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EXPERT COMMITTEE ON
ZOONOSES

Third Report

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Geneva, 6-12 December 1966

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JOINT FAO/WHO
EXPERT COMMITTEE ON ZOONOSES

Third Report

A Joint FAO/WHO Expert Committee on Zoonoses met in Geneva on 6-12 December 1966. Dr J. H. Steele was elected Chairman, Dr A. Rafii and Professor B. Babudieri Vice-Chairmen, and Dr J. A. R. Miles Rapporteur. Dr P. Dorolle, Deputy Director-General of WHO, opened the meeting and welcomed the group on behalf of the Directors General of FAO and WHO.

INTRODUCTION

The Committee faced the tasks of bringing up to date the subjects covered in the second report of the Joint WHO/FAO Expert Committee on Zoonoses and of reviewing several additional topics, including some major parasitic zoonoses and certain epidemiologic aspects of zoonoses in general, so as to improve the efficiency of control efforts.

Reports of special groups convened by WHO to consider research in, and other aspects of, major zoonoses—leptospirosis, echinococcosis (hydatidosis), arbovirus infections, rabies, and brucellosis—were of great value to the present Committee, some of whose members participated in the meetings concerned. Pertinent material from the reports of those groups concerned with leptospirosis, echinococcosis, and arboviruses has been incorporated into this report in order to give a synoptic view of the major zoonoses encountered throughout the world, with the exception of rabies and brucellosis. The Committee gave particular emphasis to and elaborated upon the zoonotic aspects of the epidemiology of these diseases. Plague, rabies, yellow fever, brucellosis, and zoonotic aspects of meat hygiene and milk hygiene are also covered by other WHO and FAO publications.

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Parasitic zoonoses

Some of the most important zoonoses are caused by parasitic animals. A large number of parasites producing infection in man have been reported in the literature but the Committee decided to deal with the epidemiology, diagnosis, prevention, and control of only the more important members of this group. The parasitic zoonoses are dealt with in sections 10 to 14. Other parasitic zoonoses are listed in Annex 2; still others were not considered to be of sufficient importance to be discussed in this report, and information on these should be sought in other sources.

Opinions differ as to whether infestation with ectoparasites, such as mites, ticks, fleas, and lice, should be considered as zoonoses. The Committee decided to include in the list only those ectoparasites that burrow into, or otherwise penetrate, the body of the host.

1. DEFINITION AND CLASSIFICATION OF ZOO NOSES

Although the term zoonoses is etymologically inexact and of little biological merit it is generally agreed that it is useful because it creates common ground for the medical and veterinary professions to explore the epidemiology of diseases that man acquires from both domestic and wild animals and to devise techniques for their control.

In a previous report zoonoses were defined as “Those diseases and infections which are naturally transmitted between vertebrate animals and man”.1 It has been argued that this definition is too wide in that it includes not only infections that man acquires from animals but also (1) diseases produced by non-infective agents, such as toxins and poisons, and (2) infections that animals acquire from man, that are merely incidental infections of no public health importance. In spite of these drawbacks the definition has been widely accepted and the Committee recommends that it should not be modified. However, any list of zoonoses should include only those infections where there is either proof or strong circumstantial evidence that there is transmission between animals and man.

It was agreed that some form of classification of zoonoses is useful, particularly for teaching, and that the classification should emphasize the epidemiologic features of the infections (see Annex 1).

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2. PREVENTION, CONTROL, AND ERADICATION

More than 150 zoonoses are now recognized (see Annex 2). Prevention, control, and eradication of some of these diseases, particularly where domestic animals are the principal reservoirs, are problems of considerable magnitude in every country. Reservoirs of zoonoses among domesticated animals are the sources of greatest danger for man since he is in closest contact with such animals. Emphasis should therefore be given to these zoonoses in the development of programmes to combat animal diseases. Notable successes have been achieved when such a procedure has been followed—for example, with bovine tuberculosis, brucellosis, and rabies.

The discharge of governmental responsibilities for zoonosis control requires adequate financial support and close collaboration between different government agencies, particularly the medical and veterinary services. The operation of inter-ministerial (e.g., health and agriculture) committees has proved to be an excellent means of achieving co-operative effort on the zoonoses and has also led to appreciable savings by the pooling of funds, personnel, and equipment. Such formal means of collaboration encourage free and frequent exchange of information on animal and human diseases, joint planning and financing of disease-control campaigns, improved food-hygiene services, and mutual assistance in laboratory and epidemiologic work. Such committees should not, however, remain as paper organizations.

Attention to the zoonoses must be given at all levels of government—local, municipal, provincial, and national. In any area, environmental conditions and local customs of the population must be studied carefully before control measures can be instituted. Measures that are successful in economically advanced countries may not be applicable to developing areas without modification.

In planning campaigns against disease, three points are important: prevention, control, and eradication. Prevention is well defined in the lexicons of all nations and there is little confusion over its meaning. Control is a more ambiguous term that means different things to different officials and workers, depending upon their training, experience, and culture. Definitions of control range from the enactment of regulations or legislation, with little or no attempt at enforcement, to quarantine, restrictions on movement, vaccination, and even destruction of animals and property. In some cases, control programmes are enacted with the purpose of complete elimination of a disease—i.e., eradication. (Examples are the elimination of glanders, rinderpest, bovine pleuro-pneumonia, and fowl plague from Europe and the Americas.) As used in this report the three terms are defined as follows:
Prevention consists of measures to protect man or animals against disease. These may frequently be independent of measures aimed at bringing the disease under control.

Control consists of measures to reduce the prevalence or incidence of disease or infection in animals and man.

Eradication is the total elimination of the etiologic agent from a region. (The term "eradication" is used by some authorities to denote elimination of disease and not necessarily of all the infective agent, especially when the chances that the agent will infect a mammalian host are very small.)

Today a nation or state that undertakes campaigns against disease must weigh many factors. Whether to follow a policy of control or one of eradication can be decided only by considering the social organization of a particular country and by weighing the various interests and claims of its economy. Many questions arise in this connexion. Is eradication of a given disease possible? If so, is it economically justifiable? Does a particular policy fit in with the social structure and customs of the country, or would it be a disruptive influence that would be resisted and thus probably fail? Is partial control feasible, or does the situation demand complete eradication and continued freedom from the infective agent or vector?

Eradication of several communicable diseases, such as malaria and smallpox, has become an international goal. National campaigns to eradicate disease include such zoonoses as plague, rabies, bovine tuberculosis, and brucellosis. In certain areas where geographic conditions are favourable in economically advanced countries some of these diseases have been eradicated. Eradication is possible in selected areas unless animal reservoirs provide inaccessible sanctuaries for infective agents (e.g., the bat and monkey reservoirs for rabies and yellow fever, respectively) and provided the cost is not too great.

The cost factor is often paramount. Economic justification of an eradication campaign—e.g., for bovine tuberculosis or brucellosis—is fairly easy in the early stages, when the returns are greatest for the money invested. When, however, the later stages of the campaign are reached and costs begin to rise for each case revealed, great doubts arise. The problem is particularly perplexing if any relaxation of effort means a gradual loss of all ground gained. If one considers the very large costs involved in finally eliminating the extremely small number of residual cases or reservoirs of disease agents, attempts at such a policy are seldom justifiable, particularly in developing countries. But even though eradication may not be practicable, a continuous effort must be made to control the disease so that it does not erupt as an epizootic or continue to take too high a toll in human disease or economic loss.
It is recognized that the goal of eradication has great public appeal and often gives to disease control campaigns support that would otherwise not have been forthcoming. However, in cases where it is clear that eradication, if achieved, would be a long and costly process, it would be less misleading and perhaps equally effective to label such campaigns "pre-eradication" or "suppression".

Operations research

The mathematical techniques of operations research, now being increasingly applied to agricultural and industrial problems, can help in the solution of particular problems that involve a choice between alternative possibilities. Operations research can be especially valuable in developing countries, because its object is to find the most economic manner in which to use limited resources of manpower and money.

An essential part of operations research analysis is the calculation of the relative costs, for the same amount of economic benefit, of alternative plans. If, for example, it had to be decided whether to undertake a programme for (1) the control or (2) the eradication of bovine tuberculosis, analysis would include costs due to losses in milk and meat production, human infections, the detection of infected animals (it costs considerably more to find 99% of such animals than 90%, and the last few per cent involve very large expenditures), and the training of the personnel that would be required for the programme. All these factors would have to be considered in predicting not only the costs and time schedules of the alternatives, but also their likely effects on the health of humans and livestock and on the agricultural economy. Clearly, there are factors in any disease problem affecting human and animal health that may be difficult or impossible to fit into such a mathematical picture. Such factors must be weighed by health and agricultural administrators. This is not an easy task; for example, what values can be placed on the social disruption and unrest that may result from the imposition of technological advances upon close-knit social groups? Nevertheless, operations research might provide a far firmer basis for quantitative analysis than has previously been available for use in deciding the kind of campaign that should be undertaken.

The training of personnel to undertake such analysis should be encouraged in all countries with a view towards their joining public health and agricultural administrations as part of the interdisciplinary team required to deal efficiently with disease problems. This will no doubt take time, but it is an essential starting point if the largely intuitive and empirical methods of assessing the consequences of disease that prevail at present are to be improved.
3. COLLECTION OF INFORMATION ON OCCURRENCE

3.1 Reporting

Reporting of zoonoses is important in the development of any programme designed to combat these diseases. Notification of the presence and distribution of disease should be made to the proper governmental authorities by veterinarians, medical practitioners, or others. Administrative practice as to the diseases to be reported and the way in which they are to be reported varies greatly from one region to another. Such variation may be justified by different conditions and different interests in this field (see Annex 3).

A system using standard nomenclature and classification has been devised by the National Institutes of Health of the US Public Health Service for the recording, retrieval, and analysis of data on animal diseases. This system has been adopted by several veterinary schools in the USA and Europe and is being considered for adoption by other agencies in several countries. For many years FAO, WHO, and OIE have jointly published the Animal Health Yearbook, an annual compilation of reports of epizootic diseases of the world, including several zoonoses. At present this is the most comprehensive source of data on disease prevalence throughout the world. OIE also collects and disseminates immediate reports of fresh outbreaks of epizootic diseases, including rabies and anthrax, and issues monthly summaries.

Much routine reporting is notoriously deficient and often inaccurate. This is true in all countries including the economically advanced ones. However, these current reports, such as they are, are essential to all control programmes.

To improve the reporting of disease, the following suggestions are offered:

(1) Information should be forwarded at regular intervals from all diagnostic laboratories to the control authorities. It should include information on infections even in the absence of disease.

(2) Reports from meat-inspection services, where these exist, can provide information on the presence and extent of specific diseases. When animals are transported, records of their origin and of the route of shipment should be provided. Such reports and records can be used to trace back to their origin conditions such as tuberculosis, parasitism, or any other disease of special interest. Where meat-inspection services are weak, their improvement should be a matter for immediate attention.

3.2 Surveillance

As Langmuir has pointed out, organizations with the necessary equipment, personnel, and financial support should consider establishing surveillance programmes that would entail "continued watchfulness over the distribution and trends of incidence [of a disease] through systematic collection, consolidation and evaluation of morbidity and mortality reports and other relevant data. Intrinsic in the concept is the regular dissemination of the basic data and interpretation to all who have contributed and to all others who need to know." 1 Such programmes are designed to provide, continually and promptly, information on the incidence of disease, and related factors, for the planning and assessment of control measures. This is done by (1) improving the reporting of morbidity and mortality caused by selected diseases, (2) improving the statistical tabulation and analysis of data so that they can be properly interpreted to reporting individuals or institutions, and (3) using laboratories to supplement basic information on incidence and prevalence and to obtain epidemiologic information that cannot be obtained through case reporting (e.g., the extent of infection compared with overt disease).

The criteria used in choosing a disease for surveillance depend on the agency involved and on the nature of the problems facing it. A surveillance programme may be desired (1) to give warning of any threatened importation of a new disease, (2) to chart the spread of a newly-introduced disease, or (3) to plot progress in a control programme where even good routine reporting would not detect the few infections that might be a starting point for a recrudescence of the disease.

3.3 Surveys

Surveys are part of any surveillance system and are a time-honoured method for obtaining rapid information on the prevalence of a disease or infection in a given area. Repeated surveys can indicate prevalence of disease or trends of prevalence. Laboratory methods, particularly serologic tests, are often the most efficient technique, but clinical surveys or surveys by questionnaire may also be used. In all types of survey, a most important requirement is a valid sampling procedure. 2

The study of factors involved in the spread of a disease or infection would probably require a more complete and detailed epidemiologic study. A useful aid to prospective and retrospective studies would be the establishment of FAO/WHO animal serum banks similar to the WHO serum banks now in use for epidemiologic studies of infections of human beings. Such

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2 For further discussion, see Wild HLth Orgn. Rep. Ser., 1966, 336.
banks collect, freeze-dry, catalogue, and store serum specimens that are released for specialized studies on request by qualified laboratories. In this connexion, the Committee endorses a recommendation, made some years ago by a WHO Study Group on Immunological and Haematological Surveys,\(^1\) that domestic and wild animal serum banks be established. The provision of standardized reagents for tests would also be most helpful.

4. ZOOONES AS OCCUPATIONAL HAZARDS AND THEIR ECONOMIC IMPLICATIONS

Zoonoses are occupational hazards faced by agricultural, industrial, and laboratory workers and animal handlers. The problems of agricultural workers have been considered by a Joint ILO/WHO Committee on Occupational Health.\(^2\) A wide variety of communicable diseases and parasitic infections considered in the present report can be classified as occupational diseases. Some diseases have significantly higher attack rates on workers in the course of their occupations than on the rest of the population. A classic example of this is the occurrence of anthrax in carpet weavers, livestock raisers, and workers with animal hair in the textile industry. Leptospirosis in rice-field workers, listeriosis in agricultural workers, erysipeloid in butchers and fish merchants, tularaemia trypanosomiasis in hunters, and creeping eruption in plumbers, trench diggers, and others are examples of occupational zoonoses that have been long recognized.

In recent years, advances in the control of animal diseases, changes in agricultural and industrial practices, and changes in the environment have contributed to shifts in the epidemiologic pattern of some of the zoonoses. Thus, brucellosis has in some regions changed from a disease primarily transmitted by the ingestion of milk and milk products contaminated with \textit{Brucella} to one transmitted by contact or inhalation, especially among meat packers and veterinarians; ornithosis has shifted from a disease of owners of pet birds to an occupational disease among workers in poultry processing plants.

The zoonoses have become, over the years, increasingly identified as occupational hazards. The list includes Q fever in abattoir and rendering-plant workers, jungle yellow fever and tick-borne diseases in woodcutters, salmonellosis in food processors, bovine tuberculosis in farmers, Newcastle disease in poultry raisers and processors, contagious ecthyma (orf) in sheep shearers, and rabies in veterinarians, field naturalists, and dog-control employees.

An important recent addition to the recognized occupational zoonoses is infectious hepatitis transmitted to man from chimpanzees and other subhuman primates. Approximately 80 instances of such transmission have been established by epidemiologic investigation during the last several years. Most of these have involved animal handlers and research biologists working with primate colonies.

The economic impact of zoonoses is extremely difficult to determine accurately, but it is known to be considerable. It includes mortality and acute and chronic debilitating illness of humans, loss of life and impairment of productivity of livestock, and consequent effects on the social fabric and economic development. It is clear that in this connexion developing countries suffer much greater losses than technically advanced countries. This is attributable to the lack of adequately organized public health and veterinary services and to particular social customs prevailing in the predominantly agricultural societies of developing countries. Economic losses caused by brucellosis, bovine tuberculosis, rabies, cysticercosis, and hydatidosis are estimated to be hundreds of millions of dollars annually in Latin American countries alone, quite apart from the human suffering and death caused by these diseases.

5. VIRAL INFECTIONS

5.1 Arbovirus infections

Arboviruses are a heterogeneous group of viruses that are defined on biological rather than morphological or chemical grounds. A WHO Scientific Group on Arboviruses and Human Disease has defined them as "viruses which are maintained in nature principally, or to an important extent, through biological transmission between susceptible vertebrate hosts by haematophagous arthropods; they multiply and produce viraemia in the vertebrates, multiply in the tissues of arthropods, and are passed on to new vertebrates by the bite of arthropods after a period of extrinsic incubation".1

It must, however, be emphasized that the bite of infected arthropods is not the only way in which arboviruses are transmitted. In certain circumstances some arboviruses have been transmitted by the alimentary and respiratory routes and in other ways.

More than 200 distinct serologic types of arbovirus have been recognized. Most of them have been classified in 27 serologic groups, but some 50 viruses remain ungrouped. Of the 200 about 80 have been reported to cause disease in man or domestic animals. The more important of those

that have been proved to have (or probably have) some vertebrate host other than man, and that have been shown to cause human disease in nature, are listed in Annex 2. Some viruses that are important in veterinary medicine have not been shown to infect man; e.g., African horse sickness viruses.

Study of the classification of these viruses and of world distribution of infections they cause is organized by WHO through the International Reference Center at the Yale Arbovirus Research Unit (New Haven, Conn., USA), various arbovirus reference laboratories in many countries, and other associated laboratories. The geographic distribution of most arboviruses appears to be limited; some, however, are very widely distributed and the same virus may be found in as many as three different continents. Furthermore, as studies are made in more and more countries, it is becoming clear that arboviruses are present on all major land masses, with the possible exception of those completely within the Arctic Circle and in Antarctica. However, there are still a number of countries where hardly any studies of the existence and significance of such viruses have been undertaken. Further studies in these countries are desirable so that a world-wide understanding of the problem may be obtained.

The known groups of arthropod vectors of arboviruses are mosquitoes, flies of the genera *Phlebotomus* and *Culicoides*, ticks, and possibly mites. To illustrate the characteristics of this group, two important examples of mosquito-borne and one of tick-borne viruses will be described.

5.1.1 *Mosquito-borne virus infections*

5.1.1.1 *Japanese encephalitis virus* belongs to the serologic group B of the arboviruses and is transmitted by mosquitoes. The disease was first reported from Japan, but it is widely distributed, occurring from the Maritime Territory of the USSR through Korea, Japan, mainland China, and South-East Asia to southern India. In Japan the virus causes summer epidemics that involve 2000-6000 cases of encephalitis, the case fatality rate ranging up to about 50%. A large number of the survivors are left with permanent neurologic sequelae. Extensive epidemics are also common in Korea and Taiwan. In Singapore and Malaya, where the disease has been quite well studied, it is normally endemic rather than epidemic, and the average case is somewhat less severe than in other areas. In many of the other countries where this disease occurs, either its significance has not yet been fully assessed or the results of such assessment are not available.

Japanese encephalitis has not been recorded south of Singapore, but epidemics due to the related Murray Valley encephalitis virus occur further south in Australia and New Guinea. Another related virus, St Louis encephalitis virus, occurs throughout the Americas and continues to cause serious epidemics in the USA.
The most extensive studies of the ecology of the Japanese encephalitis virus have been undertaken in Japan, where it has become clear that the main mosquito vector is *Culex tritaeniorhynchus*. Similar studies have been carried out in the Maritime Territory of the USSR. Many species of birds are susceptible to this virus and, following infection (particularly early in life), suffer from a viraemia that is sufficient to infect mosquitoes. Several species of such birds are highly attractive to *C. tritaeniorhynchus*. In nesting colonies of birds there can be a rapid build-up of infection, leading to a high infection rate in the vector mosquitoes. These mosquitoes have a considerable flight range and feed freely on pigs, which are susceptible to the virus and are normally kept in sites quite close to human habitations. The resulting viraemia in pigs leads to a large number of infected mosquitoes in the neighbourhood of houses, and human cases are likely to occur. Thus, although most of the evidence suggests that wild birds rather than pigs are involved in the basic cycle of the virus, the pig is an important amplifier host, acting as an intermediary in the production of large-scale epidemics in man.

Most of Japan has severe winters, during which adult mosquitoes disappear; the regular reappearance of the virus every summer therefore poses a problem. It is theoretically possible that the virus is brought north by birds migrating from tropical areas where virus activity is present throughout the year, but no objective evidence in support of this possibility has been discovered. A second possibility is the survival of the virus as a latent infection in birds that either migrate or are resident throughout the winter. The stresses of the new nesting season might lead to a breakdown of resistance and a further period of viraemia, leading to infection of mosquitoes. The possibility of such long-term latent arbovirus infections can be demonstrated in the laboratory, but there is no proof that they can occur under natural conditions. Similarly, there is no evidence that pigs can act as a reservoir of latent infection throughout the winter. Laboratory experiments have shown that infection may remain latent in hibernating bats for several months and that such bats have a further episode of viraemia when they return to normal activity. Here, again, there is no evidence that this does, in fact, occur in nature. The way in which Japanese encephalitis virus survives the winter can be clarified only by a great deal of further research.

5.1.1.2 *Western equine encephalitis virus*, a group A arbovirus whose activity extends from western Canada to Argentina, shows a similar situation. For many years this virus has caused serious epidemics of encephalitis in both humans and horses, and it has probably been more intensively investigated than any other mosquito-borne encephalitis virus.

In this case it appears probable that birds are the amplifier hosts and, particularly where there are large bird roosts, are responsible for the heavy infection of the normal vector, *Culex tarsalis*, that is an essential pre-condi-
tion for the occurrence of human and equine epideimics. Birds have normally been thought to be the reservoir hosts of this virus, as of Japanese encephalitis virus, and the same types of ecologic pattern have been postulated for both viruses. There is good evidence that latent infection can exist in birds for very long periods; the virus may occasionally be recovered almost a year after the initial infection. However, there is no reliable evidence that this actually takes place in nature.

Recent studies have shown that a number of small mammals, particularly rodents, can be infected with this virus without showing signs of illness but with viremia for a sufficiently long period for biting mosquitos to become infected. Since antibody is present in quite a high proportion of the small rodents in endemic areas, it has been suggested that they, rather than birds, may be the reservoir hosts of western equine encephalitis virus. There is good evidence that mammals, rather than birds, are the main reservoir hosts of Venezuelan equine encephalitis virus, another group A arbovirus that causes major epidemics of encephalitis in horses and a usually milder disease in man. Another interesting suggestion, differing from anything postulated for Japanese encephalitis, is the proposition that hibernating snakes may be responsible for the survival of the virus throughout the winter. It can be shown that *C. tarsalis* will bite snakes and other reptiles, that the virus can survive in the latter for long periods, and that viremia may occur for several days after they emerge from hibernation. So far there is only limited evidence that such reptiles are infected in nature, and they do not seem to be the preferred hosts of *C. tarsalis*. However, there remains a distinct possibility that reptiles may play an important role in the survival of western equine encephalitis virus throughout the winter.

It appears quite likely that in temperate zones the winter survival of mosquito-borne viruses is achieved in a number of different ways, and that for any virus more than one of those that have been postulated is significant.

5.1.2 *Tick-borne virus infections*

The main strains of tick-borne encephalitis virus are the Russian spring-summer encephalitis strain, the Central European strain and the louping ill strain. Louping ill is an important disease of sheep in the United Kingdom, but apart from infections in laboratory workers, only a very limited number of cases of human encephalitis have been proved to be caused by the louping ill virus. Many cases of Central European tick-borne encephalitis occur in man, but these are usually relatively mild and have a very low case fatality rate. Russian spring-summer encephalitis is a much more severe infection that is found mainly in the Asiatic USSR. The related Powassan virus is in North America so that the main distribution is holartic, but there are southern extensions into the tropical regions of Asia where haemorrhagic fever, rather than encephalitis, is caused by a virus of this
group. This Kyasanur forest disease virus appeared in 1955 in Mysore State, India, and has caused a series of major epidemics in both man and monkeys.

Over 100 species of mammals and birds have been shown to develop antibodies against tick-borne encephalitis viruses, and in many of these animals the levels of viraemia are adequate to infect the vector ticks. The main vectors are, for the Central European and louping ill viruses, *Ixodes ricinus* and, for the Russian spring-summer virus, *I. persulcatus*.

At least for the Central European virus there is strong epidemiologic evidence that the most important reservoir hosts are small murine rodents and insectivores. The evidence for a dominant reservoir mammal for the other strains is not so clear-cut, although similar small rodents may well be important for them also.

The survival of the virus through the seasons when no encephalitis is present is not difficult to explain. All strains have been shown to survive transtoldy in the vector ticks. Although transovarial transmission has been demonstrated in most strains, there is little doubt that the virus can survive through transtodial maintenance even if there is insufficient transovarial transmission for the latter to be of much significance.

Man and domestic animals become infected when they enter rough pasture or forest and are bitten by carrier ticks. In certain areas there is a very high rate of infection amongst forest workers. In Czechoslovakia and some other European countries, there have been extensive outbreaks of mild disease due to the Central European strain in which the infection has been acquired through the drinking of milk from infected goats.

In Central Europe tick-borne encephalitis is usually mild and may have a biphasic character, with an influenzal phase followed by a brief pyrexial period and then a second phase with signs of meningeal irritation and possibly encephalitis. The case fatality rate is usually not greater than about 0.2%. The Russian spring-summer virus causes much more severe disease and commonly there is encephalitis together with myelitis leading to a shoulder-girdle paralysis. This syndrome is very characteristic of tick-borne virus encephalitis. The case fatality rate in the Far Eastern strain is often 20-30%, and quite a high proportion of survivors show permanent muscle weakness from the myelitis that accompanies this encephalitis.

5.1.3 Control

Control of arthropod-borne viruses is at present unsatisfactory, but some success has been obtained through vector control and vaccination. In special cases where transmission does not occur directly through a vector, other means of control may be available. Knowledge of the relative importance of different vertebrate hosts is still insufficient for effective reservoir control. Since it is much easier to control ticks than most mosquitoes, the
control of tick-borne encephalitis is more practicable than that of many of the mosquito-borne virus diseases.

5.1.3.1 Control of tick-borne virus infections

(1) It is possible to reduce the number of ticks by making alterations in their habitat. In Czechoslovakia, it has been shown that ticks are most numerous in neglected pastures, and that careful management of the pastures leads to considerable reduction; while on sub-marginal land (i.e., land near the boundary between two different types of terrain) in Scotland it has been shown that the removal of wide-ranging mammals such as sheep and cattle from an area for a period of some years may greatly reduce the number of ticks even if no attempt is made to control rodents.

(2) Exposed workers should be encouraged to wear protective clothing impregnated with insect repellents or insecticides and should be trained to remove ticks from their bodies promptly.

(3) In the USSR, formalin-treated mouse-brain vaccines have been found to give good protection to those persons, such as timber workers, who have to enter heavily tick-infested epidemic areas. Greater purification has resulted in vaccines that cause fewer severe reactions than the earlier forms, apparently without any reduction in efficacy. Attempts to produce a tissue-culture vaccine are continuing with promising results. Attenuated live vaccines are also under trial, with particular attention to the possibility of using the related Langat virus from Malaya, which is of low pathogenicity for man, as a vaccine strain to give immunity to tick-borne encephalitis.

(4) The virus in milk can be destroyed either by boiling or by the maintenance of a temperature of at least 65-70°C for 20 minutes. Normal pasteurization procedures are not effective.

5.1.3.2 Control of mosquito-borne virus infections

(1) Where the vector is an urban mosquito such as *Aedes aegypti*, and particularly where such a mosquito normally rests in houses, ordinary techniques of mosquito abatement give highly effective control. Such measures have been proved extremely effective in the control of urban yellow fever.

(2) Where the main vectors are mosquitoes that have a very wide breeding area and do not normally rest in houses, control—except over very limited areas—is not at present practicable. For example, *C. tritaeniorhynchus* breeds in rice paddies, has extremely extensive breeding areas, and normally rests by day on rice and other grasses. Control over even a limited area is extremely costly and wide control would be prohibitively expensive.

(3) The housing of pigs further from habitations might lead to some reduction of infection where pigs are important amplifier hosts. There is
experimental evidence that the vaccination of pigs reduces or eliminates viraemia on subsequent challenge with live Japanese encephalitis virus. It is highly desirable that a large-scale field trial of the usefulness of this procedure be undertaken.

(4) A recently developed formalin-treated mouse-brain vaccine for Japanese encephalitis, purified by ultracentrifugation, contains very little nonspecific protein, and large-scale controlled trials in 1965 produced no evidence of allergic encephalitis following vaccination. There is good evidence that this vaccine is 60-80% effective over a period of one year. Live attenuated vaccines against the virus are being sought, but so far without satisfactory results. However, attenuated virus has been used for the production of an inactivated vaccine that is immunogenic.

Very effective formalin-treated chick-embryo vaccines have been produced for the control of equine encephalitis viruses in horses. Such vaccines, which must be administered annually, produce unduly severe reactions in man and they have been used only for unduly exposed personnel. A living modified vaccine for horses has proved effective in field trials, but has not yet been used on a large scale. An attenuated vaccine has been produced against Venezuelan equine encephalitis virus and has been found to give good immunity. The more recently developed and more highly attenuated forms of this vaccine are reported not to give unduly severe reactions.

The 17D strain of yellow fever virus is still the most satisfactory virus for production of a live attenuated vaccine against an arbovirus disease.

5.2 Influenza in animals and its relationship to human influenza

In the past, WHO has co-ordinated research on the epidemiology of animal influenza in the hope that the knowledge gained might shed light on the human problem. Recent findings can be summarized as follows.

(1) Swine influenza strains (A type) isolated from pigs in the USA during the past decade have shown slight antigenic differences from those isolated during the previous twenty years. Such differences are considerably less than those observed in other A-type strains infecting man, and in equine and avian species. Swine can be infected by human strains under natural conditions, but this has not been shown to occur frequently.

(2) Two antigenically distinct strains, A/equi 1 and A/equi 2, can cause widespread epizootics in horses. Both strains can co-exist in equine populations, although in recent outbreaks A/equi 2, first detected in Miami, Florida, in 1963, has been predominant. The equine strains are widely spread throughout the world. Man can be artificially infected by equine strains administered in high doses by the respiratory route, leading to development of clinical signs of the disease. Antibodies to equine and avian strains have been detected in aged human beings.
(3) During the past few years, numerous influenza strains of the A type have been isolated in Europe and North America from many different species of wild and domestic fowl, including the wild tern, pheasant, turkey, quail, duck, and chicken. These strains appear to form a continuous antigenic spectrum, each strain having slight but distinct antigenic differences. The isolation in both Scotland and the Republic of South Africa of almost identical strains from the wild tern, a species that migrates great distances, indicates that avian influenza strains must be widely circulating throughout the world.

(4) One case of influenza B virus infection naturally transmitted from man to a laboratory monkey has been reported. Whether or not monkeys are infected in their wild habitat is not known.

(5) Although dogs can be artificially infected with high doses of influenza A and B viruses, studies thus far indicate that dogs and cats as household pets are not of great importance in influenza epidemiology. This seems to be true of domesticated ruminants also.

(6) Serological surveys of wild rodents have yielded equivocal evidence of the presence of specific antibodies to influenza viruses.

(7) Pigs are susceptible to experimental infection by influenza B virus, and can spread such infection by contact with other pigs. Furthermore, preliminary results of a serologic survey in pig herds have indicated that pigs are naturally infected with influenza B virus. Confirmation of the latter finding is required.

(8) Serologic studies in persons born before 1889 have revealed antibodies to A/equi 2 and the related A/duck/England 62 viruses. The significance of these findings is not yet apparent.

It is clear from the above findings that further investigation of animal influenza is warranted, to determine whether lower animals can serve as reservoirs for human infection, or even as possible origins of human epidemics and pandemics. Hypothetically this could occur through mutation of an animal strain or hybridization of human and animal strains. Further studies should emphasize isolation and antigenic analysis of the viruses. Serologic surveys in animals are also most useful and should be continued.

5.3 Herpes virus infections in monkeys

5.3.1 Herpes B virus infections

This disease of monkeys is caused by *H. simiae*, a member of the herpes virus group. It is closely related to the herpes virus (*H. simplex*) that infects man. In neutralization tests, antiserum to *H. simiae* will neutralize *H. simplex* to relatively high titre: in general, antibody against *H. simplex* does not neutralize B virus, but the sera of people with a high titre of *H. simplex*
antibody usually neutralizes B virus to low titre. Rhesus (*Macaca mulatta*) and cynomolgus (*Macaca ira*) monkeys from South-East Asia have frequently been shown to be naturally infected. New World monkeys and *Cercopithecus aethiops* monkeys of Africa have not been observed to be naturally infected with *H. simiae*, although other herpes viruses have been isolated from them. The rate of infection with *H. simiae* in South-East Asian monkeys in their ordinary habitat is low, but when they are gathered in compounds to be shipped for laboratory studies, infection is rapidly transmitted to those that are susceptible. In some cases 80% of the monkeys brought into laboratories have shown evidence of infection. However, in spite of this widespread infection among monkeys, only 20-25 cases in human beings have been recorded, of which all but 2 ended fatally shortly after the onset of disease. The infection is a hazard not only to all handlers of monkeys but also to those who handle monkey tissues in the laboratory.

To reduce the hazards of this disease, laboratory use of rhesus and cynomolgus monkeys has decreased, while that of African green monkeys (*Cercopithecus aethiops*) has increased. The latter, although considered to be susceptible to Herpes B virus, do not ordinarily have the infection under natural conditions.

It is recommended that rhesus and cynomolgus monkeys newly arrived in the laboratory—the most dangerous source of infection—be placed in individual cages and kept in quarantine for 6-8 weeks. All monkeys showing herpes-like lesions (stomatitis, conjunctivitis, and vesicles and ulcers in the mouth and on the tongue and lips) should be killed, their carcasses incinerated, and their cages sterilized.

Different species of monkeys should never be mixed, and more than one species should not be transported in the same aircraft. Ideally, monkeys should at all times be caged singly; where this is not possible, the number in each cage should be small.

Monkeys to be used for long-range studies may be screened for antibodies to *H. simiae*. Since these antibodies neutralize *H. simplex* virus, the latter can be used as antigen. Only monkeys which, in two tests at least two weeks apart, show no neutralizing antibodies should be used for such studies. This precaution is used by some laboratories for all studies involving monkeys. It should be borne in mind that antibody-free monkeys are susceptible and should not be exposed to monkeys that have not passed such a test.

The finding of a stable level of antibody against herpes B virus or *H. simplex* in a clinically normal monkey probably does not mean that virus is being shed. It has not yet been determined whether such animals are liable to suffer relapses with shedding of virus under stress, as happens with *H. simplex* in man.

Handlers of monkeys should observe strict hygienic precautions. They should wear special clothing that can easily be sterilized, or disposable
garments that can be incinerated. Gloves should be worn when handling monkeys, and catching and restraining devices should be used rather than the hands. All cuts, bites, and other wounds sustained when handling monkeys or material contaminated by them should be cleaned immediately with copious quantities of soap and water. Monkey bites should be reported to supervisors, who should investigate the animals involved for clinical evidence of herpes B virus and should also consider the possibility of rabies infection. Although human infection with herpes B virus is usually sustained through a bite or wound, at least one case has been reported in which there was apparently no injury and infection was believed to have been airborne.

For monkey handlers and other persons subjected to a high risk of Herpes B virus infection, an effective vaccine would be welcome. One group in the USA has developed a killed virus vaccine that gives antibody response in most people inoculated; some, however, do not respond even to multiple injections. The vaccine has not yet been cleared for distribution. Interested parties are urged to work on this aspect of the problem.

The administration of specific hyperimmune serum or gamma globulin to persons exposed to Herpes B virus has been suggested, but there is no evidence indicating that this is an effective prophylaxis. In some animal experiments a degree of protection resulted only when specific gamma globulin was administered within one half-hour after infection.

5.3.2 Other herpes virus infections

Some New World monkeys, especially squirrel monkeys (Saimiri sciurea), are infected with a herpes virus (Herpes T or Herpes M) that has been implicated in a febrile syndrome with mild manifestations of encephalomyelitis in human beings. Marmosets (Tamarinus nigrilodis and Oedipomides oedipus) and owl monkeys (Aotus trivirgatus), also from South America, are highly susceptible to this virus, disease produced in them being almost uniformly fatal.

5.4 Poxvirus infections

5.4.1 Cowpox and related infections

Cowpox (vaccinia) is rapidly becoming a rare disease in countries with improved farm hygiene, but it is still of frequent occurrence in many countries, especially in urban dairy herds where hand milking is practised and where there is a frequent turnover of cows. The human infection is well known and is similar to that of cattle. Man can also contract vaccinia from cows infected by dairy workers who have been recently vaccinated. Buffalopox, which is caused by a closely allied virus, is frequent in countries where buffalo are used as milk producers. Its mode of transmis-
sion to man and other epidemiologic features are similar to those of cowpox.

Camelpox is common in the dromedary, the infection occurring, it is believed, invariably during early life. The lesions are generally found on the lips, muzzle, and other parts of the face and are often complicated by secondary infections. Lesions on the udders of dams are often seen at the same time as facial lesions in their calves. The infection is readily transmitted to camelmen who handle, milk, or treat the affected animals and to their families. The lesions occur on exposed parts of the body such as the face and hands.

5.4.2 Simian poxvirus infections

Monkeypox. Transmission of smallpox to monkeys in nature has not been proved, though the virus has been transmitted experimentally to several simian species in various ways, including the respiratory route. In recent years natural outbreaks of a relatively mild pox disease have occurred in monkeys after their arrival in Europe and America from South-East Asia. The causative agent, which is related to the variola-vaccinia viruses, can apparently produce a subclinical infection in monkeys for more than two months. The virus can be readily transmitted to several species of laboratory animals, but its transmission to man has not been observed or attempted. It is possible that human infection may occur if monkeys are handled without special care.

Yaba virus infection. A poxvirus isolated from spontaneous subcutaneous cellular growths in rhesus monkeys in Yaba near Lagos, Nigeria, has been found to be transmissible to man and monkeys. The growths consisted of pleomorphic polygonal cells derived from the fibrocytes of the dermis and subcutaneous tissue. There was no evidence of neoplasia. Recently, similar lesions caused by a closely allied or identical infection have been observed in monkey handlers and in monkeys in primate colonies on the west coast of the USA. Transmission appears to take place through direct contact with infected material and even by contact with apparently healthy monkeys. Simian species naturally occurring in Africa are immune to the infection.

5.4.3 Contagious ecthyma and paravaccinia

Contagious ecthyma, an exanthematous disease of sheep and goats, is almost cosmopolitan in distribution and is frequently transmitted to people who handle infected animals or the live orf vaccine. Repeated infections in man are possible, as the immunity following an attack is neither strong nor long lasting.

Paravaccinia, or milkers' nodules, is an infection of the skin of the teats of cattle and of the hands of milkers. It is milder than cowpox and differs
from it in that the lesions do not usually pass through a pustular stage. Recently a virus morphologically similar to that of orf has been isolated from human as well as bovine lesions, though the two viruses differ in certain biological characteristics.

5.5 Foot-and-mouth disease

For many years, reports of foot-and-mouth disease in man have been based mainly on circumstantial evidence. During the outbreak in England in 1966, one case was reported, with complete laboratory corroboration. There is, however, an over-all lack of valid evidence of transmission, although countless people have been extensively exposed during epizooties throughout the world. Evidence of transmission to laboratory workers is also lacking. These facts suggest that the disease is sufficiently rare in man to warrant its removal from the list of zoonoses, or at least its relegation to the status of a medical curiosity.

6. RICKETTSIAL INFECTIONS

6.1 Q fever

Q fever, caused by the rickettsia Coxiella burnetii, has a world-wide distribution and in many countries constitutes a public health and sometimes an agricultural problem.

Natural reservoirs of C. burnetii include both wild and domestic animals. Ruminants, especially goats, sheep, and cattle, are the main sources of human infection. In nature Coxiella has been found primarily in a rodent-tick-rodent cycle. From this cycle it is transmitted to domestic animals—and sometimes to man—by ticks, many species of which can carry the organism.

The disease is transmitted by tick bites, inhalation of infected dust, and—rarely—ingestion of contaminated food such as meat, milk, and milk products. Tick-borne Q fever is usually a febrile disease without any special localization, but infection by inhalation results in a pulmonary localization. In most countries the respiratory route of infection is regarded as the most important. Symptomless infections are sometimes observed. Many outbreaks in abattoirs have been recorded, and in some countries Q fever is legally recognized as an occupational disease of abattoir workers.

C. burnetii remains viable for long periods in contaminated materials such as wool, cotton, and farm dust, and infects persons who handle these

1 This disease should not be confused with a human disease called "hand, foot, and mouth disease" caused by the Coxsackie A16 virus, which is responsible for epidemics, and Coxsackie A5 and A10 viruses, which cause occasional cases.
materials. Man-to-man transmission is rare but occurs occasionally in the post-mortem room and among hospital aids. Large numbers of rickettsiae may be found in the placentae of women who recovered from clinical disease several months prior to parturition.

In the infected ewe the organism becomes activated at the time of parturition and can be found throughout the body and in the excreta. Although abortion may be rare, the placenta contains innumerable rickettsiae and these contaminate the ground. Rickettsiae are also present in the milk. Where ewes are brought into yards to lamb, large numbers of rickettsiae may be found in the dust of such yards, which is easily spread by wind. Since the organism is highly resistant to drying and is little affected by the ultraviolet rays of sunlight, such dust is highly infectious. A clear relationship between dry weather, strong wind, and the spreading of infection has been reported many times.

Even in the presence of substantial antibody concentrations, ewes may pass through a further cycle of infectivity, at least at one further parturition. The cycle in goats and cattle appears to be essentially similar to that in sheep. Dogs can become infected by eating contaminated placentae; in such cases, Coxiella can pass intact through the gut and be spread over a large area by dog faeces.

Infection of both wild and domestic birds has been demonstrated, especially in pigeons and sparrows. However, the possible importance of avian hosts in the natural history of Q fever needs further investigation.

In some countries where Q fever is endemic the disease does not show any considerable yearly fluctuation; in other countries, however, it has disappeared after an epidemic or has remained only as a sporadic infection. These phenomena indicate differences in ecologic conditions that need further clarification.

To retain its virulence, Coxiella apparently needs to pass through ticks from time to time. This has given rise to the hypothesis that in countries where the tick population is small and where wild animals are scarce (or where contacts between wild and domestic animals are difficult), Coxiella—after only mammal-to-mammal passage—loses its virulence and its ability to survive in animals.

From time to time Q fever has spread to some previously unaffected area as a result of movements of infected stock; this constitutes another problem in control of the disease.

6.1.1. Diagnosis

Isolation of C. burnetii by the inoculation of laboratory animals and by culture should be undertaken only in well-equipped laboratories where suitable precautions can be taken to protect laboratory personnel from infection.
The standard diagnostic procedure remains the complement-fixation test, but considerable advances have been made in the development of agglutination tests. The micro-agglutination test is simple to perform, economical in use of antigen, and apparently highly specific when performed by experienced workers. This test remains positive for a long time—often many years—after the infection, whereas the complement-fixation test usually becomes negative after 6-12 months. For this reason the micro-agglutination test must be considered the method of choice for epidemiologic survey work. In addition, the capillary agglutination test is a rapid and economical diagnostic test. Recently it has been demonstrated that the indirect fluorescent antibody technique is valuable in diagnosis. The direct FA procedure has been used to detect infected ticks in nature.

6.1.2 Control

With the end of epidemics and the contraction of the previously wide distribution of *Coxiella* in domestic animals, Q fever has lost its earlier importance in some countries. In other areas, however, it continues to be a significant problem that needs attention, particularly in relation to occupationally exposed persons. Some control measures that have proved effective are as follows:

1. Placentae of animals suspected of harbouring *Coxiella* must be destroyed and not left in the open air.

2. Heat treatment of milk is a measure that can be easily applied. Pasteurization by the holding (vat) method at 61.7°C for 30 minutes does not kill all the organisms, but they are inactivated at 66°C. In the high-temperature short-time (HTST) method a temperature of 75°C is required for this purpose.

3. Vaccination has been used for laboratory workers and others liable to heavy exposure, but undesirable reactions have been reported in some cases. Recently a live vaccine containing a nonpathogenic variant (M) of *Coxiella* has been tested widely, in both animals and human beings. This vaccine, which produces a milder reaction than the killed type, has been reported to give a satisfactory antibody response, but it requires further study and at present mass vaccination of human beings cannot be recommended.

4. Vaccination of cattle has been tried experimentally and promising results have been reported with the use of a killed vaccine. This procedure, however, does not appear to be sufficiently effective to justify mass application at present.

5. Routine complement-fixation or micro-agglutination testing of sera of all ruminants coming from areas of infection to areas considered free of
C. burnetii should be considered. This is important in view of the possibility that introduction of an animal carrying C. burnetii might result in the spread of the disease among domestic ruminants living in uninfected areas.

6.1.3 Treatment

Most cases of Q fever in man are mild, and patients recover without specific therapy. More severe cases respond well to broad-spectrum antibiotics.

7. BEDSONIAL INFECTIONS

The agents that cause psittacosis-ornithosis, lymphogranuloma venereum, and trachoma (the PLT group) have been isolated from diverse infections in birds, arthropods, and man and other mammals. They are obligate intracellular parasites, stain readily with basophilic dyes, and multiply by fission and a unique developmental cycle to form individual colonies of infectious units possessing group and specific antigens. The agents grow well in the yolk sac of the embryonated hen’s egg and are sensitive to certain chemotherapeutic agents, particularly tetracycline. Because of several characteristics that distinguish them from rickettsiae, it is best to consider them a distinct group, referred to as bedsonias or the PLT group.

In 1930, when outbreaks of psittacosis were investigated, filtrable but microscopically visible spherical bodies were found within reticuloendothelial cells; later, these bodies were conclusively proved to cause both avian and human psittacosis. At that time it was thought that the agents responsible for these accidental zoonotic infections occur only in the parrot family; only later was it discovered that they are widespread in other birds, mammals, and man, and that they may remain dormant for long periods in such hosts.

7.1 Avian psittacosis-ornithosis

Psittacosis is a systemic infection of psittacine birds that is directly transmissible to man. Ornithosis is the term used for similar infections in birds other than psittacines; these are also transmissible to man. The human illness contracted from either psittacine or nonpsittacine birds is termed psittacosis. Emphasis on the psittacine aspect of this disease has in many countries been replaced by interest in the infection of poultry as a public health and economic problem. Ornithosis is at times a severe disease of young ducks, turkeys, and pigeons.
7.2 Mammalian bedsonial infections

During early research on experimental infections of laboratory mice, it was discovered that many laboratory stock colonies are latently infected with the “murine pneumonitis agent,” a member of the PLT group. The first reported natural infection of a nonlaboratory mammal by a member of the PLT group was described as a respiratory distemper-like disease of cats. PLT agents have been isolated from three different species of opossums suffering from fatal meningitis and pneumonitis. Since 1950 it has become increasingly evident that agents belonging to the PLT group are the cause of disease and latent infection in many large and small mammals. However, although they cause serious economic loss, the mammalian bedsonias differ from the avian strains in that they do not cause demonstrable disease in man.

An ever growing number of mammalian species belonging to unrelated orders and families are now recognized as hosts for members of the PLT group. They include cattle, sheep, goats, hogs, and many wild mammals.

Analysis of the complex of diseases caused by PLT agents in mammals suggested possible counterparts to strictly human infections. For example, it is known that whenever sheep or hogs have generalized or merely ocular symptoms, their joints are likewise parasitized. This suggested inquiry into the etiology of arthritis in man, with the result that PLT agents were isolated from synovial material or urethral and conjunctival scrapings from five patients with Reiter’s (arthritis) syndrome in the USA and one in Great Britain.

7.3 Epidemiology

Recently accumulated knowledge emphasizes not only the world-wide distribution but also the wide variety of hosts of bedsonial parasitism throughout the animal kingdom. Natural PLT-group infections have been confirmed in 130 species of birds belonging to 12 orders, of which more than half are psittacines. At least 16 species of mammals are known to be clinically or subclinically infected. Several bedsonial disease states have been recognized in man.

In the past, psittacine birds have been recognized as the primary source of disease for man. Most infections have occurred in persons having close contact with such birds—breeders, handlers, sales persons, fanciers, and pet owners.

Ducks, turkeys, and pigeons are also major sources of infection for man. Disease from these sources has been reported among farmers, poultry processors, and rendering-plant workers, some of whom have been severely infected more than once. No disease has been traced to the consumption of poultry products. Pigeons are a world-wide source of infection for man,
especially among pigeon fanciers and handlers. Most infections are mild, although some severe cases have been reported.

In areas where psittacosis exists in wild or domestic birds, few people can avoid direct or indirect contact with this source of infection. Fortunately, few individuals develop overt disease, although a number show serologic evidence of past infection. Most of these positive serologic reactions have been thought to be caused by mild infections of avian origin, without pneumonitis or other recognizable symptoms, but this interpretation is probably not correct. Urogenital or other infections caused by human-specific *Bedsonia* agents, or occupational contact of certain groups such as veterinarians, live-stock handlers, and Eskimos in contact with fur seals, may cause the appearance of group-specific *Bedsonia* complement-fixing antibodies in the sera following unrecognized infections.

The public health hazard of free-flying pigeons in urban areas is unknown, but they are not known to have caused any human epidemics. The incidence of ornithosis carriers is lower among feral pigeons than among domestic, fancy, and poultry pigeons.

Surveillance studies conducted to discover the source of serologically diagnosed psittacosis revealed that neither the occupation of the patient nor the source of infection was determined in 191 (57%) of the 336 reported cases. It is apparent that better-defined epidemiologic studies are necessary. Some investigators believe that certain strains of *Bedsonia* have adapted to man and require no avian host. Such infective agents have been found in several similar outbreaks. They were transmitted only from fatal cases to human contacts, and then only late in the course of the disease. These agents acted like avian strains of unusually high virulence meeting man for the first time, an observation that is supported by isolation of a strain of *Bedsonia* closely resembling the Louisiana human pneumonitis agent that causes disease in snowy egrets. Furthermore, an isolate from a Chicago pigeon has been found to have all the characteristics of the agent isolated from humans in the same area. In these cases, therefore, the conception of human-adapted psittacosis-ornithosis agents is not supported. However, other isolates from the sputum of pneumonitis patients who had not knowingly been in contact with birds have been found to differ from typical psittacosis strains. Some were nonpathogenic to parakeets, were sulfonamide-susceptible, and appeared to be more closely related to lymphogranuloma venereum or the few mammalian PLT agents available at the time the studies were made.

Because of the vast number of hosts of the *Bedsonia* group, consideration of the zoonotic sources of human infection with these parasites is urgent. It is pertinent to examine the relative importance of avian and mammalian sources. There is no doubt that the overwhelming majority of recognized human cases of psittacosis have been, and will continue to be, attributed to avian origin. A recent observation suggests that psittacosis-like agents
may occasionally cause eye infections in man. It is now suspected that the
conjunctivitis observed in the past in poultry processors exposed to grossly
diseased turkeys was caused by bedsonias.

In an investigation of an epidemic of poultry ornithosis it was discovered
that litter from vacated turkey farms held at room temperature contained
viable bedsonias after at least 8 months, and that various arthropods living
in the litter apparently became contaminated. Whether or not arthropods
help to perpetuate or spread the agent among poultry or other birds remains
an open question.

Only two reports of isolation from the blood of persons exposed to
infected laboratory mammals are on record. One patient became infected
with the agent of enzootic abortion of ewes and the other with that of
bovine encephalomyelitis. Serologic surveys of groups occupationally
exposed to mammals known to be infected with bedsonias must be inter-
preted with great caution in view of the fact that venereal exchange of
atypical lymphogranuloma or conjunctivitis agents is more frequent than
is generally appreciated. Well-planned studies are needed to elucidate the
role and public health significance of mammal-specific bedsonias in the
pathogenesis of human disease.

7.4 Diagnosis

7.4.1 Demonstration of Bedsonia

In man, diagnosis is confirmed by the isolation of bedsonias from the
blood, sputum, synovial fluid, or scrapings from the conjunctiva or uro-
genital tract. This is often difficult to accomplish, especially in patients
treated with antibiotics, and repeated attempts may be necessary. Any
material suspected of containing the psittacosis Bedsonia must be regarded
as potentially infectious and dangerous to handle, unless proper precautions
are taken.

Certain diagnosis of psittacosis or ornithosis in birds is impossible by
clinical or gross anatomical examination.\textsuperscript{1}

7.4.2 Serologic tests

The complement-fixation test is valuable for the confirmation of psit-
tacosis in man and in some mammals and birds.

In man a rising titre in paired serum specimens taken 7-20 days apart,
with the first specimen taken during the acute stage of the illness, can be
considered presumptive evidence of active infection. The result of a single

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\textsuperscript{1} Details of diagnostic procedures are given in Meyer, K. F. & Eddie, B. (1964) Psit-
tacosis lymphogranuloma venereum. In: American Public Health Association, Diagnostic
serum examination may be difficult to interpret unless a high titre is obtained. LGV antigen can be used for the complement-fixation test if a reliable specific antigen is not available.

The direct complement-fixation test detects antibodies in man, psittacine birds,\(^1\) and occasionally pigeons. The indirect complement-fixation test should be used for the examination of the sera of turkeys, ducks, pheasants, and pigeons, as the direct test is not reliable in these birds. It should be noted, however, that the organism has frequently been isolated from birds and mammals, including man, that showed negative complement-fixation reactions.

Although isolation of bedsonias is the conclusive method of diagnosis in individual birds, particularly if the diagnosis of human infections is involved, complement-fixation tests can provide evidence of active infection in avairies or poultry flocks. Whenever reactions with titres above 1:16 are encountered, the psittacosis agent can be considered to be active in the flock, and further search will usually lead to its isolation.

7.5 Therapy and control

Therapy with tetracycline is highly effective in man; to avoid relapses, however, treatment should be continued for 12-14 days. Penicillin is of no value.

It has been established in laboratory and field experiments that psittacosis in parakeets can be eliminated or controlled by carefully supervised chemotherapy with tetracycline compounds given in food (see Annex 10). In addition, clean, well-ventilated premises should be maintained and overcrowding avoided. Prophylactic treatment is strongly recommended for all breeding flocks and all new additions to aviaries, zoologic gardens, and other psittacine collections. Nutrient pellets containing 0.5% chlor-tetracycline in stable form have been developed; they are readily consumed by parrots and pigeons and consistently produce satisfactory levels of antibiotic in the blood.

The control of ornithosis in poultry such as turkeys, ducks, and pigeons is difficult and expensive; antibiotic prophylaxis for breeding stock may be considered. Quarantine, isolation, and medication of new additions to disease-free flocks may be used where applicable.

There is no recommendable procedure for the control of free-flying pigeons. Costly campaigns to reduce pigeon populations in urban com-

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\(^1\) Important exceptions to the usually excellent production of complement-fixation antibodies in psittacine birds have been noted. Domestically raised budgerigars or Australian parakeets (Melopsittacus undulatus) and African grey parrots (Psittacus erithacus) have failed to produce either direct or indirect complement-fixing antibodies in a majority of birds that were known to be infected. The test is, therefore, unreliable in these species.
munities are usually unwarranted, as free-flying pigeons are seldom the cause of human infection. Control of infection among racing and fancy pigeons is an individual problem; in this connexion, antibiotics in stable nutrient pellets are of definite value.

Immunization of fowl with formalin-killed vaccines in adjuvants or with living attenuated bedsonias fails to protect against infection and therefore is of doubtful value in the control of ornithosis. No effective therapeutic or other means of control of mammalian bedsonial infections have been developed. Reduction of the incidence of enzootic abortion in ewes has been attempted by active immunization with formalin-killed concentrated bedsonias in adjuvants; the results, though encouraging, have been quite variable, and further carefully controlled field trials are necessary.

7.6 International transfer of psittacine birds

The customary holding of psittacines in isolation for 30 days in accordance with government regulations contributes to the spread of infection in an import shipment. The prevalence of bedsonial infection in psittacines caught in the bush is usually only 5% or less; by the end of quarantine, however, it may be as high as 30-40%, and newly infected birds will be in the acute phases of psittacosis, shedding enormous numbers of bedsonias. These birds serve as reservoirs and will introduce the infection to other birds and cause serious human illness. Quarantine practices should, therefore, be modified. It is imperative that preventive antimicrobial therapy be used prior to and during shipment. Simulated commercial operations, carefully analyzed by laboratory methods, have confirmed the practicability of mass chemotherapy with medicated feed. Studies based on over 200 imported psittacines indicate that satisfactory tetracycline blood levels are produced by this method and persist during shipment by air. This type of operation can be executed by animal caretakers provided they are under competent supervision.

Stringent safeguards must be provided to ensure that each bird receives the required 45 days of treatment and does not come in contact with sources of reinfection. International shipments of psittacine birds that have received prophylactic chemotherapy may consist of some birds that have been cured of infection and a much larger number, never infected, that are highly susceptible to Bedsonia. The latter may readily contract psittacosis if they are transferred by the importer to dealers whose premises house untreated infected psittacine birds. Upon arrival, all birds must be housed under sanitary conditions, isolated from untreated birds, and maintained by the importer and later the dealer on the same medicated feed until sold to the public.
8. BACTERIAL INFECTIONS

8.1 Salmonellosis

Salmonellosis may be considered as one of the most important zoonoses in which the main source of infection for man is food of animal origin. To date more than 1000 different Salmonella serotypes, all of which may be considered potentially pathogenic, have been reported. Many of the reported serotypes have been isolated only once, and others infrequently; however, some 100 have been isolated repeatedly from food, animals, and infected human beings. A few serotypes seem to have host preferences, but salmonellas may be found in all warm-blooded animals, including man, and in many cold-blooded vertebrates. The typhoid and paratyphoid organisms that are strictly parasitic for human beings are not discussed in this report, although food of animal origin can serve as a vehicle for such infections, as shown by the recent outbreak of typhoid fever in Aberdeen, Scotland.

The slight variations in occurrence of salmonellosis in different animal species that have been noted in different countries are probably related to the frequency of bacteriologic examination of these species. In most areas of the world isolation of Salmonella has been reported from domestic poultry, swine, cattle, horses, and sheep. A clear distinction should, however, be made between salmonellosis as a disease problem and subclinical Salmonella infections. Since acute or fatal disease is not frequently observed in animals other than calves, chicks, etc., the subacute or carrier state should be recognized as the main reservoir of Salmonella infections for man and animals. In this respect, subclinical infection of rodents, birds, animals in zoologic gardens, and pet animals is also significant.

8.1.1 Salmonellosis in human beings

In many countries the incidence of human salmonellosis has increased significantly in recent years. In the USA, for example, reported and bacteriologically proved Salmonella infections increased from 1700 in 1956 to 20,865 in 1965. Similar increases have been observed in many other countries. Although more efficient bacteriologic procedures and a greater interest in the problem may be contributing factors, the increase of infections is considered to be real. It has been estimated that even in countries with good reporting systems only 5-10% of the actual prevalence is reported. This is especially true during epidemics, when there is not sufficient time to send all the human faecal samples to laboratories for examination.

Studies have shown that egg products and meat products are largely responsible for outbreaks of salmonellosis. In contrast to epidemics of typhoid fever, which remain localized or limited to a community, other
Salmonelloses spread over a whole area or country continuously during the year, the number of cases reaching a peak in late summer and early autumn. Mortality due to salmonellosis is relatively low and occurs in the very young child and very old adult. Salmonellosis may cause serious problems in hospitals; carelessness in the preparation of food, for example, can lead to its becoming an "institutional" disease, and in such cases fatalities occur frequently. Other consequences of salmonellosis include the long recovery period, which may result in loss of working capacity of patients, and the danger that carriers, who may not be detected because bacteriologic examination of faeces is not completely reliable, may handle food.

In most countries Salmonella typhimurium is still the most common serotype and is responsible for 50-60% of all human cases of salmonellosis. The incidence of other serotypes in man varies from country to country; for example, S. heidelberg is prominent in the USA and the United Kingdom, S. thompson in Canada, S. bovis morbillicans in Australia and S. panama in north-western Europe. When a serotype that originally occurred sporadically becomes prominent, it seldom returns to its former status.

Salmonellosis constitutes a major health problem in countries having high standards of hygiene. This may be related to food habits in such countries, where the consumption of raw or slightly heated products of animal origin, especially meat, has become popular. The mass production and use of processed foods has increased the problem in such countries. Moreover, application of hygienic measures may eliminate bacterial flora that otherwise might either inhibit the growth of salmonellas or spoil the product so that consumers would discard it without use.

8.1.1.1 Salmonellosis apparently not associated with food

It has been reported from many countries that human salmonellosis sometimes appears to be transmitted by direct contact or by contact with fomites rather than through contaminated food. Most of these reports describe outbreaks in hospitals, particularly children's and mental hospitals, or other closed communities. In the general population, however, such a mode of transmission is difficult to prove, although direct transmission has been observed among animal attendants, poultry processors, and others having close contact with infected animals.

8.1.1.2 Foods associated with outbreaks

On the North American continent, eggs and egg products are responsible for a large number of outbreaks. Meat and meat products are the most important sources of Salmonella infections in Europe. Pork, veal, horsemeat, and poultry play a major role. Infection may be acquired from the first three by the consumption of raw or insufficiently heated products, particularly if the meat is ground or minced; from poultry meat, on the
other hand, infection is acquired from the handling and processing of contaminated birds. The decrease in Salmonella infections caused by egg and milk products in Europe is probably brought about by the increasing use of pasteurization in many of these countries.

Recently the presence of Salmonella in, and transmission of infection by, foods and additives such as dried yeast, dry milk, coconut, cotton seed protein, cereal powder, and the food colour cochineal have been reported. In some countries dried milk has also been shown to transmit human salmonellosis.

It should be emphasized that most foods are usually only slightly contaminated. During processing, however, and especially during storage, salmonellas can multiply, particularly at temperatures between 15°C and 45°C, so that their numbers reach levels sufficient to cause infection.

8.1.1.3 The human excretor

The role of the human excretor in the transmission of salmonellosis is difficult to assess. Food handlers have frequently been blamed as the source of infection because on examination they have been found to be excretors of salmonellas. Many of these food handlers, however, were probably infected by the foods they handled and thus were victims of the illness no less than were the consumers of the food. Reports have indicated that carriers may excrete salmonellas for up to 30 months. In the Federal Republic of Germany the carrier rate in the general population has been estimated to be 10 per thousand. In other countries where great epidemics have occurred in recent years the rate may be significantly higher. It should be emphasized that bacteriologic stool examination by conventional methods, even if performed repeatedly, does not necessarily prove the absence of Salmonella infection, because the excretion of bacteria is often intermittent and sometimes only very small numbers are present in the faeces.

To reduce the hazard of contamination, a high standard of personal hygiene in food handlers is necessary, and the provision of adequate means of attaining it should be required in commercial kitchens, packing plants, and meat processing factories.

8.1.2 Salmonellosis in animals

8.1.2.1 Salmonellosis in poultry

The number of Salmonella types isolated from poultry is increasing in many parts of the world. It seems that these infections are more frequently observed on the North American continent than in Europe. S. pullorum and S. gallinarum, which in recent years have markedly decreased in many countries, are still important types responsible for disease outbreaks in poultry in the USA. In 1956, for example, 30% of isolates from poultry
were salmonellas other than host-specific *S. pullorum* and *S. gallinarum*; in 1963, however, this figure had increased to 76%.

The public health significance of *Salmonella* carriers in poultry has been emphasized in many countries. The increasing world-wide consumption of broiling and frying chickens results in the establishment of larger breeding units and a consequent greater concentration of birds during transport and slaughter. This growth of the industry adds to the problem of salmonellosis. It has been shown that even though the initial number of infected birds may be low the final number is much higher, because contamination occurs during transport, slaughtering, and processing. Although poultry meat is usually not consumed raw or insufficiently cooked, infected birds may contaminate poultry and other food that has already been cooked—e.g., when the same butcher's block is used for cutting both uncooked and cooked birds.

*S. typhimurium* plays a major role in subclinical infections of poultry, but many other serotypes are also isolated. There is some evidence that human excretors occasionally have transmitted salmonellas to poultry.

**Control and prevention in poultry**: The prevalence of *Salmonella pullorum* disease in several countries has been greatly reduced by the use of blood tests and the destruction of poultry found to be infected. Blood tests with antigens of serotypes other than *S. pullorum* have many disadvantages and cannot be recommended for the detection of subclinical infections. *S. typhimurium* antigen has been used with advantage in detecting infection in turkeys.

The maintenance of hygienic conditions and the use of feed free of salmonellas are most important in reducing the carrier rate. Proper fumigation of eggs in hatcheries should be encouraged.

### 8.1.2.2 Salmonellosis in cattle

Cattle may harbour many different types of *Salmonella*. For example, *S. dublin* is particularly adapted to cattle and in many parts of the world is a cause of disease, particularly in calves. Infections with *S. typhimurium* and other serotypes are increasing. Disease caused by *S. typhimurium* infection seems to be less severe than that caused by infection with *S. dublin*, but it creates an important public health problem since it results in a high percentage of carriers.

While being fattened, calves are frequently fed artificial milk, confined within small pens, and kept in darkness. Such conditions promote clinical and subclinical *Salmonella* infections in these animals. If such infection occurs, it usually spreads rapidly. If *S. dublin* is involved, the result is usually clinical disease, but if the causative organism is *S. typhimurium* the infection is subclinical. In connexion with the carrier problem, examination
of rumen-contents in New Zealand showed them to be contaminated with
different serotypes.

Until recently, salmonellosis has apparently been of minor importance
in adult cattle. However, in the USA salmonellosis is becoming a recognized
problem among dairy and beef cattle, particularly those held for fattening
prior to slaughter.

Antibiotics and other chemotherapeutics have been widely used, espe-
cially in calves. Some breeders state that fattening of calves without prophy-
lactic or even therapeutic doses of antibiotics is not practical. The possible
consequences of such a treatment are discussed in section 8.1.8.

8.1.2.3 *Salmonellosis in pigs*

Recent investigations have shown that subclinical infections of pigs are
one of the most important sources of *Salmonella* infection in man. In some
countries up to 25% of swine have been found infected. *Salmonella* car-
rriers harbour the bacteria in the intestinal tract (particularly the caecum),
the mesenteric lymph nodes, and—to a much lesser extent—the gall bladder
and portal lymph nodes. Salmonellas are only occasionally found in
muscle tissue. Subclinical infections in individual pigs often spread rapidly,
involving the entire herd. Conditions under which the animals are sub-
jected to stress, such as transport and confinement in holding pens, pro-
mote the spread of *Salmonella* infections.

An important serotype frequently isolated from pigs is *S. typhimurium*,
but it is only one of a wide variety of serotypes that are found. Serotypes
found in healthy animals when they are slaughtered are frequently similar
to those obtained from the human population in the area where the pigs
are raised.

Infections with the host-adapted *S. choleraesuis* are widespread in
Eastern European countries and the Far East, but are decreasing in Western
Europe and on the North American continent.

*Vaccines*: Live vaccines prepared from rough variants of *S. dublin* and
*S. choleraesuis* have been reported to protect calves and pigs against disease.
Such vaccines have been used recently in the United Kingdom, but it has
not been reported whether or not such vaccines prevent subclinical infec-
tions.

*Control*: Recent investigations have clearly shown that contaminated
feeds of animal and vegetable origin are the most important sources of
salmonellas that infect pigs. Moreover, the contaminated environment
and infection of piglets in the first weeks of life are important factors in the spread
of infection within the herd. Supplying the animals with *Salmonella*-free
feeds seems to control these infections. Pigs can be raised and kept free
from salmonellas throughout their lives if they are provided with such feeds
in proper hygienic surroundings.
Salmonella-free feeds can be prepared by heating with steam or—experimentally—by irradiation (see section 8.1.9) without loss of nutritional value. The use of feeds in pellet form may be a very promising and economically practicable solution to this problem provided sufficient heat is used to kill salmonellas during the pellet-forming process. Even in infected herds the use of pellet feeds seems to result in a considerable decrease of Salmonella carriers.

8.1.2.4 *Salmonellosis in sheep and horses*

The importance of Salmonella infections in sheep has been underestimated for a long time. These infections play an important economic role in Australia and New Zealand. Although the flock mortality rate is only about 5%, a large number of animals remain carriers for a long time; furthermore, the contamination of pastures results in the reinfection of animals.

Subclinical infection in horses is of great importance in many countries (see section 8.1.3.2). The appearance of an increasing number of different serotypes in horses has been associated with their eating contaminated feed.

8.1.2.5 *Salmonellosis in other species*

Practically every animal species investigated has yielded salmonellas. It is unwise to presume that a species is seldom or never infected until a thorough investigation has been made in different areas. Surveys of dogs have shown a prevalence of 1% to more than 30% in different areas, and over 50 serotypes have been isolated from them, including the ubiquitous S. typhimurium. Surveys of cats have revealed more than 20 serotypes, the prevalence ranging up to 12% depending upon the area and conditions under which the animals lived. Chicks, ducklings, pet budgerigars (parakeets), canaries, and exotic species of birds have been incriminated as a source of Salmonella infections, especially in children. Recently it has been observed that snakes, lizards, and tortoises play a role in the transmission of salmonellosis to man. The latter, especially, have become popular pets in many countries. The unhygienic conditions under which they are kept in many pet shops and households represent a further health hazard. A number of Salmonella infections originating from them have been described recently.

Special attention should be given to the destruction of rodents, flies, and other insects that are often infected in the surroundings of slaughterhouses, food processing plants, and rendering plants.

In connexion with salmonellosis in rodents it should be re-emphasized that salmonellas should under no circumstances be used as rodenticides. Rodents rapidly develop resistance to Salmonella serotypes; thus, this method has little practical value. Moreover, it has been shown in different
countries that such practices are a public health hazard because the serotypes used are also dangerous to man.

8.1.3 Human and animal foods liable to contamination with Salmonella

8.1.3.1 Eggs and egg products

Duck eggs: Although the public-health danger of Salmonella infection of duck eggs is widely recognized in Western countries, outbreaks of salmonellosis caused by them are reported occasionally. Preventive measures, such as boiling of the eggs, have proved to be very effective; in some countries, the eggs as sold carry a printed recommendation that they be boiled. However, the potential danger of duck eggs should not be underestimated, particularly in countries where no special control measures exist, since the infection rate in duck eggs is still relatively high. Duck eggs may be infected in the ovary or oviduct or through the shell. Improved farm hygiene reduces contamination through the shell but not infection in the ovary and oviduct.

Hen eggs: Unlike duck eggs, hen eggs are rarely infected in the ovary. Examination of more than 20,000 eggs in the USA, the United Kingdom, Australia, and Ireland revealed salmonellas in only 37 (0.18%); however, a considerably higher proportion of cracked eggs has been found to be infected. Although salmonellas may enter eggs by penetrating the shells, this can be prevented if the eggs are handled hygienically.

Egg products: Frozen whole egg, liquid whole egg, egg albumen, egg yolk, and dried egg have been frequently reported as sources of salmonellosis outbreaks. The widespread contamination of these products is closely related to the high percentage of birds that are subclinically infected. Salmonella contamination and the numerous outbreaks traced to it have resulted, in several countries, in the enforcement of regulations requiring pasteurization. Such treatment has proved to be effective, if adequately checked.¹

The possibility of recontamination after heat treatment is an important problem, particularly in view of the presence in the processing plant of raw material with a high bacterial content. In some plants there is a tendency to neglect proper hygiene, since the product will be heat treated anyway and it is assumed that this will rid it of contaminants. In a number of countries, large quantities of contaminated food products reach the consumer. Severe outbreaks due to infected egg products have been reported recently—e.g., S. thompson infections in Canada, and an epidemic due to S. derby in the USA.

¹ Checking may be performed by the alpha-amylase test, as in the United Kingdom, or the Enterobacteriaceae test, as described in Zbl. Vet.-Med., 13 (1966), 273.
8.1.3.2 Meat

Poultry meat: The presence of salmonellas in fresh broiling and frying chickens on the market, and in processed chicken and turkey products, has been a source of extensive food-borne infections. Such infections are almost always the result of contamination after cooking and are therefore related to kitchen hygiene. Food-borne infections are often related to food habits. This is especially true of processed foods containing poultry meat that are consumed more widely on the North American continent than in other parts of the world.

Beef, veal, pork, and horse meat: The presence of salmonellas in these meats and products made from them is a major cause of human infections, especially in countries where the consumption of raw or insufficiently heat-treated meat and meat products is increasing. The high percentage of subclinical infections in animals brought to slaughter-houses has created a serious hygiene problem that can be solved only if Salmonella-free animals are slaughtered. As long as infected animals reach abattoirs, contamination of carcasses will occur. This is especially true for pork because of the more complex slaughtering and processing techniques used (involving scalding vats, scraping machines, etc.). Although this situation cannot be changed easily, every effort should be made to improve hygienic conditions in slaughter-houses so as to minimize contamination.

Extensive contamination of the hair and skin of calves with Salmonella organisms readily leads to contamination of the meat and organs during processing.

A special problem has developed recently in European countries where horse meat is consumed. This is particularly true when the meat is imported; 50-60% of samples of imported horse meat have been found to be infected. This meat is frequently used minced and in meat products; in both cases, cooking before consumption is often insufficient.

Hormones and other products of animal origin: Salmonella contamination of pharmaceutical substances of animal origin, such as thyroid tablets, pancreatic extracts, and adrenal cortical extracts has recently been reported in different countries.

8.1.3.3 Milk

When milk is routinely pasteurized the risk of its being a source of human salmonellosis is small. Several outbreaks of salmonellosis have, however, been traced to the consumption of contaminated raw milk, improperly pasteurized milk and milk products, or milk that has been contaminated after pasteurization. In the USA, non-fat dried milk has recently been incriminated as a source of human salmonellosis; investigations have revealed contamination with several Salmonella serotypes in cer-
tain processing plants. These findings have led to regulations requiring pasteurization of all milk prior to drying.

8.1.3.4 Fish

In temperate climates, cooked fish is seldom responsible for food infections. Where uncooked fish is eaten, however, salmonellosis sometimes occurs. In warm climates and in areas where fish are caught and shellfish raised in sewage-polluted waters, there are greater risks and further study is required before the problem can be accurately defined. Fish and shellfish are commonly contaminated by being washed in polluted waters. In recent years smoked fish has been incriminated as a source of infection; salmonellas are not killed by the smoking procedure. Consideration should be given to methods of processing such products to eliminate Salmonella contamination and prevent recontamination.

8.1.3.5 Vegetable products

In recent years, several extensive outbreaks of salmonellosis have been attributed to vegetable products such as dried yeast, cereal powder, and cotton seed protein concentrate. Dried yeast is an ingredient of a dietary supplement often given to hospital patients. These and other vegetable products may be potentially dangerous, especially when contaminated water or sewage is used in their cultivation. In view of increasing world trade, this problem may be more important than is at present realized.

8.1.4 Animal feeds and fertilizers

Animal feeds, some of which are widely distributed, have often been shown to be heavily contaminated with salmonellas. World-wide distribution causes an extensive spread of infection to domestic animals and poultry. Products such as blood, bone, feather, and fish meal can be contaminated with salmonellas, as can products of vegetable origin depending on their place of origin and the way they are processed. Products of animal origin are contaminated by unsanitary handling during storage and transport following heat-treatment. Products of vegetable origin are contaminated by birds, rodents, and other animals in the field and during storage.

Animal feeds today are not only the main source of subclinical infections in animals, but they also contaminate food for human use and ultimately result in infection of man. Conditions of sanitation in exporting countries, especially in feed-producing factories, do not usually meet the standards necessary to break the chain “feed-animal-food-man”. The use of the products of such factories in mills that prepare mixed feeds greatly increases the risk of contamination; other factors that add to this risk include the re-use of sacks and the possibility that salmonellas may be spread to other products by dust.
A number of measures, such as re-pasteurization by means of steam, irradiation, and the use of pellet formulations, can be taken to meet the danger of contaminated feeds. The use of pellet formulations in particular has given encouraging results, and it is practicable. In the manufacture of pellets the original number of Enterobacteriaceae is reduced by a factor of one hundred to one thousand. This may not always result in Salmonella-free feed, but it has been shown that subclinical infection does not occur when such products are fed to animals. The sanitary quality of pellets can be checked by means of the Enterobacteriaceae test.

In plants where feeds and fertilizers are produced, especially in rendering plants, recontamination of sterilized products is still a major problem. The "unclean" and the "clean" sections of such plants should be strictly separated, and continuous hygienic control should be maintained by trained personnel. Products should be protected during storage and transport against possible contamination by rodents, birds, reptiles, and insects.

The above remarks on the production of feeds are also applicable to fertilizers, which are often produced in the same factories. The use of contaminated fertilizers maintains the disease cycle. Recent reports in different countries have shown that these products are heavily contaminated with Salmonella.

8.1.5 Water

In recent years there have been a number of outbreaks of infection caused by water-borne salmonellas. Research has shown that some sewage treatment plants reduce the number of Salmonella organisms only relatively slightly; thus, large numbers of the organisms enter water courses with the effluent from such plants and contaminate sources of drinking water. Recreation areas used for fishing and water sports are also contaminated, creating an additional public-health danger. Raw sewage sludge should not be used as a fertilizer in parks and private gardens. These are some of the areas in which further effort is required to ensure an adequate supply of clean, safe drinking water for man and animals.

8.1.6 Control of human salmonellosis

In so far as present knowledge allows the formulation of control measures, they should include the following:

1. Reporting of cases of salmonellosis so that they and their contacts may be prevented from spreading disease.

2. Education of caterers and food handlers in a high standard of kitchen and personal hygiene.

3. Proper refrigeration of foods.
(4) Effective pasteurization of milk.

(5) Hygienic production of eggs and cold storage if possible; hygienic preparation of egg products, and effective heat treatment of the final product before distribution.

(6) Sterilization of animal feed liable to contamination.

(7) High standards of abattoir hygiene.

(8) Hygienic handling of fish and shellfish.

Pasteurization of milk and egg products has proved to be of great value in the prevention of salmonellosis in man. However, this is not possible with meat and certain meat products—the main source of Salmonella infections; here, the solution lies in the raising of Salmonella-free animals. Since a long time may elapse before significant results are achieved by the latter approach, emphasis should, meanwhile, be placed on instruction of the consumer. It should be clearly stated that foodstuffs of animal origin should not be eaten raw or insufficiently cooked. In addition to cooking, refrigeration in retail shops and households is important in the prevention of salmonellosis, even though the products may be contaminated with a small number of organisms.

A difficult situation exists with respect to Salmonella-contaminated food in international trade and commerce in general. Destruction of all such food is not at present economically feasible. Some countries have stringent prohibitions against the importation of such food, but for economic reasons other countries often find it necessary to accept it, thus removing the pressure on exporting countries to improve their sanitary practices in the production, handling, and shipping of these products. In order to meet this situation it is suggested that importing countries impose, over a period of years, progressively more stringent requirements that would force exporting countries to meet higher standards. This would cause the least disruption in international trade, and would gradually improve the hygienic quality of food products.

8.1.7 Laboratory procedures

The prevalence rates of salmonellosis in different countries cannot be compared because of the widely differing diagnostic methods that are in use. Such a variety of methods may result in wrong conclusions in the evaluation of the Salmonella problem in certain areas. Standard laboratory procedures are urgently needed, as is the continual training of laboratory personnel and hygiene supervisors in plants that produce food and feed. In addition, emphasis should be given to the phage-typing of Salmonella serotypes other than S. typhi and S. paratyphi B; this technique can be most helpful in studies of salmonellosis epidemiology.
8.1.8 Antibiotic resistance

Special attention should be given to the resistance of Salmonella to antibiotics, in view of the extensive therapeutic use of these substances in man and animals and their nonmedical use in animals and for food preservation. The increasing problem of episomally transferred drug resistance is of the utmost importance and should be thoroughly investigated, since it may become important in Salmonella infections.

8.1.9 Irradiation of Salmonella-contaminated food and feed

The preservation of food and feed by the use of ionizing radiation has been studied extensively in recent years. This is particularly true of Salmonella-contaminated products, such as meat, poultry, egg products, and feed. Surface decontamination by ionizing radiation of carcasses and irradiation of feed would be a most important aid to the solution of Salmonella problems if an economical procedure could be developed.

Work along these lines is promising and should be supported wherever possible.

8.2 Tuberculosis

8.2.1 Bovine tuberculosis

Eradication of bovine tuberculosis is a major objective in a number of countries, and it has been virtually achieved in Norway, Sweden, Denmark, Finland, the Netherlands, Switzerland, Great Britain, the USA, Canada, and Japan. The basis of these eradication programmes has been the systematic application of the tuberculin test and the removal of reactors, either by slaughter or by the establishment of separate reactor and non-reactor herds (see Annex 7). The continuing decrease in the prevalence of tuberculosis in cattle has been accompanied by a great reduction in the prevalence of infection of human beings with Mycobacterium bovis.

Although different types of tuberculin are used in different countries, purified protein derivative (PPD) is considered to be the tuberculin of choice because of its comparative purity and the ease with which it can be standardized both chemically and biologically. Strains of M. tuberculosis are usually used in the production of tuberculin; although in some countries tuberculins prepared from M. bovis are regarded as being more specific, the preponderance of evidence does not support this view. In retesting cattle, the interval between the application of tests varies according to the status of the disease in the herd; when reactors are still present, an interval of about 60 days (but not less) should elapse between tests, but when no

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further reactors are found, the interval may be increased to several months and eventually to a year or more. Even when no reactors are present, surveillance of herds and areas should be continued in order to detect infection that may be introduced.

Nonspecific reactions (i.e., those produced in reactors having no visible lesions) to tuberculin tests are a major problem both in areas where tuberculosis has been virtually eradicated and in those where infection with *M. bovis* was relatively rare to begin with. Nonspecific reactions to tuberculin vary according to ecologic factors in a given situation. They include (1) infection with *M. paratuberculosis* (Johnne's disease), (2) nonprogressive infections with *M. tuberculosis* and *M. avium* (including strains of the so-called Group III uncategorized mycobacteria), the organisms causing so-called skin lesions, and (3) various transient sensitizing infections with other mycobacteria, probably including some soil and water forms. The cause of nonspecific sensitivity can be determined only by post-mortem examination of slaughtered reactors and laboratory study of tissues from such animals, including attempted isolation and identification of mycobacteria that might be responsible. Both in established eradication programmes and in surveys of new areas, the use of quantitative comparative tests will help to establish whether or not infection with *M. bovis* is present. Comparative tests are usually performed with mammalian and avian tuberculins. In making such tests it is essential that properly standardized tuberculins (preferably PPD) be employed. Standardization should be on the basis of equal potency of the tuberculins, not merely on the basis of equal protein content. One useful dosage system is that used in Great Britain, in which 0.1 ml of mammalian tuberculin containing 10 000 IU, and 0.1 ml of avian tuberculin containing 2500 IU are injected. The increase in skin thickness is measured after 72 hours and a discrimination formula is applied, depending upon the distribution of reactions in the herd.\(^1\) When other mycobacterial sensitins are used in comparison with mammalian and avian tuberculins, adequate biological standardization on the basis of equal potency in sensitized cattle is essential to the correct interpretation of reactions.\(^2\)

Animals can also become infected from man, and a large number of reinfactions of tuberculin-free herds with human- or bovine-type strains have been traced to this source.

Infection of cattle with human strains seldom causes progressive lesions but often gives rise to a marked tuberculin reaction, frequently temporary in nature, and interferes with the application of the tuberculin test.

\(^1\) Paterson, A. B. et al. (1958) *J. Hyg. (Lond.)*, 56, 1.

As the incidence and prevalence of infection in a population decrease under the influence of an eradication programme, the importance of epidemiologic tracing and of testing procedures increases. If cattle found to be tuberculous by routine meat inspection at the time of slaughter are traced back to the herds of origin, the latter can be tested with tuberculin; this is a highly efficient technique for the discovery of infected animals, which can then be eliminated from the herds. Adequate meat inspection services and case-finding programmes can materially reduce the amount of complete area testing that is necessary.

Tuberculosis in buffaloes is a problem in some countries. Although, generally speaking, its control and eradication may be achieved by methods similar to those used to control tuberculosis in cattle, further work is necessary on the application and interpretation of the tuberculin test in the buffalo.

In some parts of the world, vaccination of human beings against tuberculosis is practised extensively. In cattle, experiments have been conducted with vaccines consisting of live cultures of the BCG and Vole strains of the tubercule bacillus, and some protection has been achieved under carefully controlled conditions. However, the Committee is of the opinion that, generally speaking, vaccination has no place in the control or eradication of tuberculosis in cattle. Vaccines such as those composed of BCG or the Vole bacillus create a sensitivity to tuberculin that interferes, for varying periods, with control and eradication programmes based on tuberculin testing.

Chemoprophylaxis and chemotherapy

The Committee recognizes that it is frequently difficult for economically poor countries to undertake control and eradication programmes based solely on test and slaughter methods. Furthermore, such countries may have great difficulty in obtaining enough calves to replace slaughtered infected cattle. Consequently, many countries have been reluctant to carry out any but the most limited attempts to control bovine tuberculosis; such attempts have frequently been quite ineffective. Recent developments in the chemoprophylaxis and chemotherapy of bovine tuberculosis should offer such countries effective and economical methods for markedly reducing levels of infection; test and slaughter procedures could be introduced subsequently.

Experiments in several countries during the past decade have indicated that chemotherapeutic agents found to be effective against human tuberculosis may also be of value against bovine tuberculosis. An extensive and carefully controlled series of trials recently completed in the Republic of South Africa showed that excellent prophylactic and therapeutic results are achieved by the administration of at least 10 mg/kg of isoniazid daily for a
period of 6 to 11 months. The drug may be given in feed, in water, or in tablet form. Prolonged isoniazid therapy results in a gradual diminution of tuberculin hypersensitivity that is related to the degree of apparent bacteriologic cure.

In situations where neither segregation of infected and non-infected cattle nor slaughter of reactors is feasible, a combination of chemoprophylaxis, chemotherapy, and selective slaughter can be used at both the beginning and the end of a 3-4 year eradication programme. This permits retention of up to $\frac{1}{2}$ to $\frac{3}{4}$ of the infected cattle for production of calves and milk, prevention of spread to susceptible cattle, and continuation of normal farming operations.

Basic requirements for these procedures are administration of drugs for long periods, accurate measurement of daily doses, proper identification of cattle, and maintenance of accurate records. Decisions as to which animals should be slaughtered at the beginning and end of such programmes must be made for each herd; this requires veterinarians with special training. Animals suffering from lung and udder tuberculosis must be removed and slaughtered.

Such programmes are particularly suitable for large government-operated dairy farms where careful supervision can be maintained. The Committee strongly recommends that chemotherapy and chemoprophylaxis should not be used in small private herds where adequate supervision cannot be exercised.

In the South African studies, excretion of isoniazid in milk amounted to 0.24 $\mu$g/ml when the daily dosage was 10 mg/kg (when the dosage was 20 mg/kg, isoniazid concentration in the milk was 0.4 $\mu$g/ml). Assuming a dosage of 10 mg/kg, and assuming that a child consumes 0.5 l of milk daily, these figures indicate the ingestion of 0.1-0.2 mg isoniazid each day. Apart from the dilution factor, it was determined that routine handling of the milk in metal containers and subsequent pasteurization results in a decrease of the isoniazid to undetectable levels.

It was found that some isoniazid resistance had developed in some of the M. bovis isolated from treated animals, but this did not affect the overall results. The virulence of these strains of M. bovis for experimental animals was markedly lower than usual; similar observations have been made with mycobacteria isolated from treated human beings. Furthermore, when uninfected cattle were exposed to cattle infected with these strains no evidence of natural transmissibility was found.

Further extensive field trials are needed to determine the value of chemotherapy and chemoprophylaxis in eliminating bovine tuberculosis. The

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Committee urges that where classical test and slaughter methods are feasible, and where effective programmes of this type are already in operation, there should be no resort to chemoprophylaxis and chemotherapy.

8.2.2 Tuberculosis in animals other than cattle

Animals other than cattle may occasionally be a source of direct infection for man. Perhaps more significantly, they may be involved in the maintenance of *M. bovis* and *M. avium* infection in livestock, so that these organisms may be transmitted to man directly from the latter. Monkeys are highly susceptible to both human and bovine types and can transmit the disease to their attendants. *M. tuberculosis*, the human tubercle bacillus, can cause disease in swine, goats, dogs, parrots, elephants, tapirs, and other animals. *M. bovis* has been isolated from cats, goats, dogs, camels, elephants, and swine and the infection is believed to have been transmitted to cattle and possibly man from such hosts on a number of occasions. Bovine tubercle bacilli have also been isolated from various animals in zoologic gardens, where they have produced progressive disease.

As recently as 25 years ago, disease caused in man by *M. avium* was considered to be an exceptionally rare event, only 13 cases having been recorded. During the last 10 years, however, the number of cases of infection with *M. avium* has been more than double this number. It is probable that this represents better recognition of infection with *M. avium* rather than increased incidence of the disease. The maintenance and spread of this infection among human beings is, in all probability, directly connected with the extent of contact with infected poultry and contaminated environments.

Much more common is human disease caused by the organisms referred to as Battey bacilli of the Group III non-photochromogens. Group III strains consistently occurring in sputum from patients with pulmonary disease are quite uniform in properties, regardless of the part of the world from which they come. Strains with similar properties have been isolated from cattle and swine. Some investigators consider them all to be *M. avium*; others prefer to separate them on the basis of lack of virulence for birds. There is no evidence of contagion in the transmission of these infections and their striking geographic distribution may be an indication of environmental sources of infection. It remains to be determined whether lower animals and man share this hypothetical environmental exposure or whether the animals play a more direct role. Such questions can be answered only by extensive epidemiologic study of animals where strains similar to Group III non-photochromogens are involved.

8.3 Anthrax

Anthrax is enzootic in both wild and domesticated animals in most parts of the world. Human infections have been estimated to number between
20,000 and 100,000 annually, most of them occurring in people living in rural districts, although infections are frequent in some industrial areas. The disease often causes serious economic losses in livestock. This is particularly true of sheep, and in many areas annual vaccination of these animals is necessary. Heavy losses are also sometimes encountered in cattle, pigs, horses, goats, and llamas. Severe outbreaks in man have been traced to wildlife, notably hippopotamuses, elephants, and other African animals whose flesh may be eaten.

The epidemiologic problem of anthrax can conveniently be discussed under its agricultural and industrial aspects.

8.3.1 Agriculture

The spore form of Bacillus anthracis is highly resistant to chemical and environmental influences and can survive for years in certain soils and in animal products such as hides, hair, and wool. When anthrax infection in livestock becomes established in a district, a relatively permanent enzootic focus of infection is created because of the inability of the soil to destroy the spores. Heavy contamination of the soil exists in many areas of the world, particularly in Asia, southern Europe and Africa. Other countries have large or small "anthrax districts", but the anthrax problem is not as serious in the western hemisphere as it is in other parts of the world.

There is considerable evidence to show that anthrax is introduced into some countries by feeds and fertilizers prepared from bones and other parts of animals that die of anthrax. Non-infected materials may also become contaminated during transport in vehicles or ships that have recently conveyed infected bones, hides, or hair. Contamination of agricultural areas may occur through the use of waste materials from wool- and hair-processing plants as fertilizers, or by the effluents from plants such as tanneries.

The anthrax bacillus can also be spread from carcasses to healthy animals by flesh-eating birds, animals, and insects.

The main source of infection in agricultural workers is contact with contaminated carcasses, wool, hair, and hides. The ingestion of insufficiently cooked meat derived from infected animals is another source of infection. Infection by inhalation is now rare.

Many factors contribute to the frequency of anthrax infection in man. Despite the familiarity of farmers with anthrax in livestock where this disease recurs periodically, the onset of an epizootic is frequently difficult to recognize because of the lack of striking signs in the hyperacute or apoplectic form of the disease that may occur at the beginning of an outbreak. For economic reasons, farmers are loath to lose the value of hides.

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1 Sections 8.3.1 to 8.3.6, inclusive, are reprinted with modifications from the second report of the Joint WHO/FAO Expert Committee on Zoonoses (Wild Hlth Org. techn. Rep. Ser., 1950, 169).
salvaged from dead animals, even where anthrax is recognized as the cause of death. At the first sign of any illness, animals are often slaughtered for meat as well as for by-products. Such practices are highly dangerous. Regulations are helpful in areas practising advanced animal husbandry, but some communities need concrete assistance from governmental authorities, in the form of low-cost or free vaccination programmes in livestock, undertaken at regular intervals. With anthrax, therefore, as with other zoonoses, the responsibilities of health and agricultural authorities are interlocked, and the following steps for control of this disease are recommended:

(a) The provision of adequate local facilities for the diagnosis of anthrax in animals. Rapid presumptive diagnosis can be based upon bacteriologic smears made directly from dead animals or upon the Ascoli precipitation test. Where facilities are available, culture and animal inoculation procedures should be used. The "pearl-string" test and gamma bacteriophage and fluorescent antibody procedures are valuable for the rapid identification of the anthrax organism.

(b) Unopened carcasses of animals that die of anthrax, or that are suspected to have died of anthrax, should be destroyed at the site where the animals died as soon as possible after death. The preferred method is incineration; however, if this is not possible, burial with lime spread over the carcass in a pit two metres deep is effective in preventing spread of the organism from the contaminated carcass.

(c) Subsidized livestock-vaccination programmes undertaken at regular intervals, using biological products of proved potency. Experience has shown that annual vaccination is necessary, and in some badly affected areas vaccination every six months may be needed.

Many different kinds of anthrax vaccine (particularly spore-suspension) have been used successfully for the prevention of this disease in animals; the Sterne vaccine has been used with considerable success in many countries. This vaccine must be carefully prepared and potency-tested in order to ensure effective protection. The Committee noted that FAO and WHO are examining certain anthrax vaccines with a view to the establishment of an international reference preparation, and are also drafting minimum requirements for anthrax spore vaccine (living). It has been observed that animals receiving antibiotic feed additives are not always effectively immunized with live vaccine.

(d) Education of the agricultural population in the early signs of this disease in man and animals. Emphasis should be placed on the dangers of contaminated wounds, scratches, and abrasions, and of eating meat from infected animals; the necessity for proper handling and disposal of carcasses should also be stressed. Suspected cases of anthrax in animals should be promptly reported to the responsible authority.
When anthrax has been diagnosed within a herd it is advisable to quarantine the entire herd for a period of two weeks after the last diagnosed case of anthrax, or two weeks after effective immunization. The quarantine implies that the animals cannot be moved, either singly or as a herd, from the premises or pastures where they were at the time of the diagnosis.

(e) The management of anthrax in dairy herds has been well covered in the first report of the Joint FAO/WHO Expert Committee on Milk Hygiene, as follows:

"Fortunately, cattle infected with anthrax do not usually excrete the bacillus in their milk since milk secretion stops abruptly. However, the danger of milk contamination arises from the environment which frequently is highly contaminated with the bacillus or its very persistent spores.

"Where anthrax actually exists in a herd, great precautions must be taken because of the possibility of the environmental contamination of the milk (warm milk provides a good medium for the multiplication of the anthrax bacillus and the formation of spores). Despite this danger, however, milk-transmitted anthrax has been very rare.

"Where adequate veterinary supervision is available and good sanitary practices are followed, precautions should include the careful observation of all animals in the herd for a period of at least two weeks after the last-observed clinical case of anthrax. During this period, any animal showing signs of illness (including a rise in temperature as indicated by a daily thermometer check) should be isolated and its milk excluded from the remainder of the supply. The rest of the milk from well-supervised herds of this kind should be pasteurized or otherwise adequately heat-treated.

"In all instances of anthrax infection in a herd, thorough disinfection of the premises should be a requirement.

"Another point of difficulty in connexion with milk hygiene aspects of anthrax occurs where dairy herds are inoculated with living-spore vaccines, with the resultant possibility of anthrax bacilli being excreted in the milk. Despite the lack of evidence of this possibility materializing, certain authorities have recommended that milk from herds where spore vaccine has been administered be not used for 3 to 30 days following administration. This often produces a decided hardship for farmers and very frequently the application of such a restriction is not practicable. A more workable procedure would be to require that all milk originating from vaccinated herds be subjected to adequate heat-treatment before consumption, and that no milk should be used from animals showing systemic reactions to the vaccine (fever, anorexia or other clinical signs). (The difficulty can be avoided entirely if the animals are vaccinated when dry.)"

(f) The recognition or suspicion of anthrax in a carcass in an abattoir calls for drastic measures. Operations should cease until rapid presumptive tests (smears or the Ascoli precipitation test) are made. If these are positive, the infected carcasses and all carcasses possibly exposed to contamination should be sterilized, and the contaminated premises should be thoroughly disinfected (with 2% lye) before operations are resumed. In well-run abattoirs such incidents occur only rarely, because animals ill with anthrax are usually recognized at ante-mortem inspection.

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8.3.2 Industry

Cutaneous infection caused by contact with contaminated animal by-products (wool, hair, hides, skins) is by far the most frequent form of anthrax encountered in industrial workers. The inhalation form of anthrax rarely occurs, although health authorities should be on the alert for focal epidemics of this type.¹

The principal sources of anthrax in industrial workers are two groups of animal by-products: (a) hair and wool, and (b) hides and skins. Nearly all cases of anthrax resulting from the handling of contaminated hair and wool are contracted during procedures taking place before the weaving and finishing operations; the spore does not usually survive the dyeing process. Anthrax associated with hides and skins occurs from the handling of these materials before the tanning and finishing operations. Goat hair and skins from areas where anthrax is highly enzootic are the greatest sources of human infection. The most dangerous wools are coarse wools originating from countries and districts where anthrax is a severe and continuing problem. "Grease" wools, even from areas where anthrax is highly enzootic, are not as contaminated with *B. anthracis* spores as are "pulled" wools, since these latter wools may have originated from animals that died of anthrax.² "Grease" wools may, however, become contaminated during handling.

Wool that is used in manufacturing carpets (coarse wool) is associated with more human anthrax infections than is the fine wool used in the manufacture of textiles. The danger is considered to be diminished after the scouring process, which reduces the content of dirt and extraneous material as well as the number of *B. anthracis* spores adhering to the wool. The dyeing of wool in its raw state also reduces the danger of anthrax infections.

Control recommendations should be made so as to disrupt the supply of raw materials as little as possible, and should not involve a cost out of proportion to the seriousness of the problem.

There are many advocates of compulsory disinfection of animal products potentially contaminated with *B. anthracis*. From an economic point of view, there is no known satisfactory inexpensive method of disinfecting hides and skins, or of treating effluents from factories. For hair and wool there is an effective process of disinfection in current use in the United Kingdom (see Annex 8). This process makes it possible to reduce *B. anthra-

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¹ An outbreak of inhalation anthrax occurred in the USA in 1957, when several cases were reported among the employees of one industrial concern within a few weeks.
² "Grease" wools are obtained by cutting or clipping wool from the live animal and are baled and shipped in the natural greasy condition. "Pulled" wools, also called "skinn" or "dead" wools, are obtained from the skins of dead animals. The wet processes used in the removal of "pulled" or "dead" wool from the skin, and in the washing or scouring that frequently follows, may result in the spread of the micro-organism to previously uncontaminated wools.
cis contamination of the raw wool and hair, thus decreasing the likelihood of anthrax infections among those who subsequently handle these materials. Because of the expense of this method of disinfection, its cost should be subsidized by governments or distributed uniformly throughout the entire industry. Gamma-ray irradiation of bales of imported wool and hair has been effectively introduced in Australia.

The procedures recommended in plants where potentially contaminated materials are handled are dealt with in Annex 9.

8.3.3 Infections from bristles

In the past, numerous cases of anthrax in man have been caused by bristles of shaving-brushes and certain other brushes contaminated with anthrax spores. It is recommended, therefore, that all bristles to be used for shaving-brushes be sterilized before being embedded in the handle.

8.3.4 Importation of animal by-products

Animal by-products, such as wool, hair, hides, skin, bones, and bone-meal, are frequently contaminated with B. anthracis and may introduce the disease into countries that import them. It would be difficult to formulate uniform regulations that could be applied to all countries. The Committee feels, however, that certain measures in connexion with import requirements are practicable and have proved useful in the past, as shown by the experience of industrially advanced countries that import these by-products.

8.3.5 Vaccines for humans

Another control measure that can be considered for the prevention of human anthrax is the use of a vaccine for the protection of all individuals who have contact with potentially contaminated materials. Various vaccines for use in humans have been prepared and administered to exposed groups. These are discussed in reports from the United Kingdom,\(^\text{1}\) the USSR,\(^\text{2, 3}\) and the USA.\(^\text{4}\) Promising results have been claimed for these vaccines.

8.3.6 Therapy

Before the advent of sulfonamides and penicillin, even the cutaneous form of anthrax had a mortality rate of up to 20%. Early diagnosis and

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\(^{2}\) Alexandrov, N. I. et al. (1959) Vo.-med. Z., 8, 27.
\(^{3}\) Alexandrov, N. I. et al. (1963) Ž. Mikrobiol. (Mosk.), 40, No. 3, 32.
treatment with penicillin or other broad-spectrum antibiotics have currently reduced the mortality of the cutaneous disease to almost zero. Successful results with penicillin treatment and broad-spectrum antibiotics have also been obtained in animals.

Anti-anthrax serum may still be useful in the treatment of systemic anthrax where toxic manifestations occur. The heterologous serum now employed can cause serum-sickness; allergic skin-tests should be employed before using serum. Further work is required on the importance of toxins in the pathogenesis of the disease, and the place of specific antitoxins in therapy.

8.4 Leptospirosis

8.4.1 Epidemiology

Leptospirosis occurs in animals and man in almost all parts of the world. The chain of transmission, with rare exceptions, stops with human infection.

For many years rats and field-mice, and later dogs, were considered to be the primary animal carriers, but, as investigation increased, a wider range of hosts, including domestic animals and a variety of wild mammals, was discovered. Leptospirosis now constitutes an economic problem in cattle and swine. In some areas sheep, goats, and horses become infected. Rodent carriers include rats, mice, voles, and other field rodents. In addition, infected bats, mongooses, shrews, hedgehogs, jackals, foxes, opossums, racoons, skunks, wildcats, deer, and other mammals have been found. In these hosts, leptospires become localized in the kidneys and may be found in the lumen of the convoluted tubules. They are shed in the urine, often over long periods.

Birds, especially wading birds living in marshes, have been found infected. The epidemiologic importance of birds seems to be relatively minor, but migrating birds could spread some leptospiral serotypes from one country to another.

Arthropods do not seem to have much importance as reservoir hosts, but some ticks can carry leptospires in their tissues. Nematode parasites of infected mammals may carry leptospires but their role in transmission is not clear.

Although leptospirosis may infect a wide variety of hosts, only a few species are able to maintain the leptospires in their kidneys for a long time and hence act as reservoir hosts. Less important hosts tend to recover quickly and stop shedding leptospires.

Sometimes more than one serotype may be found in the same host. Dogs have been found to harbour at least nine serotypes other than Leptospira canicola. On the other hand, although L. canicola is found principally in dogs, it has also been isolated from cattle, swine, and jackals.
The dispersion of leptospirosis is related to specific environmental conditions, particularly those which bring infected animals, water, mud, and man together. Animal carriers often excrete up to 100 million leptospires/ml in the urine. If the infected urine becomes mixed with water or mud that is neutral or slightly alkaline, the leptospires may survive for weeks. Susceptible animals and human beings that enter the water are exposed to the agent and may develop infections ranging from an inapparent response to an acute fulminating fatal disease.

Leptospires usually enter the body through cuts or abrasions in the skin, or through the intact mucous membranes of the conjunctivae, nose, or mouth. It is unlikely that these organisms can penetrate intact skin or the gastro-intestinal mucous membrane. Moreover, the pH of the stomach or rumen contents is such as to kill leptospires rapidly.

### 8.4.1.1 Human infections

In man, the disease caused by serotypes *icterohaemorrhagiae* and *copenhageni* is still the most dangerous of the leptospiral infections, but serious human infections can be caused by other serotypes. For example, fatal infections with *bataviae*, *grippotyphosa*, *pyrogenes*, and a few other serotypes have been reported. Although other serotypes may cause a relatively mild disease, recovery is usually slow and occasionally complications may occur. The possibility of leptospirosis should be considered in the differential diagnosis of cases of acute disease with high fever, muscle pains, redness of the conjunctivae, or jaundice, and in cases of aseptic meningitis. Early laboratory investigation to confirm the diagnosis should be carried out, especially where occupational exposure to infective material is suspected.

The disease has long been recognized among veterinarians, slaughterhouse workers, canal workers, poultry and fish handlers, kennel men, swineherds, miners, packing-house employees, plantation labourers, and others. Individuals in contact with water contaminated by urine from infected rats and other rodents are particularly exposed to the risk of infection. Workers in rice-paddies and canefields often become infected, as do farmers who handle infected livestock, particularly swine and cattle, while owners of dogs have suffered from *canicola* infection.

For many decades swimming and accidental immersion in contaminated water have been associated with *icterohaemorrhagiae* infection in humans. In recent years other serotypes, especially *pomona*, have been shown to cause disease after such exposure in Italy, Argentina, Spain, the USA, and other countries. These episodes follow a common pattern: they occur in

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1 Formerly known as *L. icterohaemorrhagiae incompleta*. 
the late summer during dry periods when ponds are stagnant and streams slow-moving, and when there is presumed contamination of the water by the urine of infected animals. Most such infections, which are characterized by signs of meningitis, occur in children and young adults.

Irrigation canals and rapidly flowing rivers have been found to be heavily contaminated and their potential infectivity increases at times of flooding.

8.4.1.2 Cattle and swine

Leptospirosis is spread to cattle and swine through contaminated water and soil, by chronic shedders among domestic animals, and probably by wild animals, especially small rodents.

Different serotypes vary in pathogenicity for cattle. Some, particularly *grippotyphosa* and *pomona*, can cause severe infections and often give rise to epidemics. *Icterohaemorrhagiae*, *copenhageni*, *hardjo*, and other serotypes may be dangerous also, but less frequently. In swine, *pomona*, *tarassovi* (= *hyos*), and *canicola* are important causes of abortion and disease. Leptospirosis is spread very rapidly among swine, dairy herds, and cattle being fattened prior to slaughter.

Increased international trade in live cattle has led to the introduction of pathogenic leptospiral serotypes into previously unaffected countries, resulting in the outbreak of limited epidemics. For this reason some countries have enacted legislation to prevent the importation of carrier animals, requiring that animals be negative to a serologic test before their importation is allowed. However, such tests cannot provide conclusive proof of freedom from infection, and further work is necessary to develop more rational criteria for excluding infected animals. In framing regulations concerning imported animals, a distinction should be made between breeding stock and animals destined for immediate slaughter in abattoirs.

8.4.1.3 Dogs

The disease may be spread from dog to dog by direct contact, by contact with urine or contaminated fomites, or by water. In some cases it can be transmitted from rodents or farm livestock to dogs. Leptospirosis is frequently epizootic in dogs in urban areas; the epizootic may persist for some months before subsiding, after which the disease may not reappear for years.

Although in some countries *canicola* is the serotype found most frequently in dogs, in other countries infections with *icterohaemorrhagiae* and *copenhageni* are prevalent. Other serotypes have been found occasionally. Despite the widespread infection of dogs with the *canicola* serotype, only a few cases ascribable to this source have been observed in man.
8.4.1.4 Rodents and other small mammals

Widespread infection in these animals is an important source of disease for domestic animals and man. The presence of carrier rodents in some areas—e.g., rice-paddies and sugar-cane plantations—may be the only reason for the persistence and endemicity of leptospirosis. Fluctuations in populations of small mammals, and changes in their age-group composition, determine the seasonal cycles of epizootics that usually precede outbreaks in man.

8.4.2 Diagnosis

The principal methods used for the diagnosis of leptospirosis are direct microscopic examination of tissue preparations and body fluids, bacteriologic culture, and animal inoculation and serologic tests. Wherever possible, all these methods should be used, although serologic tests are the most widely employed because of their practicability.

The introduction of the fluorescent antibody technique for the demonstration of leptospires in fluids and tissues offers a promising method for the diagnosis of leptospirosis. It can be particularly helpful in detecting urinary shedders when the usual culture techniques are not practicable. However, further study is required to determine the possibility of using this method for the specific identification of serotypes.

Recent reports of the existence of some leptospiral strains that are unable to grow in the usual culture media, especially on first isolation, suggest that the use of laboratory animals in isolation procedures should not be discontinued.

The microscopic agglutination test\(^1\) is the method of choice in serologic testing, but it has some practical disadvantages. The antigens are frequently unstable, and a large number of antigens made from different serotypes are required to cover the spectrum of serotypes found in a given area. This difficulty can be partially overcome by grouping related serotypes into antigens that can be used for screening purposes. The use of selected water leptospiral strains (Patoc 1 and São Paulo) that are agglutinated by human sera containing antibodies for many different serotypes of parasitic leptospires may be helpful in preliminary serologic surveys under certain conditions.

For the diagnosis of individual cases of illness, the most significant finding is a rising titre in two serum specimens taken 7-8 days apart, provided the first is taken early in the course of the disease. No definite state-

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\(^1\) This test was previously known as the agglutination-lysis test; however, electron-microscope studies have revealed that true lysis does not occur, at least by the usual ratio between antigen and antibody.
ment can be made on the basis of a single specimen, but a relatively high titre in conjunction with clinical signs is presumptive evidence of leptospirosis. Some workers have reported low levels, or even the absence, of antibodies when antibiotics have been administered very early in the disease, and in cases that are rapidly fatal.

When making serologic surveys it should be borne in mind that the length of time for which antibodies persist, and the height of the titres, vary in different individuals and with the serotype that caused the original infection. Microscopic serologic screening tests in animals, using both living and killed antigens, can be carried out at a single serum dilution of 1 : 100; a positive reaction at this dilution indicates a high probability of past or present leptosporal infection.

Complement-fixation tests, used by many workers for diagnosis, are usually inferior to the agglutination test. However, since agglutinins persist for longer periods than complement-fixing antibodies (even for several years after recovery in areas where leptospirosis is widespread), the complement-fixation test is more reliable as a diagnostic indication of current infection.

8.4.3 Classification and nomenclature of leptospires

Hitherto the genus *Leptospira* has been divided into two species: *interro
gans*, comprising the parasitic strains, and *biflexa*, comprising the saprophytic water strains. The distinction between the two species rested not only on the parasitic or saprophytic state of the strains, but also on certain biochemical differences such as resistance to copper ions, nutritional requirements, and enzymatic activity. None of these criteria, however, has proved decisive for the classification of all strains. Moreover, in recent years, strains reported to have been isolated from sick persons or animals have shown the biochemical and antigenic characteristics of serotypes hitherto considered saprophytic. In view of these difficulties the Taxonomic Subcommittee on Leptospira of the International Association of Microbiological Societies has recommended grouping all leptospiral strains in the single species *Leptospira interrogans*.

On the infraspecific level *L. interrogans* can be divided into two "complexes". The term "complex" has no official standing as a taxon but has been proposed for provisional use in dividing leptospires into the two groups for which the species names *Interrogans* and *biflexa* were previously used—but which cannot, at present, be defined with certainty.

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1 This recommendation has been endorsed by a WHO Expert Group on Current Problems in Leptospirosis Research (see *Wid Hith Org. techn. Rep. Ser.*, 1967, 380)—ED.
8.4.3.1 Serotypes

The present classification system, in which the species *Leptospira interrogans* is divided into serotypes on the basis of agglutination and cross-absorption reactions with immune rabbit sera, is still the best available.

In view of the paucity of basic information on the nature of agglutinating antigens, and in view of the large number of serotypes that could be distinguished on the basis of minor differences, some arbitrary numerical standard must be used for the official designation of different serotypes. The criterion most widely accepted at present is the residual homologous titre after cross-absorption. The 10% figure has been widely used for many years, and since there seems to be no compelling reason, in the light of our present incomplete knowledge of antigenic composition, to change it, this figure may be maintained.

The "serotype" is the basic taxon and is represented by a designated reference strain. Two strains are considered to belong to different serotypes if, after cross-absorption with adequate amounts of heterologous antigen, 10% or more of the homologous titre regularly remains in at least one of the two antisera in repeated tests.

Because of the new definition of "serotype", the term "subserotype" has been rejected, and all previously described subserotypes have been reclassified as serotypes. A list of known serotypes will be found in Annex 5.

8.4.3.2 Serogroups

A serogroup is a group of two or more serotypes that show marked antigenic relationships as disclosed by the cross-agglutination test. It is not a taxonomic subdivision, nor can leptospiral serogroups be defined precisely at present.

The current arrangement of serogroups has limitations—for example, certain strains could be allocated to more than one serogroup. Nevertheless, the concept of leptospiral serogroups has practical value for the selection of antigens and antisera for diagnostic and epidemiologic investigations.

It should be noted that for routine diagnostic purposes detailed serologic analysis of isolated strains is not necessary, and a preliminary classification by means of simple agglutination tests using standardized antisera will suffice. This, however, should not preclude submission of cultures to a reference laboratory for identification or confirmation of serotype, which is important for epidemiologic purposes.

*WHO/FAO leptospirosis reference laboratories*: A valuable function is fulfilled by the WHO/FAO leptospirosis reference laboratories (see Annex 6), which assist countries with the classification and typing of strains. These laboratories also stimulate the use of uniform methods for diagnosis and surveys, and research on improved laboratory procedures.
8.4.4 Prevention and treatment of leptospirosis

8.4.4.1 Prevention

In the prevention of leptospirosis the animal shedder, the contaminated environment, and the exposed individual or animal have each to be considered.

(a) *The animal shedder*: There has been little success in developing a practical method for elimination of the shedder state in animals through antibiotic treatment. However, some success has been reported in dogs with the use of streptomycin or tetracycline derivatives. Rodent control is desirable but is difficult to achieve economically in the agricultural areas usually affected by leptospirosis.

Mechanization of agriculture, especially in rice-paddies, reduces the contact of farm workers with contaminated water and mud, and consequently lessens the possibility of contracting the infection. A thorough knowledge of local rodent ecology is necessary to ensure success, and this information is often lacking. Under certain conditions surveillance of the dynamics of infection in rodents can provide a basis for forecasting outbreaks in man.

(b) *Contaminated environment*: Leptospires are very sensitive to disinfectants, and water and bathing pools should be disinfected with chlorine wherever possible. Contaminated barns, pigsties, etc., can be disinfected with common substances, such as cresols.

Disinfection of large tracts of land, such as rice-paddies, has been attempted with copper sulfate or calcium cyanamide, but the results have not been encouraging except under special conditions, such as those existing in some areas of Japan.

(c) *Prophylaxis in man and animals*: Protective clothing, such as boots and gloves, should be worn by hunters, fishermen, and sewer-workers, but this is often impractical for field workers, miners and other exposed groups. Protective skin creams offer some protection, but it is short-lived. Killed vaccines have been used against human leptospirosis in some countries with encouraging results. They are particularly useful where leptospirosis constitutes a hazard to certain occupational groups. If properly prepared the vaccine is safe and gives protection against clinical illness, but not against infection, especially if too few doses are administered.

Efforts should be made to develop multivalent vaccines containing the fewest possible serotypes and, particularly in areas where multiple leptospirosis is prevalent, having broad antigenic action.

Vaccines for domesticated animals would be a great advantage in countries where leptospirosis is a problem of appreciable magnitude. The results to date indicate that vaccines are of some prophylactic value in pigs,
cattle, and dogs. However, in some cases, data on vaccine trials in domesticated animals have been deficient and carefully designed trials are recommended to remedy this deficiency.

Of particular importance is the distinction between protection against symptomatic infection and prevention of carrier states; an ideal vaccine would give both forms of protection. At present, animal vaccines seem to protect against clinical infection, but there is little knowledge concerning the protection they afford against subclinical infection and the subsequent development of a shedder state. Recent experience suggests that although vaccination does not eliminate shedding, it reduces its duration and the number of organisms voided.

Another topic for further study is the persistence of titres conferred by vaccines, and hence the possibility of their interfering with serologic diagnostic tests that may subsequently be required for differential diagnosis or in control programmes.

Chemoprophylaxis for man, by means of penicillin or broad-spectrum antibiotics, may be considered if an outbreak has started, if multiple serotypes are implicated in a region, or if anticipated exposure will only be of short duration. In controlled trials, treated persons have been found to show a lower rate of infection than controls. The risk of creating sensitivity to penicillin by such programmes must, however, be taken into account.

8.4.4.2 Therapy

Early serotheraphy of Weil’s disease in man, using purified antiserum of high potency, has given excellent results. Specific gamma-globulin appears to be of some importance in therapy, particularly in the prevention of clinical disease.

Doubts have been expressed on the efficacy of penicillin and some other antibiotics in the treatment of human leptospirosis. Penicillin seems to be at least partially efficacious if administered in high doses (6-12 million units daily) at the beginning of the disease.

In cattle, swine, and dogs, treatment with antibiotics may result in considerable diminution or even temporary cessation of urinary excretion of leptospires; however, relapses often occur after the antibiotics have been discontinued, suggesting the need for prolonged treatment. Tetracycline derivatives seem to give the best results, but penicillin and streptomycin have been reported \(^1\) to be more effective in the treatment of the asymptomatic carrier (and shedder) state in dogs.

Further research is required on effective means of preventing or curing shedder states.

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8.5 Colibacillosis

Observations of outbreaks of diarrhoeal disease, the feeding of live organisms to human beings, and the study of serologic responses after natural infection have revealed that infections with enteropathogenic *Escherichia coli* (EEC) results in disease and death in infants in hospitals and nurseries, and in diarrhoea in adults. Many studies have shown that EEC pathogenic for man exist in domestic animals in the form of symptomless infections. The significance of these findings has been ignored in the past because failure to identify flagellar antigens has cast doubt upon whether these organisms were identical. Recent careful studies using fluorescent antibody techniques, as well as cultural and serologic methods, have correlated family outbreaks of intestinal infections with EEC and with the microbial flora of foods of animal origin eaten by the families, and have shown the identity of the isolates. Although attempts to trace the responsible organisms to the farms where the animals were raised have failed, studies at the plants where the animals were processed for market have revealed the same EEC organisms that were responsible for the outbreak.

A possible hazard to human beings ingesting *E. coli* of animal origin has been revealed by the discovery of the phenomenon of resistance factor transfer from *E. coli* to other intestinal organisms, including pathogens such as *Shigella* and *Salmonella*. This has been demonstrated both *in vivo* and *in vitro*. Animals consuming antibiotic-fortified feed shed *E. coli* that may be resistant to antibiotics. Through episomal transfer these “donor” organisms transmit their resistance to other intestinal organisms, which become resistant to several antibiotics simultaneously. As more and more food-producing animals are fed antibiotics, their intestinal flora may contain antibiotic-resistant *E. coli*. This phenomenon may result in the development, in man as well as in animals, of an intestinal flora that can transfer antibiotic resistance to pathogenic bacteria.

8.6 Tularaemia

The present distribution of *Pasteurella tularensis*, the causative agent of tularaemia, coincides with the area of distribution of the *Leporidae* in the northern parts of America, Europe, and Eurasia. Although tularaemia is usually a sporadic disease, it can occasionally become epidemic. It is sometimes found in domestic animals, and in sheep it may be epizootic. Strains of *P. tularensis* isolated in America and Europe show differences in biological properties and virulence. Specific vectors of the microbe are ticks, particularly the genus *Dermacentor*, and occasionally Diptera. Persistence of natural foci of tularaemia depends on animals such as ground squirrels, rats, and insectivores that are more resistant than the highly susceptible mammals such as hares, rabbits, voles, and muskrats.
The disease is transmitted to man principally by the handling of infected hares, rabbits, and other animals, by the inhalation of contaminated dust from hay, straw, and sugar beet, by the ingestion of or immersion in contaminated water, and by the bites of ticks and mosquitos. Occasionally, infections have been transmitted by bites of carnivores possibly acting as carriers. Occupational exposure occurs mainly among agricultural workers, wool shearers, commercial rabbit butchers, fur-trappers, hunters, and those in related occupations.

Control is based on avoidance of exposure, on the use of protective gloves when handling suspect material, and on adequate cooking or heating of meat or water that may be contaminated. Rodent and animal control is recommended in endemic areas, and rat-proofing of rural homes and store-houses is important. A living attenuated vaccine has recently been developed in the USSR and has been used in particularly exposed population groups with beneficial results. A living tularaemia vaccine prepared from an attenuated strain has been administered to man by scarification and has given very good results in endemic areas of the USSR. In most people the vaccine produces few side effects; newer improved vaccines have eliminated such reactions. The immunity lasts up to five years.

Streptomycin, the tetracyclines, and chloramphenicol have been found to be effective therapeutically.

8.7 Listeriosis

It is generally recognized that *Listeria monocytogenes* is virtually ubiquitous and that healthy intestinal carriers are common in many species of animals, including man. A higher percentage of isolations has been made from the faeces of slaughter-house workers than from other people. Disease due to *Listeria* is usually associated with lowered resistance or with unusually heavy exposure.

Most cases of listeriosis in human beings are believed to be derived from sources other than animals, although transmission from the latter can occur. During the past 11 years in the Netherlands 12 cases of skin infection have been traced to the handling of newborn calves. Most, but not all of these cases were benign. Two reports of zoonotic infection have implicated sick dogs as the sources of infection. Human disease is rarely caused by the eating of meat infected with *Listeria*, but one extensive outbreak was associated with the drinking of infected milk.

Altogether some 700 bacteriologically confirmed human cases have been reported in the USA, with a case fatality rate of 42%. In Sweden 60 cases have been reported—34 in the neonatal period and 26 in adults. As the organism is difficult to isolate from contaminated material, the true frequency of the disease has probably been greatly underestimated. Recently,
however, a new medium that may make isolation easier has been described.\(^1\) The fluorescent antibody technic has proved useful for diagnostic examination of tissue and spinal fluid.

The disease takes various forms, the most frequent results being encephalitis and abortion. It is a not uncommon cause of abortion in women and of infections of the newborn. Administration of cortisone increases the mortality and listeriosis has sometimes been aggravated when this drug is used in the treatment of some other condition.

8.8 Pasteurella pestis and pseudotuberculosis infections

8.8.1 Plague

Plague, caused by the organism *Pasteurella pestis*, remains a problem in many parts of the world even though it has been greatly reduced or eliminated in some areas. WHO expert committees review the problem periodically and set forth principles of control. These principles are sound and are recommended to all authorities concerned with combating plague. Since the last report of a WHO expert committee, there have been new developments in epidemiology, immunization, and treatment.

The possibility that the human flea (*Pulex irritans*) may be a vector of infection has caused much concern. A review of past epidemics as well as present-day problems points to this possibility, and emphasizes the need for personal hygiene and insect control, especially among displaced persons.

Epidemiologic studies have revealed that rabbits may act as passive carriers, as may apparently healthy dogs that have contact with infected rodents. A change in the virulence of plague has been noted in many areas. Serologic surveys indicate that latent plague in wild rodents is widespread in natural foci of Africa, Asia, and the Americas. Camels have been shown to be the source of some human infections.

There has been continuous research on human immunization, but it is apparent that present-day immunization is not satisfactory, and further investigation is necessary. The killed vaccines available at present offer a reasonable degree of protection if two injections are given, followed by boosters at 6-month intervals. There is further evidence that the widespread and promiscuous use of antibiotics, particularly at inadequate dosage levels, may lead to the development of streptomycin-resistant strains.

Subclinical upper-respiratory infections with virulent *P. pestis* have recently observed in persons who have had contact with bubonic plague cases.

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8.8.2 *Pseudotuberculosis*

Human infections with *Pasteurella pseudotuberculosis* and *Pasteurella* X are being reported with increasing frequency. Approximately 95% of such cases are mild mesenteric lymphadenitis and enterocolitis. The diagnosis is established by isolation of *Pasteurella* from the lymph nodes, blood, and stools of patients, by agglutination tests, and by intradermal reactions. Except in septicaemic infections, prognosis is excellent when the illness is treated by the administration of streptomycin and tetracycline.

Natural infection with *Pasteurella* is widely distributed among many mammals and birds and occasionally causes destructive epizootics in rabbits, sheep, and birds. Sporadic infections in cattle, horses, and dogs are well documented, and cats are frequently infected. In hogs the disease has only rarely been reported.

In the bacteriologic investigation of autopsy material or lesions of an infected animal, a negative result should not be reported until several subcultures have been made.

The ecology and epidemiology of animal and human infections deserve intensive research. It is generally believed that in most cases transmission of *Pasteurella* takes place through the digestive tract and occasionally by the ocular and respiratory routes; there is no evidence that transmission can occur through bites. Contact with infected animals is suspected as the source of human infection. In three cases the same *Pasteurella* found in patients was also isolated from animals with which they had been in contact (a cat, a canary, and a guinea pig). Since the cat remains an intestinal sheder for a long period and *Pasteurella* contaminate the fur and the anogenital region, it is suspected that transfer to man may occur by the oral route. Faecal and urinary shedding by rats and mice may contaminate food and contribute to the indirect transmission of *Pasteurella*.

Climatic factors and individual metabolic disturbances of the host may contribute to establishment of the disease. Mesenteric lymphadenitis is predominantly a disease of male children, while the septicaemic infection has been observed at all ages.

*Pasteurella* may cause mastitis in cows, in which case the milk may serve as a source of human infection.

The few reported observations indicate that pseudotuberculosis may be a zoonosis with an epidemiologic pattern similar to that of listeriosis.

8.9 *Pasteurella multocida* and *P. haemolytica* infections

Since 1913, when a case of puerperal fever in a human being due to infection with *P. multocida* was first recorded, several hundred cases of infection caused by this organism and by *P. haemolytica* have come to light. Most of these cases were mild and localized, but they also included
generalized infections that ended fatally, empyema of the lung, chronic bronchitis, one case of an ulceroglandular tularaemia-like condition, and one case of brain abscess. *P. multocida* and *P. haemolytica* have also been isolated from the normal respiratory tract and from saliva and sputum.

Cases of *Pasteurella* infection resulting from cat or dog bites and scratches are obvious examples of zoonoses. In the case of respiratory-tract infections, however, the origin of infection and the portal of entry of the causative organism are not known, and it is difficult to determine whether this type of infection is a zoonosis. It is possible that *Pasteurella* organisms found in the upper respiratory tract of man are derived from cattle, pigs, cats, dogs, rabbits, fowl, and other species that are normal hosts to these organisms. There is no evidence to show whether or not *P. multocida* type I of Roberts, the cause of haemorrhagic septicaemia in cattle, causes human infection. It appears necessary to investigate the etiology of all cases of suspected *P. multocida* and *P. haemolytica* infection in order to decide if these organisms are of zoonotic significance.

Penicillin, streptomycin, and sulfonamides are effective in the treatment of such infections.

### 8.10 Staphylococcosis

In recent years the importance of staphylococci as a cause of bovine as well as human disease has increased, and many outbreaks of bovine mastitis in dairy herds have been found to be caused by staphylococci resistant to a variety of antibiotics. In a few instances such outbreaks have been caused by important human epidemic strains, including phage type 80/81. Similarly, animals entering animal hospitals have become infected with such human epidemic strains.

Human infections with typical animal staphylococci of bovine origin occur and in different reports from 3% to 11% of staphylococci isolated from man have been found to produce the beta-haemolysin characteristic of animal strains. There is good evidence of human infection with animal strains as well as of animal infection with human strains in animal hospitals. It is clear, however, that only a small proportion of human staphylococcal infections is due to strains of animal origin. Phage typing indicates that there is no relation between bovine and human strains.

In addition to the occasional interchange of human and animal staphylococcosis, food poisoning caused by staphylococcal enterotoxin poses another public health hazard. There is convincing evidence that some outbreaks traceable to milk and milk products are caused by staphylococci of bovine origin.

Further investigation is required before the part played in human staphylococcosis by staphylococci from various animals can be assessed more fully.
8.11 Tick-borne relapsing fever

In some countries—e.g., Central, East, and South Africa—tick-borne relapsing fever is a disease of human beings and the mammalian reservoir of infection is man himself, rather than rodents or other animals. In other countries—e.g., North Africa, the eastern Mediterranean region, Central Asia, tropical and subtropical America, and many parts of the USA—relapsing fever is primarily a disease of rodents, and it may be transmitted to man only incidentally by soft ticks (Argasidae).

The carrier rodents are not usually synanthropic. They live in open country, in holes and in caves. Humans entering caves are readily attacked by ticks living there, and in this way become infected. Other animals that serve as reservoirs live in small burrows in bush land, where hunters, campers and trappers may become infected by ticks that normally transmit the relapsing-fever agent from one rodent to another.

There is still no evidence that every strain of Borrelia found in murine animals and some other small rodents is pathogenic for man, and further study of this problem is necessary.

To prevent infection, those who live in or visit endemic areas should be discouraged from sleeping or resting in caves or open land where infected ticks have been reported.

In some cases, particularly in infested caves, complete eradication of the rodent and tick population may be possible.

Broad-spectrum antibiotics are effective for the treatment of human infections.

9. FUNGAL INFECTIONS

9.1 Systemic fungal infections

Domestic animals, pet animals, wild animals and birds, and man are all susceptible to infection with fungi that are found in the environment. These infections include histoplasmosis, coccidioidomycosis, and cryptococcosis. Although animals may contribute to the contamination of the environment through their droppings—e.g., Histoplasma in the case of chickens and bats, and both Histoplasma and Cryptococcus in the case of pigeons—it is considered that both man and other vertebrates are infected in a common environment, not that each contributes in any significant way to the infection of the other.

9.2 Dermatophytes

Human and animal ringworm are a clinical entity involving the skin and its appendages and are caused by the same, or closely related, dermatophytes. The individual dermatophytes manifest varying degrees of host
specificity. Some are primarily parasites of man and others of animals; still others are free-living agents commonly found in soil.

Most of the dermatophytes in man are caused by human-type organisms. However, a large percentage of the ringworm occurring on the exposed parts of the body of the human hosts is caused by animal-type dermatophytes, with animals serving as reservoirs and vectors of infection. In urban areas, *Microsporum canis*, the common cause of dog and cat ringworm, is the principal cause of animal ringworm in man. In rural areas, *Trichophyton verrucosum* and *T. mentagrophytes* are the main animal ringworm agents affecting man. In wooded areas, small mammals have been shown to be carriers of several dermatophytes that may infect man.

Although ringworm in man and animals is of world-wide occurrence, there are few data available on its prevalence, and surveys to determine its extent should be encouraged.

The control of zoophilic dermatophyoses in human and animal populations rests upon the detection and elimination of reservoirs of infection. Thus, cases in man and animals must be traced to their sources, and such sources must be placed under proper veterinary care. Where small mammals are involved their destruction may be necessary. Examination with a Wood's light apparatus, and routine microscopic examination of suspect skin lesions by veterinarians are practical and effective methods of detecting infected animals. Fluorescent antibody techniques have worked very well in the research laboratory and now are being used in some diagnostic laboratories. Culture techniques are necessary for precise determination of the fungus species involved. In addition, attention must be given to known reservoirs of infection, including cats in breeding establishments, stray cats and dogs, and infected cattle and rodents. A successful demonstration control programme has been carried out in an area where zoophilic dermatophyte infections presented an important public health problem.¹

Grisocofulvin, an orally administered antibiotic, is preferred for the treatment of ringworm in small animals. This substance is also effective for therapy of ringworm in large animals, but its cost makes its use impractical in most such cases. Topical therapy in the form of nontoxic antifungal dips, shampoos, and sprays is a valuable adjunct to griseofulvin therapy; such treatment can be used for large animals. Grisocofulvin can also be used as a prophylactic to prevent the development of ringworm in animals exposed to dermatophytes.

The Committee recommends further surveys and research in human and animal dermatophyoses and systemic mycoses. Epidemiologic studies are also needed, particularly in rural areas. The teaching of these subjects in veterinary or medical schools should not be neglected.