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Epidemiology of Q fever

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TABLE OF CONTENTS

INTRODUCTION

Infectious diseases have always comprised an important part of medical practice. Many of these diseases are now effectively controlled either by preventive means or by curative treatment. Neither aspect of control can be achieved without some understanding of the epidemiology of the disease.

Q fever stands as a particular challenge to medicine because of its many-faceted epidemiology. Adequate control has been difficult because of the nature of its epidemiology.

Much work has been done in the study of the disease. It is not the purpose of the paper to give a comprehensive account of the work in all areas of study of Q fever. The nature of the disease and the causative agent are discussed only briefly. A more complete account is given of the historical and epidemiological aspect of the disease.

THE EPIDEMIOLOGY OF Q FEVER

THE ILLNESS DEFINED

Q fever is an acute febrile illness caused by a rickettsia, Coxiella burnetii. Following an incubation period of 16-18 days, there is sudden onset of fever, malaise, headache, weakness, and anorexia, and usually an interstitial pneumonitis. The fever usually ranges from 101°-104°, with wide fluctuations common in any given patient. Fever and a severe headache predominate. Unlike the other rickettsioses, a rash is uncommon, but has been reported in some cases. A dry cough and chest pain usually occur after about five days. Roentgenographic findings are similar to those found in primary atypical pneumonia, usually appearing by the third or fourth day of the disease. The usual course of the disease does not exceed two weeks, although in protracted cases, the fever may persist over four weeks, especially in older people. Complications are rare, but when they occur can be severely disabling and even fatal. Hepatitis, with a clinically detectable icterus, occurs in approximately one-third of patients with the protracted form. Recently the organism has been isolated from patients with subacute endocarditis, being isolated from the blood during the illness, and also being found in the heart valve leaflets

at autopsy. Marked arthritis and arthralgia are occasionally associated with the endocarditis. Further evidence of the chronicity of the infection has been demonstrated by the isolation of C. burnetii from placental tissue following clinical infection early in pregnancy.

Diagnosis of the disease can be made by isolation of the organism from the patient's blood during the acute febrile stage. A simpler and more commonly used method of diagnosis is the detection of a marked rise in antibody titer between the acute and convalescent phases of the disease.

Chloramphenicol is the drug of choice in the treatment of the disease, although oxytetracycline and chlortetracycline are also effective. This usually reduces the length of illness by about fifty percent, and also reduces the incidence of complications. Patients with proven endocarditis have failed to respond to any form of therapy for more than a short time.

Although adequate information regarding the immunologic aspects of the disease is lacking, there appears to be a permanent immunity conferred following a course of the disease. This immunity appears to be present even when antibody titers drop to nonspecific levels.

THE ETIOLOGIC AGENT

The causative agent in Q fever is a rickettsia, Coxiella burnetii. It is a pleomorphic organism, usually appearing as a bipolar rod 0.25 microns to 0.5 microns long, but varying from large forms resembling bacteria to minute granules which pass Berkefeld N filters or collodion membranes with pore diameters of 500 millimicrons. It resembles the other rickettsiae in staining reactions and in photographs made with the electron microscope. It is unlike the others in that it is filtrable; it is resistant to physical and chemical agents; and it does not develop cold agglutinins or agglutinins to Proteus OX19, OX2, or OXK.

The feature which makes this organism most unique is its resistance to physical and chemical agents. This was first demonstrated by Derrick in his original work with the organism. After 64 days in the refrigerator at temperatures below 40°F. the organism was found to remain infective. This was unlike any other rickettsia. Further work has substantiated these findings. The organism has been isolated from dust on the premises of infected herds of cattle and sheep; it has been incriminated as the source of infection in patients who inhabited premises which

were previously inhabited by infected animals. The infectious agent has also been carried in straw over long periods of time. The common methods of milk pasteurization are not adequate to completely destroy the organism. Experimental studies with chemicals have shown that C. burnetii is more resistant to chemical destruction than are the other rickettsia.

HISTORY OF THE DISEASE

Q fever was first reported as a new clinical entity by E.H. Derrick in Australia in 1935. The disease was given the name "Q fever" because of the many "queries" which remained unanswered concerning the disease. The initial description of the disease was based on its manifestations in 9 farmers and meat workers who were infected. Derrick carefully studied the disease, recognizing in it certain elements which were not characteristic of atypical pneumonia which it so closely resembled.

Derrick found that he was able to reproduce the disease in guinea pigs by injecting blood or urine from infected patients into the guinea pigs' peritoneum. He further noted that infection with the agent apparently conferred immunity, in that

repeated injections of the infectious agent into a convalescent guinea pig did not produce another infection. Although he was able to accurately describe the disease, Derrick did not isolate the infectious agent. He felt that it was probably a virus because of the nature of the illness. Furthermore, he was unable to grow the organism on any available culture media, and was unable to visualize the organism microscopically with any of the staining techniques which he used. The "virus" was noted to remain infective for long periods of time when kept under refrigeration at less than 40°F. One specimen remained infective after 64 days of such storage.

The epidemiology of the disease remained obscure. Derrick noted that all of the original cases occurred among farmers and meat workers. He was unable to find any common source of infection or any reservoir of the disease.

Samples of the infective material were given to F. M. Burnett, who had done a great deal of work with viruses and rickettsia. He was able to reproduce the disease in monkeys and mice, as well as in guinea pigs. He also found that the organism survives on the chorio-allantois of the chick embryo. Burnett was able to successfully stain the organism in impressions of spleens of infected animals. Microscopically the organism

resembled the rickettsia. Burnett's further work established the identity of the organism as being a rickettsia, and the name Rickettsia burnetii was given to it. He further observed the formation of agglutination when a semi-purified rickettsial suspension was combined with immune human and monkey sera. This reaction was found to be specific, a factor which has subsequently proven useful in the study of the epidemiology of the disease.

In 1938 Davis and Cox reported the isolation of a filter passing organism from the wood tick, Dermacentor andersoni, collected near the Nine Mile Creek in Montana. This organism was described as rickettsia-like in nature, and was found to be filtrable. It was also found to be infective to guinea pigs. This infection could be produced by injection of the infectious agent or by allowing infected ticks to feed on the guinea pigs. Because of the organism's filtrability the name Rickettsia diaporica was suggested. Later work by Dyer in this country and by Freeman and Burnett in Australia established the identity of the organism as being the same as R. burnetii.

Following the identification of the organism and its isolation from ticks, additional work was done in an effort to determine if there were other arthropods which were susceptible to the organism,

and whether these might play a role in the transmission of the disease either as vectors or reservoirs. Much of this work was done by Derrick and Smith in Australia and by Davis and Cox in this country.

The first possible vector-hose relationship to be studied was that between the tick, Haemophysalis humerosa, and the Australian bandicoot which it commonly infests. This came about because of the isolation of R. burnetii from both of these animals. It was further noted that the organism could be transmitted from the tick to uninfected animals. It was shown that the organism lives in the intestinal tract of the tick, and that tick feces have a high degree of infectivity. Infection of the host animal occurs by contamination of the tick bite wound with tick feces.

Experimentally, it was shown that infection could be produced in the dog tick, Rhipicephalus sanguineus, and that this tick was capable of transmitting the organism to test animals. The cattle ticks, Boophilus annulatus, Haemophysalis bispinosa, and Ornithodorus sp. were also found to be experimentally infective.

This mode of transmission was soon verified by reports of such naturally occurring host-vector relationships. Infected cattle ticks were found occurring naturally in cattle. This has also been reported in dogs and sheep.

Since these early studies of the disease, considerable interest has been generated in evaluating it further. Subsequent studies in many parts of the world have begun to reveal the cosmopolitan nature of the disease.

As the organism was more carefully studied, it became evident that it had characteristics which set it apart from the other rickettsia. These differences included its extreme pleomophism, its resistance to physical and chemical destruction, its filtrability, and its failure to react with any of the Proteus antigens. Because of its unique characteristics, this organism was placed in a new genus under the family Rickettsiaceae. The name given was Coxiella, after Harold Cox, who has done much work with the organism.

THE EPIDEMIOLOGY OF THE DISEASE

Methods of Study

Derrick originally recognized Q fever as a new disease entity by isolating the causative agent. He did this by animal inoculation of blood from infected patients during the febrile stage of the disease. He found that the immunity which this illness confered was specific in that it gave no immunity to

diseases which had been previously described. This included the other rickettsioses which he considered when working with Q fever. Isolation and immunologic studies of the organism have been used to identify the etiologic agent in subsequent outbreaks of the disease.

Serologic methods have been developed to detect antibody titer in sera. These methods have markedly simplified diagnosis by permitting comparison of acute and convalescent sera for significant rise in titer. These methods also lent themselves to studies on large population groups to determine incidence of the disease.

A complement-fixation test was initially developed which was found to be highly specific at fairly high titers. This was the most commonly used method in early studies of the disease. The chief problem with this test was that it was not entirely specific at low titers. This has resulted in confusion in the literature as to which antibody titer should be considered significant. Some investigators used 1:4, while others considered it significant only above 1:8. This has resulted in inconsistent reporting. The chief usefulness of the complement-fixation test lies in the determination of changes of titer during the acute and convalescent phases of the

disease. Thus it remains an important diagnostic tool.

The capillary Agglutination test was developed by Luato in 1953. It lends itself more readily to use in serological surveys. It is particularly useful in that nonspecific reactions are not common, and therefore undiluted serum can be used. In comparative studies it has been reported to be more sensitive than the CFT. It can also be used for titration where specific levels are desired.

Another method which has been more recently developed is the Microscopic Slide Agglutination Test. This is even more sensitive and more specific than the others. It does not lend itself to detecting levels in titer, however.

Welsh and others made a comparative study of the four serologic techniques employed. This included the Complement-Fixation Test, the Standard Rickettsial Agglutination Test, the Capillary Agglutination Test and the Microscopic Slide Agglutination Test. According to their studies, the first three were about equal. The last method was reported as more specific and more sensitive.

Another serious problem has been encountered in evaluating reports of the disease based on serologist findings. This problem is the wide range of antigenicity among the strains of C. burnetii which have been used as antigens. Some strains have been shown

to be more sensitive than others by comparative studies of different strains tested with the same sera. The severity of infection which was produced in guinea pigs when infected with similar doses of the organism varied with the strains used. Topping and others in 1946 made a comparative study of strains using the Italian (Henzerling), Balkan, Panama, American (Dyer), Fort Bragg, and Australian. These strains had been used to produce antigens for serological studies in their respective countries. It was found that the Balkan and Italian strains were considerably more reactive than the American or Australian. It was found that many sera which tested negative with the American strain, tested moderately to strongly positive when using the Italian strain. Since that time, the more sensitive strains have been used as antigens in serological studies.

Even under ideal conditions, using the most sensitive and specific strain, as well as employing the most sensitive serologic techniques, there are still factors which contribute to inaccurate evaluation of incidence in a given animal or human population. One of these factors is that antibody titer may drop to undetectable levels within 1 to 2 years following infection. Another is that animals may be actively shedding the organism in their excreta or products

of parturition without showing any serologic evidence of the disease. The reason for this is not clearly understood.

Geographic Distribution

The recognition of Q fever throughout the world slowly followed its initial description in Australia in 1935. This was not because of absence of the disease, but rather because of lack of recognition of it as a separate disease entity. For several years its study remained confined to the laboratory, although isolated cases were being reported in Australia and the United States. The epidemic potential of the disease was recognized during World War II, when large numbers of American and German troops acquired the disease in Italy, Greece, and other Balkan countries. Since that time the disease has been found endemic in every country of the world, except the Netherlands, New Zealand, Poland and Scandanavia. In the United States it has been reported in all but 14 of the states. Most of the data regarding its prevalence has come from serological testing of human and animal sera, although in many instances diagnoses of the active disease process have been made. Although there are areas in which Q fever has not been reported, this probably is due to the

fact that no efforts have been made to find evidence of the disease in these areas, rather than due to an absence of the infection.

Incidence of the Disease

The incidence of Q fever varies widely with geographic areas. Surveys which have been undertaken to evaluate its incidence have approached it primarily from three aspects. (1) Its incidence in domestic or wild animals in a given area; (2) Serologic evidence of infection in humans in the area; (3) Actual incidence of disease by means of clinical and serological diagnosis.

Initially, the main emphasis appeared to be a study of possible animal reservoirs and vectors of the disease. Because of the association of the first reported cases of the disease with farm animals, these became the first area of inquiry. Following the outbreak in Australia which Derrick first reported, serologic studies in that area showed an incidence in cattle of up to five percent. Since 1950, numerous surveys have been undertaken in the United States. These surveys consistently show evidence of the disease in dairy cattle. Among the most extensive of these surveys has been the one in the Los Angeles area in southern California. Over fifty percent of the milk samples coming into

The Los Angeles area showed positive antibody titer. Repeat surveys indicate that the incidence is increasing. This is well demonstrated by the fact that the animals moved from a sero-negative herd to a seropositive herd usually become seropositive within a month or two. In many herds the incidence of the disease reaches 90-100 percent. In Washington, surveys taken in 1949 and repeated in 1960 showed a fourfold increase in the incidence of serologically positive cattle. In Montana the incidence among dairy cattle increased from 0 percent in 1952 to 3.5% positive herds in 1960. In the Bitter Root Valley, where particularly intense studies are being conducted, an increase from 3% infected herds to 20% was noted between 1958 and 1960. Incidence in other parts of the country varies considerably. Surveys in Nebraska report approximately 10% positive. Pennsylvania reports 25%.

The Pennsylvania report describes the clinical aspects of the disease in cattle, which heretofor had been considered insignificant. Studies on a small herd of sick cows with rhinitis, conjunctivitis, dyspnea and decreased milk production, showed all but three to have significant complement-fixing titers. These animals represented a replacement herd of animals which had been removed 7 months earlier for a similar condition.

Studies on beef cattle have failed to show any significant degree of infection in these animals.

Work has been done on a vaccine to be used in dairy cattle in highly endemic areas, such as southern California. Studies have shown that the rate of active infection, as indicated by growth of the organism from milk or tissues from the infected animal, has been approximately one third as great in the vaccinated group as in the nonvaccinated group.

Although active disease in cattle is not commonly reported, cows do attain a high degree of infectivity. This has been demonstrated in studies on milk from infected herds. This milk has been shown to contain enough organisms to produce disease when injected into guinea pigs. The placentae and vaginal discharges of cattle have also been found to be highly infective. Extremely high concentrations of the infective organism have been found in these organs. Contamination of soil by these placentae during calving is believed to be a major source of airborne infection. The organism is also excreted in the urine and feces of infected cattle. Studies have repeatedly shown that infection can be present to a high degree without there being any serologic evidence of the disease. This fact is particularly significant in that it suggests an even higher

incidence of the disease than is commonly reported.

In areas where Q fever is endemic, its incidence in sheep is high. This is demonstrated by the recovery of the organism from the milk and from the products of parturition. Serologic studies are also used for this purpose. No illness has been demonstrated in sheep which can be traced to infection with C. burnetii.

The number of reports dealing with sheep infection is small compared with the number of reports which are available on studies in cattle. One of the reasons for this is that cattle sera are so much more readily available because of mandatory testing for brucellosis in cattle. In endemic areas where studies have been made on sheep, the reported incidence is as high as fifty to one hundred percent. One of the most extensive surveys of this nature was taken in northern California where the sheep population is high. It was in that survey that the above percentages were obtained. Although reports of percentage of infection are not as readily avilable, there are reports of infection in sheep with C. burnetii in most parts of the world.

Goats are a third major source of infection in domestic animals. Studies in England, Italy, and California suggest that

the incidence is similar to that seen in sheep. An interesting outbreak of human infection occurred on a shipment of goats being sent from California. There was a high incidence of infection among the goats on this shipment. There was also a high percentage of positive antibody titer.

The only other domestic animals in which C. burnetii have been found to occur spontaneously have been dogs and horses. These have been reported on premises where infection was known to exist in other animals such as cows or sheep. Among birds studied, chickens and pigeons have been reported to carry the infection. A report from England gives an incidence of 11.8% in chickens in an endemic area.

Infection of wild animals with Q fever has been well documented whereever studies have found the disease to be endemic. Particular attention has been focused on this aspect of the disease's natural history because of the conviction among many early researchers that a reservoir of infection must exist in wildlife, similar to that seen in the other rickettsioses. The first wild animal to be incriminated in this quest was the Australian bandicoot, which is a small mammal commonly seen in the endemic areas in that country. Derrick not only found serologically positive

animals, but he also found some of these animals to carry the tick, Haemophysalis humerosa. He found that some of these ticks were infected and that they were capable of transmitting the disease to uninfected animals. Shortly after Derrick's findings were reported, C. burnetii was isolated in this country from the wood tick, Dermacentor andersoni.

Several other species of the genus Haemophysalis have been found to experimentally transmit the disease to rodents and to cattle.

The dog tick, Rhipicephalus sanguineus, has been found to be infective experimentally. This tick has also been reported as the source of a naturally occurring infection in dogs.

Initially, it was felt that the existence of the disease in wildlife constituted a major reservoir of the infection. Current investigators, such as Marmion in England, feel that the primary source of infection may be in cattle, sheep and goats, and that the infection seen in wild animals is a "spill over" of this infection.

Serologic evidence of Q fever in humans has been reported from most areas of the world where the disease is known to be endemic. The most extensive studies have taken place in England and in the United States, especially in those areas where

heavy animal infection has been noted. Routine surveys have been conducted, using blood samples brought into Red Cross blood centers, or drawn on routine hospital admissions. These surveys represent general population groups. The incidence of serologically positive blood in these groups has usually been from 0.75 to 1 percent.

Markedly increased rates of infection have been reported among select population groups. Surveys made of persons living on farms with infected cattle on the premises have shown an incidence of up to 25%. Where raw milk was drunk by these persons, an even higher incidence was reported. Packing house workers also show increased incidence of infection. In a survey among packing house workers in Omaha an incidence of 4.76% was reported. This compared with an incidence of less than 1% among the general population in Omaha. Laboratory workers working with C. burnetii are frequently infected with the disease in spite of strict precautionary measures.

Clinically and serologically proven cases of Q fever appear to be as cosmopolitan as are the cases of past infection based on serologic surveys. Derrick first described Q fever as a new disease entity among 9 farmers and meat workers. Since that time numerous outbreaks have been reported involving from one case to several

hundred cases. Individual sporadic cases have been reported from many parts of the world.

The outbreaks which attract the most attention are those in which large numbers of persons are involved. This is in part due to the fact that it takes an outbreak of significant proportions to call attention to the fact that the disease involved is actually Q fever. Many individual cases and small outbreaks are written off as atypical pneumonia, "flu", fever of unknown origin, etc. This may be due to the fact that in most areas Q fever is not even considered in a differential diagnosis. Another factor is that many patients do not manifest enough clinical symptoms to warrant medical attention. As an increasing awareness of the existence of the disease develops, there will be an associated increase in the number of cases reported. As the disease become more widespread among animals, there is also an absolute increase in the incidence of cases.

One of the first major outbreaks to be studied and reported was among American troops stationed in Italy during World War II. Approximately 800 men were involved in a series of outbreaks in the years 1944 and 1945. There was also a continuation of this epidemic among troops who returned to this country at that time. Most of

the cases reported in that series of outbreaks were diagnosed clinically and serologically. Serological diagnosis was made by studying paired, acute and convalescent, sera. Where the facilities were available the diagnoses were further confirmed by reproduction of the disease in guinea pigs. These studies showed that the men involved appeared to be highly susceptible to the disease upon first exposure to it. This was reported on the basis that a high percentage of men, who were transferred to an area where the disease appeared to be highly endemic, became infected. Although no specific etiological factor was found at that time, it was believed that the men involved in the various outbreaks were infected by a common source. It was in the followup of these studies that it was noted that the antibody titer can drop to non-specific levels as soon as a year after infection. There was no evidence, however, that the immunity was not permanent.

In contrast to the epidemics involving the troops during World War II, studies in California have shown a more constant rate of new cases in the endemic area. Newcomers to an endemic area appear to be particularly susceptible to infection. During abnormally dry lambing seasons, increases in incidence have been reported in surrounding areas. This is believed to be due to the

organism being carried by air more readily when the ground is dry and dusty.

On the basis of the studies in California, it would appear that the rate of infection is lower among people living in an endemic area. This is not an accurate supposition, however, because it has been shown that antibody titer may drop to nonspecific levels within 1 year after infections. These persons are apparently immune to reinfection, but are not reported as seropositive in group surveys.

Transmission of the Disease

When Derrick first described Q fever, he was unable to clearly demonstrate any means of transmission of the disease to the patients. This has continued to be a serious obstacle in the study of the epidemiology of the disease. Various modes of spread have been considered and studied. The more work that is done in this area, the more evidence accumulates that there is not one, but several means of transmission.

When Q fever was first recognized as a rickettsial disease, it was felt that it should be transmitted like other rickettsial diseases. For this reason Derrick and other early investigators

persued the theory that there must be an arthropod vector which was capable of transmitting this disease. Potential and actual vectors were soon demonstrated. Cox in this country isolated Coxiella burnetii from the tick, Dermacentor andersoni. Derrick in Australia isolated the organism from the tick Haemophysalis humerosa, which was found on the bandicoot. Following this, it was found that various ticks could become infected with the organism by feeding on an infected laboratory animal. Furthermore, it was soon found that the bandicoot and other small mammals, wild and domestic, were naturally infected with C. burnetii.

These various studies established the existence of a potential source of infection to man and other animals in small mammals and the arthropods which they carried. The problem which then presented itself was that of finding a means of transmission of the organism to man and to other animals. Only on rare occasions have cases of the disease been reported in which contact with ticks as the sole source of possible infection has been established. This, however, does not eliminate the vector host relationship of arthropods and small mammals as a possible reservoir of the disease. The available evidence certainly suggests that this is one means by which the disease is propagated in nature. Originally it was

thought that this was also the source of infection in higher mammals. More recently investigators believe that they represent a spill-over from infected domestic animals.

As the reporting of human cases of Q fever has become more prominent, so has the question of the source of infection in humans. Most of the cases reported have had some association with animals. These people included farmers, packing house workers, shepherds, dairy employees, laboratory workers, etc. This contact has been both direct and indirect. Indirect contact was believed to be the source of infection of most of the troops involved in the outbreaks in Italy and the Balkan countries during World War II. These men were housed in areas which had recently housed sheep, cattle, and goats. Although the organism was never isolated from these premises it was believed that the organism was probably present, either in the dust which had accumulated or in rodents and birds which infested the premises. This and subsequent outbreaks in which no direct contact with animals could be ascertained strengthened the idea that the organism might be spread by the airborne route. It had already been determined in early studies of C. burnetii that the organism was resistent to drying, and that it could survive for long periods of

time at room temperature, or in specimens of tick feces and other highly infectious material.

In 1959 the organism was isolated from soil samples collected in California on ranches which were known to have infected herds of sheep and cattle. This work has since then been reproduced in California and also in other areas. In Australia the organism was isolated from the dust surrounding a water hole with which infected patients had been in contact. Not only has the organism been isolated from soil samples, it has also been isolated from dust collected on air filters, demonstrating that the organism actually is readily airborne. It was this finding that confirmed the speculation of many investigators who have ruled out all other means of infection, and who have postulated that this must be the source. Several major outbreaks have been reported which have included persons with no contact with animals or animal products. The only explanation given in these cases was that the persons infected lived in an area covered by wind currents which passed over a heavily infected premise.

Direct contact with animals is an important means of transmission. As has been pointed out, a high percentage of cases occur among livestock workers. Sheep, goats, and cattle have all

been incriminated in this regard. In controlled studies, it has been shown that there is a markedly higher incidence of infection in persons associated with these animals than in those who have had no such association. Infection in these instances may also be attributed to aerosol spread, but direct contact with the animals is also known to be a source. There has been noted a marked rise in incidence of infection during the lambing and shearing seasons among persons who work with sheep. This is due to the highly infective nature of the products of parturition which are shed at that time. In areas where dairying is the predominent industry, the incidence of infection is not as closely related to the seasons. This is because calving occurs throughout the year, thereby providing constant exposure to parturient animals.

Another important means of spread is through milk. It has long been determined that infected animals shed the organism through this means. Milk may be infective even when the animal is reported as serologically negative. Surveys in southern California and in England have shown a higher incidence of infection among persons who drink raw milk, than among those who do not. This study was made among persons who lived on farms which were known to have seropositive herds. Although the incidence of

infection by serological testing was increased, yet the actual cases of clinically recognized disease was markedly diminished. These same findings were also noted in England. It has been speculated that because of a lower infecting dose that the cases are milder. Some workers have postulated that the presence of a whey antibody which is present in the milk of infected animals modifies the course of the disease. This is rather doubtful, because of the action of digestive processes on orally ingested antibodies.

When studying the resistence of C. burnetii to various physical and chemical factors, it was found that the organism was not entirely destroyed by the usual means of pasteurization. All organisms were apparently destroyed when the temperature in the vats was raised from the usual 143° to 145°. The flash method of pasteurization, which requires subjecting the milk to a temperature of 161° for 15 seconds, is apparently adequate to destroy the organism.

Laboratory workers are another group in which outbreaks have not been uncommon. These have occurred among persons actually handling the cultures of C. burnetii, as well as other people in the same area who have had no apparent contact with the disease.

This again suggests the multiple means of transmission of the organism. Some were apparently infected by direct contact and others with the aerosol route. In an outbreak at Fort Detrick, Maryland the disease occurred among personnel who had been immunized. The cases were all mild, but apparently the immunization was not entirely effective.

Person to person spread of the disease has been reported, but if this occurs, it is indeed rare. Cases have been reported following autopsy of an infected individual.

CONTROL OF Q FEVER

Whenever a disease involves as many people as does of fever, the question of control becomes important. Generally the disease is not of any serious consequence and is readily treated. However, there are a small number of patients with serious complications. In other instance the disease has been fatal. Even in patients who readily recover, the disease is often diabling during the acute phase. It would seem, then, that there is enough cause for concern about control.

Control has been considered from various aspects. Immunization of cattle has been tried, resulting in a reduction of infection

by 2/3. Human immunization among laboratory workers has been tried. Mild disease has been reported in immunized laboratory workers exposed to C. burnetii.

More careful control of milk pasteurization with a 2° temperature increase in holding vat has resulted in destroying the organism in milk.

Additional work is needed to provide a reliable vaccine for cattle as well as for persons in close contact with infected animals. Where feasible, more sanitary means should be provided to dispose of product of parturition. This might help reduce this incidence of airborne infection to man as well as to other animals.

SUMMARY AND CONCLUSION

Q fever is an acute febrile illness, characterized by fever, malaise, headache, weakness, anorexia, and usually an interstitial pneumonitis. The disease is caused by a rickettsia, Coxiella burnetii. It is usually a readily treatable disease, but complications may be severe and even fatal. The disease is fairly "new", being described by Derrick in Australia in 1935. Since that time it has been found to be endemic in all parts of the world. Epidemics of the disease have been reported involving several cases to several hundred cases. The disease has been diagnosed by isolation of the organism. The development of serologic methods which measure antibody titer has made diagnosis much simpler. These methods have also been used and are being used to determine incidence of infection in any given population group.

The disease has been recognized in man, cattle, sheep, goats, and several other wild and domestic animals. It has also been isolated from ticks which commonly infest the above animals. Because Q fever was recognized as a rickettsial disease, it was believed that an arthropod vector was necessary to explain the infection in man and domestic animals. More recent work suggests that the major source of infection is among cattle, goats, and sheep.

It is from these sources that most cases of human infection have arisen. It is also believed that small animals and arthropods are infected by contact with the above domestic reservoirs, rather than the opposite being true. At first it was though that a vector was necessary to transmit the disease from animal to animal, but it is now known that contaminated dust is an effective means of spread. Perhaps the most highly infectious means of spread of C. burnetii is the product of parturition from infected animals. This causes infection by direct contact as well as by contamination of the dust and air.

Milk from infected animals is another important source of infection in humans. This is one area, however, where effective control is possible. While the ordinary vat storage method of pasteurization at 143°F. for 30 minutes is not adequate to completely destroy the organism; raising the temperature to 145°F. for the same length of time is adequate. The flash method of pasteurization is also effective in destroying the organism.

Attempts to produce an effective vaccine against C. burnetii have not been entirely successful. Thus far the vaccine has reduced, but not eliminated, infection in cattle. Human cases have also been reported despite immunization. These cases were milder than usual,

however.

Much time and effort has gone into the study of Q fever and its etiologic agent since its initial recognition in 1935. Out of these studies have come assorted objective findings and opinions. The agent has been accurately described. The disease and its complications have been exhaustively described. In recent years, a clearer picture of the epidemiology of the disease has been forming. This has been clarified to the point that researchers now know in what directions efforts to control the disease should go.

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