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THE EPIDEMIOLOGY OF Q FEVER IN GREAT BRITAIN AN ANALYSIS OF THE FINDINGS AND SOME CONCLUSIONS*

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Perhaps the most lasting impression left by a survey of the literature of Q fever is of the remarkable diversity of the ecology of *Rickettsia burneti*. Its pattern of maintenance in animal or insect hosts differs strikingly from one part of the world to another, and the particular local variant which has evolved may have much significance for the infection of man. Thus, for example, the infection of sheep in the central valley of California or in southern Europe is accompanied by an appreciable morbidity among the human beings in contact, whereas the presence of the organism in the rabbits and ticks (*Hyalomma excavatum*) of the Nefifik forest, Casablanca, is an inapparent infection of seemingly little consequence to the visitors to this popular holiday resort (Blanc and Bruneau, 1956).

The extensive information about Q fever has been reviewed in detail many times (Derrick, 1953; Berge and Lennette, 1953; Kaplan and Bertagna, 1955; Stoker and Marmion, 1955a) and attempts have been made to form a unified view of the ecology of the rickettsia (Derrick, 1944; Marmion, 1954). These have not, perhaps, been particularly successful, but they do serve at least to indicate those ecological problems which need further exploration—for example, that of the relation between the cycle of maintenance of the rickettsia in ticks and small animals in various parts of the world and in the larger domestic animals, such as cattle, sheep, and goats.

Sporadic cases or outbreaks of the human disease have often been found in areas of intensive cattle or sheep farming, and the work of the Californian investigators (Huebner and Bell, 1951; Lennette and Clark, 1951) in particular has done much to unravel the way in which infection spreads from these animals to man. However, methods of animal husbandry in California have some unusual features, and the experience there cannot necessarily be used as a model for other countries. Q fever appears to be rare or entirely absent in certain agricultural countries such as Denmark, Finland, Norway, the Netherlands, and New Zealand. This may possibly be related to the infrequent importation of cattle and sheep into these countries (Kaplan and Bertagna, 1955), but the factors responsible may be more

complex, as the prevalence of the disease in cattle has been found to vary quite strikingly within the boundaries of a single county in England.

The work of Giroud and his colleagues in the Belgian Congo and French Equatorial Africa suggests that the ecology of the rickettsia and the epidemiology of the human disease may differ both qualitatively and quantitatively in tropical as compared with the temperate areas of the world.

Italian workers (Babudieri and Moscovici, 1952) found that pigeons and geese may be naturally infected with *R. burneti*, and Czechoslovakian workers (Brezina and Táborská, 1956; Raska *et al.*, 1956; Syruček and Raska, 1956) have extended our knowledge in this field by demonstrating natural infection in certain wild and domestic birds as well as in various rodents. The former finding is of some interest in view of a Russian report (Zhmaeva *et al.*, 1955) that *R. burneti* has been isolated from nestling field sparrows and two species of bird mites in an endemic focus of infection in Central Asia. The mites, it appears, were of a variety which sometimes attacks man and were collected from some of the numerous sparrows nesting near a village where human cases of Q fever had occurred.

These examples of the more unusual geographical variants of the ecology of the organism have been chosen deliberately to give point to Derrick's (1953) statement that "the history of 'Q' fever is full of paradoxes and surprises and changes of emphasis" and to make it clear that our understanding of the ecology of *R. burneti* is still incomplete.

There are therefore good general grounds for investigating Q fever in each country where it has been detected—quite apart from the need for public health workers to know about the local reservoirs of infection for man.

The investigation of the disease in England started in 1949, when Stoker found serological evidence of infection in two patients with pneumonia. Later in the same year the organism was isolated from patients in a small outbreak of Q fever at a hospital in London (Harman, 1949; MacCallum *et al.*, 1949). The epidemiological investigation of this outbreak (Marmion and Stoker, 1950) established that cattle in this country were infected and that the human cases were not the result of isolated importations of the disease.

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Subsequent epidemiological investigations fell into two stages. In the first, conducted from Colindale and Cambridge, patients with Q fever in many parts of the country were followed up to find out how they had been infected. This approach to the problem yielded some information, summarized in the paper by Marmion *et al.* (1953). However, the retrospective investigation of sporadic cases or outbreaks has limitations—due principally to the absence of epidemiological information about control groups of uninfected human beings or animals. In the second stage, therefore, certain areas and groups of the population were studied in a controlled way so as to assess the significance of various possible sources or modes of spread of infection to man which had been uncovered in the earlier investigation. This work was carried out from Cambridge as a joint responsibility of the authors and with support from the Medical Research Council and Cambridge University. Attention was concentrated on Kent and East Anglia—areas of high and low prevalence of the disease. Systematic surveys of possible animal reservoirs of Q fever in these two areas were undertaken and three main epidemiological investigations were carried out. For the sake of brevity the latter will subsequently be called the “survey of healthy adults,” the “rural area investigation,” and the “urban area investigation.”

In the first of these the epidemiological histories of blood donors with Q fever antibody who were living in Kent or East Anglia were compared with the histories of randomly selected and negative donors living in the same areas (Marmion *et al.*, 1956). In the second a comparison was made of the prevalence of Q fever in a sheep-raising area, the Romney Marsh, and in a geographically similar area of Fenland—Chatteris-Witchford R.D.—with few sheep (Marmion and Stoker, 1956). In the third, the residents of two towns in north-east Kent were studied to determine the part played by cows' milk as a vehicle of Q fever infection (Marmion and Harvey, 1956).

In other parts of the country and about the same time, surveys of Q fever infection in cattle and cows' milk were undertaken by Dr. Slavin, of the Weybridge laboratory of the Ministry of Agriculture and Fisheries (Slavin, 1952). The disease in human beings and animals was also investigated by Drs. A. D. Evans, W. F. Lane, and J. C. Walker at the Public Health Laboratories in, respectively, Cardiff, Bedford, and Luton, and also by Dr. N. R. Grist at the Virus Laboratory, Ruchill Hospital, Glasgow.

It is the purpose of this paper to assemble the results of all these studies and to present them, together with some fresh information, in an effort to provide a composite picture of our national epidemiology.

The reservoirs of infection in this country and their possible interrelationships are described first of all, then the ways in which infection spreads from them to man.

1. NATURAL HOSTS OF *R. BURNETI* IN GREAT BRITAIN AND MAINTENANCE OF THE ORGANISM

Cattle

R. burneti has been isolated on numerous occasions from the pooled milk of herds of cattle kept in many parts of England, Wales, and Scotland (Marmion and Stoker, 1950; Slavin, 1952; Marmion *et al.*, 1953; Evans, 1956; Grist, 1956). The survey by Slavin was the most comprehensive, and covered 3,374 herds, of which 6.9% in England, 2%

in Wales, and 0.8% in Scotland were infected as judged by the isolation of the rickettsia from the herd milk. The intensity of infection appeared to vary from county to county, doubtless owing mainly to uneven sampling, but nevertheless it was probably a valid observation that herds in East Anglia were much less often infected than those, for example, in Kent, Devon, Stafford, or Cheshire.

Few observations have been made on the distribution and progress of infection within herds of cattle in this country. The scanty information available suggests that the number of cows in a herd which are excreting rickettsiae in the milk may be small and that the infection may smoulder in the herd in an undramatic way. Thus in six infected herds in Kent and East Anglia 12 (10%) of 116 cows were shedding the rickettsia in the milk, and 24 (21%) of 114 cows had serological evidence of infection. Infection was found to persist for at least as long as two years in some Kentish herds which were sampled repeatedly.

Serological surveys of cattle at large—carried out mainly by testing sera submitted to veterinary laboratories for other diagnostic purposes—suggested low rates of infection; only 2 of 446 cattle in Kent and none of 609 cattle in East Anglia had Q fever antibody. Slavin found rather higher rates—12 (2.3%) of reactors among 509 sera collected from cattle in the country as a whole. When it is remembered that *R. burneti* was isolated from 8 to 12% of herd milks in Kent it is clear that surveys of bovine sera are an insensitive method of detecting or excluding the presence of Q fever in countries with a prevalence of infection at levels such as ours.

The rates of infection found by Huebner and his colleagues in Californian cattle were much higher than those just described—the milk from two-thirds of 63 dairies in Los Angeles contained the rickettsia (Huebner and Bell, 1951) and over 15% of 120,000 dairy cattle at large had serological evidence of infection (Luoto *et al.*, 1952). Such frequencies of infection seem to be of a different order of magnitude to those in British cattle. This might be due either to the less intensive methods of dairy farming in this country or it might represent a fundamental difference in the modes of spread of infection among the cattle. Presumably *R. burneti* is excreted in the placenta of English cattle as in Californian (Luoto and Huebner, 1950), but in a small series of tests we failed to isolate the organism from 32 placentas collected from cattle in herds with evidence of infection.

Sheep

Serological evidence of infection with *R. burneti* has been found in sheep in several parts of Great Britain. Fifteen (1.6%) of 906 sera from sheep killed in Kent slaughterhouses were found to have antibody, and higher rates of infection were found in certain flocks associated with cases of Q fever in the Romney Marsh area of the county (Marmion *et al.*, 1954). Eleven (3.5%) of 317 sheep in a rural area of Cardiganshire about 12 miles from Aberystwyth were found to have Q fever antibodies (Report to the P.H.L.S., 1956). Further south in Wales it was found that 2.7% of nearly 2,000 sera from sheep in 13 sanitary districts had Q fever antibody (Evans, 1956). Grist (1956) found a few positives among sheep coming to the Glasgow abattoir.

The significance of these serological observations was confirmed and enhanced by the isolation of *R. burneti* from 2 of 96 placentas collected from ewes in a flock with serological evidence of infection and kept in the Romney Marsh (Stoker *et al.*, 1955). The rickettsia was also isolated from pieces of wool collected from around the vulva of some ewes in the same flock. The frequency of serological positives and of the isolation of the organism from the placenta suggests a less intense infection than that found for example in North Californian or Italian sheep (Lennette and Clark, 1951; Davoli and Signorini, 1951).

We do not know how infection commonly spreads among sheep in this country—whether it is by the respiratory tract

after inhalation of infected aerosols, or by the digestive tract after the ingestion of water or pasture contaminated with the rickettsia, or even by arthropod vectors. Although *R. burneti* was found in the ticks (*Haemaphysalis punctata*) which heavily parasitized one infected flock in the Romney Marsh, infection was also found in another flock which was virtually free from ticks.

Spread of Infection from Sheep to Cattle

Early in the investigation of Q fever in Kent it was noted that the herd milks from cattle in the sheep-rearing areas of the county were more often infected than those elsewhere. A detailed survey of herds in two parts of the county was undertaken, therefore, to explore this lead. The parts chosen were agricultural census areas 8, 9, and 10 on the one hand and area 2 on the other. (See Fig. 1 (a).) Samples of the herd milks from the cattle in these areas were inoculated into guinea-pigs by Dr. E. R. Jones, of the County Pathological Laboratory, Maidstone, and the sera from the guinea-pigs, collected some six weeks after inoculation, were tested for Q fever antibody in our laboratory. In addition, samples of milk were obtained for us by medical officers of health in the two areas and tested in guinea-pigs at Cambridge. It will be seen from Table I that

TABLE I.—Isolation of *Rickettsia burneti* from Herd Milks of Cattle in Various Areas of Kent with Differing Populations of Sheep

Agricultural Census Area	Animals per 100 Acres of Crops or Grass			Cattle: Herds with		Total
	Cattle	Sheep	Pigs	Positive Milk	Negative Milk	
2	26.8	14.9	16.8	0	82	82
8, 9, 10	21.3	57.3	22.2	12	91	103

the two test areas were roughly similar in their numbers of cattle and pigs but differed strikingly in their number of sheep. It is clear that the proportion of herd milks which contained *R. burneti* was much higher in agricultural census areas 8, 9, and 10 than in area 2.

This difference in the rates of infection in the herds of cattle in the two areas could, of course, be due to other factors unrelated to exposure to sheep. Consequently an attempt was also made to find out whether the herds in the two areas differed in their size, methods of maintenance and replacement, exposure to sheep, infestation with ticks, and so on. This was done by sending a questionnaire to the farmers whose herds had been sampled. An analysis of the results is shown in Table II. The herds in the two areas were similar in respect of size, methods of maintenance, and grazing practice, but those in areas 8, 9, and 10 were more

TABLE II.—Analysis of the Answers to a Questionnaire Sent to 35 Farms in Area 2 and 63 Farms in Areas 8, 9, and 10

	Agricultural Census Areas			
	2		8, 9, and 10	
	No.	%	No.	%
No. of cattle in herd:				
< 10	1	3	6	10
10-30	20	57	28	44
31-50	7	20	12	19
51-70	6	17	8	13
> 70	1	3	9	14
Herds maintained from:				
(a) Calves born in herd	34	97	58	92
(b) Calves from outside herd	1	3	6	10
(c) Adult cattle from outside herd	10	29	17	27
Grazing practice:				
(a) Cattle graze with sheep	8	23	18	29
(b) Cattle graze on pasture used by sheep	7	20	17	27
Flock of breeding ewes on same farm:				
(a) At present time	4	11	22	35
(b) In the past	9	26	39	62
Flock of "fat" sheep on same farm	6	17	6	10
Ticks:				
(a) On farm dogs	4	11	5	8
(b) On cattle or sheep	2	6	20	32
Total farms	35	100	63	100

FIG. 1.—Sketch maps of Kent, divided into agricultural census areas (1 to 9 and the Romney Marsh) and showing (a) the number of sheep per 100 acres of crops and grass in the various areas of the county, (b) the number of cattle per 100 acres of crops and grass, (c) the distribution of sporadic cases, and outbreaks of Q fever (the numbers in the squares), and (d) the proportion of blood donors with Q fever antibody in the various areas.

commonly found on farms where there was a flock of breeding ewes—either at the time of replying to the questionnaire or in the past—and the farmers also reported that ticks were more often found on the cattle or sheep.

There is thus some evidence for an association between the infection of cattle and the presence of sheep or sheep ticks, or both, in this region of Kent. This conclusion is also supported by the findings in East Anglia, where the sheep population is low and the cattle are infrequently infected (Marmion *et al.*, 1953; Marmion and Stoker, 1956).

Goats and Pigs

Slavin (1952) isolated *Rickettsia burneti* from the pooled milk of a herd of goats in Devon. More recently we have failed to isolate the organism from the milk of five of the larger herds of goats in Kent.

So far as we are aware, there is no substantial evidence that pigs can act as a source of Q fever, although some workers (Giroud and Jadin, 1951; Giroud and Goulon, 1952; Davoli and Signorini, 1951; Monaci and Nuvolone, 1953) have found antibody in their sera. The epidemiology of an outbreak of Q fever on a farm in Kent (Stoker and Thompson, 1953) suggested that farrowing sows might be a source of infection for man. This conclusion stimulated a search for more certain evidence of infection among pigs in this country. As a preliminary some pigs were inoculated artificially to determine the nature of their serological response to infection with *R. burneti*. Both complement-fixing and agglutinating antibody were formed, but the rickettsia was not excreted in the placenta of a sow inoculated during pregnancy (Stoker and Betts, 1953). Tests for these two types of antibody were then carried out on the sera from 106 bacon pigs and 401 sows slaughtered in bacon factories and abattoirs serving a wide area of the country, but the results were negative. In addition placentas were collected from 101 sows, mostly on dairy farms in Kent, but *R. burneti* was not isolated by guinea-pig inoculation. Other material which was tested and proved to be negative included post-mortem specimens from four sows coming from farms where infection was known to be present either in human beings or in dairy cattle.

Rabbits

Bengtson (1941) and Fiset (1957) have shown that rabbits artificially inoculated with *R. burneti* form agglutinating and complement-fixing antibodies, and other workers have shown that infection sometimes occurs in Nature (Davoli and Signorini, 1951; Blanc and Bruneau, 1956).

The organs from 229 rabbits, mostly trapped in the Romney Marsh, were examined by guinea-pig inoculation, but *R. burneti* was not isolated. Professor C. P. Beattie, of the Department of Bacteriology, University of Sheffield, kindly provided 172 rabbit sera which had been collected during a survey of the distribution of *Toxoplasma*. These showed neither agglutinating nor complement-fixing antibody to *R. burneti*.

Birds

Chickens

Our colleagues Drs. Fiset and Barber have examined sera from domestic hens which were obtained through the courtesy of Miss M. J. B. Wheatley and Mr. John Edwardson, of the Veterinary Inspection Service in Kent and of the Director of the Houghton Poultry Research Station in East Anglia. The method of indirect complement-fixation (Rice, 1948) was used to test for Q fever antibody and with an antigen made from the Nine Mile strain of *R. burneti*.

Sera from 390 birds were tested and 46 (11.8%) gave a positive inhibition test at titres of 1/10 or more. A comparison of sera collected from Kent, where Q fever is endemic, and East Anglia, where infection is rare, showed that 46 (13.5%) of 341 Kentish fowl sera were positive (some with titres of 1/80) but none of 49 sera from East Anglian fowls. There was also an indication that the

proportion of positives in Kent was the highest in flocks of hens running on pastures used by sheep.

The serological infection rate in Kentish fowls was of the same order as that—15%—found by Syruček and Raska (1956), who, however, used the direct complement-fixation test on fowl sera from Czechoslovakian farms where Q fever had occurred in man and domestic animals. These authors, and Sobeslavsky, also studied the excretion of the rickettsia and antibody formation in experimentally infected fowls. *R. burneti* was recovered from the droppings of one bird during the period from the 7th to the 40th day after inoculation. Complement-fixing antibody formation as measured by the direct test was rather irregular: only 3 out of 12 hens developed antibody, and even then not until six weeks after infection.

Wild Birds

The organs of 166 wild birds of various species taken in the Romney Marsh were examined, but *R. burneti* was not isolated.

Ticks

R. burneti was isolated from two batches of *Haemaphysalis punctata* collected from the flock of sheep in the Romney Marsh which had provided the infected placentas and wool clippings (Stoker and Marmion, 1955b). Ticks collected at the same time from other flocks in the Romney Marsh were negative, but an equivocal isolation was made some years before from *H. punctata* collected on the northern Kent marshes. Large batches of *Ixodes ricinus* from Cumberland and Scotland and a small number of *Dermacentor reticulatus* from Devon were negative (Marmion *et al.*, 1953).

Miscellaneous Animals and Ectoparasites

The organs from 30 assorted small animals—mice, rats, shrews, moles—and several pools of rabbit fleas, mostly collected in the Romney Marsh, were examined by guinea-pig inoculation with negative results.

2. TRANSMISSION OF INFECTION TO MAN

General Epidemiology of Human Q Fever

Geographical Distribution of Cases

Patients with Q fever have been detected in most parts of the Midlands and southern England. Relatively few cases have been reported in the north, and they appear to be especially rare in Lancashire, Westmorland, Cumberland, and the North and East Ridings of Yorkshire (Stoker, 1949; Manderson, 1949; Crofton *et al.*, 1951; Cameron, 1951; Marmion *et al.*, 1953, and unpublished data; Erooga and Shaw, 1956). The absence of Q fever in these northern counties, which are agricultural areas with large numbers of sheep, is most probably due to the fact that a systematic search has not been made. On the other hand, there are certain areas in East Anglia where, despite a rigorous search for patients with Q fever, only one or two have been found. This fact and the relatively infrequent finding of Q fever antibody in healthy members of the local population make it certain that the disease is genuinely absent and not merely undetected (Marmion *et al.*, 1953, 1956; Marmion and Stoker, 1956). In fact, the disease may have a patchy distribution even within the boundaries of a single county. Thus in Kent most of the patients with Q fever were found in the eastern half of the county, although admittedly the distribution is weighted by the inclusion of patients in the "urban" and Romney Marsh areas, which were the subject of special study. Despite this, the results of a serological survey of healthy adults (blood donors) throughout the county does support the idea of an irregular distribution of infection which more or less coincides with the case distribution. (See Fig. 1 (c) and (d).)

Sporadic cases or outbreaks of Q fever have also been found in many parts of Wales (Forbes, 1950; Evans, 1956; Report to the P.H.L.S., 1956). Little evidence of human

infection has yet been obtained in Scotland in spite of finding infected cattle in Dumfries, Clydebank, and Aberdeen (Grist, 1956; Slavin, 1952).

Age and Sex Distribution of Sporadic Cases

An analysis of the first 69 patients with Q fever showed that 58 were males and only 11 females. Of the patients, 92% were between 20 and 60 years old—that is, of working age (Marmion *et al.*, 1953). An analysis of cases since 1953 shows similar trends. The youngest patient in our records was aged 6.

Seasonal Prevalence of Cases

Fig. 2 shows the distribution of 104 patients with Q fever in England and Wales by their month of onset of illness. Over half of these had been found in Kent—an area of

FIG. 2.—Seasonal distribution of 104 sporadic cases of Q fever in England and Wales. Those in Kent are represented by black squares and those elsewhere by open squares.

was predominantly among those supplied with pasteurized milk at home, so that infection from a source other than raw milk must be postulated. Lastly, Fig. 3 (c) shows that the vernal prevalence of infection was most striking in the Romney Marsh area of Kent, where sheep were almost certainly the source of infection. On the other hand, cases in the urban area in the north-east of Kent, where milk was the most probable source of infection (see below), occurred all the year round.

Modes of Spread of Infection from Animals to Man

Occupational Q Fever

Classically, Q fever is a disease of those working with the domestic ruminants, but in fact only 8 (11.6%) out of the original series of 69 sporadic cases of Q fever in this country had such exposure. Nevertheless, in accord with the pattern of the disease elsewhere, patients with Q fever have been found among farmers and farm workers, shepherds, slaughterhouse workers, and veterinary surgeons. The serological survey of healthy adults in Kent and East Anglia showed that antibody was almost twice as common in persons who were occupationally exposed to cattle and sheep (or materials from them) as in those who were not. The low incidence of the clinical disease among those most closely exposed was probably due to pre-existing immunity—a point more fully explored in the discussion.

Residence Near Sources of Infection

Elsewhere in the world, in Los Angeles or Italy for example, it has been found that people living near certain sources of infection (cattle, sheep, or goats, particularly when giving birth to their young) have an increased risk of

getting Q fever. In England, however, there is little evidence from the investigation of Q fever patients in general that such "residential" contact plays a significant part in the epidemiology of the disease. This conclusion is supported by the finding that healthy adults in Kent and East Anglia who had lived within 200 yards (183 m.) of farm stock did not have Q fever antibody any more frequently than those not so exposed. This divergence from the experience in Los Angeles and elsewhere is probably accounted for by our wetter and less dusty atmosphere, the generally low incidence of Q fever in English cattle and sheep, and the less intensive and concentrated dairy farming.

There was, however, one group of 10 patients with Q fever in a small town in north Kent (Fig. 1 (c), area 6) where a form of "residential" exposure probably did play a part. Investigation of these patients showed that they had probably not been infected from milk or the local cattle and sheep, and the only remaining source seemed to be a large glue and fertilizer factory, around which most of the cases of Q fever either lived or worked. The factory received, among other materials, the offal from animals slaughtered in abattoirs in various parts of Kent and Sussex—bones, horns and hooves, intestines, and parts of the genital and urinary tracts. Some of this material—namely, the udder, the uterus with placenta and birth fluids, and the intestines—may have contained *R. burneti* from time to time, or indeed any of it may have been contaminated with the excreta of the rats which were inevitably to be found in the area.

If the factory was the source of infection then it is far from clear how infection was disseminated to the local inhabitants. Simple wind-borne carriage of infected dust from the factory during the processing of various tissues seems hardly credible, as some of the patients lived or worked more than half a mile (0.8 km.) away. Some interesting conclusions about the distance which infected aerosols can

FIG. 3.—Seasonal distribution of sporadic cases and outbreaks of Q fever in Kent: (a) all cases, (b) showing the household milk supply at the time of illness, and (c) showing the area of the county from which the cases were drawn.

spread from a rendering and fertilizer factory have recently been given by Spendlove (1957). After an outbreak of psittacosis had occurred at a factory which processed infected turkeys it was found that "tracer" bacteria placed on the material being macerated could be recovered in small numbers in an air sampler placed on a road skirting the factory and some 100 feet (30 m.) down-wind from the factory chimney. A more credible if quite unproved explanation would suggest that infected dust was carried out of the factory on the floors of transport vehicles or on the clothing or hair of the factory workers and subsequently liberated into the air of places at a distance—for example, the packing bays of adjoining factories, or in local shops, public houses, or cafés, and so on. Presumably the intensity of such infection would be greatest in the vicinity of the factory but would diminish much more slowly with the distance from the source than would simple wind-borne carriage of infected dust.

Direct Contact with Infected Cattle and the Use of Infected Raw Milk

Although there have been one or two episodes in which bystanders other than the herdsman or veterinary surgeon have been infected at the birth of a calf, the main vehicle by which Q fever comes from cattle to man in England appears to be the milk. The part played by milk in causing Q fever was shown in two towns in area 8 of Kent. (See Fig. 1 (c).) In these towns it was found that there was a preponderance of users of raw milk among Q fever patients when compared with a control group of patients suffering from other forms of fever or pneumonia. The majority of the cases of Q fever, and also the highest proportion of healthy adults with serological evidence of infection, were found among the customers of five particular retail dairies out of a total of 16 or 17 selling milk in the two towns. The rickettsia was demonstrated in the milk supplied to two of the five dairies.

Infection from sources other than milk seemed improbable in these two towns because a history of occupational or any other form of contact with animals or animal products, or of regular contact with persons working in trades with animals, was no commoner among the Q fever patients than among the controls.

The results of the survey of healthy adults in all parts of Kent and several counties of East Anglia provided an independent confirmation of the importance of milk-borne infection. In both areas it was found that after due allowance had been made for exposure in other ways the proportion of healthy adults with Q fever antibody was significantly higher among those who had used raw milk at home for all or part of the period 1942–53 than among those who had used only pasteurized milk.

Sheep as a Source of Infection for Man

The part played by sheep in the epidemiology of human Q fever in England was explored in the Romney Marsh area of Kent, which has a very large sheep population. As already mentioned, several flocks with serological evidence of infection were found in this area and the rickettsia was isolated from placental and wool samples collected from the sheep in one such flock. A serological survey of patients in the Romney Marsh who had suffered from pneumonia or undiagnosed fever during the period 1949–54 showed that some 14% of them had probably had Q fever. The majority of the patients with Q fever became ill in April, May, and June—that is, at a time when lambing, shearing, and other work with the sheep is at its height. (See Fig. 3 (c).) Several of the patients with Q fever were farm labourers or shepherds in close contact with sheep, and in at least three episodes it seemed very probable that the patients had been infected from the lambing ewes. The other Q fever patients in the area were not working with sheep, but some were in contact with shepherds or other persons handling sheep or materials from them. An investigation of the milk supplies of the cases of Q fever showed that some were using

pasteurized milk, while others were using supplies of raw milk and that one of these was infected with *R. burneti*. This last supply may have been the source of infection for a few of the cases (Marmion *et al.*, 1954; Marmion and Stoker, 1956).

The investigation of a small outbreak of 15 cases of Q fever in a sheep-rearing area of Cardiganshire (Report to the P.H.L.S., 1956) provided additional evidence that sheep may be responsible for human infection in Great Britain. As with the series of Q fever patients in the Romney Marsh only a proportion, 10 of the 15 patients, had obvious occupational exposure to animals. The remaining patients—a salesman in a mobile clothing-shop, a physician, a newspaper reporter, a carpenter, and a domestic worker—had either visited farms or had some contact in their spare time with persons who were engaged in sheep farming. It seems probable that they were exposed to infection in some undefined way during these activities.

The epidemiological pattern of the Welsh outbreak and that of some of the Romney Marsh cases resembles that found in the outbreak at Colusa, North California, by Clark *et al.* (1951). These workers considered that some persons who were not directly exposed to sheep may have been infected by the inhalation of dust containing *R. burneti* which was carried into town on the clothing of sheep farmers or other fomites. We have recovered *R. burneti* from the dust taken from the clothing of a Romney Marsh shepherd in charge of an infected flock (Marmion and Stoker, 1956), and it is easy to imagine how such persons dressed in their working clothes could carry infection into local shops, cafés, hairdressers, or public houses, or to any other place at some distance from the infected sheep.

Possibility of Infection from Other Domestic Animals, Birds, and Arthropods

Goats.—These animals are known to play a part in the epidemiology of Q fever in some parts of the world. Although infection has been demonstrated in goats in England (Slavin, 1952) their small number probably makes them of little importance as a cause of human Q fever in this country. Reliable statistics of the goat population are difficult to obtain, as many goats are kept on holdings of less than an acre, which are not included in the agricultural returns. In the 1951 census 995 goats were recorded in Kent—a trifling number compared with some 120,000 cattle and 400,000 sheep. Goats are sometimes kept instead of cows to provide milk for farm households in the Fenland areas of Cambridgeshire, and are probably commoner there than in Kent. It is significant, therefore, that the Fens are largely free from Q fever. The survey of healthy adults in Kent and East Anglia revealed that only 5% of the sample of nearly 400 persons who were interviewed had bought or consumed goat's milk during the period from 1942 to 1953. Those who had done so did not have Q fever antibody more frequently than the remainder of the sample.

Pigs.—The survey of healthy adults in Kent and East Anglia did not show any increased frequency of Q fever antibody in human beings in contact with pigs. In fact, those persons living in areas of Kent and East Anglia with the largest populations of pigs showed the lowest rates of serological infection. These findings, together with the failure to demonstrate infection in pigs (see above), indicate that the pig is at best a very infrequent source of infection for man in this country.

Miscellaneous Animals, Birds, and Insects.—There was no increased frequency of Q fever antibody among the healthy adults in Kent or East Anglia who had kept dogs, cats, rabbits, chickens, or various psittacine birds at or near their homes during the survey period from 1942 to 1953. Similarly infestation (generally slight) of the house or outbuildings with mice, rats, or mosquitoes was without significance. A history of tickbite was very uncommon among both the healthy adults and the patients with Q fever, and there is no good evidence of the infection of man by this means. There were a few reports of the presence of ticks on dogs,

cats, or ferrets, and it is possible that an occasional patient might be infected while removing them—as in the incident with dogs and *Ixodes ricinus* described by Hengel *et al.* (1950).

DISCUSSION

It is difficult to make an accurate estimate of the prevalence of clinical Q fever and the size of the problem it presents in this country. This is partly because of the indefinite clinical picture and partly because there is considerable variation in the frequency of the disease from area to area (for example, in Kent and East Anglia) and also between town and country. It is not altogether surprising, therefore, that figures derived from the central examination of the sera from patients with pneumonia or unexplained fever (mostly from urban areas) show low rates of infection (MacCallum, 1954). In some well-studied areas such as the Romney Marsh, or the small urban area in Kent, some 14% of patients with pneumonia probably had Q fever, and it is significant that the local medical practitioners at first did not distinguish the sporadic cases of Q fever from the bulk of those with pneumonia or fever due to other causes. Evans (1956) draws attention to the discrepancy between, on the one hand, the evidence of infection in cattle and sheep in South Wales and the frequency of antibody in the healthy residents of the area, and, on the other hand, the infrequent detection of clinical Q fever (15 (0.6%) of 2,482 cases of non-bacterial pneumonia). These findings might mean either that human infection was occurring at the time of the survey but was almost entirely subclinical in nature, or, as antibody may persist for six or more years after infection, that the antibody in the healthy population was from past infection and that the rickettsia was no longer spreading from cattle (or sheep) to man in this area. A recent change to the use of pasteurized milk could, for example, bring about such a dissociation between serological and clinical evidence of infection.

In general terms the finding of antibody in a population with no clinical Q fever might indicate a past acquisition of immunity and resistance to present exposure to infection. Relatively few of the Kentish cases of Q fever occurred among persons occupationally exposed to animals, although antibody was commonly found among such workers. In both the urban area and the Romney Marsh investigations it was noted that the newcomer to the area bore the brunt of the clinical Q fever—an observation most easily explained by postulating an immunity in residents of longer standing. Such an immunity might be the result of childhood exposure and acquired from infected milk—which appears to produce a high ratio of subclinical to clinical infections. An analogous situation appears to exist in South Africa, where most of the adult population are apparently immune and patients with Q fever are seen mostly among newly arrived immigrants from overseas or in South-African-born children (Report, 1954; cited by Kaplan and Bertagna, 1955).

The main conclusion from the investigations in Great Britain is that human beings in the areas studied were infected primarily from cattle and to a less extent from sheep. Although a few persons may have been directly or indirectly infected at the birth of a calf, the chief way in which the rickettsia spread from cattle to man appeared to be in the milk—at least in the sporadic cases of Q fever. No epidemiological evidence was obtained that goats, pigs, dogs, cats, rats, mice, domestic fowl, psittacine or other birds, ticks or other insects were a significant source of infection.

Although there is convincing evidence that Q fever can be contracted from the use or consumption of infected raw milk from cows—not only from the pioneer observations of Huebner and his colleagues in Los Angeles (Huebner *et al.*, 1948; Beck *et al.*, 1949; Bell *et al.*, 1950), but also from our own experience with the survey of healthy adults and the urban area investigation—the situation has nevertheless some puzzling features.

Infected milk may contain large numbers of rickettsiae—5 to 500 guinea-pig-infective doses per ml., and sometimes even more. Superficially it might be thought that drinking infected milk would be more dangerous, in terms of concentrations of organisms in contact with the oropharynx, than inhaling an infected aerosol. Yet the consumption of infected milk appears to be responsible for sporadic cases of Q fever at most. It is often assumed, possibly correctly, that this low incidence of clinical Q fever in drinkers of raw milk is due in some way to the greater resistance to infection of the oropharynx or intestinal tract as compared with the lower reaches of the respiratory tract. The recent demonstration (Abinanti and Marmion, 1957) of the protective or neutralizing properties of whey antibody in infected milk offers another possible explanation—namely, that contact with the antibody-coated rickettsiae leads to subclinical rather than clinical infection as with the guinea-pig inoculated with a mixture of rickettsiae and immune serum.

The ratio of subclinical (antibody-forming) to clinical infections among the users of an infected milk supply is a matter of some interest. In the absence of much-needed and accurate data from an institutional population supplied with infected milk we can only make a very rough estimate of the proportion of clinical cases of Q fever to persons with antibody for the customers of dairies A and B of the urban-area investigation. Probably about 7,000 to 8,000 people were getting milk from these two dairies. It can be estimated that during the period 1948–54 there were some 94 cases of pneumonia in this group and that of these about 30 were probably due to Q fever. From the results of antibody tests on the samples of healthy adults using milk from dairies A and B it can be calculated that some 1,070 persons among the customers had antibody—a proportion of one patient with Q fever for every 35 persons with antibody.

There have been several experimental investigations of the effects of pasteurization on infected raw milk (Huebner *et al.*, 1949; Marmion *et al.*, 1951). Essentially these have shown that treatment of the milk at 161° F. (71.7° C.) for 15 seconds in the high-temperature-short-time (H.T.S.T.) process and 145° F. (62.8° C.) for 30 minutes in the vat-holding process is generally sufficient to destroy the rickettsiae in naturally infected milk. A recent reinvestigation of the problem (Enright *et al.*, 1957) has confirmed these findings. Examination of milk purchased in the open market and pasteurized by the H.T.S.T. or vat-holding process has revealed a few samples in which the rickettsia has survived (Huebner *et al.*, 1949; Lennette *et al.*, 1952; Evans, 1956). This is probably of little practical significance, for the results of our investigations show clearly that persons using pasteurized milk have a lower probability of contracting Q fever or of exhibiting antibody than those in the same area who use raw milk. The great increase in the pasteurization of milk which has taken place during the last ten years in this country should substantially reduce the number of sporadic cases of Q fever in urban dwellers who are not otherwise exposed, although unpasteurized tuberculin-tested milk will presumably still remain as a potential source of infection.

Although the sporadic cases of Q fever may be brought under control the outbreaks of the disease may well continue, as they appear to be part of a different epidemiological problem. The source and occasion of infection has only been determined with certainty in one of the seven British outbreaks investigated—that at the Royal Cancer Hospital in London. Four of the outbreaks occurred in the spring and at the time of lambing and shearing, but the remaining two were at quite different times of year. Perhaps the most puzzling of all was that among the students at the College of Arts, Canterbury, where no obvious contact with domestic animals, rodents, or birds could be demonstrated (Harvey *et al.*, 1951).

A number of the students at this college came from the farming community and a few from sheep farms on the edge of the Romney Marsh. In view of the recovery of

R. burneti from air-borne dust by the Northern Californian workers (DeLay *et al.*, 1950) and their suggestions about fomites-borne infection (see Welsh, 1951), and also of our own isolation of *R. burneti* from dust collected from the clothing of a Romney Marsh shepherd, it is tempting to look back at this outbreak and speculate on the possibility that infected dust may have been brought to and disseminated in the college by a student rather than on the exterior or the contents of a packing-case, as tentatively suggested at the time.

The recent discovery that certain rodents and chickens can be infected and excrete the rickettsia points to another possibility which should be explored in future outbreaks where cattle, sheep, or goats are not obviously involved. Even if *R. burneti* is not regularly maintained in rats or chickens it may well be that these creatures can act as "short-term" or "secondary" hosts to the rickettsia and carry it into domestic or other environments well away from domestic ruminants, their products, or fomites directly contaminated by them. To mention this possibility is only to return to the theme of the variability of the ecology of *R. burneti* which has been stated in the introduction. Our information about the epidemiology of the disease in Great Britain as a whole is still quite limited. The indications from the most closely studied county, Kent, are of localized and complex endemic focus in which ticks and sheep are infected, with spread of infection from the latter to cattle and possibly to other creatures in contact, such as chickens. The distribution of sporadic cases and outbreaks of Q fever in man corresponds to the intensity of stocking with sheep in Kent, but it is clear that infection does not always spread from them to man by the most direct route. Studies elsewhere in Great Britain might well show different combinations of hosts and different routes of spread of infection.

Summary

Investigations of the epidemiology of Q fever in Great Britain since 1949 have shown that the disease is widespread in the country.

Rickettsia burneti has been isolated from the milk of cows and goats and from the placenta and wool of sheep. It has also been isolated from the sheep tick, *Haemaphysalis punctata*, but not from *Ixodes ricinus* or *Dermacentor reticulatus*.

There was some evidence of an increased frequency of infection in cattle in areas of Kent with large numbers of sheep and in some sheep ticks.

Limited attempts to find a reservoir of infection in small wild animals or wild birds were unsuccessful. Serological evidence of infection was found in chickens, but there are, at present, no grounds for assuming that these birds are an important reservoir of infection in Great Britain.

Infection in man has not been limited to those persons working with animals, but has been found in all sections of the community. Sporadic cases and outbreaks of Q fever occurred at any time of the year, but, in the areas studied, were commonest in the months from April to July.

Studies of the transmission of *R. burneti* to man have shown that sheep or cows were directly or indirectly the main sources of infection. Good evidence was obtained of the importance of unpasteurized cows' milk as a vehicle of infection.

REFERENCES

- Abinanti, F. R., and Marmion, B. P. (1957). *Amer. J. Hyg.*, **66**, 173.
 Babudieri, B., and Moscovici, C. (1952). *Nature (Lond.)*, **169**, 195.
 Beck, M. D., Bell, J. A., Shaw, E. W., and Huebner, R. J. (1949). *Publ. Hlth Rep. (Wash.)*, **64**, 41.
 Bell, J. A., Beck, M. D., and Huebner, R. J. (1950). *J. Amer. med. Ass.*, **142**, 868.
 Bengtson, I. A. (1941). *Publ. Hlth Rep. (Wash.)*, **56**, 327.
 Berge, T. O., and Lennette, E. H. (1953). *Amer. J. Hyg.*, **57**, 125.
 Blanc, G., and Bruneau, J. (1956). *Arch. Inst. Pasteur Maroc*, **5**, 87.
 Brezina, R., and Táborová, D. (1956). *Csl. Epidem.*, **5**, 152. Abstracted in *Trop. Dis. Bull.*, 1956, **53**, 1415.
 Cameron, H. (1951). *Brit. med. J.*, **1**, 1367.
 Clark, W. H., Romer, M. S., Holmes, M. A., Welsh, H. H., Lennette, E. H., and Abinanti, F. R. (1951). *Amer. J. Hyg.*, **54**, 25.
 Crofton, J. W., Fawcett, J. W., James, D. G., Scadding, J. G., Macrae, A. D., and Marmion, B. P. (1951). *Brit. med. J.*, **2**, 1368.
 Davoli, R., and Signorini, L. F. (1951). *Ann. Sanità pubbl.*, **12**, 67.
 DeLay, P. D., Lennette, E. H., and DeOme, K. B. (1950). *J. Immunol.*, **65**, 211.
 Derrick, E. H. (1944). *J. Hyg. (Camb.)*, **43**, 357.
 — (1953). *Med. J. Aust.*, **1**, 245.
 Enright, J. B., Sadler, W. W., and Thomas, R. C. (1957). *Amer. J. publ. Hlth*, **47**, 695.
 Erooga, M. A., and Shaw, J. B. (1956). *Tubercle (Lond.)*, **37**, 114.
 Evans, A. D. (1956). *Monthly Bull. Minist. Hlth Lab. Serv.*, **15**, 215.
 Fiset, P. (1957). *Canad. J. Microbiol.*, **3**, 435.
 Forbes, J. (1950). *Lancet*, **2**, 267.
 Giroud, P., and Goulon, M. (1952). *Bull. Inst. nat. Hyg. (Paris)*, **7**, 877.
 — and Jadin, J. (1951). *C.R. Acad. Sci. (Paris)*, **231**, 86.
 Grist, N. R. (1956). *Scot. med. J.*, **1**, 173.
 Harman, J. B. (1949). *Lancet*, **2**, 1028.
 Harvey, M. S., Forbes, G. B., and Marmion, B. P. (1951). *Ibid.*, **2**, 1152.
 Hengel, R., Kausche, G. A., and Sheris, E. (1950). *Dtsch. med. Wschr.*, **75**, 1505.
 Huebner, R. J., and Bell, J. A. (1951). *J. Amer. med. Ass.*, **145**, 301.
 —, Jellison, W. L., Beck, M. D., Parker, R. R., and Shepard, C. C. (1948). *Publ. Hlth Rep. (Wash.)*, **63**, 214.
 —, —, and Wilcox, F. P. (1949). *Ibid.*, **64**, 499.
 Kaplan, M. M., and Bertagna, P. (1955). *Bull. Wild Hlth Org.*, **13**, 829.
 Lennette, E. H., and Clark, W. H. (1951). *J. Amer. med. Ass.*, **145**, 306.
 —, Abinanti, M. M., Brunetti, O., and Covert, J. M. (1952). *Amer. J. Hyg.*, **55**, 246.
 Luoto, L., and Huebner, R. J. (1950). *Publ. Hlth Rep. (Wash.)*, **65**, 541.
 —, Winn, J. F., and Huebner, R. J. (1952). *Amer. J. Hyg.*, **55**, 190.
 MacCallum, F. O. (1954). *Trans. roy. Soc. trop. Med. Hyg.*, **48**, 203.
 —, Marmion, B. P., and Stoker, M. G. P. (1949). *Lancet*, **2**, 1026.
 Manderson, W. G. (1949). *Ibid.*, **2**, 1085.
 Marmion, B. P. (1954). *Trans. roy. Soc. trop. Med. Hyg.*, **48**, 197.
 — and Harvey, M. S. (1956). *J. Hyg. (Camb.)*, **54**, 533.
 —, Rowlands, A., MacCallum, F. O., and Thiel, C. C. (1951). *Monthly Bull. Minist. Hlth Lab. Serv.*, **10**, 119.
 —, Stewart, J., Richmond, P., Barber, H., and Stoker, M. G. P. (1954). *Lancet*, **1**, 1288.
 — and Stoker, M. G. P. (1950). *Ibid.*, **2**, 611.
 — (1956). *J. Hyg. (Camb.)*, **54**, 547.
 —, McCoy, J. H., Malloch, R. A., and Moore, B. (1953). *Lancet*, **1**, 503.
 —, Walker, C. B. V., and Carpenter, R. G. (1956). *J. Hyg. (Camb.)*, **54**, 118.
 Monaci, V., and Nuvoione, U. (1953). *Boll. Ist. sieroter. milan.*, **32**, 62.
 Raska, K., Syruček, L., Sobeslavsky, O., Pokorný, J., Privora, M., Havlík, O., Lim, D., and Záštera, M. (1956). *Csl. Epidem.*, **5**, 246. Abstracted in *Trop. Dis. Bull.*, 1957, **54**, 280.
 Report (1954). South African Institute for Medical Research, Johannesburg. Annual report for the year ended December 31, 1954. Cited by Kaplan and Bertagna (1955).
 Report to the Public Health Laboratory Service (1956). *Monthly Bull. Minist. Hlth Lab. Serv.*, **15**, 10.
 Rice, C. E. (1948). *J. Immunol.*, **59**, 365.
 Slavin, G. (1952). *Vet. Rec.*, **64**, 743.
 Spindlove, J. C. (1957). *Publ. Hlth Rep. (Wash.)*, **72**, 176.
 Stoker, M. G. P. (1949). *Lancet*, **1**, 178.
 — and Betts, A. (1953). Unpublished data.
 —, Brown, R. D., Kett, F. J. L., Collings, P. C., and Marmion, B. P. (1955). *J. Hyg. (Camb.)*, **53**, 313.
 — and Marmion, B. P. (1955a). *Bull. Wild Hlth Org.*, **13**, 781.
 — (1955b). *J. Hyg. (Camb.)*, **53**, 322.
 — and Thompson, J. F. (1953). *Lancet*, **1**, 137.
 Syruček, L., and Raska, K. (1956). *Bull. Wild Hlth Org.*, **15**, 329.
 Welsh, H. H. (1951). *J. Amer. med. Ass.*, **145**, 316.
 Zhmaeva, Z. M., Pchelkina, A. A., Mishchenko, N. K., and Karulin, B. E. (1955). *Dokl. Akad. Nauk. S.S.S.R.*, **101**, 387. Summary in *Trop. Dis. Bull.*, 1956, **53**, 430.

"The control of dark smoke can be achieved if the representatives of local authorities accept the responsibilities that the full implementation of the Clean Air Act, 1956, involves. The common practice of waiting for smoke nuisance complaints from the public before action is taken is over. All areas should be subject to constant inspection and contraventions should not be allowed to persist. In many cases the co-operation of the owners or occupiers of the premises is readily available once their attention is drawn to such contraventions, and persuasion rather than compulsion is the answer; on the other hand there is sometimes a hard core of resistance to be overcome, and in such cases the local authority should ensure that the enforcement of legal proceedings can be carried out. If the representatives of local authorities who are in fact the policy makers do not accept the responsibilities placed upon them by the Clean Air Act, 1956, then I suggest that one of the ideas of this Society, 'To encourage the adoption of methods to reduce and prevent atmospheric pollution,' will be of no avail."—Mr. G. W. FARQUHARSON, chief smoke inspector for Birmingham, speaking on October 1 at the annual conference of the National Society for Clean Air.