

OVINE ENZOOTIC ABORTION

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INTRODUCTION

Ovine enzootic abortion (OEA) is caused by a member of the chlamydia, *Chlamydia psittaci*. It was some 25 years ago that the potential significance for the pregnant woman of infection with *Chlamydia psittaci* of ovine origin was first recognised. It was only in the 1980's, however, that following a spate of case reports of maternal illness and abortion due to OEA that it gained more widespread attention, and even elicited questions in the House of Lords.

Ovine enzootic abortion also presents major problems to sheep farming in the UK as it is the most frequent cause of abortion of ewes in the UK, and its spread has proved resistant to available vaccines.

THE AGENT

The chlamydiae are well-established pathogens for man, being first recognized as the cause of trachoma in the early part of the century. Chlamydiae are distinct organisms belonging to one family. They have a unique intracellular replication cycle and can only be isolated in living host cells. They are resistant to many antibiotics, but usually sensitive to tetracycline and erythromycin. There are three species now recognized, namely *C. trachomatis*, *C. pneumonia* and *C. psittaci*. *C. trachomatis* infects only man and is the causative agent not only of trachoma but also a wide spectrum of disease including non-specific urethritis in the male, pelvic inflammatory disease, and conjunctivitis. *C. pneumonia*, previously known as TWAR, is becoming an increasingly recognized cause of respiratory tract infection in humans, although diagnostic tests are not yet readily available.

Chlamydia psittaci is one of the commonest infectious agents encountered in the animal kingdom. Psittacosis of man was first described in the 1870s in Switzerland and a number of outbreaks in Europe in the late nineteenth and early part of the twentieth century lead to the recognition of the association with 'exotic' or psittacine birds. Particular attention to the disease was brought by the pandemic of 1929-30, when without the availability of antibiotics mortality rates up to 20% were described. In the 1950's the importance of other birds, such as poultry, was recognized as a source of psittacosis. Although the term ornithosis has been used to imply infection from non-psittacine birds, the distinction is unnecessary as the diseases are essentially identical from whichever species of bird it is caught. Although perhaps parrots are the most common source, a wide range of other birds such as pigeons, turkey and ducks can be responsible, and many outbreaks have been described in turkey and duck-processing factories. Psittacosis of man is virtually always acquired from birds, with human-to-human transmission being described rarely. Avian chlamydiosis is now recognized in at least 130 species of bird. The intestinal

tract of the bird, which may well be asymptomatic, is the usual site of infection. Clinical manifestations are often precipitated by stress and the bird develops wasting and diarrhoea. The organism is shed in the faeces, contaminates the environment, including the feathers of the bird, and further spread occurs by aerosol.

The number of cases reported annually to the Communicable Disease Surveillance Centre has steadily increased over the years from 100-200 in the late 1970's, to 400-600 in the late 1980's. The cause for this apparent increase has been debated, but is uncertain. It has been reported that in only some 20-30% of cases of psittacosis is a likely avian source identified, and this certainly is in accord with local experience. It is uncertain whether the remaining cases are due to unidentified contact with psittacine birds, eg visiting friends with parrots or pet shops, or having been infected from more mundane birds, eg pigeons. They may even reflect infection with mammalian *C. psittaci* described below. Certainly some cases are due to *C. pneumonia*, as one of the consultant paediatricians in Lancashire and South Cumbria can attest, and we now have all sera showing rising or elevated titres to chlamydia group antigen (CGA) by complement fixation test (CFT) retested at the Institute of Ophthalmology, London by immunofluorescence (IF) for antibody against the different chlamydia species or strains. Often, but not always, this can distinguish infection with *C. pneumonia* from that with *C. psittaci*. Sometimes elevated CFT titres are found which are unconfirmed by IF, leading to difficulties in interpretation and in assessing the significance for the patient's illness.

Although *C. psittaci* infect many species of animals, the only recognized animals which may transmit infections to humans are sheep, cattle and the cat. Sheep are the source of OEA, also known as enzootic abortion of ewes (EAE), and will be considered in the remainder of this review. Bovine chlamydial infection may cause pneumonia, enteritis, conjunctivitis, abortion, and a wide range of other manifestations in the cow. There are a few descriptions in the literature of apparent human infection with bovine chlamydia, including a fatal case of pneumonitis, but there are doubts about the certainty of diagnosis in some. Feline *C. psittaci* primarily causes a chronic conjunctivitis in cats. There have been a small number of reports of transmission to humans resulting in conjunctivitis, fever with hepatosplenomegaly, and endocarditis, but in each case once again there was perhaps some doubt as to diagnosis.

OVINE ENZOOTIC ABORTION IN SHEEP

Although ovine enzootic abortion in sheep was probably first recognized some 150 years ago, attention was first drawn to infection in the UK in 1950. A description of laboratory-acquired human infection followed in 1955,

although the patient suffered a psittacosis-like respiratory illness which may have been coincidental.

Chlamydial infection of pregnant ewes may result in abortion, stillbirth, prematurity or delivery of 'weak' lambs. Ovine strains of *C. psittaci* show a predilection for placental tissue with necrosis and haemorrhage. Usually the infection does not become evident until the last four weeks of gestation and if abortion occurs the foetus usually has no apparent abnormality. It is uncommon for the ewe itself to show any ill health. Surviving lambs are often of poor health and may suffer conjunctivitis. Many are latently infected and they themselves may have affected pregnancies in following years.

In an affected flock up to 30% of pregnant ewes may suffer an adverse outcome of pregnancy, so the financial implications for the farmer are apparent. OEA is the most common cause of abortion in sheep, accounting for perhaps 40-50% of fetal losses, and the numbers are steadily rising, even using relatively insensitive reporting procedures (Table 1) which probably grossly underestimate the scale of the problem.

Year	Great Britain	Lancashire and Cumbria
1975	184	1
1976	265	3
1977	214	1
1978	340	8
1979	407	9
1980	654	7
1981	901	6
1982	920	30
1983	1110	13
1984	1109	12
1985	1338	18
1986	1277	45
1987	1665	75
1988	1814	115
1989	1707	122
1990	1734	139

Table 1. Number of reports of ovine enzootic abortion in sheep (Central Veterinary Laboratory; personal communication)

The mode of transmission in sheep is of interest as asymptomatic enteric infection occurs, both of surviving lambs and infected ewes. Chlamydial infection is commonly introduced into a healthy flock by the introduction of sheep with such an asymptomatic enteric infection. Infected ewes remain asymptomatic until the following lambing season when the infection manifests itself with the adverse consequences for pregnancy. Further, and probably the most important, spread occurs from infected fetal membranes and uterine discharges which contaminate the lambing environment. Up to three-quarters of sheep in a flock may become infected. In some cases, if infected before the end of pregnancy, that pregnancy itself may suffer, but usually the presence of OEA in the flock does not become apparent until

the next lambing season. Because infection is so often inapparent and the problem within the flock has not yet appeared, it is easy to see how spread between flocks occurs.

Control can be attempted by antibiotic treatment of remaining pregnant ewes after diagnosis of the first case, blanket antibiotic therapy of a flock and segregation of aborting ewes.

Vaccines have been available for many years and are continuously being developed. Their use offers some protection, but often insufficient to prevent infection, particularly when levels of exposure are high as in intensively managed sheep.

OVINE ENZOOTIC ABORTION IN HUMANS

Reports of human infection due to OEA date from the 1950's, although for the early reports there was only circumstantial support. These included reports of febrile illness, pneumonia, and conjunctivitis. Since these early reports, and in the last 10 years or so, there have been few published human cases of OEA not involving the pregnant woman. One report of infection in a male described a flu-like illness only.⁽¹⁾ The possible benign nature of the infection in the non-pregnant person is well demonstrated by a series of eight employees producing an OEA vaccine from a newly-introduced strain. It is likely that all eight were infected during a short period and, although the OEA strain may be considered attenuated, the only symptoms noted were minor upper respiratory tract symptoms in six, and flu-like illness in two.⁽²⁾

There have now been a number of reports of chlamydial abortion due to OEA where there was laboratory evidence to support the diagnosis⁽³⁻¹²⁾. A remarkable feature of reports has been that almost all cases described are from the UK, many from Scotland. As OEA is a widespread disease of sheep one finds it difficult to comprehend why there have not been reports from other countries - we can hardly believe other authors and ourselves would have missed more than the occasional case in the literature.

Where available we have given details of many of the reported cases in Table 2. Characteristic features of these cases include the majority being between late 2nd trimester and middle 3rd trimester, the severity of the illness suffered by the mother, with one death, and the poor outcome for the fetus, with only one survivor. The patients usually present with a 2-7 day history of a febrile, 'flu-like' illness with headaches, neck, back and abdominal pain, and feeling generally unwell. This has progressively worsened to lead after a few days to a septicaemic-type illness with disseminated intravascular coagulation (DIC) and possible renal, hepatic and cardiac failure. In one case (case 7) pneumonia was present. Intensive care support has often been needed. Appropriate therapy, such as tetracycline, has led to improvement, but even then abortion has soon followed (case 1). In most cases improvement has only followed delivery of the fetus, whether spontaneously, by induction, or by caesarian section, although the one woman who died (case 3) did so after delivery, albeit very soon, and other cases (eg case 7) have worsened. In one case (case 2), although erythromycin therapy was started early, improvement did not occur until delivery. That delivery of the fetus is often but not always beneficial to recovery of the mother supports the findings in sheep that the main focus of infection with OEA is the placenta. The placenta may appear grossly normal, however, although some infarction may be apparent. Histological examination of the placenta usually shows a

Case (ref)	Gestation	Source/occupation	Diagnostic findings	Maternal illness/outcome	Fetal outcome
1(3)	6 months	Lived near farmland	Rising CF titre to CGA	Febrile, recovery	Abortion
2(4)	34 weeks	Farmer's wife, lambing	Rising CF titre to CGA	Febrile, DIC, recovery	Caesarean section, healthy baby
3(4)	36 weeks	Farmer's wife, lambing	Circumstantial	Febrile, DIC, death	Stillbirth
4(5)	28 weeks	Farmer's wife, lambing	Rising CF titre to CGA. IF rising titre	Flu-like illness, DIC, recovery	Stillbirth
5(5)	25 weeks	Veterinary surgeon. Autopsies of aborted ewes	Rising CF titre to CGA. IF rising titre	Febrile, DIC, recovery	Neonatal death
6(6)	28 weeks	Farmer's wife, lambing	Rising CF titre to CGA. IF rising titre. Ovine chlamydia in placenta/fetus	Febrile, DIC, recovery	Stillbirth
7(7)*	15 weeks	Sheep-farmer's wife, but denied sheep contact	Rising CF titre to CGA. Ovine chlamydia in placenta	Febrile, DIC, jaundice, recovery	Abortion
8(8)	29 weeks	Farmer's wife, lambing	Elevated CF titre to CGA	Febrile, DIC, recovery	Neonatal death after caesarean section
9(9)	26 weeks	Farmer's wife, but denied sheep contact	Falling CF titre to CGA	Febrile, DIC, recovery	Abortion
10(10)	14 weeks	Farmer's wife	Ovine chlamydia in fetus	Febrile, DIC, recovery	Abortion
11(11)	27 weeks	Farmer's wife, lambing	Rising CF titre to CGA. Ovine chlamydia in placenta	Febrile, DIC, recovery	Abortion
12(12)	19 weeks	Abattoir worker	Rising CF titre to CGA. IF rising titre. Ovine chlamydia in placenta	Febrile, DIC, recovery	Abortion

* Also had 'Q' fever and influenza A in preceding weeks

Table 2. Some reported cases of OEA in pregnancy

patchy inflammatory infiltrate. Chlamydia antigen has been detected in the cytoplasm of both trophoblastic and inflammatory cells, with *C. psittaci* having been isolated on occasion, and further identified as the ovine strain. Chlamydia has also been isolated from fetal liver and lung (case 6). In one case (case 5) a recurrent fever which responded to rifampicin suggested that a persistent infection had been established. There is no further evidence that persistent infection may occur, and some women described above have later had normal pregnancies with a good outcome.

Although most cases had recently had direct contact with lambing ewes, in some cases close contact was denied, suggesting that infection may have been transmitted by fomites, or even airborne. The correct diagnosis has usually not been suspected in the first few days of illness, and hence appropriate therapy with erythromycin or tetracycline was not initiated early. On occasions the unsuspected diagnosis was probably achieved retrospectively when the "viral screen"

showed a rising titre to chlamydial group antigen by the complement fixation test.

DIAGNOSIS

It is apparent that the first step in achieving correct diagnosis, and hence appropriate therapy, is a high index of suspicion. OEA should be considered in any pregnant woman from a farming community, particularly if she has had recent contact with lambs, who presents with a febrile or septicaemic-like illness. Specific diagnosis can be achieved, albeit often retrospectively, by examining acute and convalescent sera for complement-fixing antibody to the chlamydial group antigen ("psittacosis/LGV"), a test available from any diagnostic virology service. More specific diagnosis of ovine chlamydial infection may be achieved serologically by using immunofluorescent techniques. The most likely site to find the organism itself is the placenta,

and if delivery occurs, which is most likely, part of the placenta should be stored dry at +4°C for isolation, rather than all being fixed in formol-saline. Occasionally we are asked to test for prior exposure or 'immunity'. There is no available serology for such a purpose, and indeed in case 6 the failure to demonstrate specific IgM suggests a probable reinfection.

LOCAL STUDIES AND EPIDEMIOLOGY

The major problem with performing appropriate seroepidemiological studies to ascertain the frequency of infection in farmers is that current antibody assays cannot distinguish between antibodies to the many different *C. psittaci* strains, except possibly during an acute infection. Hence what surveys have been done have simply looked for antibodies to *C. psittaci* in general, and not specifically for past infection with the ovine strain. A study of farmers in Northern Ireland did suggest an increased prevalence of *C. psittaci* antibodies, although there were only retrospective controls for comparison.⁽¹³⁾ A study we performed in North-West England revealed no difference from non-farming controls, or between farmers who did or did not have contact with sheep.⁽¹⁴⁾ There was no difference in outcome of previous pregnancies for women from farms, compared with non-farming controls, although the numbers were small. Similarly there were no differences observed in antibody prevalence if the information was analysed according to various parameters of likely degree of contact with sheep, such as tending sickly lambs in the home, assisting at delivery of lambs and milking sheep. Another similar study was conducted in South Wales and Devon⁽¹⁵⁾ and this also showed no difference between antibody prevalence or of titres suggesting recent infection between those having contact with sheep known to have OEA and controls. In collaboration with a group in Hereford, and funded by the Health and Safety Executive, we are currently performing another study of exposure to zoonoses in farmers, and this includes *C. psittaci*.

On a national scale, the number of reports to the Communicable Disease Surveillance Centre of psittacosis steadily increased during the 1980's to about 500 per annum (personal communication; Communicable Disease Surveillance Centre). Of these, from 1976 to 1989, some 29 specifically noted contact with sheep, although many also had other possible exposures. In addition to these there were 8 cases of *C. psittaci*, presumptively ovine infection, in pregnant women, although there is little further detail for most, and a number are probably included in the table.

CONCLUSION

The reported cases of OEA present a number of questions that need addressing. How frequently are farmers infected? What are the manifestations of infection in the non-pregnant person – are we missing the diagnosis? What is the outcome of infection in the first and early second trimesters – are we missing abortions because they are not accompanied by a severe maternal illness? Does late pregnancy infection occur without severe maternal illness?

In a rural population, the possibility of OEA must be considered in the differential diagnosis of febrile illnesses and abortions, stillbirths or intrauterine death. Pregnant women must continue to be advised not to have contact with lambs, recently delivered ewes and ovine placentae, a message now being disseminated not only by the Archers and farming publications, but also in leaflets being distributed by the Department of Health.

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