Contagious agalactia of sheep and goats

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Summary: Contagious agalactia is a form of mycoplasmosis which is usually enzootic, and can be recognized clinically by the syndrome of mastitis, arthritis and keratitis. Formerly confined to the Mediterranean basin, it now occurs on every continent. Its course is usually chronic, but can be acute in certain local circumstances and with some strains of the causal organism.

Diagnosis can be performed in any laboratory which has the appropriate culture media. Identification of the three mycoplasmas responsible is relatively easy on the basis of cultural and biochemical characteristics, confirmed serologically. A clinical diagnosis within a herd can be confirmed by detecting serum antibodies by the complement fixation or ELISA techniques, which are also suitable for epidemiological surveys.

The only effective treatment is by certain antibiotics administered in adequate dosage for several days. The protective ability of inactivated vaccines is variable. Attenuated vaccines are to be preferred in countries which authorize their use.

Infected animals are the chief reservoir of the mycoplasmas, and hygienic precautions form a major part of eradication schemes, which can be successful only if there is concerted action within the affected region.

KEYWORDS: Agalactia - Diagnosis - Disease control - Epidemiology - Goat diseases - Mycoplasma agalactiae - Mycoplasmosis - Sheep diseases.

INTRODUCTION

Definition

Contagious agalactia of small ruminants is a transmissible mycoplasmosis of sheep and goats caused by Mycoplasma agalactiae. The three principal signs of mastitis, arthritis and keratitis constitute the contagious agalactia syndrome. Two other mycoplasmas may also be responsible for this syndrome in goats: Mycoplasma mycoides subspecies mycoides of the caprine biotype (large colony form) and Mycoplasma capricolum (12, 60, 61).

Economic importance of the disease

The economic importance of the typical enzootic form is considerable within affected regions (11). The main target organ of the mycoplasma is the mammary gland, and the infection within a flock is manifested by a fall in milk production (in the case of dairy breeds) which may be considerable, and the loss of many young animals in the meat breeds.

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Control measures are far from being efficacious, and breeders have to become accustomed to living with the disease. The morbidity rate varies from year to year, but the consequences for infected animals are serious.

The economic future of affected animals is compromised, and often it is best to cull them prematurely. Productivity and profitability of such flocks remain poor, particularly in zones where traditional husbandry is practised, or where financial equilibrium depends on a period of transhumance in order to utilize alpine pastures. This unfortunately involves mixing flocks, which encourages the spread of infection and perpetuation of the enzootic state.

**HISTORY**

Contagious agalactia has been known for a long time in Europe, having been first described in Italy (under the name “stornarella”) by Metaxa in 1816.

Using this fairly precise definition of the characteristic signs, Mara reproduced the disease by inoculation in 1841.

Its contagious nature was demonstrated in Apulia (Italy) by Dinella and Provinziano in 1862, who observed that animals became infected after grazing a pasture previously occupied by an infected flock (“mal del sito”: disease of the place).

Its present name is attributable to Brusasco, who published a comprehensive monograph in 1871.

At the beginning of this century some discoveries were made about the nature of the causal agent, when Celli and Blasi showed that it was filtrable.

The pathogenesis, aetiology and clinical course were studied by Carré between 1912 and 1921, who concluded that “mal de Lure” was a pyobacillosis secondary to agalactia.

In 1923 Bridre and Donatien isolated, cultured and described the specific agent, and demonstrated the therapeutic effect of Stovarsol sodium (10).

An oedematous disease of goats in Greece was identified by Debonera in 1937 as an atypical, severe form of contagious agalactia, the aetiology of which was confirmed. Recently it has been shown that a mycoplasma very similar to *M. mycoides* subsp. *capri* is responsible (11).

The first vaccine was produced by Zavagli in 1952. Since then numerous inactivated vaccines and attenuated strains have been developed.

**CLINICAL FEATURES**

**Mammary localization**

This is the commonest localization of the agalactia syndrome, and may be the only sign in a lactating animal.

The first sign varies from a fall in milk yield to complete loss of milk. The milk may look normal, but often becomes thick or even a yellowish fluid, with milk clots
which may obstruct the teat duct. At first the pH of the milk becomes slightly alkaline for some days, and the leukocyte count increases.

The three causal mycoplasmas can be isolated from the milk when mastitis is present, and they may also be present in large numbers in apparently normal milk. The catarrhal or parenchymatous mastitis is usually bilateral. The udder becomes hot, swollen and tender. Later it undergoes atrophy, with lumps of indurated tissue.

**Localization in joints**

This form, which is seen often in affected flocks, ranges from a simple stiffness of limb joints to severe lameness which may prevent the animal from standing.

Joints affected most often are the tarsus, carpus and hock. The joint is hot and swollen, with accumulation of synovial fluid. The lesion may be confined to simple synovitis without involvement of the cartilage, arthritis being present only in severe cases (42, 50).

**Ocular localization**

This rarer form commences with conjunctivitis and congestion, lacrimation and photophobia, followed by vascularization of the cornea, inflammatory foci and parenchymatous keratitis; severe cases progress to panophthalmitis with loss of the eye.

Most cases recover completely within a month. The lesions are unilateral or bilateral, and are most severe in unweaned young (61).

**Pulmonary localization**

This is often benign in adults, and may pass unobserved in the presence of other major symptoms. It may develop into bronchopneumonia, in which case the causal agent can be easily recovered from the lungs after death; the lungs have necrotic lesions and there is fibrinous pleurisy (3, 22).

In young animals pneumonia may be the sole external sign, and severe cases may prove fatal (53, 34, 25).

**General signs**

The first sign of infection, some days before the localized manifestations appear, is general malaise. The animal is weak, with more or less pronounced hyperthermia, inappetence and a slightly alkaline reaction of the blood, signalling the septicaemia which precedes implantation of the causal agent at sites of localization (46, 60).

**Other disorders**

According to the degree of infection, abortion may take place towards the end of gestation. Severe cases may have enteritis in addition to the other symptoms, or fibrinous pericarditis or disorders of the central nervous system. Pustular vesicles may be visible on parts of the skin not covered by hair. Males may develop posthitis and balanitis. Some cases of granular vulvovaginitis have been described. The uterus or the entire genital tract may become infected (27, 28, 47). In some Asian countries the ocular form may be the sole visible lesion.
Complications occur when the body is invaded by other bacteria. "Sparta oedema" is a severe, atypical form in which other symptoms are absent (11, 36). One superinfection is pleuropneumonia. Bacteria are also found in subcutaneous abscesses (4).

EPIDEMIOLOGY

DESCRIPTIVE EPIDEMIOLOGY

Geographical distribution (1, 4, 11, 14, 16, 26, 35, 40, 44, 51)

Contagious agalactia has long been observed in most Mediterranean countries, and no continent is presently free of the disease. In some countries (Australia, Sweden, Federal Republic of Germany, Great Britain, Canada) there are only sporadic cases, or there may have been just a single outbreak which has been controlled successfully (6, 7, 11, 27, 43).

The endemic status may extend over large areas in countries where effective control measures are considered uneconomic (too many animals affected, inadequate disease control measures, mixing of flocks at alpine grazing, etc.). In all such regions, agalactia has a long history, with periods of low intensity, or even prolonged absences on occasion (61).

When the disease is confined to a local breed, members of which are seldom taken to other regions, it is truly endemic and rarely extends beyond the area of origin.

Evolution

Acute form

This is rarer than the chronic form, and is found in flocks recently infected (through the introduction of infected carriers), before there has been opportunity for immunity to develop.

General malaise is prominent, corresponding to the septicaemic stage. In less than a week the animals are affected by hyperthermia (over 41°C), prostration and inappetence. Pregnant females near full term may abort. Some animals may die without showing any other sign, but the usual course is for severe mastitis to develop, followed by arthritis and unilateral or bilateral keratitis.

The flock is severely affected, with a mortality rate among adults of 10-15%, and higher mortality among unweaned young. After a few weeks of illness the remaining animals will recover, but with sequelae, particularly mastitis and a milk yield which is much below the seasonal average.

Chronic form

This form occurs in regions where the disease has been endemic for a long time. The general illness is less severe and may pass unnoticed, while the localized forms are dominant. The symptoms develop progressively, but at a slower rate.

Only part of the flock is affected. In mild cases the syndrome may be incomplete. However, more or less pronounced agalactia and mastitis are the rule. Animals which have recovered from a previous infection are more or less protected from reinfection.
Importance

The disease is generally enzootic. Under conditions of traditional husbandry, its seasonal character becomes evident at the time of parturition. Once introduced into a region, the causal agent persists for a long time, with flare-ups interspersed with prolonged periods of attenuation or even latency.

Among flocks in frequent contact with each other (as on alpine pastures or common grazing), the disease occurs regularly, and although the mortality rate is low, morbidity is by no means negligible and economic losses may be severe.

ANALYTICAL EPIDEMIOLOGY

Within an infected flock contagion occurs directly by contact between animals. Contaminated milk forms an ideal culture medium for the causal agent. The young become infected directly at sucking, and adults by means of the milker’s hands or by bedding contaminated by infected milk; the bedding may provide rich cultures of mycoplasmas.

The lungs are susceptible to infection, particularly in young animals, and transmission by the respiratory route is highly likely.

Transmission by the digestive route seems to be important. Animals can become infected by ingesting small amounts of the bacteria (e.g. from a communal water trough), and infection may remain dormant for months until conditions favour its development (as at the start of lactation).

The introduction of a carrier animal into a healthy flock results in illness among non-immune animals. The causal agent may also be spread by feed and footwear.

The main reservoir of mycoplasmas is the infected animal, in which the bacteria can persist after clinical recovery from one year to another. Such animals are an inapparent source of infection. Females are most susceptible during lactation, and the appearance of symptoms at this time may be no more than an activation of latent infection (30). Other species of animals can serve as reservoir hosts (33, 39).

It has been shown recently that the external ear can harbour various mycoplasmas, including those responsible for agalactia. Certain parasites such as mites could serve as a reservoir host and vector (13, 15, 52).

The environment plays a definite role. Although the mycoplasmas are said to be quite fragile, they can survive for three years under anaerobic conditions at 37°C, and for months at lower temperatures (10, 20). Dung and compacted soil can harbour the bacteria for a long time, justifying the Italian term “mal del sito” (disease of the place) used in the last century.

However, transmission from an infected locality is inexplicably haphazard (61), for under identical conditions it may take place regularly in some cases, and not at all in others.

The haphazard nature of infection also applies to experimental infection, because only half of the infected, lactating females may develop clinical illness, unless massive septicaemia is induced.
DIAGNOSIS

CLINICAL DIAGNOSIS

This is easy when a flock is severely affected. The three major symptoms are present within the flock, sometimes in the same individual.

The mild form is difficult to detect, for the localized forms may not be present in the flock. Sometimes only one localization is manifest, particularly the mammary form. Isolated cases of pulmonary infection may be seen among the young animals.

An acute course can also be misleading in the presence of septicaemia without specific local signs. General illness with hyperthermia should be treated as suspected agalactia. However, once this occurs it is often too late to avoid widespread infection of the flock, and losses may occur before the characteristic signs of the disease appear.

DIFFERENTIAL DIAGNOSIS

The three mycoplasmas responsible produce an identical illness and can be differentiated only in the laboratory. However, the course is more likely to be chronic with *M. agalactiae* while, among goats, the other two mycoplasmas (*M. mycoides* subsp. *mycoides* caprine biotype and *M. capricolum*) usually produce acute or hyperacute infection, often with pulmonary complications.

It is possible to confuse the disease, particularly in young animals, with that caused by the pneumotropic mycoplasmas (*M. arginini* and *M. ovipneumoniae*).

Superinfection with *Pasteurella* species or a virus may complicate diagnosis. In such cases it is important to establish exactly which pathogens are present in order to provide appropriate antibiotic therapy. Laboratory diagnosis will then be capable of elucidating the aetiology.

LABORATORY DIAGNOSIS

This provides the only means of verifying the nature of the pathogen.

Microbiological diagnosis

The pathogen is usually isolated (and identified) from milk from a case of mastitis or from synovial fluid. Isolation can also be accomplished from an ocular or nasal swab, provided that there is no superinfection.

At post-mortem examination the mycoplasmas can be isolated from udder tissue, retromammary lymph nodes, joints, lungs and, when septicaemia is present, from various other organs and lymph nodes.

Samples must be submitted rapidly and in a cooled state. They can be stored for a few days at +4°C, and for many months at -25°C. Addition of penicillin is recommended for samples not taken under sterile conditions.

(a) Isolation

Various culture media are suitable, with more or less enrichment. The agalactia mycoplasmas grow well and are not difficult to isolate by using standard media.
Recommended media include the “medium B” of Freundt et al. (21) and “medium 45” of Fallon et al. (19). Another is the Oxoid ready-to-use medium, which gives rapid growth:

- base: 80% (to be autoclaved)
- G supplement: 20% (pre-sterilized)

The supplement includes thallium acetate, but it is necessary to add penicillin.

It is best to seed a liquid medium first, followed by an agar gel plate. Five to ten drops of milk or synovial fluid, or fluid aspirated from lung tissue by sterile syringe, are added. Two or three dilutions are made in the culture media, which are incubated at 37°C.

The contents of the culture tube should become cloudy after 1-3 days. If not, blind subcultures are made three times in succession after three or four days before assessing the result as negative. If the tubes are cloudy from the start (after milk has been added), subcultures should be made systematically every two or three days.

For greater certainty of a flock diagnosis by isolation, it is advisable to take several samples (such as milk), for only a few animals may be actually excreting the pathogen.

(b) Identification

In general it is difficult to identify mycoplasmas, because this requires a range of biochemical and serological tests, some of them lengthy and delicate (18, 21). However, the three mycoplasmas responsible for agalactia can be identified readily by their cultural and biochemical characteristics, taken as a whole. Serological testing is useful to confirm this identification if the necessary immune sera are available.

1. Cultural characteristics

In liquid media the caprine biotype of subspecies mycoides and capricolum are among the mycoplasmas which grow the fastest (in one or two days), producing the most intense turbidity. In this case the presence of one of the two can be suspected, while their presence can be discounted if the growth rate is slower (three to five days) and the turbidity less intense, providing the biochemical properties are in agreement.

The growth rate of M. agalactiae is a little less rapid (two or three days) and the turbidity obtained rather less pronounced, at least in the early stage. By five to ten days, crystals start to form and they give a final turbidity similar to that of the other strains. These crystals are characteristic of M. agalactiae (and a few other species); they are very refringent and show up brilliantly under phase-contrast microscopy (objective x 40, phase 2), while the mycoplasmas themselves appear as black dots. They are round with a scalloped edge, while the crystals of the culture media are angular with smooth edges.

On agar medium M. mycoides is unique among mycoplasmas in its formation of large colonies (1-2 mm diameter) when these are well separated. This distinguishes them particularly from the biotype of M. mycoides which causes contagious bovine pleuropneumonia. This feature is not always reliable, for sometimes the size of colonies remains normal (57). It is possible to distinguish the two biotypes on certain growth media (54).
Colonies of *M. capricolum* are of normal size and appear within a few days.

Colonies of *M. agalactiae* produce soaps which spread out in the form of a film and spots, equivalent to the rounded crystals found in liquid media. The surface of the agar assumes a characteristic satin appearance. However, this phenomenon is not seen until several days, or even a week or more, have elapsed, and it may not be very pronounced with certain strains.

### 2. Biochemical characteristics (21)

Apart from the digitonin test which distinguishes *Acholeplasma* from *Mycoplasma*, four other tests are used: catabolism of glucose and arginine, phosphatase activity and digestion of coagulated horse serum. Table I summarizes the responses of the three mycoplasmas responsible for agalactia to these tests, and to the triphenyl-tetrazolium chloride (TTC) test, together with the responses of *M. ovipneumoniae* and *M. arginini*, which can be found in the lungs of small ruminants.

**TABLE I**

**Biochemical characteristics of the principal types of mycoplasma pathogenic for sheep and goats**

<table>
<thead>
<tr>
<th></th>
<th>Arginine</th>
<th>Glucose</th>
<th>TTC*</th>
<th>Serum coagulation</th>
<th>Phosphatase</th>
<th>Films or crystals</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>M. agalactiae</em></td>
<td></td>
<td></td>
<td>+/-</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><em>M. mycoides</em></td>
<td></td>
<td></td>
<td>+/-</td>
<td></td>
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<tr>
<td><em>mycoides</em></td>
<td></td>
<td></td>
<td>+/-</td>
<td></td>
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<tr>
<td><em>caprine biotype</em></td>
<td></td>
<td></td>
<td>+/-</td>
<td></td>
<td></td>
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<tr>
<td><em>M. capricolum</em></td>
<td></td>
<td></td>
<td>+/-</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><em>M. ovipneumoniae</em></td>
<td></td>
<td></td>
<td>+/-</td>
<td></td>
<td></td>
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<tr>
<td><em>M. arginini</em></td>
<td></td>
<td></td>
<td>+/-</td>
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<td></td>
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</tr>
</tbody>
</table>

* TTC = triphenyltetrazolium chloride.

+/- (TTC) = aerobiosis/anaerobiosis.

v = variable.

These characteristics are quite clear-cut. However, they have to be interpreted as a whole. In the case of arginine and glucose there should also be one tube containing phenol red and arginine (or glucose) not inoculated, and an inoculated tube containing phenol red and neither arginine nor glucose. It then becomes easier to distinguish the difference in colour between negative and positive results.

The culture film does not appear for several days. With a little practice it is easy to identify the crystals by phase-contrast microscopy. Digestion of coagulated serum may not be very pronounced. The phosphatase test often gives the best results in liquid media. These characteristics do not appear until after several days or even a week of culture. A fluorescence technique has been proposed to provide rapid results within an hour (9).
Identification is practically certain if these cultural and biochemical characteristics are supported by the typical location (in milk or synovial fluid) and by the clinical picture (if available).

3. Serological tests (21)

The clear-cut specificity of these tests enables the identity of an isolate to be confirmed, if it is still in doubt.

**Growth inhibition** on agar is easy to perform, but requires considerable amounts of antisera. There is usually a quite clear zone of inhibition in the case of agalactia mycoplasmas, but if the growth of colonies is exceptionally rapid the zone becomes blurred in outline and smaller. For this reason it is advisable to permit an inhibitory serum to diffuse away from the disk or well for several hours at room temperature before placing it in the incubator.

The concentration of the inoculum should be adjusted, because if the colonies are too close together the zone is narrowed and the result is difficult to read; if they are too far apart the limit is no longer visible. An optimum density is about $10^4 - 10^5$ organisms per ml. It is advisable to set up 3 plates inoculated with densities above, at and below this figure.

Other important factors are the composition of the medium, incubation temperature and amount of antiserum. The test becomes all the more reproducible if these factors are accurately controlled.

The technique of wells punched in agar uses less antiserum than the disk technique, and provides wider zones of inhibition. To increase the sensitivity of the technique further, conditions for suboptimal growth can be selected, for example, by reducing the incubation temperature and decreasing the serum content of the medium, or even by omitting yeast extract in the case of rapidly-growing strains.

There may be variation in the zone of inhibition between strains of the same species, probably due to antigenic variation. In such a case a mixture of immune sera prepared against several strains can be employed.

The **inhibition of metabolism** test can be considered as growth inhibition in liquid medium. However, this test is more delicate to carry out, and its use is confined to taxonomic studies in specialist laboratories.

Epi-immunofluorescence is just as specific as the above tests, and it uses very little antiserum. It is performed on colonies growing on agar.

Impression smears of the colonies are fixed on a slide in hot water, or a block of agar supporting unfixed colonies is placed directly onto the slide. Reaction with antiserum then takes place, acting against crude membrane proteins which have not been denatured by heat. The technique gives good results, even though the process takes rather longer.

Whether the direct technique with fluorescent rabbit serum or the indirect technique with an anti-rabbit fluorescent conjugate is used, it is necessary to use diluted reagents which have been calibrated beforehand. Diluted conjugate cannot be kept for more than a week, but the antiserum can be kept for at least a month, and can be frozen and thawed repeatedly.
The colonies used are small and therefore young, growing from an inoculum suitable for providing well separated colonies, as in growth inhibition (about $10^5$ organisms per ml). To avoid non-specific fluorescence it is best to use a medium poor in serum, if possible. Control tests of the antiserum with specific and non-specific colonies should remove all doubt. A single conjugate is required, and higher dilutions of antiserum can be used.

This technique is rapid (two hours), economical with antiserum, and easy to interpret and perform. Therefore it is the best way of identifying mycoplasmas.

An indirect immunoperoxidase technique has been tried, in comparison with immunofluorescence (41).

**Serological diagnosis**

This done for two reasons. Firstly, it can confirm a clinical diagnosis when it has not been possible to isolate mycoplasmas. High antibody titres are present in animals at the end of illness or recently recovered, and these fall gradually over two or three months. This type of diagnosis is valid only if a sufficient number of samples is tested — at least 10% of the flock, or a minimum of 10-20 serum samples.

Secondly, serological testing shows if a flock is free from infection or latently infected. The same stipulation about numbers applies, particularly if antibody titres are low and close to the threshold limit.

The complement fixation test (38) is used widely and benefits from many years of experience in many laboratories. However, it must be performed with great care, and there may be considerable variation in the results. It gives good results only in the hands of experienced personnel.

Enzyme-linked immunosorbent assay or ELISA (31, 45) is more recent and less widely used so far. Its crude results (expressed in terms of optical density) are also subject to variation but the more refined results (expressed in units) show a remarkable stability, provided of course that a reference serum is used for each test. It is a reliable and simple technique which can be performed in any laboratory equipped with a plate reading device and supplied with reagents already standardized.

At present this technique is used by only a few specialist laboratories. However, its principle of a single dilution makes it suitable for epidemiological studies, thanks to the large number of samples which can be tested at each session. Moreover, it is more sensitive than complement fixation, and is capable of detecting the low antibody titres found in latent infections.

Whenever possible, it is best to use ELISA, particularly for large-scale testing, falling back on complement fixation if ELISA is unavailable, bearing in mind that a negative result, even in an entire flock, does not exclude the presence of the agalactia mycoplasmas.

Other tests are capable of providing additional information, such as haemagglutination, growth inhibition, immunofluorescence and immunodiffusion. When such a range of tests is used, it is found that no animal of an infected flock is positive to all the tests, and many are positive to just one or two tests (32). Many serum samples remain completely negative.
As a consequence, the diagnostic value of testing is a function of the number of samples tested, and a negative result can never be taken as evidence of freedom from infection.

**TREATMENT AND PROPHYLAXIS**

**Treatment**

The antibiotics normally used against bacteria are ineffective. Others, such as the macrolides and their derivatives, and the tetracyclines, depend for their action on the dose employed (8, 23, 24, 37, 48, 49). Other drugs like zinc sulphate (56) and arsenicals (Stovarsol) are also effective.

Treatment must be applied systematically, as otherwise the results may prove to be disappointing. A badly conducted treatment, even with efficacious antibiotics, favours the development of resistant pathogens and jeopardises the result of future treatment.

To be effective, treatment must be given early, at the first clinical signs, and kept up for at least three to five days. These two requirements often make the treatment uneconomic for use in sheep and goats, and it is easy to understand the reluctance of an owner to agree to the treatment of a disease which will regress spontaneously once it becomes chronic.

Badly applied treatment (inadequate duration or dosage, treatment of only part of a flock, an ineffective antibiotic) has the undesirable effect of creating carrier animals. In any case, it is by no means certain that even suitable treatment can eliminate all the pathogens, some of which may remain in joints or lymph nodes, leading to recurrence when conditions are suitable.

**Immunoprophylaxis**

Most of the inactivated vaccines have a very limited efficacy under experimental conditions. Under field conditions the mode of transmission of the disease may allow sufficient time for vaccinated animals to respond satisfactorily, but field trials may not give useful results if the flock has not been divided into comparable groups. An endemic develops over a period of years, and it is difficult to evaluate the long-term effectiveness of a vaccine. However, certain inactivated vaccines seem to have shown their worth, at least on a small scale, and in particular against the caprine biotype of *M. mycoides* (5). The route of inoculation, dose and revaccination are important factors.

Attenuated vaccines provide better protection (2, 11, 59) but carry the potential risk of resumption of virulence. The vaccine may protect the animal against clinical signs of the disease, but it will not prevent subsequent establishment of infection by a virulent strain. Thus an adequately vaccinated flock can be allowed to mix with infected flocks without much risk, but they will probably become inapparent carriers of the pathogen, since a lactating animal, for example, may excrete virulent mycoplasmas in its milk without mastitis being present.

Consequently, the use of such a vaccine should be accompanied by certain precautions. Vaccination must be avoided during lactation, for some strains can
produce a temporary fall in milk yield. The recommended dose must be adhered to, for an excessive dose can produce mastitis (11), while an inadequate dose is likely to be ineffective (2). It is advisable to confine vaccination to an infected area, because of the risk of resumption of virulence of the vaccine strain. Vaccination should preferably form part of a local or regional programme for the control of agalactia, so that all flocks which may be mixed later, e.g. during summer grazing, are vaccinated simultaneously. Revaccination must be planned to take account of the duration of immunity conferred, as well as of additions to the flock. Antibiotic treatment should be avoided after vaccination, because the antibiotic could destroy the delicate attenuated strain (58).

Hygienic precautions

(a) At the flock level

Sick animals must be segregated from the rest of the flock, or even killed if severely affected. Handicapped animals should be culled. The premises and contaminated materials are disinfected and kept empty of animals for at least a month, before the introduction of healthy animals. Animals coming from a suspect area are to be tested and placed in quarantine. A negative serological test does not, however, exclude the presence of the pathogen beyond doubt. A healthy carrier may pass undetected because it will have very low titres of circulating antibody in the absence of infection.

At the time of parturition, if there is a risk that the pathogen will be transmitted to the newborn by milk it is possible to heat the colostrum to 56°C for an hour in order to kill the mycoplasmas without destroying the protective antibodies. Subsequently the young can be fed pasteurised milk. If this solution is too costly, those females giving healthy milk are retained, while the others are culled (17).

(b) At the regional level

It is evident that concerted action, voluntary or imposed, is essential. In an endemic zone transmission occurs mainly on alpine pastures when flocks intermingle. To avoid introducing infected animals it is necessary to screen all the flocks serologically before transhumance, and to ban those which contain one or more positive animals.

In zones where sporadic cases occur, there should be surveillance of all commercial transactions. In the absence of legislation, there should be serological testing not only of purchased animals but also of a part or the whole of the flock of origin. This may prove to be difficult, and will increase the purchase price.

(c) At the international level

In the case of trade between countries, the International Animal Health (Zoo-Sanitary) Code, 5th Edition, recommends the following precautions for contagious agalactia (Article 3.3.3.1.):

"Veterinary Administrations of importing countries should require, for sheep and goats, the presentation of an international zoo-sanitary certificate attesting that the animals:

1) showed no sign of contagious agalactica on the day of shipment;
2) were kept since birth or for the six months prior to shipment in an establishment where no case of contagious agalactia was officially reported during that period;  
3) were kept in a quarantine station for the twenty-one days prior to shipment."

**REFERENCES**

(see p. 694)