

Special Article – Bacterial Diseases

Contagious Agalactia: Economic Losses and Good Practice

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Introduction

Contagious agalactia (CA), a disease of dairy sheep and goats mainly caused by *Mycoplasma agalactiae*, is known to have been present in Europe for over 200 years (Nicholas et al 1998). While it can present as a mild disease in small ruminants CA has proven difficult to eradicate as it may persist on farms contaminating successive flocks. The disease is first noticed when milk production falls usually a few days after the introduction of healthy carriers or from mixing with affected herds at pasture, markets or water sources. Milk becomes abnormal in appearance, mastitic then production ceases in one or both udders, often permanently. Keratoconjunctivitis and arthritis are chronic sequelae, particularly severe in the young preventing them from keeping up with the rest of the group during transhumance and other animal movements. CA is found wherever sheep and goats are kept but concentrated in countries surrounding the Mediterranean and western Asia, especially in Iran and Mongolia where large numbers of outbreaks are reported [1].

Unusually for a World Association for Animal Health (OIE)-listed disease four agents, all mycoplasmas, are listed as causing a clinically indistinguishable syndrome although *M. agalactiae* accounts for more than 80% of outbreaks; the other three pathogens, *M. mycoides* subsp. *capri*, *M. capricolum* subsp. *capricolum* and *M. putrefaciens* are more often found in goats. There are indications that the disease is spreading in Europe with increase numbers of cases seen in France and new outbreaks in Corsica [2].

Economic Impact

The economic costs of CA as a result of deaths, treatment, lowered milk production, spoiled products, abortions and animal welfare problems are not widely known. Previously the impact of the disease was thought to be most severely felt by farmers using traditional husbandry for producing milk products on a small scale essentially destroying their livelihoods [2]. However the disease probably also has a major impact on the larger commercial farms [3]. Made the first attempts at estimating the economic losses of acute disease suffered in Greece between 1997-1994 using official data. The losses,

made up of milk reduction, abortions, neonatal deaths and dead animals, were estimated at 24.5 million euros per year. However, the author stated that these losses were almost certainly under estimated because the compulsory reporting of the disease in Greece leads to severe restrictions resulting in farmers often not reporting their affected flocks. Furthermore, the impact of the subacute or chronic disease, which causes physical weakness and clinical complications, is very hard to measure. Other figures not taken into account are the significant costs of vaccination and veterinary costs.

More recently, we studied the losses from two different farm types in Sicily: A large commercial farm of mixed small ruminants and smaller family farm. The first farm was located in the Enna district and comprised over 1000 sheep and goats. Milk production suddenly dropped from 650 to only 100litres/day in October 2015. Every day of the outbreak 10-15 animals developed characteristic clinical signs of CA. The course of the infection stopped in January 2016 when all animals entered the dry period following vaccination with an inactivated CA vaccine on two occasions. The disease was found to have arrived on the farm through a group of 120 apparently healthy Etna goats in March 2015. Those goats were newly lactating animals without any unusual signs until the new parturition season the previous July when 18 goats delivered weak kids and an unexpected drop in milk production. As is normal practice, the goats had not been screened for CA before introduction to the farm. After this, clinical signs began to develop in the goats and in September, CA spread eventually to 30% of the 1000 susceptible ewes.

Following notification of the disease, costs incurred included: Slaughtering of 200 sick sheep and all 240 goats; administration of a full course of commercial autogenous vaccine according to manufacturer's recommendations to all remaining animals; and purchasing of replacement animals and milk from other farmers to maintain the dairy business. Although the disease appears to have been controlled on this farm the cost of the disease was estimated at over 100,000 euros to the farmer (Table 1).

The second farm located in Palermo District and smaller than the previous one consisted of only 200 sheep and goats. The outbreak was confirmed on May 2016 when milking production dropped 27% down from 150 to only 110 litres/day. Twenty ewes were reported as showing clear signs of CA. The clinical course of the infection stopped in June 2016 when all animals, after a single vaccination of inactivated CA vaccine, became dry. Surprisingly there were no other losses probably because the disease developed on the farm around the time of the dry period (from May to June 2016); the pathogen consequently did not have the opportunity to infect all ewes during the period of lactation. The disease incursion on this farm was on a smaller scale, occurring just prior to the end of the lactation period. To help control the disease, 20 sick sheep and 15 goats were culled. The purchasing of replacement lactating animals and the use of vaccination to control

Table 1: Economic losses caused by contagious agalactia on a large commercial farm of over 1000 small ruminants.

Item	Number	Cost (Euro)
Sheep lost	200	26,000
Goats lost	240	50,000
Lamb and kids affected	400	20,000
Cost of extra milk	400 litres	25,000
Vaccine	30 vials	2,550
TOTAL		approx. 127,550

Table 2: Economic losses caused by contagious agalactia on small family farm of 200 small ruminants.

Item	Number	Cost (Euro)
Sheep lost	20	2600
Goats lost	15	1950
Lamb and kids	1-2	scant
Losses of milk	40 litre	1680
Vaccine	9 vials	370
Total		approx. 6600

the disease meant that the farmer incurred losses of several thousand euros (Table 2).

As can be seen the loss of animals, dairy production, and the additional expenditure on disease control and restocking, means that the economic costs of CA disease incursions on Sicilian small ruminant farms incurred by individual farmers are substantial. Both farms will continue to vaccinate for 3-4 years in order to reduce the pathogen burden and clinical disease in the flocks and, ultimately protect the new stock of lactating ewes, which are very susceptible to the infection. The additional vaccine will add to the costs of control. Extrapolated over the whole of Sicily with almost 8,700 farms of which we estimate that 6% are affected -which is probably an under estimate as many are chronically affected so difficult to identify- this represent a major burden to the local economy.

Good Practice

The main impediments to successful control of CA are a lack of awareness and agreement internationally on the way forward. France favours culling of affected flocks while Italy, Spain and Greece use a mixture of antimicrobials and vaccination in their endemically affected areas [2]. Recent in vitro data has shown that most antibiotics are still effective against *M. agalactiae* which is in sharp contrast with the closely related pathogen of cattle, *Mycoplasma bovis*, reflecting the industrial scale of most cattle production where, because of wide-spread use, virtually all classes of antimicrobial agents are poorly effective [4]. However, the actual experience of antibiotic usage on small ruminant farms is much less satisfactory and their use, while bringing about a quick clinical improvement, leaves long-term shedders contaminating the environment and posing risks to susceptible animals as well posing a small risk of antimicrobial resistance.

Vaccination also leaves a lot to be desired. The majority in use today are formalin-inactivated whole cell vaccines, containing *M. agalactiae* and one or more of the other causative mycoplasmas, with limited

or no published efficacy. One inactivated vaccine could not protect sheep from natural challenge despite three annual vaccinations over the previous three years [5]. More recently in a small trial no potency was evident in a similar commercial product following contact challenge [6]. Interestingly a live attenuated vaccine, used successfully in Turkey for many decades, was safe and protective. While larger trials on commercial products are necessary, consideration should be given to using live vaccines (which are presently not allowed in Europe) in endemically affected areas. The development of DNA vaccines or recombinant vaccines have been reported but have not yet been tried in the field. Sadly based on developments in other areas of animal disease, there is little evidence that these innovative products will greatly improve the health of small ruminants affected with CA.

Despite its endemicity confirmed by the massive sales of vaccines and antibiotics directed at mycoplasma infections, mostly CA, the number of outbreaks reported officially in Southern Italy is remarkably low. Only handfuls of outbreaks were reported between 2012 to the present day. Consequently the present numbers of reported outbreaks represent a large under estimate. The disease itself is not a zoonosis and relatively easy to control as it is only spread by direct contact or via contamination by the hands of milkers or associated dairy equipment; in addition the environment does not play much of a role in the epidemiology particularly as the pathogen is sensitive to commonly used disinfectants. Similarly vectors, particularly blood suckling parasites are not thought to be involved in transmission of CA but have not yet been fully investigated.

Simple improvements in biosafety on the farm are of course necessary but this requires, initially, an education programme for farmers. As discussed above antibiotics are mostly effective and annual vaccination with approved vaccines can hold the disease in check. Unfortunately, the inability to control CA in some parts of southern Europe is largely the result of unnecessarily strict local veterinary legislation which discourages farmers and veterinarians from reporting outbreaks. The prohibition of selling milk and delays in lifting restrictions can have a serious impact on the income of these small farmers. These restrictions, like the declaration of infected area which can cover a 3km area in Italy often involving other adjoining farms which will suffer the same restrictions, are more appropriate to more serious diseases like sheep pox and foot and mouth disease. The result of these restrictions is to discourage the notification of outbreaks by farmers and private veterinarians as can be seen in the under reporting in official statistics.

More recently, the introduction of EU regulation 2016/429 complements local legislation but also reduces the amount of intervention. Worryingly, however, there are proposals that some traditionally notifiable diseases like CA and enterotoxemia of sheep and goats will be removed from new EU disease listing process with control being devolved, presumably, the national or even local level. This apparent downgrading of CA's importance may badly affect international collaboration on control across borders and make this disease a less likely area for research funding.

Biosafety measures to be taken on the farm must be sufficiently flexible, appropriate to the type of production and the species concerned, must also take into account local circumstances, and crucially must be shared with the competent authorities. Moreover,

in the light of a policy of prevention of communicable diseases, the EU encourages the development of local guidelines for good practices and/or special rules for diseases considered “less dangerous” like CA but which still have large local economic impact. It is therefore the duty of responsible bodies to provide veterinarians and field operators, with guidelines or good practices that, on the one hand respect the existing regulations, and on the other, take into account the level of risk and the epidemiological factors of the area involved.

We propose here that whenever an outbreak is confirmed the competent authority and owner should be informed and this properly recorded. Susceptible animals should be identified and animal movements banned from leaving and entering the infected farm/holding or if the area is difficult to define, then all land within 1km surrounding the affected farm. The culling of infected animals should be encouraged at a slaughterhouse following normal sanitary arrangements or quarantined. Milk from affected animals should be prohibited from purchase or heat-treated on the premises if destined for food animals. Milk from unaffected animals should only be used if permission is granted by the competent authority. All forms of transport used for the animals, shelters, resting areas, milking areas, milk storage areas, tools and utensils with particular reference to those destined to come into contact with milk should be disinfected following standard procedures using authorised products.

Infected and suspected mastitic animals on the affected farm should be isolated immediately in a quarantine area sufficient to prevent contact with other animals. Treatment with the most appropriate antibiotic should be carried out under the instructions of a veterinary surgeon. In addition vaccination of the entire flock, including affected animals, with a licensed inactivated vaccine should be mandatory with two doses given at a 15 day interval followed by another 2 doses 6 months apart for at least two to three years. As the pathogen and antibody may persist in sub-clinical or healthy carriers for over one year, even in those animals vaccinated, the sanitary measures should be maintained until the mycoplasma is completely cleared in bulk milk, or, preferably, in individual milk. This can be confirmed by negative results in two repeated PCR tests under the supervision of the veterinarian. Stricter controls should be put in place for animals exported to CA-free countries.

Conclusions

Estimating the economic impact of CA is a complex issue, probably because it is connected with traditional husbandry typical of Mediterranean areas; invariably, however, CA has a strong impact on the local economy because of its high morbidity rate which is why

it is often known as “the shepherd’s nightmare” [2,7,8]. Moreover, due to the indirect effect on the quality of milk produced, it is likely that the impact of CA is underestimated especially in dairy livestock. In this paper we have focused on estimating the economic costs to two different farm types: a small family farm and large commercial holding. Extrapolated across Southern Italy, where most of these farms are located, these represent significant losses to this poorer sector where there is little or no compensation. We have also put forward some recommendations to improve the control of this disease though its impact could be reduced by the EU’s proposals to downgrade the disease to national or even local importance. Such a development could affect cross border control and make this a less attractive area for research funding. Many objectives still remain if we are to improve control of this disease. This includes: The development of a safe vaccine which provides greater and longer lasting protection; a pen-side test which can assess quickly the infection status of a herd; and finally a greater awareness amongst national and international authorities of the true social economic impact of this disease.

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