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Administration of antibiotics to ewes at the beginning of the dry-period

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The objective of the present paper is to review the significance of administration of antibiotics at the end of a lactation period/beginning of the dry-period in ewes. During the stage of active involution, there is an increased risk of new mastitis cases and recrudescence of subclinical infections that had occurred during the previous lactation period. The main pathogens involved in the so-called 'dry-period mastitis' are coagulase-negative staphylococci. The principle of antibiotic administration at the end of a lactation period involves the intramammary infusion of a preparation to both mammary glands of ewes in the flock. Although a variety of products is licensed for administration in ewes, preferably the product for administration should be selected on the results of susceptibility testing of bacteria to be isolated from samples from ewes in the flock. In many clinical studies from around the world, performed in dairy- or mutton-production flocks, administration of antimicrobial agents at the end of a lactation period has been found beneficial in curing intramammary infections present at cessation of a lactation period, as well as in minimising the risk for intramammary infections during the dry-period. In dairy flocks, there are also benefits from increase in milk yield and decrease flock bulk milk mean somatic cell counts during the subsequent lactation period. Antibiotic administration at drying-off may be performed to all animals in a flock ('complete') or only to those considered to be infected ('selective'). In all cases, after administration of the antibiotic, definite and complete cessation of the lactation period is essential for success of the procedure. Moreover, maintenance of the prescribed withdrawal periods is essential to safeguard public health. The procedure should always be applied as part of a strategic udder health management plan in a flock; implementation improves the welfare of animals and affords significant financial benefits to the farmer. A mastitis prevention scheme during lactation will minimise the incidence of the disease; effective treatment of cases of the disease during lactation will decrease the bacterial populations in the flock and limit risk of infection of other animals. Administration of antibiotics at the end of a lactation period will complement the above procedures and will contribute to improved mammary health for the forthcoming lactation period.

Keywords: Dry-period, intramammary treatment, mammary involution, mastitis.

The mammary gland fulfils a diversity of physiological, immunological and biochemical functions (Oliver & Sordillo, 1989). As part of the reproductive system of mammals, it undergoes repeated cycles of structural development, functional differentiation and regression (Hurley 1989; Hurley & Loor, 2011). During these cycles, the mammary gland of adult animals undergoes three distinct functional transitions: (i) from involution to lactogenesis (including the colostrogenesis), (ii) from lactogenesis to lactation and (iii) from lactation to involution. In each of these phases, marked changes occur in the size, structure and function of the organ; moreover, distinct changes also occur in the mammary secretion during each of the above physiological transitions (Oliver & Sordillo, 1989). In ruminants, mammary involution occurs at the end of each lactation period and is characterised by the reduction of numbers of mammary epithelial cells coupled with the extensive proteolytic degradation of the extracellular matrix (Quarrie et al. 1996; Flint et al. 2005).

In sheep, in dairy-type production systems, mammary involution can be effected either progressively (i.e. milking frequency is gradually decreased over a period of several days or weeks) or abruptly (i.e. milking is stopped at once) (Gelasakis et al. 2010). In mutton-production systems,

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cessation of lactation, and consequent mammary involution, is always abrupt, taking place when lambs are removed from their dam (Sargison, 2008). From the viewpoint of udder health management, recent work has shown that the procedure for udder drying-off (i.e. progressive or abrupt cessation of lactation) does not affect the risk of subsequent intramammary infection and development of mastitis (Petridis et al. 2013).

The period from complete cessation of milk removal until the beginning of the subsequent lactation period (i.e. parturition) is termed the 'dry-period'. The dry-period is distinguished in three distinct stages: (i) stage of active involution, (ii) stage of the 'steady-state' involution and (iii) stage of redevelopment and lactogenesis (including colostrogenesis). The dry-period is of importance in the health management of sheep for optimum milk production in the subsequent lactation period (Contreras et al. 2007; Fthenakis et al. 2012).

During the stage of active involution, there is (i) easier invasion of pathogens, owing to dilatation of the teat orifice and duct as a result of milk accumulation into the mammary gland and consequent increased pressure to the teat, whilst the protective keratin plug which seals the teat canal is not yet formed (Dingwell et al. 2004), and (ii) impaired defensive ability of the mammary gland as a result of decreased concentration of lactoferrin and lactoferrin:citrate ratio (Smith & Oliver, 1981; Nickerson, 1989; Oliver & Sordillo, 1989), decreased phagocytic ability of leucocytes (Sordillo & Nickerson, 1988; Tatarczuch et al. 2000, 2002) and reduced amount of immunoglobulins in lacteal secretions (Sordillo et al. 1987). The above predispose the mammary gland to new mastitis cases during involution and support recrudescence of subclinical infections that had occurred during the previous lactation period (Orphanou, 1987; Barkema et al. 1998; Saratsis et al. 1998).

Remodelling of the mammary gland during involution, characterised by the renewal of damaged or senescent mammary epithelial cells, is essential for optimum milk production during the subsequent lactation period (Capuco et al. 1997). Intramammary infections during that period would adversely affect normal development of mammary epithelial cells and, thus, quality and quantity of milk to be produced (Sordillo & Nickerson, 1988).

Udder health management at the end of a lactation period aims (i) to cure infections which have occurred during the previous lactation period and (ii) to prevent development of new intramammary infections during the dry-period (Fthenakis et al. 2012). Initially, clinical examination of the mammary glands of ewes in the flock should be carried out; that way, ewes with mammary abnormalities can be identified. The udder of all ewes in the flock is examined by palpation, whilst the animals are run through a race (Orphanou, 1987; Saratsis et al. 1998). If mammary abnormalities are suspected, animals should be individually examined. Diffuse hardness, abscesses and nodules in the mammary glands are the most common clinical findings during the examination (Saratsis et al. 1998). Samples (e.g. mammary secretion, abscess material) should also be collected for bacteriological examination (Fthenakis, 1994; Saratsis et al. 1998; Mavrogianni et al. 2005).

Based on the results of the clinical examination of the udder and the ancillary tests performed (e.g. bacteriological examination) the following categories of ewes should be considered for culling: (i) animals with at least one mammary gland permanently damaged, (ii) animals chronically affected and (iii) animals that had shown incidents of relapsing mastitis or had not fully responded to mastitis treatment during the preceding lactation period. The benefits of culling such animals include: (i) decrease of veterinary expenses for mastitis control in the flock, (ii) elimination of sources of potential infection for other animals in the flock and (iii) decrease of flock bulk somatic cell counts in the subsequent lactation period (Mavrogianni et al. 2011). Moreover, lambs (especially in large litters) from ewes with extensive mammary lesions do not thrive well and may require additional feeding (Fthenakis & Jones, 1990a), which increases expenses and labour in the flock.

The above procedures should be complemented by administration (preferably by the intramammary route) of antibiotics, which is an integral part of udder health management (Fthenakis et al. 2012). The objective of the present paper is to review the significance of administration of antibiotics at the end of a lactation period/beginning of the dry-period in ewes.

Pathogens involved in 'dry-period mastitis'

The main pathogens involved in the so-called 'dry-period mastitis' are primarily coagulase-negative staphylococci (Saratsis et al. 1998; Croft et al. 2000; Chaffer et al. 2003; Gonzalo et al. 2004; Shwimmer et al. 2008; Spanu et al. 2011). Reservoirs of these microorganisms are the subclinically infected mammary glands, although these bacteria are also part of the normal flora of the udder skin, which renders their control difficult. In sheep, these organisms are frequent aetiological agents of clinical or subclinical mastitis and elicit a strong host response (Fthenakis & Jones, 1990b; Pengov, 2001). Various coagulase-negative staphylococcal species are involved in the aetiology of the disease. Phenotypic tests (e.g. API Staph ID 32) are used often for speciation of these organisms. Genotypic methods can provide information (Sampimon et al. 2009) for use in epidemiological studies, e.g. regarding increased prevalence and persistence of infection by some staphylococcal species in flocks.

Other organisms involved in dry-period mastitis are streptococci (Chaffer et al. 2003; Linage & Gonzalo, 2008) and *Trueperella pyogenes* (Saratsis et al. 1998). As these bacteria are not frequent aetiological agents of mastitis in lactating mammary glands, the findings raise a question regarding a possible increased susceptibility of involuting ovine mammary glands to those organisms.

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Benefits of administration of antibiotics at the end of a lactation period

Intramammary administration of antibiotics

The principle of antibiotic administration at the end of a lactation period involves the intramammary infusion of a pharmaceutical preparation to both mammary glands of ewes in the flock. In all published work carried out in dairy flocks, a significantly greater cure rate of mammary abnormalities recorded at the end of lactation has been achieved after administration of the antibiotics. Pharmaceutical preparations used in the studies include combinations of antibiotics, which afford a broader spectrum of antibacterial activity. Although a variety of products is licensed for administration in ewes, preferably the product for administration should be selected on the results of susceptibility testing of bacteria (Constable & Morin, 2003; Mavrogianni et al. 2011) to be isolated from samples (e.g. mammary secretion, abscess material) from ewes individually examined, as detailed above. Moreover, antibiotic administration has led to a smaller incidence of new infections during the dry-period, which indicates the preventive role of the procedure during a period of high risk for intramammary infections and underlines the usefulness of strategic administration. The beneficial effects of the administration are clearly shown in the subsequent lactation, when increased milk yields of treated ewes have been recorded.

Chaffer et al. (2003) found that prevalence of intramammary infections in ewes at drying-off was 45%; cure rate after intramammary administration of a combination of benzylpenicillin, nafcilin and dihydrostreptomycin at the end of lactation period was found to be 65% 15–20 d after the subsequent lambing, compared with 6·5% cure rate in control animals. In a similar study, Shwimmer et al. (2008) reported that prevalence of intramammary infections in ewes at drying-off was 47·5%; cure rate after intramammary administration of the above combination at the end of lactation period was found to be 71% 2–4 weeks after the subsequent lambing, compared with 8% cure rate in control animals. These authors also documented that mean milk yield throughout the lactation period subsequent to antibiotic administration increased by 19% and flock bulk milk mean somatic cell counts during the same period decreased to $1{\cdot}0 \times 10^6$ from $2{\cdot}5 \times 10^6$ in the previous lactation period (Shwimmer et al. 2008). De Santis et al. (2001) reported that cure rate of intramammary infections in ewes after intramammary administration of cloxacillin at the end of the lactation period was >60% 4–59 d after the subsequent lambing, compared with <50% cure rate in control animals. De Santis et al. (2001) and Spanu et al. (2011) also documented that treated ewes had significantly smaller somatic cell counts in the subsequent lactation compared with controls. However, Gonzalo et al. (2009) found beneficial results in decreasing flock bulk milk somatic cell counts only in machine-milked ewes and not in hand-milked animals.

Linage & Gonzalo (2008) reported that prevalence of intramammary infections in ewes at drying-off was 49%; cure rate after intramammary administration of a combination of penethemate and framycetin at the end of the lactation period was 82% 5 d after the subsequent lambing, compared with 13% cure rate in control animals. Moreover, these authors found that incidence risk of new intramammary infections, during the dry-period was 8% in treated and 23% in control ewes. Gonzalo et al. (2004) found that prevalence of intramammary infections in ewes at drying-off was 54·5%; cure rate after intramammary administration of a combination of penicillin and novobiocin at the end of a lactation period was 61·5% at the subsequent lambing. Moreover, these authors indicated that milk yield of ewes increased by 7% in the lactation period subsequent to antibiotic administration, as a result of decreased incidence of new intramammary infections during the dry-period (Gonzalo et al. 2004).

Finally, Petridis et al. (2012) reported that cure rate of intramammary infections in ewes, after administration of a combination of procaine penicillin and neomycin at drying-off was ⩾ 50% 10 d after the subsequent lambing, significantly higher than that in untreated glands. The authors observed these beneficial effects independently of the procedure used for drying-off (i.e. progressive or abrupt).

Thus, it becomes evident that in dairy ewes intramammary administration of antimicrobial agents at the end of a lactation period is effective in curing intramammary infections present at cessation of a lactation period, as well as in minimising the risk for intramammary infections during the dry-period. Moreover, there are further benefits from a potential increase in milk yield and a decrease in flock bulk milk somatic cell counts during the subsequent lactation period.

The procedure has been found to be just as beneficial in ewes in mutton-production systems (Hendy et al. 1981; Watson & Buswell 1984; Hueston et al. 1989). In mutton-production systems, healthy mammary glands of the dam and increased milk yield during the first month of a lactation period are important for optimum growth rate of lambs (Fthenakis & Jones, 1990a).

One might suggest that differences in the length of the dry-period, which reflect differences in production systems, may potentially affect the efficacy of intramammary administration of antibiotics at the end of a lactation period. However, Linage & Gonzalo (2008), who studied this particular factor in their work, did not find any significant differences in the efficacy of administration between groups of ewes with varying length of the dry-period.

Injectable administration of antibiotics

McCarthy et al. (1988) proposed the intramuscular administration of procaine penicillin to ewes at the end of a lactation period, after administration of which prevalence of subclinical mastitis at lambing was found to be 27% in treated animals and 31% in controls. Croft et al. (2000)

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indicated that the subcutaneous injection of tilmicosin one month prior to the expected start of the lambing period, concurrently with the anti-clostridial vaccination, led to a 43% decrease in mammary abnormalities at the subsequent lambing. Moreover, the latter authors documented that mean bodyweight of 50-d-old lambs of treated ewes was greater by 520 g than that of lambs of control ewes and attributed the benefit to cure of pre-existing intramammary infections in treated ewes, which led to increased milk yield by the animals (Croft et al. 2000).

In comparison with intramammary administration, it is noteworthy that an advantage of injectable administration is the minimal risk of potential iatrogenic contamination of the mammary glands, as handling of the udder is avoided.

The publications regarding administration of antibiotics to ewes at the beginning of the dry-period are summarised in Table 1.

'Complete' or 'selective' antibiotic administration?

Administration of antibiotics to ewes at drying-off may be performed on all animals in a flock ('complete') or only on those considered to be infected ('selective'). The need for selective administration was developed owing to public concerns regarding (i) potential antibiotic residues in the food chain and (ii) increased incidence of antibiotic-resistant bacterial strains in animals. Moreover, selective administration has a smaller cost to the farmer and a decreased risk of potential iatrogenic contamination of the mammary glands (Mavrogianni et al. 2011).

In the selective administration approach, there may be a query regarding criteria to be used in the selection of animals that will receive the antibiotic preparation. Clinical examination of all animals in the flock, as discussed above, has a small cost and can be used to identify animals in need of antibiotic administration. The procedure can be complemented with bacteriological examination of samples collected from clinically affected udders, which will support the decision for selection of the most appropriate antibiotic (Orphanou, 1987; Saratsis et al. 1998). Milk somatic cell counting alone, as a means of identifying ewes in need of antibiotic administration, may not be a useful method, because somatic cell counts have been found to increase physiologically at the end of a lactation period, i.e. even in healthy ewes (Fthenakis, 1995), and hence are not indicative of intramammary infection. Gonzalo et al. (2004) did not find any significant differences between the two methods (i.e. complete or selective) in the cure of pre-existing intramammary infections. Bogolin & Vasiu (2008) used selective treatment in ewes with subclinical mastitis and reported a cure rate of 78·5% in the treated animals.

A disadvantage of selective administration is the incomplete protection of the untreated ewes in the flock against new intramammary infections during the dry-period (Berry & Hillerton, 2002; Bergonier & Berthelot, 2003), especially during the stage of active involution when there is an increased risk of mastitis (Orphanou, 1987; Barkema et al. 1998; Saratsis et al. 1998).

Potential concerns regarding intramammary administration of antibiotics at the end of a lactation period

Administration of the antibiotic preparation should be performed under good hygienic conditions and thorough disinfection of the respective teat, in order to prevent insertion of pathogens, which may subsequently cause mastitis. Organisms that may be introduced into the teat at that point include *Pseudomonas aeruginosa* and *Aspergillus fumigatus* (Las Heras et al. 2000; Bergonier & Berthelot, 2003; Spanu et al. 2011) for which organisms the antibiotics usually administered are not effective.

It has been proposed, during intramammary antibiotic administration, to use partial insertion of the tip of the tube or to use short-tipped tubes, with the aim of avoiding excessive dilatation of the teat canal and destruction of its protective lining (Bergonier & Berthelot, 2003; Bergonier et al. 2003). The results of Gonzalo et al. (2004) indicated that the procedure was as effective as complete insertion of the tip of the tube into the teat. In view of previous findings, which pointed out the significance of damaged teats as a risk factor for development of mastitis (Mavrogianni et al. 2006; Fragkou et al. 2007), this may be a useful suggestion. Moreover, this method allows some antibiotic to be left inside the teat canal, in that way preventing bacterial invasions into the mammary parenchyma.

After administration of the antibiotic, definite and complete cessation of the lactation period is essential for success of the procedure (Fthenakis et al. 2012). This implies that ewes should not be milked again after administration of the antibiotic, whilst in mutton-production systems, lambs should have been removed from their dams before that.

Finally, some concerns have been voiced regarding potential problems with residues of the antibiotics in milk of the subsequent lactation (Chaffer et al. 2003; Linage & Gonzalo, 2008; Shwimmer et al. 2008). Nevertheless, it should be noted that, at least in the European Union, veterinary pharmaceutical products are only licensed if adequate scientific evidence can be presented about residues in the animal products (e.g. meat, milk) and if appropriate withdrawal periods have been calculated (Athanasiou et al. 2009). Calculation of withdrawal periods for intramammary veterinary pharmaceutical products at the beginning of the dry-period takes into account minimum length of the dry-period, as well as minimum time after parturition that milk cannot be given for human consumption. For example, in the study by Linage & Gonzalo (2008), no antibiotic residues in milk were detected as early as 54 h after the lambing subsequent to antibiotic administration. Therefore, maintenance of the prescribed withdrawal periods is essential to safeguard public health.

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Table 1. Summary presentations of publications regarding administration of antibiotics to ewes at the beginning of the dry-period

Reference	Route of administration/antibiotics used	Summary of findings
Bogolin & Vasiu (2008)	Intramammary/cloxacillin	'Selective' administration in ewes with subclinical mastitis; cure rate at lambing was 78·5%, compared with 23% in controls
Chaffer et al. (2003)	Intramammary/benzylpenicillin, nafcilin, dihydrostreptomycin	Cure rate of intramammary infections 15–20 d after the subsequent lambing was 65%, compared with 6·5% in controls
Croft et al. (2000)	Subcutaneous/tilmicosin	Cure rate of mammary abnormalities at the subsequent lambing was 43%; bodyweight of 50-d-old lambs of treated ewes was greater by 520 g than that of lambs of controls
De Santis et al. (2001)	Intramammary/cloxacillin	Cure rate of intramammary infections 4–59 d after the subsequent lambing was >60%, compared with <50% in controls; treated ewes had significantly smaller milk somatic cell counts in the subsequent lactation compared with controls
Gonzalo et al. (2004)	Intramammary/penicillin, novobiocin	Cure rate of intramammary infections at the subsequent lambing was 61·5%; milk yield in the subsequent lactation period increased by 7% compared with controls; no difference between 'complete' and 'selective' treatment in cure of intramammary infections
Gonzalo et al. (2009)	Intramammary/penethamate, benethamine penicillin, framycetin	Treated machine-milked, but not hand-milked, ewes had significantly smaller milk somatic cell counts in the subsequent lactation compared with controls
Hendy et al. (1981)	Intramammary/procaine penicillin, dihydrostreptomycin	Prevalence of mammary abnormalities at mating 1·5% in treated ewes and 4·5% in controls
Hueston et al. (1989)	Intramammary/cephapirin	Untreated ewes had a 2·6-times higher risk to developing intramammary infections at the early stage of the subsequent lactation period
Linage & Gonzalo (2008)	Intramammary/penethemate, framycetin	Cure rate of intramammary infections 5 d after the subsequent lambing was 82%, compared with 13% in controls; incidence risk of new intramammary infections during the dry-period was 8% in treated ewes and 23% in controls; no differences in efficacy of administration with regard to length of the dry-period
McCarthy et al. (1988)	Intramuscular/procaine penicillin	Prevalence of subclinical mastitis at lambing was 27% in treated ewes and 31% in controls
Petridis et al. (2012)	Intramammary/procaine penicillin, neomycin	Cure rate of intramammary infections in ewes 10 d after the subsequent lambing was found to be $\geqslant$ 50%, significantly higher than in controls; beneficial effects independent of the procedure used for drying-off
Shwimmer et al. (2008)	Intramammary/benzylpenicillin, nafcilin, dihydrostreptomycin	Cure rate of mammary abnormalities 2–4 weeks after the subsequent lambing was 71%, compared with 8% in controls; milk yield increased by 19% and bulk milk somatic cell counts decreased by 60% compared with ones in the previous lactation period
Spanu et al. (2011)	Intramammary/cephapirin	Treated ewes had significantly smaller milk somatic cell counts in the subsequent lactation compared with controls
Watson & Buswell (1984)	Intramammary/cloxacillin	Prevalence of intramammary infections at lambing 1% in treated ewes and 3·5% in controls; increased (up to 7%) bodyweight gain in lambs of treated ewes

Concluding remarks

Implementation of intramammary administration of antibiotics at the end of a lactation period improves the welfare of animals and affords significant financial benefits to the farmer. These benefits are pretty obvious in dairy production systems, but they can also be significant in mutton-production systems. The procedure will provide maximum benefit in flocks with increased incidence of intramammary infections, where it can bring dramatic improvement in the financial performance of the flock. Although no premium payment schemes based on milk somatic cell counts are

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enforced in the European Union, if such schemes were to be applied, financial benefits would increase greatly; flock bulk somatic cells counts decrease in the subsequent lactation period, which would lead to higher payment for milk produced.

The procedure should always be applied as part of a strategic udder health management plan in a flock. A mastitis prevention scheme during lactation will minimise the incidence of the disease; effective treatment of cases of the disease during lactation will decrease the bacterial populations in the flock and limit risk of infection of other animals. Administration of antibiotics at the end of a lactation period will complement the above procedures and will contribute to improved mammary health for the forthcoming lactation period.

References

Athanasiou LV, Orfanou DC, Fragkou IA, Gougoulis DA & Nerou C 2009 Proposals for withdrawal period of sheep milk for some commonly used veterinary medicinal products: a review. *Small Ruminant Research* **86** 2–5

Barkema HW, Schukken YH, Lam TJGM, Beiboer ML, Wilmink H, Benedictus G & Brand A 1998 Incidence of clinical mastitis in dairy herds grouped in three categories by bulk milk somatic cell counts. *Journal of Dairy Science* **81** 411–419

Bergonier D & Berthelot X 2003 New advances in epizootiology and control of ewe mastitis. *Livestock Production Science* **79** 1–16

Bergonier D, De Cremoux R, Rupp R, Lagriffoul G & Berthelot X 2003 Mastitis of dairy small ruminants. *Veterinary Research* **34** 689–716

Berry EA & Hillerton JE 2002 The effect of selective dry cow treatment on new intramammary infections. *Journal of Dairy Science* **85** 112–121

Bogolin I & Vasiu C 2008 Treatment of subclinical intramammary infections in small ruminants. *Bulletin USAMV Veterinary Medicine* **65** 298–303

Capuco AV, Akers RM & Smith JJ 1997 Mammary growth in Holstein cows during the dry period: quantification of nucleic acids and histology. *Journal of Dairy Science* **80** 477–487

Chaffer M, Leitner G, Zamir S, Winkler M, Glickman A, Ziv N & Saran A 2003 Efficacy of dry-off treatment in sheep. *Small Ruminant Research* **47** 11–16

Constable PD & Morin DE 2003 Treatment of clinical mastitis: using antimicrobial susceptibility profiles for treatment decisions. *Veterinary Clinics of North America Food Animal Practice* **19** 139–155

Contreras A, Sierra D, Sanchez A, Corrales JC, Marco JC, Paape MJ & Gonzalo C 2007 Mastitis in small ruminants. *Small Ruminant Research* **68** 145–153

Croft A, Duffield T, Menzies P, Leslie K, Bagg R & Dick P 2000 The effect of tilmicosin administered to ewes prior to lambing on incidence of clinical mastitis and subsequent lamb performance. *Canadian Veterinary Journal* **41** 306–311

De Santis EPL, Mencarelli A, Nieddu MP, Farina S, Mazzette R, Sanna S & Virdis S 2001 [Efficacy of the administration by the intramammary route of benzathine cloxacillin for the treatment of intramammary infections of sheep during the dry-period] (It.) *Large Animal Review* **7** 1–9

Dingwell RT, Leslie KE, Schukken YH, Sargeant JM, Timms LL, Duffield TF, Keefe GP, Kelton DF, Lissemore KD & Conklin J 2004 Association of cow and quarter-level factors at drying-off with new intramammary infections during the dry period. *Preventive Veterinary Medicine* **63** 75–89

Flint DJ, Boutinaud M, Tonner E, Wilde CL, Hurley W, Accorsi PA, Kolb AF, Whitelaw CBA, Beattie J & Allan GJ 2005 Insulin-like growth factor binding proteins initiate cell death and extracellular matrix remodeling in the mammary gland. *Domestic Animal Endocrinology* **29** 274–282

Fragkou IA, Papaioannou N, Cripps PJ, Boscos CM & Fthenakis GC 2007 Teat lesions predispose to invasion of the ovine mammary gland by *Mannheimia haemolytica*. *Journal of Comparative Pathology* **137** 239–244

Fthenakis GC 1994 Prevalence and aetiology of subclinical mastitis in ewes of Southern Greece. *Small Ruminant Research* **13** 293–300

Fthenakis GC 1995 Somatic cell counts in milk of Welsh-Mountain, Dorset-Horn and Chios ewes throughout lactation. *Small Ruminant Research* **20** 155–162

Fthenakis GC & Jones JET 1990a The effect of experimentally induced subclinical mastitis on milk yield of ewes and on the growth of lambs. *British Veterinary Journal* **146** 43–49

Fthenakis GC & Jones JET 1990b The effect of inoculation of coagulase-negative staphylococci into the ovine mammary gland. *Journal of Comparative Pathology* **102** 211–219

Fthenakis GC, Arsenos G, Brozos C, Fragkou IA, Giadinis ND, Giannenas I, Mavrogianni VS, Papadopoulos E & Valasi I 2012 Health management of ewes during pregnancy. *Animal Reproduction Science* **130** 198–212

Gelasakis AI, Valergakis GE, Fortomaris P & Arsenos G 2010 Farm conditions and production methods in Chios sheep flocks. *Journal of the Hellenic Veterinary Medical Society* **61** 111–119

Gonzalo C, Tardaguila JA, De La Fuente LF & San Primitivo F 2004 Effects of selective and complete dry therapy on prevalence of intramammary infection and on milk yield in the subsequent lactation in dairy ewes. *Journal of Dairy Research* **71** 33–38

Gonzalo C, Linage B, Carriedo JA, Juarez MT, Beneitez E, Martinez A & De La Fuente LF 2009 Effect of dry therapy using an intramammary infusion on bulk tank somatic cell count in sheep. *Journal of Dairy Science* **92** 156–159

Hendy PG, Pugh KE & Harris AM 1981 Prevention of post-weaning mastitis in ewes. *Veterinary Record* **109** 56–57

Hueston WD, Boner GJ & Baertsche SL 1989 Intramammary antibiotic treatment at the end of lactation for prophylaxis and treatment of intramammary infections in ewes. *Journal of the American Veterinary Medical Association* **194** 1041–1044

Hurley WL 1989 Mammary gland function during involution. *Journal of Dairy Science* **72** 1637–1646

Hurley WL & Loor JJ 2011 Mammary gland growth, development and involution. In *Encyclopedia of Dairy Sciences*, 2nd edition, pp. 338–345 (Ed. JW Fuquay). San Diego: Academic Press

Las Heras A, Dominguez L, Lopez I, Paya MJ, Pena L, Mazzucchelli F, Garcia LA & Fernandez-Garayzabal JF 2000 Intramammary *Aspergillus fumigatus* infection in dairy ewes associated with antibiotic dry therapy. *Veterinary Record* **147** 578–580

Linage B & Gonzalo C 2008 Influence of an intramammary infusion at drying-off of combined penethamate hydriodide, benethamine penicillin, and framycetin sulfate on intramammary infections and somatic cell counts in dairy sheep. *Journal of Dairy Science* **91** 3459–3466

Mavrogianni VS, Fthenakis GC, Brooks H, Papaioannou N, Cripps PJ, Taitzoglou I, Brellou G & Saratsis P 2005 The effects of inoculation of Mannheimia haemolytica into the teat of lactating ewes. *Veterinary Research* **36** 13–25

Mavrogianni VS, Cripps PJ, Papaioannou N, Taitzoglou IA & Fthenakis GC 2006 Teat disorders predispose ewes to clinical mastitis after challenge with *Mannheimia haemolytica*. *Veterinary Research* **37** 89–105

Mavrogianni VS, Menzies PI, Fragkou IA & Fthenakis GC 2011 Principles of mastitis treatment in sheep and goats. *Veterinary Clinics of North America Food Animal Practice* **27** 115–120

McCarthy FD, Lindsey JB, Gore MT & Notter DR 1988 Incidence and control of subclinical mastitis in the intensively managed ewes. *Journal of Animal Science* **66** 2715–2721

Nickerson SC 1989 Immunological aspects of mammary involution. *Journal of Dairy Science* **72** 1665–1678

Oliver SP & Sordillo LM 1989 Approaches to the manipulation of mammary involution. *Journal of Dairy Science* **72** 1647–1664

Orphanou E 1987 *Post-weaning Mastitis in Ewes: a Clinical and Bacteriological Investigation*. M.Sc. Project Report, London School of Hygiene and Tropical Medicine, University of London. pp. 50

Pengov A 2001 The role of coagulase-negative Staphylococcus spp. and associated somatic cell counts in the ovine mammary gland. *Journal of Dairy Science* **84** 572–574

Petridis IG, Mavrogianni VS, Gougoulis DA, Amiridis GS, Brozos C & Fthenakis GC 2012 Effects of drying-off procedure of ewes' udder, with intramammary antibiotic administration, in subsequent mammary infection and development of mastitis. *Journal of the Hellenic Veterinary Medical Society* **63** 273–282

Petridis IG, Mavrogianni VS, Fragkou IA, Gougoulis DA, Tzora A, Fotou K, Skoufos I, Amiridis GS, Brozos C & Fthenakis GC 2013 Effects of drying-off procedure of ewes' udder in subsequent mammary infection and development of mastitis. *Small Ruminant Research* **110** 128–132

Quarrie LH, Addey CV & Wilde CJ 1996 Programmed cell death during mammary tissue involution induced by weaning, litter removal, and milk stasis. *Journal of Cellular Physiology* **168** 559–569

Sampimon OC, Zadoks RN, De Vliegher S, Supre K, Haesebrouck F, Barkema HW, Sol J & Lam TJGM 2009 Performance of API Staph ID 32 and Staph-Zym for identification of coagulase-negative staphylococci isolated from bovine milk samples. *Veterinary Microbiology* **136** 300–305

Saratsis P, Leontides L, Tzora A, Alexopoulos C & Fthenakis GC 1998 Incidence risk and aetiology of mammary abnormalities in dry ewes in 10 flocks in Southern Greece. *Preventive Veterinary Medicine* **37** 173–183

Sargison ND 2008 *Sheep Flock Health. A Planned Approach*, pp. 465. Oxford: Blackwell

Shwimmer A, Kenigswald G, Van Straten M, Lavi Y, Merin U, Weisblit L & Leitner G 2008 Dry-off treatment of Assaf sheep: efficacy as a management tool for improving milk quantity and quality. *Small Ruminant Research* **74** 45–51

Smith KL & Oliver SP 1981 Lactoferrin: a component of non-specific defense of the involuting bovine mammary gland. *Advances in Experimental Medicine and Biology* **137** 535–554

Sordillo LM & Nickerson SC 1988 Morphologic changes in the bovine mammary gland during involution and lactogenesis. *American Journal of Veterinary Research* **49** 1112–1120

Sordillo LM, Nickerson SC, Akers RM & Oliver SP 1987 Secretion composition during bovine mammary involution and the relationship with mastitis. *International Journal of Biochemistry* **19** 1165–1172

Spanu C, Berger YM, Thomas DL & Ruegg PL 2011 Impact of intramammary antimicrobial dry treatment and teat sanitation on somatic cell count and intramammary infection in dairy ewes. *Small Ruminant Research* **97** 139–145

Tatarczuch L, Philip C, Bischof R & Lee CS 2000 Leucocyte phenotypes in involuting and fully involuted mammary glandular tissues and secretions of sheep. *Journal of Anatomy* **196** 313–326

Tatarczuch L, Bischof RJ, Philip CJ & Lee CS 2002 Phagocytic capacity of leucocytes in sheep mammary secretions following weaning. *Journal of Anatomy* **201** 351–361

Watson DJ & Buswell JF 1984 Modem aspects of sheep mastitis. *British Veterinary Journal* **140** 529–534

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