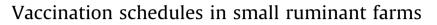
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ABSTRACT

Development and implementation of health management plans is the cornerstone of profitable farms; prevention of microbial diseases by means of vaccination is an integral part of such a plan. In every production type and management system in small ruminants, microbial diseases have a major significance, hence their proper control must be based in good health management practices, including use of effective and safe vaccines. Development of various types of vaccines is evolving very quickly in recent years and the improvement of new type of vaccines offers prospects. The article reviews and discusses vaccination programs and latest advances in development of vaccines against diseases that cause major economic losses in small ruminants. Specifically, vaccination schedules for the following diseases are reviewed: bacterial abortion (abortion associated with Brucella melitensis, Campylobacter spp., Chlamydophila abortus, Coxiella burnetii, Salmonella abortus ovis or Salmonella brandenburg), caseous lymphadenitis, clostridial diseases, colibacillosis, contagious echtyma, epididymitis caused by Brucella ovis, footrot, mammary diseases (contagious agalactia, mastitis), paratuberculosis and respiratory diseases (respiratory disease caused by Mannheimia haemolytica or other Pasteurellaceae).

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1. Introduction

Small ruminant farmers have improved their professionalism during the recent years and, although there are still traditionally managed farms coexisting with those with high technical intervention level, veterinarians active in that field need to offer improved services adjusted to the varying management systems. This veterinary consultancy service includes the development of health schemes designed according to individual needs, but within the framework and the particular conditions prevailing in each region and country and adapted to the practiced production system (Ganter, 2008). A good health management plan is the foundation for a thriving farm and with that approach veterinarians will support farmers, developing a mutually beneficial collaboration.

A complete health management program must deal with prevention of pathological conditions and increase of farm production, in the simplest way for the farmers, in order to minimise their work, at the same time promoting animal welfare. Scott et al. (2007) mentioned that a veterinary flock health plan must serve several purposes: reduction of economic losses due to

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http://dx.doi.org/10.1016/i.vetmic.2015.07.018 0378-1135/© 2015 Elsevier B.V. All rights reserved. disease, improvement of farm capacity due to increased production and reduction of adverse welfare effects of diseases.

For a correct health management program, several parametres should be taken into account: production type (meat/milk/wool), breed of animals, management system (extensive/semi-extensive/ semi-intensive/intensive/mixed, shepherding/non-shepherding), climate of the area, production targets in the farm, pathological conditions prevailing in the farm and the region, available facilities and the human resources (farmer and supporting staff).

Before each vaccination, it is imperative to confirm the health status of the animals. Vaccination is an active process, where the immunological system of the animal is requested to mount an adequate response against the antigen administered. For improved results, an anthelmintic treatment can be performed in advance (at least 15 days) of the vaccination; that way, an improved immune reaction can be mounted. However, in practice, often, anthelmintic treatment and vaccinations are carried out simultaneously. In most cases, there are no incompatibilities between vaccines and anthelmintic drugs administered to sheep or goats, although, occasionally, adverse reactions have been reported in relation to specific vaccinations (e.g., possible adverse reaction in case of administration of moxidectin and foot-rot vaccine; RUMA Guidelines, 2009); hence, one should be aware of those possibilities.

The present review will focus in vaccination programs for prevention of diseases applied as part of health management









schemes, i.e., against common enzootic diseases of small ruminants. It does not present epizootic diseases, which are outside the scope of routine health management schemes and are monitored with surveillance schemes implemented by national veterinary authorities.

2. Methodology

The review includes primarily references published in journals cited at the Web of Knowledge database (wok.mimas.ac.uk); papers published in these journals have been refereed. Various search terms have been employed to identify relevant publications (e.g., 'sheep', 'goat', 'vaccine, 'control', 'prevention' coupled with disease name and/or the respective causative agent e.g., 'abortion' and 'Chlamydophila' or 'mastitis' and 'Staphylococcus'). Subsequent-ly, the full papers have been retrieved through the websites of the respective journals. Moreover, material from selected books is also discussed in the paper.

3. Bacterial abortion

Infectious ovine abortion is a major health problem in sheep worldwide and causes significant financial and welfare implications (Menzies et al., 2011, 2012; Longbottom et al., 2013). The main microbial agents causing abortion in ewes or does are Brucella melitensis, Chlamydophila (Chlamydia) abortus, Coxiella burnetii, Campylobacter spp. and Salmonella spp.; depending on the world region, significance of the various abortifacient agents would differ. Repeated surveys carried out in Europe have indicated C. abortus as a significant abortifacient agent in small ruminants (Buxton and Henderson, 1999; Chanton-Greutmann et al., 2002; Longbottom and Coulter, 2003; Navarro et al., 2009), although other pathogens can emerge occasionally, e.g., C. burnetii was the cause of an extensive outbreak in the Netherlands in the late 2000s. In southern European countries, as well as in many Asian and African regions, B. melitensis is also a significant pathogen in small ruminant farms, against which extensive, state-supervised control campaigns have been undertaken over the years. In contrast, in New Zealand, Campylobacter spp. and Salmonella brandenburg are the primary microbial abortifacient agents, whilst C. abortus and C. *burnetii* infections have never been diagnosed in that country (Orr, 1998; West, 2002). Campylobacter spp. is a significant cause of small ruminant abortion also in North America (Sahin et al., 2008; Hazlett et al., 2013). Knowledge of the specific agent mainly responsible for abortion in a population of sheep or goats is important, because it would help to design the vaccination program against the most prevalent pathogens.

3.1. Abortion associated with Brucella melitensis

Brucellosis, caused by the zoonotic agent *Brucella melitensis*, is a significant abortion-causing disease, widely spread. The disease has a tremendous significance, due to veterinary and socioeconomic effects, which include a public health significance. Vaccination policy against the disease can be reviewed and discussed in a paper on its own; a recent, comprehensive review has been presented by Blasco and Molina-Flores (2011) and the reader is referred to that for a detailed account of the topic. Vaccinations should be part of any control and eradication plan. However, vaccinations alone would not suffice for success of the plan. Other parts of the plan include choice of the appropriate diagnostic test, long-term plan and commitment of the supervising authorities, availability of human and financial resources and training of farmers involved.

The attenuated *B. melitensis* Rev 1 is a vaccine available and widely used worldwide, as it has been repeatedly found to be

effective in sheep and goats (Blasco, 1997; Blasco and Molina-Flores, 2011). The vaccine is administered by the conjunctival route (individual doses of $1 \times 10^9 - 2 \times 10^9$ c.f.u.) and confers fully effective immunity. The antibody titres thus evoked make this route of administration acceptable in campaigns to control the disease, which are based on vaccinations and 'test-and-slaughter'.

The main approach in a long-term control strategy of brucellosis is to vaccinate female replacement animals (3–4 month old) exclusively. The rationale is that if replacements would be vaccinated every year, then in four to six years all female animals in a population would be immunised. Vaccination of pregnant animals may induce abortions and vaccination of lactating animals may lead to excretion of the vaccinal strain to milk (Blasco, 1997). However, there are drawbacks in the recommended approach, especially in countries with large populations of small ruminants under extensive or semi-extensive management systems, e.g., several visits to the same farm might be necessary for vaccination of all animals, tags of vaccinated animals might be lost over the years etc. Thus, alternative strategies need to be applied; for example, an initial mass vaccination of all animals in a farm can be performed, that will be followed by annual vaccination of replacement animals and, after two to three years, by a repeat mass vaccination and again subsequent annual vaccination of replacement animals, a scheme that will provide immunisation of all animals in the population, at the same time fully continuing the long-term protection strategy of the population (Blasco and Molina-Flores, 2011). However, the above schedule would require extensive resources for its application and would need a suitable time-point for applying the mass vaccination: the end of a lactation period, before start of the mating season, has been suggested as such (Blasco and Molina-Flores, 2011), as there are no risks for abortion or excretion of the vaccinal strain in milk. To note that in high-yielding breeds of sheep with long lactation periods, this may be difficult, as the end of a lactation period may often coincide with the initial stage of pregnancy.

3.2. Abortion associated with Campylobacter spp.

Cases of *Campylobacter*-associated abortion in sheep are due to *C. fetus* subsp. *fetus* or *C. jejuni* and have been widely reported around the world; in contrast, in goats *Campylobacter*-associated abortion has been rarely described (Menzies, 2011, 2012). Transmission occurs mainly by the oral route (e.g., from ingesting contaminated feed or water), as well as by direct contact with infected placenta or foetuses. Then, abortion can occur during late pregnancy.

The significant genetic variations of isolates of the organism with the consequent inefficient protection conferred by the vaccinal strains (Fenwick et al., 2000) and the lack of cross-protection between *C. jejuni* and *C. fetus* subsp. *fetus* (Diker and Turutoglu, 1995) might have contributed to the reported vaccination break-downs. Currently, there are few vaccines licenced for sheep, none of these in Europe; two vaccines with inactivated *C. jejuni* and *C. fetus* subsp. *fetus* are licenced in the USA and Canada and another one with three strains of *C. fetus* subsp. *fetus* and one strain of *C. jejuni* is licenced in New Zealand and Australia. That last vaccine is considered to confer good protection against all *Campylobacter* species implicated in cases of ovine abortion in New Zealand (Mannering et al., 2003), although Fenwick et al. (2000) have reported that *Campylobacter* strains causing abortion in sheep in that country, differ from those included in the licenced vaccine.

In the USA, where a tetracycline-resistant clone of *C. jejuni* (clone SA) has been isolated, the efficacy of the locally licenced vaccines has been tested specifically for protection against that clone; Burrough et al. (2011) reported, based on studies carried out in guinea pigs, that only one of the two available vaccines was

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