CONTROL / PREVENTION

Successful eradication programmes have always been costly, long, and hard to carry through. The difficulties in controlling and eradicating brucellosis stems from a variety of issues, the most important of which is the animal management conditions (extensive breeding, transhumance, co-existence of several livestock species, etc.). Most often, endemic areas are in countries with structural weaknesses, an aggravating circumstance since efficient use of current vaccines requires proficient veterinary services. This requirement relates in part to some of the limitations of currently available brucellosis vaccines, and it seems likely that an ideal vaccine could greatly facilitate control and eradication. The ideal brucellosis vaccine should: (1), trigger a solid and life-long immunity; (2), protect against infection by *Brucella* species other than those typical of a given host; (3), be innocuous regardless of the physiological state of the animal; (4), be effective in a single dose; (5), not interfere with serological diagnostic tests; (6), not be virulent for humans or carry resistance to antimicrobial drugs; (7), not be shed in the environment; (8), be stable; and (9), be affordable. Indeed, some of these requirements have become apparent only after using the classical brucellosis vaccines for more than half a century. To what extent has those requirements been met and what approaches have been followed to solve some of the problems?

The two best vaccines developed in the past century (*B. abortus* S19 and *B. melitensis* Rev 1) are both attenuated (live) vaccines with a certain degree of residual virulence. Strain 19 is used in cattle and Rev 1 in goats and sheep, not only against *B. melitensis* but also against *B. ovis*. Both vaccines carry a smooth (S) lipopolysaccharide (S-LPS) with an O-polysaccharide similar to that of the wild type *Brucella*.

Limitations of the Rev 1 vaccine are the abortifacient effect if applied during pregnancy, interference in serological diagnosis, virulence for humans and resistance to streptomycin and tendency to dissociate into ineffective rough [R] mutants. These limitations can be partially overcome by vaccinating animals conjunctivally when they are less than 4 months old which reduces greatly the interference in serological diagnosis and avoids vaccine-induced abortions; a minimal personal protection makes Rev 1 vaccination safe; and there are well-established quality control protocols. Rev 1 has been crucial wherever *B. melitensis* eradication has been achieved and, moreover, vaccination with Rev 1 is economically sound. Since cattle may become infected with *B. melitensis* (and by some *B. suis* biovars), it has been suggested...
that Rev 1 could be used in these ruminants. However, the protective efficacy against *B. melitensis*, innocuousness and safety of Rev 1 in cattle is not known. *B. melitensis* infections in cattle can be controlled with the help of S19 but there is a paucity of studies with regard to *B. suis*.

With the exception of a handful of countries with favorable geographical and management conditions, all successful programs in cattle have used S19. Subcutaneously, standard S19 doses generate immune responses interfering in diagnostic tests and may induce abortions if applied during pregnancy and genital lesions in males. Moreover, a small proportion of animals may develop subclinical infections and shed the vaccine. Conjunctival vaccination with reduced doses when animals are less than 4 months old avoid the abortions as well as the serological interference and udder infections. It is not known whether this route and doses make S19 safe in males, a point that would be worth investigating. Conjunctival vaccination is also adequate for vaccinating adult cattle since abortions and milk shedding are reduced to less than 1%.

Despite their limitations, S19 and Rev 1 have been successfully used in some developed countries to eradicate brucellosis. However, their use in eradication programmes poses the problem of distinguishing infected from vaccinated animals in serological tests. Although it is important to stress that this problem is of little or no significance in countries unable to implement testing and slaughtering programmes, this has been considered the major drawback of these vaccines.

*B. abortus* RB51 is an R mutant obtained by passage on media with rifampin and penicillin. It carries a mutation in the O-polysaccharide gene wboA but also other and unknown genetic defects. Concerning protection, controlled experiments show that RB51 is inferior to S19. RB51 does not elicit significant amounts of antibodies to the O-polysaccharide so that its interference in brucellosis tests that use smooth *Brucella* suspensions is minimal. However, the antibodies induced by RB51 are detected in tests apparently specific for Smooth *Brucella* spp. RB51 can induce abortions and can be excreted, and its use should be limited to non-pregnant animals. Since RB51 is more attenuated, it should be less dangerous than S19, and only very few human cases have been described. Although introduced over 12 years ago, no country using RB51 has eradicated cattle brucellosis although success has recently been suggested in the Azores, Portugal. However, such field observations are either contradictory or controversial because of the implementation of additional control measures and the absence of appropriate control groups. RB51 does not protect sheep against either *B. melitensis* or *B. ovis*.

Given the successful eradication of *B. abortus* and *B. melitensis* in some developed countries, it may be asked whether this research is necessary at all. The answer is that the organization and favorable environmental conditions found in these countries were a decisive factor in eradication. Those conditions are unlikely to be reached soon or even be possible in many areas where brucellosis is endemic and control and eradication can be facilitated only by an ideal brucellosis vaccine. Moreover, vaccines for reindeers, water buffaloes, yaks, camels, and swine, all susceptible animals that are important in the economies of many countries, are still missing.