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# Letter to the Editor

# The Challenges Inherent in the Control and Prevention of Bovine Papillomaviruses

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Several cattle diseases represent significant issues to livestock man, particularly those that is viral associated and with great spread potential. BPV infection became important in the context of livestock because the disease leads to economic depreciation of herd, deterioration of animal leather; decrease of general animal sanity and, in the severe cases, death of the animal. The decision of the farmer in managing the diseases that affect the herd is very private. The problem is that the presence of a disease in a property imposes a threat to adjacent properties and therefore requires an additional response by the involved properties or public agencies [1]. Particularly for bovine papillomatosis, the lack of accuracy in the data and the lack of information related to the costs of the disease and efforts to its control hinder interventions to minimize its impact.

Since it is a viral infection, the best prevention strategy for papillomatosis will be the vaccinal immunization [2]. Although BPV has been successfully used as an experimental model to previous studies that culminated in the development of vaccines against human papillomavirus [3,4], to date there are no commercial vaccines.

Early attempts to immunization against BPV were based on virus preparations obtained from papillomas of infected animals [2,5]. These approaches aimed to activation of Antigen-Presenting Cells (APCs), whereas in natural infection, the virus is restricted to the epithelial layer and its contact with the APCs is limited. However, this protection is type specific [3]. For this reason, although this approach is the most common technique for controlling papillomatosis, it is a strategy with unstable satisfactory rates of healing, being avoided as a preventive treatment.

The subsequent vaccine strategies were based on the use of recombinant versions of BPV L1 protein obtained from prokaryotic expression systems, or by production of VLPs (Virus-Like Particles) through employment of eukaryotic cells [4,6]. Although associated with the production of neutralizing antibodies in immunized animals, these approaches have two major obstacles that impede their business disposals for protection against BPV: the viral diversity, since it is type-specific, and the cost of production [3]. This context makes the use of these vaccines uninteresting by livestock farmers, especially in developing countries like India, Brazil and China (the three countries

with the largest herds of cattle in the world) [7].

A promising vaccine strategy for a new generation of BPV vaccines explores the immunization against minor viral capsid protein L2 [3]. Vaccination based on the L2 protein provides cross-protection against various types of human papillomavirus [8] - due to homology of neutralizing epitopes found at the N terminus of L2 protein [9] - and the vaccine antigens can be generated in bacterial systems, which reduces production costs compared to those of vaccines based on VLPs [3]. However, a major obstacle is the titers of neutralizing antibodies produced against L2, much smaller than L1 VLPs [10].

In this context, there is a set of therapies with limited efficacy for treatment of BPV-infected animals [11,12]. The traumatic removal of the lesions is frequently recommended when the animal presents few papillomas as well as the chemical treatment. The great demand for an efficient product for the treatment of papillomatosis, due to the difficulties encountered in its control and the increasing in incidence observed in recent years. In the extreme case occurred in the Japanese herd [12], the control of hematophagous insect populations in the fields can be effective to stop the transmission of BPV, although the main mechanism of viral spread is the direct or indirect contact with the source of infection.

Although regarded as an old disease, new discoveries about BPV infection such as identification of new variants, co-infection by multiple genotypes, viral spreading through non-epithelial sites and heterologous infection, gave to this disease, an increasing importance [13]. The stress out the lack of understanding and implies the urgency for more studies on this subject, as well as the need for developing control strategies against bovine papillomatosis. Main goal should be establishing an effective and affordable vaccine approach, in opposite to the current expensive and low effective strategies. Challenges faced with anti-HPV vaccines show a long way to be coursed.

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