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The Veterinary Journal 170 (2005) 289–299
The Veterinary Journal
www.elsevier.com/locate/tvjl

Review

# Recent developments in veterinary vaccinology

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**Abstract**

Advancement in technology and science and our detailed knowledge of immunology, molecular biology, microbiology, and biochemistry among other basic science disciplines have defined new directions for vaccine development strategies. The applicability of genetic engineering and proteomics along with other new technologies have played pivotal roles in introducing novel ideas in vaccinology, and resulted in developing new vaccines and improving the quality of existing ones.

Subunit vaccines, recombinant vaccines, DNA vaccines and vectored vaccines are rapidly gaining scientific and public acceptance as the new generation of vaccines and are seriously considered as alternatives to current conventional vaccines. The present review focuses on recent advances in veterinary vaccinology and addresses the effects and impact of modern microbiology, immunology, and molecular biology.


*Keywords:* Vaccinology; Veterinary vaccines; Vaccine development

## 1. Introduction

Vaccinology was born with Edward Jenner's discovery of smallpox vaccine that changed the world of medicine forever. He discovered that immunisation with antigenically related but less virulent virus (Cowpox virus) protects against a more virulent virus (smallpox virus). The first century-and-a-half after Jenner's discovery were mostly spent trying to establish and understand the principles of the science, and in the past five decades, the marvels of vaccinology have been shaped. Worldwide eradication of smallpox and drastic reductions in other infectious diseases such as polio, diphtheria, tetanus, pertussis, measles, mumps and rubella are attesting to the fact that vaccination is the most feasible and cost effective strategy to prevent, control and eradicate infectious diseases (Andre, 2003).

As a multidisciplinary science, vaccinology incorporates several scientific disciplines such as immunology, microbiology, molecular biology, biochemistry and statistical sciences, and also engages in several other issues such as regulation, licensing and ethical considerations. Vaccines were primarily considered to prevent infections and lately scientists have been working on the ideas to design vaccines against cancer, for birth control, and vaccines for lowering immune responses (e.g., in autoimmunity or allergy).

Veterinary vaccinology addresses a broad spectrum of objectives. Providing cost effective approaches to prevent and control infectious diseases in animals, to improve the animal welfare and to decrease the cost of production in food animals are primary goals (Walker, 1992; Pastoret, 1999). However, the mass vaccination of animals has been seriously considered as a means of preventing the incidence of zoonoses. Moreover, due to mass vaccination programmes, consumption of different veterinary drugs has been reduced significantly, and this has resulted in a reduction in their environmental

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doi:10.1016/j.tvjl.2004.07.004

impact, their side effects and residues in food animal products (Pastoret, 1999). In summary, veterinary vaccinology besides improving the animal health sector itself, has also substantially enhanced public health.

Traditionally, most current licensed veterinary vaccines are killed or live modified vaccines. Although widespread use of these vaccines has contributed considerably to the improvement of animal and public health throughout the world they have serious shortcomings and are far from perfect. Conventional vaccines are generally expensive to produce, require adjuvants and multiple inoculations to induce optimal immunity, may interfere with maternal antibodies, and consequently confer little or no protection in neonates (Chappuis, 1998; Pastoret, 1999). Toxoids induce reliable humoral immunity but little or no cell mediated immunity. Killed whole cell vaccines contain both immunogenic and non-immunogenic components, and immune responses against the non-immunogenic components are entirely irrelevant to the prevention of infection and may even interfere and reduce the immune responses to immunogenic components. They may also cause adverse side effects due to undesirable components such as endotoxins (Wegener et al., 1998).

Live modified vaccines are attenuated and capable of inducing both humoral and cell mediated immune responses, and in the last several years, there has been a large amount of research and debate regarding the current protocols and recommendations for vaccination with live modified vaccines. It merits consideration that live modified vaccines are available only for a limited number of pathogens, and the potential of pathogenicity in immunocompromised animals and the risk of conversion to wild type and pathogenic form are serious disadvantages of live attenuated vaccines (Moos, 1995; Terpstra and Kroese, 1996a,b).

This review will not probe into all details of the vaccines and vaccination in the global animal health sector but will attempt to focus on the aspects of interest in food animals and public health.

## 2. Host defence against pathogens

The main aim of vaccination against infectious diseases is to stimulate host adaptive immune responses to counteract the infection. In contrast to innate immunity, recognition of foreign antigens by an adaptive immune system is highly specific (Takahashi, 2003). Principally, adaptive immunity consists of humoral and cell-mediated immunity (Germain, 1994). Production of antibodies is a major effector function of B-cells (plasma cells) and an indicator of activation of humoral immunity. Strong humoral immunity can be protective against extracellular infections. Extracellular pathogens reside and replicate outside host cells in alimentary, urogenital and respiratory tracts and avoid phagocytosis and subsequent killing by host monocytes, neutrophils and macrophages. Hence, the main effector function of host immunity to control and clear the extracellular infection will rely on the production of specific antibodies and activation of complement system. However, most of the aetiological agents of endemic, epidemic or emerging infectious disease of veterinary interest are intracellular pathogens such as viruses, certain bacteria and parasites.

Immunity against intracellular pathogens is a complex process and requires strong cell mediated immune responses. In general and during the course of infection, intracellular pathogens should adhere to host cells, enter the cell and grow intracellularly. Interfering with any of these stages by the immune system may prevent the disease. Inhibiting the adherence and entry may be the most effective method to prevent the pathogenesis of intracellular pathogens. A strong humoral immunity can prevent the adherence of the pathogens to the host cells that do not carry Fc receptors (Fluckiger et al., 1998). Also, antibodies can opsonize the pathogens and make them prone to internalisation by phagocytes that carry Fc receptors. Internalisation by phagocytes is detrimental to majority of pathogens and results in degradation of phagocytosed organisms (Hostoffer et al., 1994; Mosser, 1994).

After entry into the host cells, the pathogen will be relatively inaccessible to humoral immunity and therefore a strong cell-mediated immunity is required to restrain and clear the internalised pathogen. Intracellular pathogens reside either in membrane bound vesicles (phagosome) or in the cytoplasm of the host cell. *Salmonella* and mycobacteria inhabit and even replicate in the vesicles, whereas *Listeria monocytogenes* and most viruses reside and replicate within cytoplasm (Goossens et al., 1995; Kaufmann and Hess, 1999).

As a general rule, antigens from vesicular intracellular pathogens are processed and presented in the context of major histocompatibility complex (MHC) class II molecules to activate naïve or reactivate memory CD4+ T-cells (van Bergen et al., 1999), and the antigens from cytoplasmic intracellular pathogens are processed and presented via class I processing and presentation pathway to CD8+ T-cells (Germain, 1995; Reimann and Schirmbeck, 1999). However, it has been shown that antigens expressed extracellularly (exogenous) may be presented via the class I pathway, and by using fusion to different peptides Kim et al. (1997) directed the fate of an antigen for presentation by a particular MHC molecule.

CD4+ T-cells are potent effectors, and CD4 dysfunction is associated with increased susceptibility to various infections. The dominant role of CD4+ T-cells in defence mechanisms includes both induction (antigen recognition and T-cell activation) and effector (cytokine