Another Look at the "Dismal Science" and Jenner's Experiment

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KEYWORDS

• Immunology • Adverse reactions • Memory • Vaccines

KEY POINTS

- Defense of the vertebrate body comprises 3 layers: physical barriers, innate immunity, adaptive immunity.
- B cells and antibodies recognize whole proteins; T cells recognize processed proteins.
- Innate immunity contributes to adverse reactions and vaccine efficacy.
- Overall effectiveness of vaccines and memory depends on the life style of the pathogen.

Immunology is a course that most veterinary students suffer through; many would consider its reappellation as the "dismal science" more than appropriate. One carrot in the course is the lectures on vaccines, because even a pedestrian pre-veterinary experience would indicate the continued relevance of the now 200 years plus-old gutsy, if not totally original, "experiment" of Edward Jenner[1]; vaccination remains a backbone of practice and the stuff of preventative medicine. The chapter on vaccines in immunology textbooks generally contains a table listing the advantages and disadvantages of live versus dead (inactivated) immunogens.[2] Live vaccines confer a broader, longer lasting immunity, require fewer doses, and are less likely to stimulate "hypersensitivity," whereas inactivated vaccines are stable and "safer" because they are less virulent and do not replicate in the vaccine. Beyond the midterm and final examinations in immunology class we have all internalized these "facts" at some level and consciously or unconsciously routinely apply them in practice. But, what features of the immune response and characteristics of pathogens and respective vaccines validate, or invalidate, our working assumptions? How does an understanding of the basic science of "vaccinology" avert oversimplification, thereby avoiding unrealistic

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expectations of vaccine efficacy and duration of immunity, and misunderstandings regarding "adverse reactions" (to vaccines)? And, how do more recent studies in the dismal science broaden our understanding and suggest further applications for vaccination? This review is an attempt to again address this subject for the practicing small animal veterinarian; hopefully, being both at least somewhat practical, and not overly soporific.

A BRIEF OVERVIEW OF THE "DISMAL SCIENCE": IMMUNOLOGY

Conceptually, defense of the vertebrate body can be seen to consist of 3 overlapping layers. The first layer comprises constitutive anatomy, microanatomy, and physiology. The skin, the body's largest organ, is the most obvious example of a physical barrier. Ciliated epithelium and the overlying "mucous," that is actually a complex cocktail, comprise the "mucociliary escalator" that perform housekeeping functions in the respiratory tract.[3,4] A similar microanatomical/physiologic barrier is found in the gastrointestinal tract.[5] These barriers keep the respective mucosal surfaces "scrubbed" of pathogens. In recent years, the microbiota or "normal flora" of various body systems, especially the mucosae, have been much studied as a modulator of colonization by pathogens.[3,4,6] All of these protective constitutive structures and functions can be affected by a variety of co-factors ranging from poor nutrition to the number of air changes in a boarding kennel, thereby precluding the possibility that vaccination can be the "silver bullet" solution to every (management) problem.[4,7]

If the constitutive barriers are breached by pathogenic microbes, the next layer, the innate immune response, comes into play. Although innate immunity has long been recognized as an ancient part of vertebrate defenses,[8] it is only in the last couple of decades that it has been intensively studied, more fully characterized, and taught to any extent in veterinary curricula. The plethora of molecular interactions that comprise the innate immune response is perhaps best summarily thought of as an inflammatory response involving a variety of cells that are spread throughout the body, including neutrophils, eosinophils, natural killer cells, and monocytes and macrophages; soluble mediators, notably type I interferons; and the often memorized and forgotten cascade, complement.[9–11] Traditionally, innate immune responses have been considered to be "nonspecific" and devoid of "memory."

If invaders persist in defiance of an innate immune response, adaptive or acquired immune responses are triggered; that part of the overall response that medical professionals have generally paid most attention to, because it is these responses that have been traditionally associated with the use of vaccines. Even the most immunophobic of veterinarians, of course, remember that the adaptive response comprises both "humoral" or antibody responses involving B lymphocytes and plasma cells, and cell-mediated immunity responses involving acronym-shrouded, too complicated subpopulations of T lymphocytes and the cytokines they produce.[12] Historically, specificity and memory differentiate adaptive responses versus innate responses.

HOW DOES THE IMMUNE SYSTEM "SEE THE WORLD," AND WHAT ARE THE IMPLICATIONS FOR VACCINE CHOICE AND EFFICACY?

As with all the rest of life on the planet, interactions between the immune system and the outside world unavoidably, ultimately, come down to biochemical reactions; in this case receptor-ligand interactions, a common modus operandi in most body systems. Generically, in the case of the innate response, the ligands are biochemical motifs or patterns that are "foreign"; not found in vertebrates. Notable examples include