Pediatric Immunology and Vaccination

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While the majority of scientific evidence indicates that foals are immunocompetent at birth, vaccination is complicated by interference by passively transferred maternal antibody. In addition, there is considerable clinical evidence of poor resistance to disease or response to primary vaccinations in the first year of life. Against this background it is critical to identify and develop potent vaccination regimes to generate effective immune responses in foals. Author’s address: School of Veterinary Medicine, University of Wisconsin, 2015 Linden Dr. West, Madison, WI 53706. © 1997 AAEP.

1. Introduction
This paper reviews our current understanding of the development of equine immunocompetence, and against this background it discusses the interactions between vaccines and the immune system. A subsequent paper discusses current foal vaccination strategies.

2. Development of Equine Immunity
A. Ontogeny of the Equine Immune System
There have been few studies of the prenatal development of the equine immune system. As in other species, the thymus is the first lymphoid organ to develop, and mitogen responsive cells can be identified there from day 80 of the 340-day gestational period of the horse.1 Subsequently these cells appear in peripheral blood at 120 days, in lymph nodes at 160 days, and in the spleen at 200 days. Cells responsive in mixed lymphocyte reactions are detectable in the thymus from 100 days and in the spleen at 200 days. Immunoglobulin production is detectable prior to 200 days, and newborn foals typically have IgM concentrations in their serum of approximately 165 µg/ml. Overall, it appears that functional T lymphocytes are present by day 100 and B lymphocytes by day 200 of gestation. When immunological competence of the equine fetus is assessed in terms of specific antibody responses, in utero immunization of foals in late gestation with keyhole limpet hemocyanin in an alum adjuvant results in detectable specific antibody production and T-cell responsiveness at the time of birth.2 In addition, the equine fetus can respond to coliphage T2 at 200 days and to Venezuelan equine encephalitis virus at 230 days.3,4

B. Immunocompetence in Foals
1. Passive Transfer of Immunity
There is no transplacental transfer of immunoglobulins across the diffuse epitheliocorial placenta of the foal. Consequently, foals are born essentially agammaglobulinemic, and they must absorb passively transferred maternal immunoglobulins from colostrum if they are to survive.5 Although foals are capable of de novo immunoglobulin synthesis at birth, endogenously produced immunoglobulins will not reach adequate levels until the foals are 2 months of age. The importance of failure of passive
transfer of immunoglobulins in causing morbidity and mortality in foals has been extensively documented and represents a major problem in the horse industry. Equine colostral antibodies include all the isotypes present in serum, and in similar proportions and concentrations. It is possible to substitute bovine colostrum to achieve a level of immune protection in foals, although the resulting immune protection may be suboptimal.

2. Primary Immune Responses in Foals
Infectious disease in neonatal foals is associated with high morbidity and mortality. Although failure of passive transfer is a major cause of this problem, immaturity of the immune system has also been considered a potential contributing factor. As a result, a number of studies of neonatal immunocompetence have been completed. Neutrophils are generally found to be fully functional from birth; however, their function is significantly impaired prior to absorption of colostral antibodies, which are required for opsonization. Alveolar macrophages recovered from bronchoalveolar lavages may be low in number up to 2 weeks of age and have impaired chemotactic function. Lymphocyte blastogenesis responses may be depressed on the day of birth; subsequently, they rapidly rise to adult levels. Overall these studies indicate that the normal foal is immunocompetent but immunologically naive at birth. Although the foal can respond to foreign antigens from the day of birth, a factor that significantly affects de novo immune responses in foals is the suppressive effects of passively transferred maternal antibodies. The rate of decline of these antibodies varies for both individuals and different infectious agents. For many important pathogens, the concentration of maternal antibodies in foals falls to nonprotective levels by 2–3 months of age. However, the remaining antibody can still render the foal unresponsive to vaccination for weeks or even months to come. In the case of equine influenza virus infection, maternal antibodies can persist until 6 months of age and prevent immune responses in foals vaccinated prior to reaching that age.

3. Immunodeficiency in Foals
Primary immunodeficiencies of foals are addressed elsewhere in these proceedings. Causes of secondary immunodeficiency in the horse have been associated with failure of passive transfer (see above), malnutrition, in utero equine herpesvirus 1 infection, lymphosarcoma, and pregnancy. In addition, Prescott proposed immunodeficiency as an explanation for the high frequency of respiratory tract infections affecting foals in the period from 1 to 6 months of age. One particularly important form of respiratory disease in horses of this age group is Rhodococcus equi infection. This pathogen can cause epidemic disease in foals, and currently the only effective prophylactic measure for foals is the administration of plasma from hyperimmunized donor horses prior to exposure. This intracellular pathogen parasitizes macrophages, and it appears to be able to resist defense mechanisms in the age groups of foals in which it causes disease. Although there is considerable circumstantial evidence for decreased resistance to infectious disease in foals, no specific immunodeficiency syndrome has been defined that explains this phenomenon. In certain instances, infections with pathogens such as Pneumocystis carinii or Candida albicans in young horses certainly are consistent with a diagnosis of immunodeficiency. However, given the current limitations of objectively measuring immunocompetence in horses in field conditions, it is difficult to determine whether the high rate of respiratory infections in young horses represents an immunodeficiency state or a normal age-dependent susceptibility to respiratory infections that is exacerbated by current husbandry practices.

3. Vaccination for Prevention of Disease
A. Introduction
Veterinarians can manipulate the equine immune system in a number of ways to prevent disease. Examples include providing passive immunity through plasma transfusions, stimulating active immune responses through vaccination or the administration of specific or nonspecific immunostimulants, or reconstituting a normal immune response through resolving immunosuppressive disease states such as nutritional deficits. The remainder of this paper reviews current and future strategies for the immunization of horses against infectious disease. Current vaccination strategies can be broadly divided into the administration of live and dead vaccines. Live vaccines include attenuated microbes and recombinant vaccines that utilize a living vector, whereas dead vaccines include killed whole pathogens, soluble pathogen subunits, or protein subunits. Live vaccines, although often successful in generating immunity, can be dangerous in immunocompromised or pregnant hosts, can revert to pathogenicity, and may be contaminated with other pathogens. Dead vaccines may be safer in use but frequently fail to induce appropriate and protective immune responses, despite the intense investigation of novel adjuvant strategies.

Currently a wide variety of vaccines are available for use in horses, but the efficacy of these products varies widely despite the fact that many of these vaccines are similar in design, as they contain killed organisms or toxoids combined with simple adjuvants. A significant reason for this is that this single type of vaccination strategy will stimulate only one array of immune responses. In the case of infections such as tetanus, the inactivated toxoid vaccines generate neutralizing antibodies that are highly successful in providing long-term complete protection. However, in the case of viral infections, such as equine influenza virus, current inactivated
virus vaccines fail to induce the complete spectrum of immune responses required for lasting and effective protection. The first step to overcoming the limitations of current vaccines is to understand what types of immune responses are required to protect against a specific pathogen.

B. Equine Immunity to Infectious Disease

The basic host defenses against infectious disease are outlined in Table 1. Immune defenses include both innate and adaptive responses, but only adaptive responses can be induced by vaccination. The specificity of adaptive responses, mediated by antibodies or by effector cells such as cytotoxic T lymphocytes (CTL’s), is responsible for their capacity to protect an animal completely against a particular pathogen. For many years immunologists have observed that while the horse is subject to several diseases whose control requires an improved understanding of equine immunological defenses, our ability to design better vaccines is limited by our knowledge of equine immunobiology. However, in the past decade many of the technological barriers to performing detailed immunological investigations in horses have been removed by the development of numerous monoclonal antibodies and the cloning of important cytokine and T-lymphocyte receptor genes. Although this scientific effort is admirable in itself, when will it result in new and more efficacious vaccines? The production of these new reagents does not resolve the questions surrounding the pathogenesis of disease, but it does provide researchers with the tools to address these issues. Progress in this regard is demonstrated by several recent studies identifying the importance of cellular immunity for protection against equine herpesvirus 1 (EHV-1) or equine infectious anemia virus infection, mucosal immunity for protection from influenza virus infection, or the effects of exercise stress on immune defenses. The goal of investigators is to properly understand what type of immune responses can protect against a disease, so that vaccines can be designed that can themselves induce the same protective responses.

### Table 1. Barriers to Infection

<table>
<thead>
<tr>
<th>Physical barriers</th>
<th>Immunity</th>
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<tbody>
<tr>
<td>skin</td>
<td>innate immunity</td>
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<tr>
<td>mucociliary escalator</td>
<td>chemical poisons</td>
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<tr>
<td>cough response</td>
<td>complement</td>
</tr>
<tr>
<td></td>
<td>phagocytic and cytotoxic cells</td>
</tr>
<tr>
<td></td>
<td>neutrophils and macrophages</td>
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<tr>
<td></td>
<td>natural killer cells</td>
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<tr>
<td>Adaptive immunity</td>
<td>lymphocytes</td>
</tr>
<tr>
<td>antibodies</td>
<td>cellular immunity</td>
</tr>
</tbody>
</table>

### Table 2. Effector Molecules and Cells of the Adaptive Immune System

<table>
<thead>
<tr>
<th>Effector</th>
<th>Accessory Factors</th>
<th>Infectious Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>Complement, neutrophils</td>
<td>Bacteria (strept., tetanus, etc.), viral neutralization</td>
</tr>
<tr>
<td>IgA</td>
<td>Alternative complement pathway</td>
<td>Respiratory, enteric and genital infections; viral attachment</td>
</tr>
<tr>
<td>IgE</td>
<td>Mast cells</td>
<td>Intestinal parasites</td>
</tr>
<tr>
<td>IgM</td>
<td>Complement, macrophages</td>
<td>Encapsulated organisms</td>
</tr>
<tr>
<td>CTL (CD8+)</td>
<td>Perforin, lymphotoxin</td>
<td>Viruses and mycobacteria</td>
</tr>
<tr>
<td>Th, lymphocytes</td>
<td>Macrophages</td>
<td>Mycobacteria, viruses, fungi</td>
</tr>
</tbody>
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The types of immune effectors, and the infectious agents against which they are most effective, are listed in Table 2. This is a simplified overview. For example, IgG is considered as a single type of immunoglobulin, while in reality there are different subtypes of IgG with different functions. To understand how these different types of immune responses are induced, one must have at least a rudimentary understanding of the biology of T lymphocytes, as it is these cells that govern the adaptive immune responses that we need to generate with vaccines. Two concepts in particular have to be grasped. The first is the process of antigen presentation to T lymphocytes, and the second is the division of T-helper lymphocytes into two subsets.

C. Antigen Presentation

A critical division of T lymphocytes is into CTL’s that express the CD8 molecule, and helper T lymphocytes (T helper or Th) that express the CD4 molecule. Expression of these molecules outside of the thymus is mutually exclusive, which means that T lymphocytes must be either CD4 or CD8 positive. The next thing to understand is that T lymphocytes don’t respond directly to antigens present on the surface of a virus, for example. Instead they recognize small processed antigen fragments that are present on the surface of either infected cells, or on cells that are specialized for capturing foreign antigens and presenting them on their surfaces, such as macrophages. This latter type of cells is termed an antigen presenting cell. These antigen fragments are always presented by major histocompatibility (MHC) molecules, which can be divided into MHC class I molecules, which are present in all cells, and MHC class II molecules, which are only present in specialized antigen presenting cells. Antigens are processed for presentation either by the endogenous pathway, resulting in presentation by MHC I molecules, or by the exogenous pathway, resulting in presentation by MHC II molecules. What this means is that antigens absorbed from outside the cell, by phagocytosis for example, are presented by MHC II molecules. Antigens produced inside the cell, as is the case during viral infection, are pre-
Th1 cells, which can activate the macrophage by the macrophage requires help from inflammatory the appropriate T-helper response. An example of pathogen is to be produced, vaccination must induce such infection in foals.26 In order to overcome such infection the Th1 subset produces the cytokines interleukin 2 (IL2) and interferon gamma (IFN-\(\gamma\)), which are necessary for the development of CD8+ T-helper lymphocytes? These lymphocytes, as their name implies, help other effector cells to fight off pathogens. Currently it is believed that two different subsets of T-helper cells, characterized by their cytokine production profile, may be responsible for determining the nature of the immune response to infectious agents.48,49 The subsets are the T-helper 1 subset (Th1), which stimulates cytotoxic and inflammatory functions, and the T-helper 2 subset (Th2), which stimulates strong antibody and allergic responses. The Th1 subset produces the cytokines interleukin 2 (IL2) and interferon gamma (IFN-\(\gamma\)), which are necessary for the development of cell-mediated immune responses, while the Th2 subset produces IL4, IL5, IL6, and IL10, which favor the development of humoral immune responses. These two types of T-helper subsets and the cytokines they produce tend to suppress each other, so that in an immune response to a particular pathogen either the Th1 or the Th2 will predominate, resulting in either an inflammatory–cytotoxic or a humoral immune response.

Therefore, if an appropriate immune response to a pathogen is to be produced, vaccination must induce the appropriate T-helper response. An example of such a circumstance may be R. equi infection in foals. Like other intracellular pathogens, such as Salmonella spp., this organism survives by parasitizing macrophages.26 In order to overcome such infection the macropage requires help from inflammatory Th1 cells, which can activate the macrophage by secretion of cytokines such as IFN-\(\gamma\) and GM-CSF. In contrast, a Th2 response may be ineffective in combating these intracellular organisms and may actually be counterproductive by suppressing Th1 activity.

Several factors have been identified that may influence whether a Th1 or Th2 type of response will predominate, and these include the type of antigen presenting cell, the dose of antigen and adjuvant, the immunization route, specific antigen-MHC combinations, and the cytokines present during antigen presentation. The type of T-helper cell induced by vaccination will determine whether the vaccine is either helpful or possibly even detrimental in protecting against disease. Therefore, a key issue in vaccine development is the ability of different vaccination strategies to stimulate specific T-helper subsets.34,38

An example of the practical implications of this can be found in equine influenza virus infection.

E. Immunity to Equine Influenza Virus Infection

Equine influenza remains one of the most important infectious diseases of the horse throughout the world and is enzootic in North America. Strenuous attempts are made to control equine influenza virus infection by vaccination, but this approach is of limited value because currently available commercial vaccines may offer protection for as little as 2–4 weeks.50 Natural equine influenza virus infection confers complete clinical immunity for over 6 months and partial immunity for over 1 year.51 Long-term protective immunity against infection is therefore obviously possible, and a successful equine influenza vaccine should stimulate the same type of immune responses as infection does.

In murine models it has been demonstrated that influenza-specific IgA in respiratory secretions protects against influenza virus infection. To date there have been few descriptions of local antibody responses in the horse,52 although high levels of IgA have been demonstrated in the upper respiratory tract. For this reason we recently undertook an experiment to compare local and circulating antibody responses and protection resulting from a conventional commercial vaccination or natural influenza virus infection.53 The horse possess a particularly complex array of immunoglobulin isotypes, with four subtypes of IgG: IgGa, IgGb, IgGc, and IgG(T), in addition to the other immunoglobulin isotypes. These different types of antibody responses can be distinguished by using recently developed monoclonal antibodies.41

In our experiment, we found that 3 months after the administration of two doses of a conventional vaccine, ponies were left unprotected when subjected to a challenge infection. In contrast, 3 months after being given an initial influenza virus infection, ponies were completely immune to a repeat challenge infection. A critical difference between natural infection and vaccination was that infection induced high levels of IgA in nasal mucosal secretions, whereas vaccination induced no IgA antibodies. In addition there were marked differences in the isotypes of IgG induced by infection compared with
those induced by vaccination, with natural infection inducing IgGa and IgGb responses and conventional vaccines inducing IgG(T) responses. It is interesting to note that in the horse the IgGa and IgGb subisotypes are capable of mediating important antiviral activities such as complement fixation and antibody-dependent cellular cytotoxicity, whereas IgG(T) responses can actually inhibit complement fixation and are better adapted to neutralizing toxins such as those produced by the Clostridia spp.53,54

On the basis of this experiment, it is apparent that the local and systemic humoral immune responses to current conventional influenza vaccination are very different from those resulting from natural infection, and that this difference correlates with the level of protection induced. The local IgA responses in particular were characteristic of a mucosal antibody response, and such mucosal immunity may be critical for protection from many respiratory and enteric pathogens.

F. Effective Vaccination Strategies

The current range of vaccines includes some very effective products, as well as some relatively ineffective products. Vaccines tend to be effective when they are specific for diseases that normally result in protective immunity in patients who survive the disease, and when the vaccines mimic the immunological effects of the disease itself. The less efficacious vaccines frequently fail to induce the type of immune responses that result from natural infection. However, there is another scenario in which the natural infection itself does not normally induce long-term protection, such as in the case of herpesvirus infection. In this instance we are trying to produce vaccines that improve on the natural immune response, and this is a formidable challenge. In fact, effective immune responses to a particular disease may be undesirable as they may result in severe immunopathology, and there may be a biological advantage to coexistence with the pathogen. For example, an effective CTL response to a neurotropic virus could result in large-scale and permanent destruction of neurons.37 The most attractive infections in which to search for more effective vaccination strategies may therefore be those in which nature has already demonstrated that long-term immunity is both possible and desirable.

In the discussions above, three types of T lymphocytes have been identified that mediate immunity: the CTL, which can destroy virus infected cells; the Th1 lymphocytes, which can provide proinflammatory signals to activate cell mediated immunity (e.g., macrophage activation); and the Th2 lymphocyte, which can drive antibody production. In some cases we know which of these types of immune responses we need. For example, CTL’s may be essential for eliminating EHV-1 infection, macrophage activation may be necessary to fight R. equi, and IgG antibodies can protect against tetanus while mucosal IgA antibodies can prevent influenza virus infection. This may represent an oversimplification because a combination of immune responses is often used to effectively fight infection. In the case of both EHV-1 and influenza virus, a mucosal immune response may prevent viral entry while a simultaneous CTL response may clear any virus that does penetrate the defenses. What then are the tools that are available to try to generate these different immune responses?

1. Modified Live Versus Killed Vaccines

We have already seen that CTL’s have to see antigens presented with MHC I molecules. However, antigens that are transported into cells from the extracellular environment by phagocytosis will only be presented by MHC II molecules. This means that killed or inactivated vaccines are unlikely to be capable of generating a CTL response, and they are far more likely to generate only humoral immunity. This is one important reason for the success of attenuated or modified live vaccines (MLV’s). Generally MLV’s are far more effective than killed vaccines because they induce all the appropriate effector mechanisms. A viral MLV will produce proteins in the cytosol, which will be presented by MHC I molecules and induce CTL’s. Nevertheless, MLV’s have practical drawbacks. Attenuation of MLV’s is generally achieved by growing the virus in abnormal conditions. The mutations that result are often poorly defined, and reversion to virulence is a constant threat. In the future MLV’s may be available in which specific mutations are produced, using recombinant DNA technology, which cannot be reversed. Another concern with MLV’s is that they may produce disease themselves, and animals may require rest and a stress-free environment at the time of vaccination. In the case of diseases that cause abortion, this problem prevents the use of MLV’s during pregnancy.

For these reasons killed vaccines remain attractive, but if they are to be effective, new delivery systems and adjuvants must be developed. The success of killed vaccines depends on the adjuvant system used, as adjuvants can determine the form of immune response that will be stimulated, through stimulating either the Th1 or Th2 regulatory lymphocyte subsets. Current adjuvants such as alum tend to stimulate Th2 responses, whereas Freund’s complete adjuvant stimulates Th1 responses. However, although FCA can induce Th1 responses, this adjuvant cannot be used because of its side effects. Considerable current research is directed toward developing new adjuvants for this purpose.34,55

The explosion of knowledge in the field of recombinant DNA technology has led to the identification and in some instances synthetic production of many of the specific antigens that are important for immunity to pathogens. Unfortunately, these purified proteins are typically poorly immunogenic by themselves and still cannot overcome the barriers that prevent MHC I presentation. An ideal vaccine
might contain such a synthetic peptide combined with a new adjuvant that renders the peptide immunogenic and can transport it into the cellular compartments that will allow for MHC I presentation and CTL induction. This is currently an area of intense investigation, and one of the most promising adjuvants for this purpose is the immune stimulating complex (ISCOM) that can be prepared from the Quil A plant bark saponin. This technology is described in greater detail elsewhere. Briefly, ISCOM adjuvants have been associated with greatly increased antigen-specific antibody responses, and a wide range of T-cell responses including the induction of cytotoxic T lymphocytes. This latter finding suggests that ISCOM's may allow soluble antigens to enter the endogenous antigen processing pathway in a physiological manner and be presented with MHC I. There is already evidence of the efficacy of influenza virus ISCOM vaccines in horses, and a commercial equine influenza virus ISCOM vaccine has been available for several years in Sweden and more recently in Great Britain. Dr. Jenny Mumford and Dr. Duncan Hannant at the Animal Health Trust, Newmarket, UK, have completed a series ISCOM vaccination trials in horses. In one study they reported protection 5 months after intramuscular vaccination, whereas another study indicated that protection could last as long as 15 months.

2. Mucosal Vaccination
The desirability of inducing mucosal immune responses to pathogenic organisms has already been emphasized by using the example of equine influenza virus infection. However, attempts to stimulate mucosal immunity by vaccination are frequently met with little success despite the repeated administration of high doses of antigen. As an alternative to the local administration of MLV's with their associated drawbacks, two strategies that show considerable potential for generating equine mucosal immune responses are the use of either cholera toxin or the same ISCOM adjuvants described above. Cholera toxin administered at mucosal surfaces is both strongly immunogenic and a powerful adjuvant for other coupled or coadministered antigens. Cholera toxin is the enterotoxin produced by Vibrio cholerae and is responsible for the excessive enteric secretion of electrolytes and fluid in humans suffering from cholera. The mucosal administration of small amounts of relatively nonimmunogenic protein antigens can elicit vigorous mucosal IgA when these proteins are coupled or admixed with cholera toxin. A disadvantage of using cholera toxin is that it can produce cholera diarrhea in humans, although it is well tolerated in other species. Protection against equine influenza virus infection is a highly appropriate large-animal model in which to study cholera toxin as a mucosal adjuvant, because mucosal immune responses are critical in protection against influenza virus infection and large domestic species are resistant to the toxic effects of cholera toxin. In preliminary experiments recently completed in our laboratory, we found good evidence that cholera toxin may be an excellent respiratory tract mucosal adjuvant when administered by nebulization to horses. However, although cholera toxin may prove to an excellent tool for examining mucosal immunity, its practical application in equine vaccines may be limited by its extreme toxicity to humans at the doses required to generate mucosal immunity.

G. DNA Vaccination
Given the limitations or potential side effects of current live or dead vaccines, it is important to continually examine new vaccination strategies. The most novel vaccination technique currently under investigation is DNA vaccination. This is a radically different form of vaccination that may offer considerable advantages over conventional strategies, and it is based on the administration of plasmid DNA (variably termed genetic, nucleic acid, or DNA immunization). DNA vaccination results in the in vivo synthesis of antigenic proteins in a manner identical to that occurring in natural infection. This endogenous production results in presentation of antigens by MHC I and presentation to CD8+ T-cytotoxic lymphocytes, and uptake and presentation of soluble proteins by MHC II to CD4+ T-helper lymphocytes. As a result, DNA vaccination has been shown to induce both potent CTL and antibody responses. To date no undesirable side effects have been associated with the use of DNA vaccination, although the potential risks of long-term antigen expression or integration of plasmid DNA into host chromosomes require further evaluation. Overall, DNA vaccines can deliver the immunogenic advantages of live vaccines but at a low cost and with minimal safety concerns. The intense scientific interest in DNA vaccination can be gauged by visiting the World Wide Web site maintained by Dr. Robert Whalen.

In collaboration with Dr. Chris Olsen (University of Wisconsin—Madison) and Geniva (Madison, WI) we are currently using DNA vaccination in horses to protect them from influenza virus infection by vaccinating with the DNA sequence that codes for the critical hemagglutinin protein. We are particularly interested in generating mucosal immune responses by this method, and therefore we are experimenting with vaccination of both skin and mucosal surfaces. In this project, DNA vaccination of nasal mucosal surfaces is performed by using a gene gun, which employs a high-energy microparticle bombardment method to fire DNA-coated gold beads into target tissues. This system has been compared with other types of DNA inoculations and found to be by far the most efficient. Preliminary results have given a strong indication that this method of vaccination does protect horses from influenza virus infection, and does so by inducing appropriate antibody isotype responses.
4. Special Considerations for Vaccinating Foals

We know that foals appear to be immunocompetent at birth, but we also know that immune responses to vaccines can be limited by interference that is due to maternal antibodies. In addition there is considerable clinical evidence of a high incidence of infectious disease in foals in the first year of life, and also of a poor response in this age group to vaccination regimes. These facts argue strongly that new and powerful vaccines are required if we are to vaccinate foals effectively against pathogens such as influenza virus, EHV, or R. equi. In order to vaccinate effectively in the face of maternal immunity, more potent vaccines, such as MLV’s, may be indicated. Recently it has been shown that a canine parvovirus MLV can effectively overcome a significant level of maternally derived antibody interference. Even so it was necessary to use a low-passage MLV, meaning that the vaccine virus was relatively less attenuated during production. In addition a high titer of vaccine virus was necessary. When it is necessary to modify MLV’s in this way, the safety margin of vaccines is decreased. For this reason investigations of safer killed vaccines combined with more potent adjuvants will continue. In addition there is reason to anticipate that DNA vaccination may circumvent interference by maternal antibodies, although this has yet to be established in horses.

Although it is always tempting to bank on the development of more powerful vaccines to protect animals, it is critical to remember that no vaccine will protect in the face of a high pathogen load. This is particularly true in debilitated or young animals. Therefore vaccines must be seen as a single component of our response to the threat of infectious disease, and as veterinarians we must continue to emphasize the critical importance of good husbandry in disease prevention.

References and Footnotes


