Impact of Parasites on the Immune System of Cattle. Gary L. Zimmerman, BS,MS,PhD,DVM, College of Veterinary Medicine, Oregon State University, Corvallis, Oregon 97331-4802.

All cattle have parasites. Even low worms burdens, often considered normal, can have an economic impact on productivity. The major effects of parasitism are not from competition for host nutrition, but rather from phenomenon such as damage to host tissues, alteration of physiological functions, host reaction to the parasites, and adverse immune interactions. Consequences of the interactions between the host immune system and parasites can be dramatic. In order to survive in immunocompetent hosts, parasites either modulate or avoid the host immune responses. When parasites actively modulate host immunity, the results can range from the inapparent to severe pathologic changes that compromise the health and survival of the animal. The majority of these changes have some adverse effects on productivity. Suppression of host immune responses can increase susceptibility to other parasites as well as bacteria and viruses. Parasite-induced suppression of host immune systems may reduce responses to vaccines, which can be misinterpreted as vaccine failure. A practical consequence of the immune response to parasites is the production of antibodies that can be detected by various techniques. The complex immune interactions and a wide diversity of parasite transmission patterns require more than a cursory consideration to achieve maximum production efficiency. The astute bovine practitioner must consider the overall parasite-host interface in order to develop a more integrated approach to herd health programs.

Introduction

The theme of this meeting is "Challenges of the Bovine Industry in the Twenty-First Century." Improving herd health and production efficiency are among the greatest challenges facing practitioners. Parasites decrease productivity more than any other disease agent. Although clinical parasitism occurs in many parts of North America, low-level parasitism is more widespread and causes more overall production losses. Parasites burdens, as demonstrated by fecal egg per gram (EPG) counts as low as 10-20 EPG, can reduce productivity.[1] Recommendations for treatment should be based on the producer's return on investment (ROI). This decision is made with consideration of the current burden of parasites, and the potential of

further pasture contamination. All cattle carry burdens of parasites. Calves become infected shortly after birth and face various parasitic insults for the duration of their lives. Actual burden of parasites depends upon a myriad of diverse factors. A common misconception is that losses due to parasites result from competition with the host for nutrients. There are few cases when this is true. Host-parasite interactions are far more complex and have more significant consequences than previously recognized. Adverse effects of parasites result from physiologically active substances, toxins, and other products of parasite metabolic processes, direct physical or mechanical damage caused by the parasites, and immune mediated interactions. The dynamic immune interactions initiated upon the entry of these foreign organisms into the bovine host may prove to be among the most important factors affecting overall production. This paper is not written as a complete review of the host-parasite immune interactions that adversely affect production, but rather to stimulate practitioners to consider the various immunological interactions between ruminant hosts and helminth parasites that can either directly or indirectly affect productivity. A few selected reports are discussed as they relate more directly to bovine practice.

The physical or mechanical damage caused to hosts can be dramatic. Many worms damage hosts by burrowing into or migrating through tissues. As the worms develop and mature to adult stages, their size increases dramatically, with resultant pressure on and damage to host tissue. Substances originating from parasites can be toxic to host cells, suppress appetite, suppress hematopoiesis, and/or otherwise alter functions such as digestion, absorption, and metabolism. The diversity of these adverse affects are well documented. Less well known are the immune system interactions between the hosts and the parasites. While the host immune systems evolved as mechanisms to eliminate foreign invaders, the parasites of necessity evolved mechanisms to avoid or suppress host immunity. The immune responses are far more complex than just cell mediated and antibody mediated responses. Recent evidence also shows neuronal and hormonal interaction with the immune system. Such interactions are poorly understood and too complex to address in this presentation. However, knowing they exist further demonstrates the complex and interactive nature of the host-parasite immune interactions.

Immunomodulation and Immunopathology

Host immunomodulation and immunopathological reactions have been described for a number of the more common and important helminth parasites. Oesophagostomum radiatum infects parts of the small intestine, cecum, and proximal colon of cattle, resulting in inflammation and formation of nodules in the mucosa. A 25,000-35,000 mw fraction of the excretory-secretory products (ESP) from larvae of O. radiatum undergoing the molt from 3rd to 4th stage inhibits expansion of immunoreactive clones of bovine lymphocytes. By inhibiting the expansion of local antigen-specific lymphocyte clones, the parasite can effectively decrease the ability of the host to elicit a protective immune response.[2] Part of the tissue damage resulting from Ostertagia ostertagi infections is linked to the massive local infiltration of eosinophils in the mucosa of the abomasum. A lectin-like eosinophil chemotactic factor isolated from ESP of O. ostertagi stimulates the accumulation of these cells.[3] Reactive components of the eosinophils can be more damaging (Type I hypersensitivity) to the host tissues than to the parasite against which the immune response was intended. Circulating total and O. ostertagi specific IgE levels decrease in heavy worm burdens. IgE is sequestered on inflammatory cells and participates in the Type I hypersensitivity reactions.[4] Adverse immune responses have a role in the pathogenesis of O. ostertagi in cattle. Suppression of T-cell, but not B-cell activity, occurs during the first 8 weeks of infection.[5] Both O. ostertagi and Cooperia oncophora may immunosuppress calves, increasing the susceptibility to Dictyocaulus viviparous.[6] In mouse models, O. ostertagi interfered with immunity to unrelated antigens.[7] Suppression of antibody responses of Fasciola hepatica infected mice may be one of the means by which general or specific antibody responses are suppressed.[8] Liver flukes modulate the immune response of sheep, although specific studies have yet to demonstrate a similar phenomenon in cattle.[9]

Immunodiagnosis

A useful consequence of host-parasite immune interactions is the development of circulating antibodies, directed against parasite antigens, that can be demonstrated by a variety of laboratory techniques. There are advantages of immunodiagnosis compared to traditional parasitological techniques such as fecal examination for parasite eggs.

Antibodies directed against parasites can usually be detected during the pre-patent period. Various ELISA techniques are used to detect either circulating antibodies directed against the antigens or the antigens themselves. Modifications of the ELISA can detect antigens of gastrointestinal parasites in the feces of the host. When properly developed and field tested, emerging biotechnology techniques should provide an ever-increasing potential for improving diagnosis of parasitic infections. Direct detection of parasite DNA/RNA or gene products based on probes for nucleotides or monoclonal antibody probes should enhance epidemiological studies as well as diagnosis on an individual animal or herd basis. Such advances have been demonstrated in the diagnostic approaches to fascioliasis. The direct ELISA has been used to diagnose F. hepatica in cattle[10] and sheep approximately 6-8 weeks post-infection (PI).[11] A modification of the ELISA, the Dot-ELISA, detects antibodies to F. hepatica as early as 2 weeks PI in sheep[12] and cattle.[13] These ELISA techniques all utilize antigens obtained directly from the parasites. Monoclonal antibodies directed against components of the excretory-secretory products from flukes will prove increasingly useful in future diagnostic tests.[14] A DNA-probe described for the detection of fluke infected snails could be useful for epidemiological studies to estimate the risk of infection.[15] Similar biotechnology tools being developed at several universities will likely provide new diagnostic procedures for additional helminth infections such as ostertagiasis. Each of these techniques provides improved and early diagnosis of selected parasitic infections, allowing the practitioner to initiate treatment regimes before severe economic losses have occurred.

Immunoprotection

Bovine hosts develop various degrees of resistance to the different helminth parasites. With natural infections, protection is seldom if ever complete, due in part to the ability of the parasites to modulate host immune responses. The intent of vaccination against parasites is to improve on nature by stimulating protective responses while preventing host immunomodulation by the parasites. Antigens contained in either somatic extracts or ESP are most often considered as candidates for stimulating protective immunity. By selecting only specific fractions of these antigens that stimulate protective immune responses, the potentially immunosuppressive products from the parasites would not be

introduced into the host. Partial protection using antigens derived from nematodes, cestodes, and trematodes has been reported. One example is the demonstration that antigens derived from adult Oesophagostomum radiatum induced an 85% protective immunity in challenge infections in calves. The protection was highly correlated with IgG_2 isotype antibodies and with cellular immune reactivity.[16] As a novel candidate for inducing protective immunity, glutathione S-transferase (GST) isolated from Fasciola hepatica induced a 78% protection of sheep against challenge infection. Apparently the immune response to GST was directed against the juvenile.[17] The literature contains many studies reporting varying degrees of protection for many of the common helminth parasites of cattle. In spite of the advances in molecular biology and biotechnology, no commercial vaccines are available for the immunoprotection of cattle against helminths in the United States.

Summary

Host-parasite immune interactions are complex attempts by the host to eliminate the parasites and by the parasites to evade or suppress the host responses, with only limited success on either front. The ensuing immunopathological reactions that occur are often more severe than the direct damage caused by the parasite. Some helminth infections can be diagnosed by immunological techniques. Although there are no successful commercial vaccines for helminth parasites, immunoprotection is a future potential. Our knowledge and ability to conduct procedures (biotechnology) in the laboratory far exceeds our knowledge and understanding of the immune system and parasites. Premature attempts to apply biotechnological procedures have been discouraging and at times embarrassing.

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