Immunodeficiencies Caused by Infectious Diseases

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KEYWORDS

• Feline immunodeficiency virus • Feline leukemia virus
• *Anaplasma phagocytophilum* • *Ehrlichia canis*
• Distemper virus • Parvovirus

The classic example of immunodeficiency caused by an infectious agent is the acquired immunodeficiency syndrome, caused by human immunodeficiency virus (HIV). Similarly, the best known pathogens of companion animals causing immunodeficiencies are the feline retroviruses feline immunodeficiency virus (FIV) and feline leukemia virus (FeLV). However, several other pathogens are capable of disrupting normal immune function. Many infectious agents disrupt host barriers to infection. This may result from the inflammatory response to a pathogen or direct damage by the microbe itself. Examples include disruption of the gastrointestinal mucosal barrier by canine parvovirus, destruction of nasal turbinates by *Aspergillus fumigatus* in canine sinonasal aspergillosis, or paralysis of the respiratory cilia by *Bordetella bronchiseptica*. *Anaplasma phagocytophilum* disables neutrophil function, ensuring its survival within a cell normally charged with antimicrobial substances. Viruses, such as canine distemper virus, cause lymphopenia; the outcome of infection depends on the balance between viral destruction of the immune system and the ability of the remaining immune defenses to eliminate the virus.

Disruption of immune function by infectious agents may serve to promote the infectious agent's survival through host immune evasion. Immunosuppression having the greatest impact clinically often occurs as a result of infection with organisms that are able to persist within the host. Ideally, a pathogen is able to adapt such that it can coexist with the host, without causing death of the host or severe illness, in a way that maximizes the pathogen's transmission efficiency.

The types of opportunistic infections that occur in patients that are immune compromised as a result of an underlying immunosuppressive infection depend upon the mechanisms of immunosuppression. Impairment of normal host barrier function or the function of granulocytes is generally associated with a broad spectrum of bacterial

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Vet Clin Small Anim 40 (2010) 409–423
doi:10.1016/j.cvsm.2010.01.006 **vetsmall.theclinics.com**
0195-5616/10/$ – see front matter. Published by Elsevier Inc.

infections and sometimes infection with opportunistic fungi, such as *Aspergillus* spp Impairment of cell-mediated immunity (CMI) results in infections with opportunistic pathogens, such as *Nocardia* spp, *Mycobacterium* spp, *Toxoplasma gondii*, and a variety of fungal pathogens. Reactivation of dormant pathogens, such as feline herpesvirus, may also occur with depression of CMI.

The purpose of this article is to highlight some of the mechanisms by which persistent infectious microorganisms cause acquired immunodeficiency in companion animal species, and the consequences of the resulting disturbance in immune function.

VIRAL INFECTIONS CAUSING IMMUNODEFICIENCY

Canine Distemper Virus Infection

Canine distemper virus (CDV) causes canine distemper, a common disease of dogs worldwide that is associated with a high degree of morbidity and mortality. The virus also infects several other species, including foxes, raccoons, skunks, ferrets, and free-ranging and captive felids. Disease in dogs is most prevalent in regions where vaccination of young dogs against the disease is either not performed or is poorly timed, and epidemics continue to occur in shelter environments in developed countries.[1]

Canine distemper virus is a Morbillivirus related to measles virus and has been used to study the pathogenesis of measles virus infection. Morbilliviruses are enveloped RNA viruses that survive poorly in the environment. Based on genetic variation within the viral hemagglutinin (H) gene, a multitude of different strains of CDV exist that vary in their geographic distribution, cell tropism, and virulence. Although CDV infects a variety of different cell types, including epithelial, mesenchymal, neuroendocrine, and hematopoietic cells, the marked tropism of CDV for immune cells is critical in respect to its ability to cause immunosuppression. Viral components involved in CDV-induced immunodeficiency include the viral hemagglutinin; the V protein (a nonstructural phosphoprotein); and the nucleocapsid (N) protein.

Dogs are generally exposed to CDV through contact with infected oronasal secretions. The virus initially infects monocytes within lymphoid tissue in the upper respiratory tract and tonsils and is subsequently disseminated via the lymphatics and blood to the entire reticuloendothelial system. Direct viral destruction of a significant proportion of the lymphocyte population, and especially CD4+ T cells, occurs within the blood, tonsils, thymus, spleen, lymph nodes, bone marrow, mucosa-associated lymphoid tissue, and the hepatic Kupffer cells.[1–3] This viral destruction is associated with an initial lymphopenia and transient fever that occurs a few days after infection. Subsequently, there is a second stage of cell-associated viremia, after which CDV infects cells of the lower respiratory; gastrointestinal tract; central nervous system; urinary tract; and red and white blood cells, including additional lymphoid cells.

Elimination of CDV by the host depends on humoral and CMI.[1,4] Because the virus is lymphocytolytic, the outcome of infection depends on the rate at which the host is able to remove the virus before the virus has sufficient time to cause severe immune system injury. Dogs mounting a partial immune response may undergo recovery from acute illness but fail to eliminate the virus completely, leading to a spectrum of more chronic disease manifestations that often involve the uvea, lymphoid organs, footpads, and especially the CNS. Opportunistic infections may also have the chance to develop in these dogs.

Dogs with canine distemper may develop profound lymphopenia and leucopenia. Lymphopenia results from generalized depletion of T and B cells in a variety of tissues