Proceedings of the 33rd World Small Animal Veterinary Congress

Dublin, Ireland - 2008

Next WSAVA Congress:

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Vaccination and the Immune Status of the Cat
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The immune system
The feline immune system consists of the thymus and bone marrow, the peripheral lymphoid system (the lymph nodes, the lymphatic vessels, the spleen, and tonsils) and the extralymphatic organs: Peyer’s patches, cecum and bronchial lymphoid tissues.

All animals, including cats, have an innate immune system that functions via inherited responses to major common antigens (Ags) and includes white cell basic defenses (neutrophils/polymorphonuclear leukocytes - pmens) as well as the immune system itself. This innate system is invaluable for initial immune responses. The acquired immune system includes both antibody dependent and independent responses. This system comprises lymphoid cells, macrophages and other antigen presenting cells. These cells release cytokines that expand the immune response to include other body defense systems i.e., pmens, eosinophils, and macrophages.

Antigenic material triggers changes in lymph node structure through many interactions between lymphocytes, macrophages and their chemical messengers. Over a period of 7-10 days, plasma cells respond (humoral response) and produce immunoglobulins (Igs/antibodies). The initial response is regulated through IgM, and the amnestic/sustained response is mainly through IgG. Macrophages and T lymphocytes are the effector cells of the cell mediated immune (CMI) response to the antigenic stimulation.

Lymphocytes
There are three types of lymphocytes:
1. B-lymphocytes are antigen specific cells functioning through Ag-specific-antibody immunoglobulin receptors. Adult levels of B cells are attained by 12 weeks of age. Plasma cells represent the end stage of B cell differentiation. and are located in the medullary cords of lymph nodes, the red pulp of the spleen and in the sub epithelium of mucous membranes. Plasma cells are found at mucous membranes and any location where there is environmental contact. They are generally tissue bound but can circulate. They may be found in non-lymphoid tissue when chronic antigenic stimulation is present such as in stomatitis or IBD.
2. T-lymphocytes process specific Ag on their surfaces. 32-41% of peripheral blood lymphocytes are T cells. There are three types:
   - T helper (CD4) cells collaborate with B cells and facilitate Ab production
   - T suppressor (CD8) cells depress antibody formation by B cells
   - T-effector cells function in CMI reactions
3. Natural Killer (NK) cells (‘null cells’ or ‘large granular lymphocytes’) can destroy some tumour cells and virus-infected cells. They constitute 20% of feline lymphocytes.

Macrophages
These play several roles in the immune response. They:
1. process and present Ag to T cells
2. produce cytokines
3. lyse tumour cells using toxic metabolites and proteolytic enzymes
4. are effector cells in some forms of CMI (i.e., Type IV/ delayed hypersensitivity reaction).

How does the immune system work?
Humoral antibody production
Cats are not immunocompetent to all antigens at birth. Normal Ig levels vary considerably in cats depending on the environment they are reared in. IgG and IgA are found in serum and membrane secretions, IgA also in intestinal and respiratory mucus. IgM is important in the primary response to certain antigens and is secreted into colostrum, secretions and nasal mucus. Reaginic IgE is found in skin, mucous membranes and lung and has a high affinity for mast cell membrane receptors. It is involved in Type I (immediate) hypersensitivity responses.

Cell mediated immunity
CMI involves the interaction between T effector lymphocytes (or macrophages) with a specific antigen to release lymphokines. These act to a) kill cells the lymphocyte contacts, b) inhibit macrophage and leukocyte migration from the site and/or c) induce blastogenesis of lymphocytes. Cats have very well developed CMI.

The phagocytic system
Cats have an efficient phagocytic system that consists of fixed tissue histiocytes, splenic cells, lymph nodes, peritoneal macrophages and monocytes. The phagocytic system is highly developed and consists of fixed tissue histiocytes, splenic cells, lymph nodes, peritoneal macrophages. Circulating monocytes increase in chronic infection; they are transformed into macrophages. Neutrophils are highly phagocytic. Neutrophils participate in mast cell events and anaphylaxis.

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**Infectious Disease**

Cytokines are a large group of short acting soluble messenger polypeptide molecules, which mediate interactions, and effector functions of the immune responses. This large group of polypeptides also plays a role in the regulation of inflammatory and reparative host responses. There are four major groups of cytokines:

1. those which mediate natural immunity
2. those which regulate lymphocyte growth, activation and differentiation
3. those which activate inflammatory cells
4. those which stimulate hematopoiesis

**Membrane immunity**

Mucous membranes and the skin are the main barriers against microbial invasion. They protect mechanistically as well as with complex immune processes. Early in infection, epithelial cells secrete interferon, which protects against viral invaders until other facets of the immune response are activated. Complement binding facilitates phagocytosis and lysis of bacteria. These events precede humoral and cell mediated immune responses.

**Immunomodulatory events**

What day- to-day factors affect the immune system and thus determine when and whether vaccines should be administered?

**Stress**

This may be psychological, environmental or physical and encompasses a wide variety of insults. Acute stress causes epinephrine release; chronic stress induces cortisol release. Stress is especially detrimental in local immunity in mucous membranes. Glucocorticoids have been shown to convert latent infection to an active state and transient to permanent infections (e.g., rhinotracheitis, FeLV infection, hemobartonellosis and toxoplasmosis). Stressors include pregnancy, parturition and lactation; premature or rapid weaning; sleep deprivation; general anesthesia; severe weather or weather changes, extremes of humidity or temperature; prolonged travel; excessive handling and grooming; overcrowding and regrouping; exercise, trauma, illness, etc.

**Age related**

Maternal immunity protects kittens during the first 12 weeks of their life by providing antibodies while their own immune system is maturing, however, it also interferes with response to exogenous immunization. The higher the dose or virulence of a microbe, the earlier latency will be. Weaning before 6-8 weeks of age creates physiologic stress that makes the kitten more vulnerable. Conversely, as maternal immunity is waning, the queen’s nutritional stress level is maximal, increasing susceptibility to infectious agents as well as activating latent infections /shedding. The younger a kitten is at the time of infection, the greater the likelihood of severe illness, chronic complications, or death. Ideally, avoiding exposure of kittens to all infectious agents is preferred, regardless of maternal immunity.

Maternal immunity consists of immunity derived from colostrum, and locally protective lactogenic immunity. Colostrum is produced by the queen for five days but is only absorbed by the kitten over the first 24 hours. It contains high concentrations of IgG and IgA and provides systemic immunity to the neonate for the first 12-16 weeks of life. Lactogenic immunity involves antibodies in milk, which protect kittens against intestinal pathogens (via IgA) for the first few weeks of life. Oropharyngeal protection is provided via IgA as well as IgG and IgM. These Ab must be antigen specific and must be provided continuously as the kitten cannot mount a humoral response of its own at this age.

Age related disease resistance also occurs (e.g. in FeLV). Cats under 16 weeks of age are most susceptible to infection with FeLV; if their first exposure occurs after one year of age, they are significantly less likely to become infected. As a cat ages, CMI and humoral responses decline. T helper cells (CD4) decrease with thymic involution and the peripheral lymphoid population changes from a naïve one to a memory cell population. The bone marrow is unaffected by aging. Ag processing and presentation are minimally affected.

**Husbandry practices** may significantly affect the immune response. High population density, poor sanitation and inadequate ventilation lead to increased exposure to pathogens and also cause social stress, which impairs immunocompetence. Housing cats of various ages together increases the exposure for immunologically fragile cats, as adult cats carry and/or shed pathogens such as FHV-1, FCV, enteric coronavirus, chlamyphila, mycoplasma, enteric pathogenic bacteria, ecto- and endoparasites. Inbreeding and 'line-breeding' allow some forms of congenital immunological weaknesses to persist (e.g., Chediak-Higashi syndrome in Persians).

Nutrition can play a significant role in the effectiveness and function of immunity and the effects of malnutrition on immune functions are complex. In general, severe nutritional deficiencies cause a decline in T cell function but, surprisingly, spare B cell function. The net result may be suboptimal CMI with negligible or no effect on humoral immunity. Serum immunoglobulin levels remain unchanged; complement levels decline and neutrophils and macrophage chemotaxis is impaired. Malnutrition results in altered resistance to infectious disease. In malnutrition, bacterial diseases are more severe but because viruses require a healthy host, malnutrition can result in an increased resistance to viral infection! The effect on parasitism is variable. Starvation causes...
generalized immunosuppression. Effects of some specific nutrient deficiencies have been recognized.

- Vitamin A, polyunsaturated fatty acid and some B vitamins decreased Ig levels
- Magnesium B cell induced decreased Ig levels
- Vitamin A, B12, folic acid decreased CMI
- Vitamin D decreased poor macrophage development
- Zinc low thymus weight, impaired cytotoxic T cell activity, decreased B cell activity, NK cell function (in swine) and in pregnant animals, zinc deficiency results in immune dysfunction in offspring
- Copper decreased number and function of neutrophils, T cell and NK numbers, impaired mitogen responsiveness; mast cells become more prone to release histamine
- Selenium impaired function of most immune cells
- Taurine impaired function and numbers of neutrophils, impaired B cell activity

Supplementation with selenium up regulates the expression of some interleukins and prevents oxidative injury to immune (and other) cells. Chromium supplementation also enhances some aspects of immune responsiveness. Recently, numerous studies have shown that anti-oxidants enhance the humoral response to vaccination. But, over nutrition may increase susceptibility to viral infection; obesity is a major stressor in many respects.

Regular moderate exercise enhances immune function, but strenuous exercise results in oxidative stress and enhances vulnerability to infectious diseases. Severe trauma results in immunodeficiency and may result in sepsis and death due to the massive release of corticosteroids, prostaglandins, and suppressive active peptide all of which are immunosuppressive. Routine surgery has no significant impact on the response of healthy animals to vaccination.

Concurrent illness may impair immune responsiveness. Conditions resulting in protein loss may decrease Ig production. Thyrotoxicosis and diabetes mellitus are immunosuppressive. FeLV infection results in a loss of CD4 cells; in kittens, lymphoid atrophy (or hyperplasia) may be seen. B cell activity is normal in FeLV and FIV infected cats, so vaccination is recommended for these animals. Killed products, rather than modified live vaccines (MLV) are preferred. Cats with major illness, debilitation or a high fever should not be vaccinated. Mild respiratory or gastrointestinal disease may not preclude vaccination.

Some cytotoxic drugs cause significant immunosuppression. Other medications may suppress bone marrow resulting in leukopenia and immunodeficiency, e.g., clindamycin, chloramphenicol, griseofulvin. Prolonged corticosteroid use may make the use of killed vaccines preferable over MLV. Vaccination in the face of corticosteroid use may result in a less than optimal (but still valuable) immune response.

Any MLV or avirulent live vaccine component administered during pregnancy has the theoretical risk of crossing the placenta, invading the fetus and causing fetal damage. This has only been demonstrated in panleukopenia seronegative queens receiving MLV vaccine, resulting in cerebellar hypoplasia in kittens. A pregnant or lactating queen could be more prone to adverse events because of the high physiological load the she is already under.

To quote Niels Pederson: ‘The immune system does not operate in a vacuum but is influenced at many points and in subtle ways by environmental, host and pathogen-related factors. The cat is not an immunologic cripple; its great problem with infectious diseases is largely due to the practices of man, not to its own deficiencies.’