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Basic Immunology

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INTRODUCTION

The immune system can be thought of as a surveillance system to discriminate between "self" and "non-self." From simple life forms such as insects to advanced life forms such as humans, all living organisms have some form of host defense mechanism. Most have multiple, overlapping mechanisms ranging from very non-specific resistance to highly specific immunity. White blood cells forming "pus" around a splinter is representative of non-specific host resistance to invasion while immunity to IBR virus after vaccination or following recovery from active infection is representative of specific active immunity.

These host defense systems protect livestock and man from the millions of microbes that attack the body every day. Without them, living creatures would die rapidly from the constant, and sometimes successful, attempts by disease agents to invade the body.

Host defense mechanisms also protect livestock and man from invaders within. For example, abnormal cells such as cancer cells are detected and destroyed every day by this surveillance system. The abnormal cells may also be those infected with viruses. Viruses cannot multiply by themselves and require living cells to do their replicating. The immune system detects and destroys these virus-altered cells.

Most producers have some knowledge of the immune system. They know that with certain vaccines, livestock can be protected from infectious disease. They also are aware that the immune system has "memory"-----the ability to remember past disease or past vaccinations for a long period of time. For example, calves given blackleg vaccine at branding and weaning are generally immune to this disease for life.

Producers are also aware that the immune system is under genetic control. They have seen that cross-bred calves and yearlings are more disease resistant than most purebreds. From news reports, they know that you cannot transplant a kidney or heart from one person to another unless the donor and recipient are genetically very similar in blood and tissue type, factors controlled by our genes. Even then, the body still recognizes the donor organ as slightly foreign, so the immune system must be suppressed by drugs to prevent rejection. So, producers are aware that the immune system can differentiate "self" from "non-self."

NON-SPECIFIC RESISTANCE MECHANISMS

The body has many innate ("born with") resistance factors to prevent disease agents from gaining entry into the body. These include physical barriers such as skin and the mucous

membranes of the eye and respiratory, digestive and reproductive tracts. Chemical barriers such as stomach acid and enzymes in body secretions destroy many microbes. Normal bacteria on body surfaces interfere with colonization by abnormal, disease-causing bacteria.

Once a foreign agent or substance gains entry into the body, many cells and proteins attempt to destroy it. Inflammation is a normal body process to contain disease organisms and to prevent spread. Products of inflammation assist in recruiting cells from the bloodstream that are capable of ingesting and digesting the disease organism. These white blood cells are mainly neutrophils and macrophages and are collectively called phagocytes (phago = to eat). With many bacteria, blood proteins with enzymatic activity are activated that kill them. Fever is often beneficial; for example, some viruses are very temperature sensitive and cannot replicate at temperatures above normal.

It is important for producers to realize that the non-specific resistance mechanisms can be enhanced by specific immunity. For example, it is difficult for phagocytes to engulf many bacteria because the bacteria have slippery coatings. But if antibody against that bacteria are present, the phagocytes have receptors for the other end of the antibody. Thus, a strong linkage binds the bacteria to the phagocyte until it can be eaten and destroyed. So, pre-existing immunity can enhance the more primitive defense mechanisms. Stimulating immunity before disease exposure is the very basis of vaccination. If a vaccination is successful, then immunization has occurred.

ACQUIRED IMMUNITY

Unlike innate resistance, acquired immunity is very specific and directed against the foreign microbe, toxin or cell. Anything foreign and recognizable by the immune system is called an antigen. A single microbe may have dozens of different antigens that are recognized. The immune system has an infinite capacity to recognize antigens. Some ranchers and veterinarians worry that they will overwhelm the immune system by giving too many antigens at once (for example, a 7-way clostridial vaccine and a 4-way viral vaccine at the same time), but in non-stressed livestock, this is probably not a significant problem.

CELLS OF THE ACQUIRED IMMUNE SYSTEM

White blood cells called lymphocytes are the primary cells that respond to a specific antigen. They reside mainly in blood, lymph nodes, spleen and thymus. They arise from the bone marrow. The two main types of lymphocytes are B cells and T cells.

DUALITY OF THE IMMUNE RESPONSE

There are two arms of the immune system. Proteins called antibodies or *immunoglobulins* are produced by B lymphocytes. Antibodies bind to microbes or toxins that are free in body fluids such as blood or mucus. This immunity is called *humoral immunity* or *antibody-mediated immunity*. Microbes that are inside cells, such as viruses, are protected from antibody, so a second arm of the immune system is required to destroy the entire infected cell. This immunity is called *cellular immunity* or *cell-mediated immunity* and is produced by T lymphocytes. Both

types of immunity are often needed for complete protection from an infectious disease.

PASSIVELY ACQUIRED IMMUNITY

A newborn calf has a highly developed and functioning immune system. Most work would indicate that it is comparable to an adult's. In fact, fetuses can respond in utero at about 150 days of gestation. The problem with a newborn calf's immune system is that it is naive; the neonate has not been exposed to disease agents and has not developed immunity.

Newborn calves acquire specific immunity from the dam via antibodies in the colostrum milk. Antibodies are concentrated in the first few milkings that the calf takes. These antibodies are transported across the gut wall and absorbed into the bloodstream. Thus, the calf receives immunoglobulins that reflect the cow's past disease and vaccination exposure. However, the window of opportunity for absorption is very short, generally less than 24 hours. About one-half of the calves born to first calf heifers will have failure or partial failure of passive transfer of maternal antibodies.

ACTIVELY ACQUIRED IMMUNITY

For the immune system to recognize an antigen, it first must be processed (digested) and presented to the lymphocytes before they can be activated to respond against that particular microbe. A cell called the macrophage is the primary cell that does this processing. It is important that producers understand that processing for antibody-mediated immunity takes place differently than for cell-mediated immunity. The two arms of the immune system do not recognize the same antigens from the same disease agent. Also, the antigens are recognized only when presented to the lymphocytes in association with proteins produced by our genes that are responsible for controlling the immune response.

WHY SHOULD YOU CARE?

By now, you should understand that the body has a number of ways to help prevent infection. After infection or vaccination, the microbes are digested and antigens presented to the B and T lymphocytes so that an active response can occur. The two different arms of the immune response recognize different antigens. The B lymphocytes produce antibodies that can bind and neutralize or kill microbes or toxins that occur in the blood or body fluids but they cannot get inside cells to destroy pathogens that may reside there. To destroy abnormal infected cells requires that the entire cell be killed; this is the function of cell-mediated immunity mediated by the T cells. Keeping this in mind, vaccine selection is dependent on the type of microbe and its site of replication in the body.

VACCINES AND VACCINE SELECTION

Virtually all vaccines that are made by injecting killed bacteria (bacterins), inactivated toxins (toxoids), or killed viruses result in the production of antibodies but not the T cells responsible for cell-mediated immunity. These vaccines are generally effective against disease

agents that multiply or exist outside of cells although their duration of immunity is often less than desired. In most instances, a minimum of two doses of killed or inactivated vaccine is necessary to stimulate good immunity. Read the label and follow directions.

When dealing with agents that can live inside cells such as brucellosis and viral agents, killed vaccines are generally ineffective once infection has occurred. Although antibody may help prevent the body from getting infected, if cellular invasion occurs, then humoral immunity is pretty much ineffective. It cannot get inside the cell to destroy the invader. Cell-mediated immunity is required to recognize altered cells and destroy them.

Except for experimental vaccines, stimulation of cellular immunity in livestock has required the use of attenuated or modified live vaccines. These vaccines cause a transient, low grade infection that mimics natural infection. Both antibody and killer T cells are produced. The safety record of the modified live virus (MLV) vaccines is very good when used according to label. Some cannot be used in pregnant cows and some MLV vaccines should not be used in the face of a disease outbreak. It should be noted that one company is now claiming that their killed viral vaccines will stimulate cellular immunity, but publication in a peer-reviewed journal has not yet occurred.

Most research would indicate that you cannot vaccinate calves at branding and expect significant immunity against respiratory viruses. The notion has persisted that passive antibody from the dam will interfere with immunity by binding with antigen and preventing a protective response. However, some recent work has shown that cellular immunity in response to the MLV vaccines can occur despite the lack of a significant antibody response. So, with diseases like PI-3, IBR, and BRSV, vaccinating with a MLV vaccine at branding may be beneficial, especially on ranches that experience viral pneumonias before weaning. Further confirmation is needed, and work on BVD vaccine remains to be done.

Many producers are using MLV vaccines pre-weaning in calves on pregnant cows (off-label) without adverse effects. Whether this becomes an accepted use by the USDA remains to be seen.

SUMMARY

By understanding the inner workings of the active immune response, producers and veterinarians can question conventional thinking and make informed decisions with regard to vaccine selection. It is not enough just to listen to advertising hype. Ask for detailed research data and peer-reviewed journal articles to support claims.

Vaccine selection should be based on the type of disease agent involved. For those that replicate in body fluids and outside of the body's cells, killed or inactivated vaccines are generally adequate to stimulate protective antibody. For agents that replicate inside body cells, different processing of the antigens is needed to stimulate the cell-mediated arm of the immune system. Modified or attenuated live vaccines are generally much more effective in stimulating this arm of the immune system.