Basics of Immunology: Pork Industry Handbook
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Basics of Immunology

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Definition of Immunity

Immunity is the ability of an animal to resist infections. Immunity is not an absolute phenomenon but exists in varying degrees. Thus a limited state of immunity can be suppressed by certain adverse environmental factors or can be overwhelmed by a large number of highly infectious bacteria or viruses. Immunity is classified into natural and acquired resistance.

Native or natural immunity is the genetically determined resistance present at birth. Examples of defense mechanisms that fall into the category of natural immunity include barriers such as skin that prevent entry of infectious agents into the animal, secretions that coat the respiratory and intestinal tracts and function to dilute or wash away microorganisms, and the chemical makeup of body components such as the acid content of the stomach in which bacteria are unable to survive.

Acquired immunity is provided by the actions of certain classes of white blood cells called lymphocytes and macrophages; these primarily arise from specialized tissues in the spleen, lymph nodes, tonsils, intestines, respiratory tract, reproductive tract, and mammary glands. Acquired immunity appears in swine after they have come into contact with agents that are foreign to them. Foreign agents may be bacteria, viruses, parasites, or any large molecule that is not normally found within the pig's body. When a foreign agent enters the body, it encounters lymphocytes that trigger an immune response. The immune response may take one of two forms. It is likely that both forms of immunity will develop, and it is rare to have only one form of immunity. One possibility is the production of antibodies by specialized lymphocytes. Antibodies are large molecules specially shaped to correspond to surface characteristics of the particular foreign agents that triggered their production. Antibodies adhere to foreign agents and interfere with their ability to infect and replicate. When bacteria are coated with antibodies they become more susceptible to killing by substances in the blood and are more easily engulfed by macrophages whose job it is to eat and thus destroy bacteria. The second form of immune response is effective against viruses or bacteria that are able to grow within cells of the body and so are protected from the actions of antibodies. Specialized lymphocytes are produced to combat intracellular pathogens. These lymphocytes are able to destroy a virus-infected cell or can release activating substances that stimulate other phagocytic cells to destroy infected cells.

The immune system has at least two subcomponents, the mucosal and the systemic immune systems, based on location and function of the cells involved. Lymphocytes and macrophages that make up the mucosal immune system are found diffusely spread along the respiratory tract, the intestinal tract, the urogenital tract, and the mammary glands. Cells of the systemic immune system are in the spleen and lymph nodes. The systemic and the mucosal immune systems produce antibodies that differ from each other in structure, function, and location. The systemic immune system produces predominantly antibodies of the classes IgG and IgM. IgG and IgM circulate in the blood and are effective against systemic diseases in which disease organisms spread through the circulation. Lymphocytes in the mucosal immune system produce antibodies that are primarily of the IgA class. In the process of their secretion onto mucosal surfaces, the IgA antibodies are first transported through epithelial cells which line the mucosal surfaces, acquiring in the process a special protein — secretory component — which is produced by the epithelial cells. After IgA combines with secretory component, it is known as secretory (S) IgA. SIgA is the predominant form of IgA found in the secretions, whereas most IgA in serum lacks the secretory component. The unique structure of SIgA antibodies allows them to adhere to the lining of mucosal surfaces in the intestine and respiratory tracts as well as making them more resistant to being broken down by enzymes found in secretions. This ability makes locally produced SIgA the antibody of choice for combatting gastrointestinal, respiratory and other mucosal infections.

Development of the Immune System of the Pig

The immune system begins to develop in fetal pigs at about 50 days of gestation. By 70 days of age the fetus is able to respond to foreign agents with the production of antibodies. However, in most cases the uterine environment is sterile, and piglets are born without having produced any antibody. Therefore, the newborn piglet is dependent upon antibodies contained in the sow's colostrum for the first few weeks of life until its immune system can respond to antigenic challenge from the many infectious agents it encounters in the environment. The first milk produced by the sow — the colostrum — contains very high concentrations of mainly IgG antibodies directed against diseases endemic (resident) in the herd. The newborn piglet's intestine is able to absorb antibodies from colostrum and these antibodies are passed intact into the piglet's blood stream. This assures that the neonate passively acquires IgG antibodies in its serum similar to the serum antibodies present in the mother which then provide protection against infections until the neonate actively produces its own serum antibodies. Twenty-four to 48 hours after the piglet has suckled, the intestine is no longer able to absorb antibodies. Subsequently, the SIgA antibodies contained in the sow's milk continue to provide local protection against intestinal infection as long as the piglet continues to nurse an immune sow. In fact, milk is so rich in antibodies that the amount of antibody taken into the intestine daily through the milk is greater than the amount of antibody of the entire circulatory system of the piglet.

The antibodies in the sow's colostrum and milk are so effective in combining with disease organisms that very few infectious agents are able to penetrate this defense and contact the piglet's immune system. Consequently, antibodies produced by the piglet do not begin to appear in its circulation until about 10 days after birth.

Stimulation of Immunity

Whether an animal develops immunity against a certain infection depends a great deal upon how the animal first encounters the agent. If a small dose of infectious organisms gain access to the site in which they would normally cause disease, natural defense systems or passive immunity may be able to keep them in check while active immunity builds. If the dose of organisms is too large, natural defense systems and passive immunity may be overwhelmed and clinical disease may occur before the pig has time to generate an active immune response.

Piglets receiving antibodies in the milk from their dam (passive immunity) may develop only low levels of or no active immunity even though infectious agents are in their intestines. The passive antibodies from the sow combine with the infectious agents and neutralize them so that the piglet's immune system is not strongly triggered. Other infectious agents like those in the respiratory tract and certain vaccines (pseudorabies) will stimulate immunity even when piglets are receiving antibodies in the milk. Also if the level of passive antibody is low, it can be overcome by high doses of pathogens.

Whether immunity develops actively in response to invasion by infectious organisms or is acquired passively from antibodies supplied in the sow's milk, it tends to diminish over time. Passive immunity is lost when the antibodies in serum decay or break down over time (about 4 to 6 weeks after birth) or when the pig is weaned and no longer receives the passive antibodies present in milk.

Factors that Inhibit Immune Function

A number of factors have been shown to directly or indirectly affect resistance to infectious disease in swine. Understanding of these effects provides a basis for establishing criteria for housing and management.

Cold—Both extremes of constant temperature and fluctuations in temperature have been shown to reduce resistance to disease. In neonatal swine, one mechanism by which chilling increases susceptibility to infection is in reducing the amount of colostrum consumed and possibly absorbed. In addition to the effect on consumption of colostrum, extremely low temperatures may contribute to infection by reducing body temperatures. If the environment is cold enough to cause a drop in rectal temperature, the resulting lower body temperature is less conducive to optimum phagocytosis of infectious agents by macrophages.

Behavior and Social Stress—Various social stresses such as weaning, mixing strange pigs together, and physical restraint have been shown to suppress the function of the immune system. Various stresses increase levels of cortisol and other hormones in the pig's circulation. The cortisol acts to diminish the strength of the immune response to foreign agents. The interaction between the stockman and the pigs can also have significant effects on resistance. Rough handling of pigs causes elevations of their blood cortisol levels. Weaning causes an abrupt loss of passive antibodies provided in milk and coupled with other stresses at this time may account for the pigs' enhanced susceptibility to enteric diseases after weaning.

Nutrition—Energy and protein levels below NRC (National Research Council) requirements have been shown to reduce the immune response generated by the pig. This effect was apparent even when the level of dietary protein was lowered only from 16 to 12%. In other studies the addition of vitamin E and selenium to deficient rations has been shown to significantly increase the humoral response to disease.

Mycotoxins—Swine consuming feed containing mycotoxins are less resistant to infections.

Ammonia—Atmospheric ammonia contributes to respiratory disease in swine because of its effect on cells lining the respiratory tract. Ammonia triggers excess production of mucus in airways with an associated decrease in the ability of ciliated cells to move the mucus out of the tract.

Other Diseases—There are many examples of infection with one disease causing pigs to be more susceptible to infection with another disease. Frequently viral infection or even vaccination with a live virus vaccine may suppress immune function.

Principles of Vaccination

After a vaccine has been administered, immunity develops over a period of days or weeks. Usually a first dose of vaccine is given to sensitize the immune system to the organism. The level of antibodies produced after this first dose is very low. Then 2 to 6 weeks later a second dose is given that stimulates a high level of antibodies that will provide continuous protection. A modified live vaccine may induce strong immunity after one dose if the vaccine organism grows in the host. The immunity that develops after an animal has been vaccinated or has undergone infection is called active immunity, because the animal's own immune system was activated to provide protection. With diseases that affect older pigs there is adequate time to

immunize pigs prior to the anticipated time of infection. Vaccination of the animals at risk is a sensible option in these cases. On the other hand there are many diseases that affect baby pigs soon after they are born. With diseases such as colibacillosis that affect newborns it is more reasonable to vaccinate the sow and rely on her to provide antibodies to the piglets through her milk. Piglets that receive immunity from the sow are said to be passively immunized, since they are able to resist the disease, yet their own immune systems have not been activated.

Vaccines are principally used in two ways; to provide protection through passive immunity or to stimulate active immunity.

1. Vaccines to provide passive immunity—Some vaccines are used to stimulate antibody production in the dam which is passed on to the piglets through nursing. For diseases such as colibacillosis and transmissible gastroenteritis which infect pigs shortly after birth, it is important to provide immediate protection.

Two routes can be used to immunize the sow; oral feeding of live, virulent organisms or injection of killed or modified organisms. An example of using live organisms is the Kohler method of growing *E. coli* in milk and feeding it to sows and gilts before farrowing. Another example is feeding intestines from piglets that died from TGE to sows in gestation. These procedures are most effective because they stimulate the "gut-mammary immunologic axis" in the mother. This results in the production of SIgA antibodies in the gut of the sow and the migration of these IgA-producing cells from the gut to the mammary gland. These cells secrete SIgA antibodies in the milk with specificity against intestinal disease agents which the sows have previously encountered. The SIgA antibodies provide active immunity in the gut of the sow and passive immunity in the gut of her nursing offspring.

The use of modified live (ML) or killed vaccines are much less effective than the live, virulent organisms in stimulating this kind of immunity in sows which have not been previously exposed to the disease. However, in sows which have had prior natural exposure (herds in which the disease is resident) it is possible to boost or enhance the levels of SIgA antibodies in their milk by oral or parenteral (IM or SC) vaccination with killed or ML organisms. Thus *E. coli* pili vaccines or ML TGE vaccines may help to control these respective diseases in herds which have had previous natural exposure to these disease agents (test positive for antibodies in their blood).

2. Vaccines to stimulate active immunity—Some vaccines are used to stimulate active immunity in the animals receiving them. Examples include vaccines for porcine parvovirus and leptospirosis that induce immunity in sows against reproductive diseases. Frequently these vaccines contain killed or inactivated organisms. Some may contain ML organisms. Newer vaccines may contain only a part of the infectious organism (subunit or gene deletion vaccines).

Vaccines do not provide complete protection against all diseases. This is due to a number of reasons including the nature of the vaccine and the route of administration. Most vaccines are made of either viruses or bacteria that have been grown in the laboratory and then killed or modified so that they are no longer harmful to the animal. A new generation of vaccines is currently under development which will consist of injecting only the immunogenic subunit of the organism or will involve vaccinating animals with a live recombinant DNA vaccine which expresses this subunit when it replicates. When the altered organisms are injected into the pig they trigger the immune response without causing disease. If the pig later encounters live organisms, it will have antibodies structured to bind to the organisms. One reason for the failure in this system to provide perfect immunity lies in the fact that viruses and bacteria are structurally changed in the process of altering them to be harmless. Therefore the antibodies generated in response to the vaccine may not exactly resemble those that would have been produced in response to pathogenic organisms. Second, by injecting vaccines, the systemic immune system is stimulated resulting in production of IgG and IgM antibodies that will circulate in the blood stream. Circulating antibodies are not very effective against diseases that affect the intestinal or respiratory tract, but are effective against pathogens which infect systemic tissues or are spread to other target tissues via the blood stream. Finally, other reasons for vaccine failure are that the vaccine was given too early and maternal antibody inhibited active immunization, or vaccine immunity was not protective because it failed to induce an adequate level of cellular or humoral immunity.

Deciding for which Diseases to Vaccinate

Producers want to know what vaccines to use that will give them the best return in terms of both health and profit. Unfortunately there is no pat answer. Because of varying disease prevalences, management styles, and farm types, no one is able to develop vaccine recommendations for even a minority of the farms in a given location. Before deciding whether to vaccinate, consider the following points:

1. The cost of the disease—In a 100-sow farrow-to-finish farm the following decreases in production are shown with their associated economic losses:

Loss of .1 litter/sow/year	$3,000
Loss of .1 pig born alive/litter	700
One percent preweaning mortality	600
One percent postweaning mortality	800

Therefore if *E. coli* scours is causing an increase of about 5% in deaths before weaning, the loss would amount to $3,000 plus treatment costs in a 100-sow unit.

2. The cost of the vaccine—Vaccines vary in cost from a few cents to a dollar or more per dose. Also ordering, handling, and administration add about 50% to the cost of the vaccines.

3. How effective is the vaccine—Intramuscular or subcutaneous administration of a vaccine stimulates the systemic immune system to produce IgM and IgG classes of antibody. Because SIgA production is not stimulated to any extent, vaccines may not be effective against infectious diseases which primarily involve mucous surfaces in the intestinal or respiratory tracts. Also, a killed vaccine cannot be expected to stimulate cellular immunity since this type of resistance is generally induced only by live organisms. The development of a new generation of adjuvants may improve the nature of the immunity induced by killed or future subunit vaccines.

4. The risk that the herd will become infected—Some diseases such as leptospirosis, erysipelas, *E. coli*, rotavirus, and parvovirus are very widespread in nature and should be considered as potential disease agents on all farms. Other diseases such as atrophic rhinitis, *Actinobacillus*

pleuropneumoniae, and pseudorabies affect a large percentage of swine farms, but there are many others that appear free of the diseases. Acute transmissible gastroenteritis is very sporadic in appearance both by year and geographic location. A local veterinarian or extension specialist should be consulted regarding the prevalence of each disease in the area.

5. If other alternatives for control exist—At best, vaccination can only be expected to assist in the reduction of disease, not eliminate it. As one swine consultant put it, "No vaccine is a magical barrier against a particular disease; microorganisms don't break and run, fleeing the herd, just because a vaccine was administered." When disease is a problem the solution is not vaccination or changes in management; the solution is vaccination with changes in management or changes in management without vaccination.

Sanitation is a major tool in control of diseases affecting baby pigs. This includes thorough cleaning of farrowing facilities, washing sows prior to placing them in farrowing crates, and daily removal of manure. Proper temperatures maximize animal resistance. Management of animals is also a major contributor to health. Pigs of different age groups should be housed separately. Moving and mixing of animals should be minimized. Good exposure of replacement gilts to the breeding herd prior to their first mating will allow them to develop acquired immunity to many of the resident microorganisms in the herd.

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