HEIFER DEVELOPMENT: A HEALTHY START TO FUTURE PROFITS

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INTRODUCTION

A replacement heifer's normal development consists of several stages. The first stage consists of a pre-natal period. The second is the transition from fetal organism to independent animal. The third stage consists of the neonatal period (from birth to approximately three weeks of age). The next stage is from neonate to weaning, followed by the step from weaning to puberty. The final stage in developing a productive heifer is the breeding to calving stage.

In order to maximize herd performance, replacement dairy females must become productive members of the herd by about 24 months of age. They must also be capable of maximizing their genetic potential. These two stipulations require certain management goals be met. These goals must be met in the areas of environment, nutrition, and immunology. Each of these areas must be considered throughout the heifer's developmental stages, along with the changes and challenges that are unique to each developmental stage.

IMMUNOLOGY

Immunology probably has changed more dramatically than most other scientific fields in the last ten years. Our understanding of mammalian immune systems has vastly improved. As always, there are many more questions that arise with each new *answer discovered.* To paraphrase **TQM** (Total Quality Management) guru Stephen Covey, we'll begin with the end in mind. Figure 1 is an attempt to graphically represent the adaptive or active branch of the immune system. This represents what is probably the most commonly held view of the immune system. However, this represents only the active branch or the adaptive system. There are many other vital parts that comprise the immune system that we as managers, investigators, veterinarians, nutritionists, and industry professionals often neglect.

The Immune System

The immune system is composed of two main branches, essentially a defensive structure with an active surveillance system. One branch we call the ***innate system*** and the other the ***adaptive system***. This system develops during the first and second trimester of gestation and it is during this time the animal's immune system learns to distinguish itself from non-self. Generally by the third trimester the fetus is immumo-competent but immuno-naive. As with every other adaptive system or organism, this system is ignorant in the beginning, but has the capacity to learn. Because of the thickness of the bovine placenta the normal calf is born without protective antibodies and specialized cells. The innate ability to respond to immunological challenges is present but it has no protection other than the physical barriers with which to respond.

The Innate System

The innate branch is a group of *barriers* both active and passive. These barriers are: physical, chemical, microbiological, and cellular in nature.

- Physical barriers: intact skin, mucous membranes, and the tracheal mucociliary elevator. These barriers prevent infectious agents access to vital organs.

- Chemical defenses: lysozyme, an enzyme in secretions such as tears that destroys infectious agents; the compounds isolated from mammary glands such as nisin that have anti-bacterial properties; stomach acid kills many agents with its low pH, thereby preventing infections in the intestinal tract; and complement, a group of proteins that circulate throughout the body. Most are enzymes with the sole purpose of attaching themselves on infectious agents to *puncture* invaders and/or facilitate phagocytosis.

- Microbiological barriers: the unique ecosystem that exists between mammalian cells and bacterial populations that essentially covers the entire body.

- Cellular defenses: white blood cells such as neutrophils and macrophages that constantly patrol the body looking for foreign material to phagocytize or *chew-up* to rid the body of an invader.

The disruption of any of these barriers constitutes a major compromise of the animal's immuno-integrity. Cut or abraded skin is much more easily infected than intact, healthy skin. Salmonellae are very susceptible to the low pH of stomach acid. Humans who frequently use antacids are considerably more susceptible to Salmonella infections. They have decreased part of their chemical barrier by increasing stomach pH. It takes approximately 10^8 or 10^9 Salmonella organisms to infect a horse to the extent that diarrhea will develop. However if the horse is given penicillin, the infectious dose of Salmonella decreases to about 100 organisms to generate the same signs because we have decreased the animal's microbiological barrier. **BLADS** (bovine lymphocyte adhesion deficiency syndrome) is a genetic defect in the cellular barrier group. The cells cannot sufficiently *grab onto* invaders; therefore these cells are not able to engulf and destroy their targets as effectively as they should.

The Adaptive System

As in the innate branch of the immune system, there are both passive and active parts to the adaptive branch of the immune system. Each part is composed of a humoral or antibody component and a cellular component. Passive immunity stems from the fact the animal itself does not manufacture this protection. There are local aspects as well as systemic ones and the two do not communicate very well.

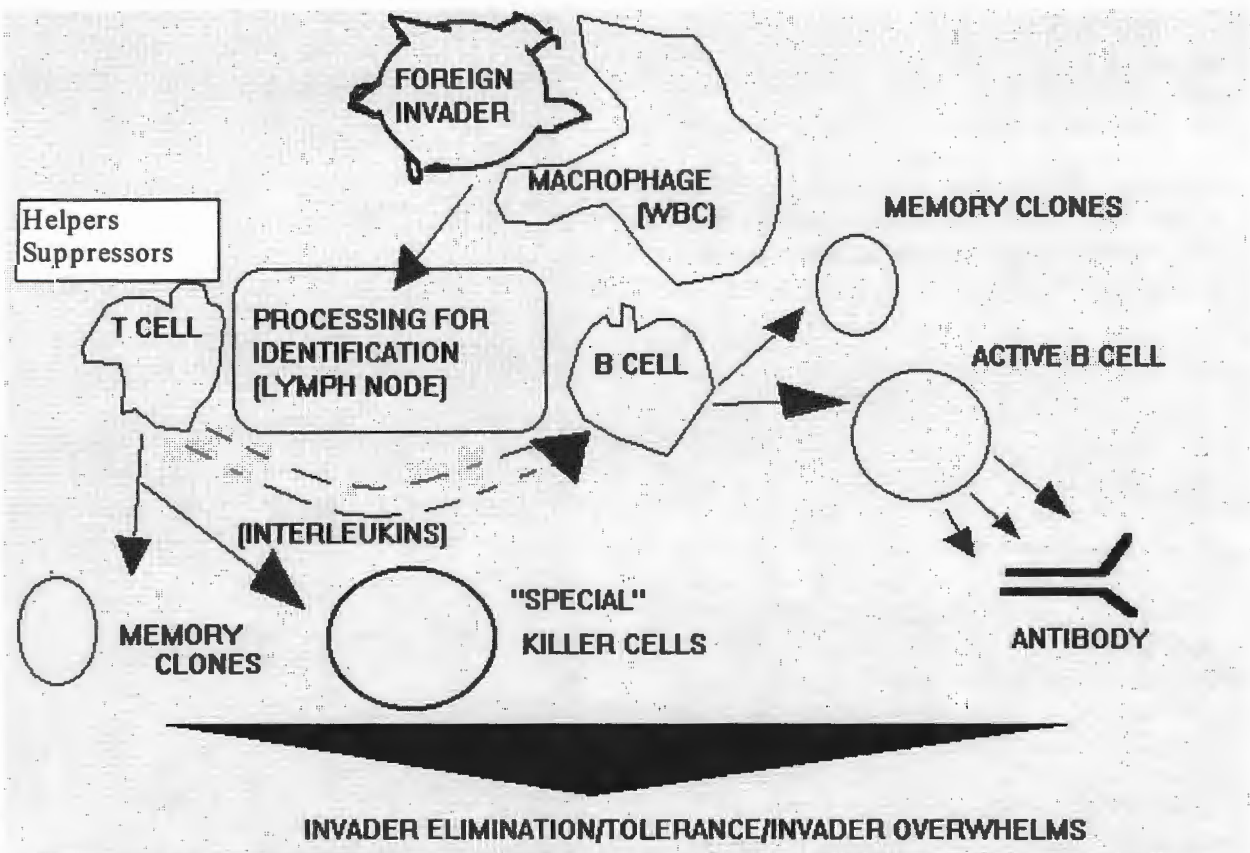

Figure 1. Graphical representation of stimulation of active branch of the immune system.

The Humoral Component

Basically this is the component of the adaptive branch of the immune system we have known about for decades. It is this component that various animal health companies have traditionally used for extensive marketing campaigns. The humoral component consists of antibodies, also called immunoglobulins (**Ig**) which are three-dimensional Y-shaped protein structures. B-cells (derived from bone marrow) are the actual manufacturers of antibodies. The antibodies are divided into various classes depending on their shape and function. IgG_1 and IgA are both secretory antibodies (IgG_1 being unique to cattle). These two are most commonly found in mucus lining airways or the gut and are the primary antibodies of colostrum. IgG_2 and IgM are antibodies that spend their time traveling through the circulatory system and deep body tissues. There is also an IgE that deals primarily with large objects such as parasites and is involved with immediate hypersensitivity allergic reaction. Antibodies have two primary functions: neutralizing and opsonizing invaders. Neutralizing involves surrounding the invader with antibodies so the invader is biologically inactive. It cannot attach to anything to cause dysfunction. Opsonization involves attaching to the invader thereby providing a handle for macrophages to attach more easily. Ig's are measured in dilution factors called *titer*, whereby serial dilution of the blood serum is performed until there is no longer a reaction between the antibodies in the blood and the material being tested.

The Cellular Component

The cellular component of the adaptive branch may be best thought of as the command and control apparatus of the immune system. This component is composed of what are called **T-cells** (they also are derived from bone marrow but undergo further *training* in the thymus). T-cells are divided into subgroups because of their different physical and functional aspects. T-helpers are responsible for communicating and directing the immune response and T-suppressors for controlling and ending the response. There are also cytotoxic T-cells or killer cells. T-cells control and direct through various chemical agents called cytokines. Essentially these cells detect foreign cells and eliminate them; direct antibody production by the B-cells; and restrain the immune response when the invader has been removed. Until recently, evaluation of cell mediated immunity (**CMI**) was not practically possible. However in the last ten-plus years methods have been defined that allow assessment of CMI.

Passive Immunity

Passive immunity is primarily thought of as the colostrum a newborn receives shortly after delivery. However, there are a few other sources such as tetanus antitoxin and various anti-sera. These are pre-formed products delivered into the neonate for protection. These pre-formed protectors are not self-manufactured and they are generally not long lived. Colostrum is by far the most important concern to a newborn. This is ***the elixir of life*** for the bovine neonate. Again antibodies traditionally have been the primary concern and the amount of Ig absorbed by the neonate has a vast effect on its health and performance. But we have learned the cellular component of colostrum seems to also play a very important role in the immune system. We will continue colostrum discussion in a separate section.

Active Immunity

The active section of the adaptive branch of the immune system (Figure 1) is the part most commonly considered when discussing the immune system. This is the surveillance and reactive component of the immune system. This section has the capacity to learn and to remember, but this effort requires vast amounts of inputs. The macrophage's task is to present information to the active section so that a response may be initiated. This is the first step in an immune response. From this point it is up to the command and control structure to identify and trigger the appropriate responses that lead to elimination of the invader. This is where nutrition becomes critical to the immune system. Massive amounts of inputs are required to drive the active section. Some of the components that make up the system such as T-cells and macrophages may have lives of months to years. This is probably part of why prior nutritional effects or deficiencies can contribute to poor performance much later in life and also why simply supplying adequate nutrition in the present generally will not correct a nutritional problem for an extended period of time.

COLOSTRUM

The following are some points gleaned from field and research studies. Studies indicate 20 to 30% of neonates will have below acceptable Ig levels or have

Figure 2. Change in milk composition postpartum for cows milked twice daily.

	Milking Number			
Component	1	3	5	11
% total solids	23.9	14.1	13.6	12.9
% total protein	14.0	5.1	4.1	4.0
% Ig's	6.0	2.4	0.1	0.09
% fat	6.7	3.9	4.3	4.0
% lactose	2.7	4.4	4.7	4.9

none. The National Animal Health Monitoring System (**NAHMS**) showed 67% of calves sampled had less than acceptable levels of circulating antibodies. The NAHMS data suggests that increasing serum Ig alone will decrease pre-weaned heifer mortality by 30%. Several studies have also shown that low Ig levels contributed to decreased daily gain, especially through the weaning period. A study in the late 1980's in a large field trial found a correlated 8.5 kg increase in ME Milk for each increase in serum Ig level (mg/ml) in the heifers 24 to 48 hours after birth. Other studies have shown failure-of-passive-transfer (**FPT**) calves have 9.5 times greater risk of becoming sick as compared to calves with acceptable Ig levels. The statement that absorbing maternal antibody is the single most important factor influencing calf morbidity and mortality continues to be supported. So why don't we do a better job? Failure-of-passive-transfer occurs at any of three points: poor formation of colostrum by the dam; poor ingestion of colostrum; and poor absorption.

Colostrum Quality

The modern dairy cow is geared to produce milk, not colostrum. The dilution effect is tremendous. Figure 2, from work at the University of Minnesota, shows how significant the effect can be. Too often calves are not getting colostrum, they are getting transition milk. This is especially true in situations where colostrum is pooled and occassionally when stored for later use. Too often the colostrum that is saved and stored is actually transition milk. As for storage, freezing is probably the preferred method. Estimates are that frozen colostrum is good to use for up to 1 year. The important factor is that the colostrum should be thawed slowly. The Ig's are proteins and heat denatures protein. Another aspect to consider is that freezing destroys the cellular material in colostrum. Recent work indicates these cellular components play significant roles in defending the neonate as well as possibly *training* the neonate's immune system in antigen processing.

As for manufacturing quality, some cows simply do not do an adequate job of producing Ig-dense colostrum. Some method of assessing quality should be employed. The colostrometer is a relatively good tool for this purpose provided the temperature of the sample remains constant across samples. Also studies indicate that heifers' colostrum contains less protective factors than that of a mature cow. Dry period length also has an effect on quality. Ig concentration is highest in cows with dry periods from 40 to 90 days. Nutrition and vaccination also play important roles in the quality of the colostrum formed.

Colostral Antibodies

After Ig's are absorbed they circulate within the neonate. They may be effective in disease protection but they will have very minor effects on the majority of agents that cause calf scours. Most of these agents are non-invasive and therefore the circulating antibody is not in position to protect the calf. IgG_1 is actually transported back into the gut lumen to aid in protecting the calf from disease. However this appears to be of short-lived duration due to rapidly decreasing concentration levels in the gut lumen in only about a week.

Colostrum Quantity

This may be the most critical factor of colostrum management, getting an adequate volume into the calf. Several studies have consistently

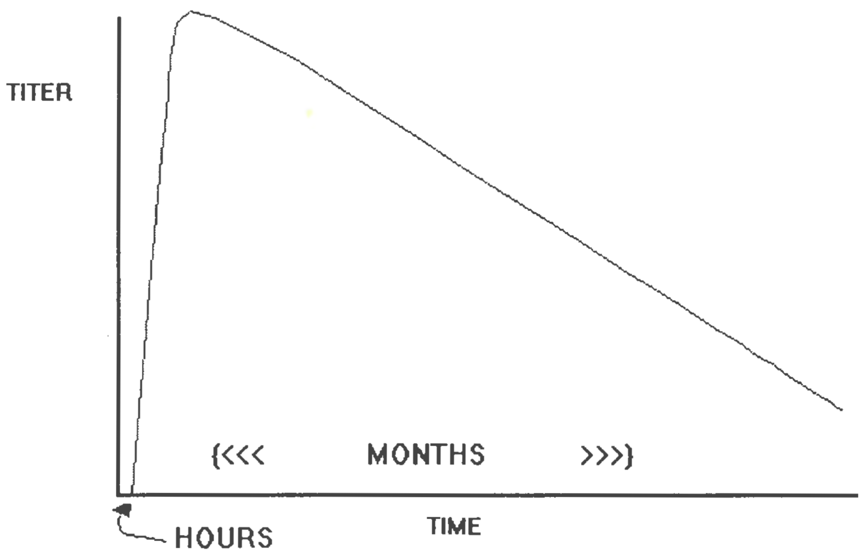

Figure 3. Calf serum maternal antibody levels post-suckle

shown the benefits of ensuring colostrum ingestion. Calves that were fed a total of four liters with esophageal feeders were consistently healthier, as measured by morbidity and mortality, than calves allowed to nurse on their own. Two liters should be ingested as soon after birth as possible with two more liters following within another six to twelve hours. Ideally the goal is to have the calf ingest 10% of its body weight in colostrum within the first twelve hours of life. By twelve to sixteen hours post partum the gut has become impermeable to IgA. This time limit is the reason for early administration of colostrum.

VACCINATION CONSIDERATIONS

The feto-placental unit has been occassionally called a successful parasite. One of the means parasites achieve success is by down-regulating the host's immune response. This is also an effect of the feto-placental unit. Some of the consequences of this action are that generally most fetuses survive and are born healthy instead of the dam's immune system detecting and rejecting the fetus. Some of the other consequences are that the dam tends to shed more infectious organisms near calving and that some aspects of both the dam's and the calf's immune system have been somewhat *put to sleep*. These factors need to be considered along with the effects of maternal protection when designing vaccination programs. Figure 3 is a schematic of what we typically see in Ig levels in a calf after successful colostral absorption.

Vaccination of the neonate is a controversial area. Classical thinking has it that immunization cannot be accomplished in the face of maternal protection. It has been thought that as maternal antibody protection decreases the calf becomes more susceptible to infection (or immunization). Immune response requires the invader be recognized. If the invader is removed before the calf's immune system has the opportunity to recognize and respond, immunization cannot occur. In this situation infection occurred, but neither disease nor immunization occurred.

The conditions that cause this scenario to occur are not completely known. Past studies of vaccinations of young calves typically have shown no increase in serum titer levels, lending support to the theory that immunization of these animals had not occurred. However, more recent work has indicated that in some situations cellular immunity may be stimulated even in the presence of considerable amounts of maternal antibodies. The key to accomplishing this feat probably lies in the ability to successfully initiate or stimulate the calf's immune processing system. This begins the training of the recognition phase of the immune system. This means the animal's defenses must be active, especially the macrophages. This also means the antigen must be detected, captured, and processed by the appropriate macrophage (as clonal theory of recognition dictates any given macrophage is only able to recognize a certain particular antigenic shape).

Neonates' cellular defenses are tremendously down-regulated by the hormones present during the birth process. This effect generally lasts several days and research indicates the effect is not completely gone for approximately a month. This makes vaccination of the neonate essentially useless until several days after birth. Vaccination of the calf past the first two weeks of life is a less clear situation. The calf's immune system is much more able to respond, but the presence of maternal antibodies presents a tremendous challenge to effective recognition of antigen. The work that has shown some success in stimulating the calf's immune system does indicate limited training occurs of the T-cell population.

So the question of timing to reasonably ensure successful immunization still remains cloudy. Numerous varied vaccination schemes have been published. However, to successfully prepare a vaccination regime requires knowledge not only of the underlying immunology but also of the unique nature of the operation to which the program is to be applied. Generally it does appear the initial stimulation and training of the immune response may have a significant impact upon the system's later performance. A good education will carry you a long way. Human infants nursing their mothers have been shown to be slightly healthier and heavier than their artificially nursed cohorts. The major difference is the cellular components that were transmitted through lactation, as antibodies are able to transverse the human placenta. Research has also shown living organisms stimulate better cellular responses. Once the initial training is accomplish the method of stimulation is probably of lesser importance than simply ensuring occasional stimulation occurs.

HEIFER PRODUCTION

The cow has to be in good physical condition and have been on an adequate diet to manufacture the quantity of antibodies and specific cells necessary to provide high quality colostrum. She should also have been properly immunized and *rested* during her dry period. Environmental considerations need to be addressed. Sanitation levels and population density can dramatically impact the health of the calf due to its effects on pathogen levels as well as levels of hormones that adversely impact the immune system's function.

Once the calf is delivered, colostrum administration is vital along with iodine treatments applied to the navel cord. After this procedure, removal of the neonate from the surroundings of the mature cow herd is beneficial in greatly reducing the challenge load confronting the neonate. Isolation is one of the best principles that can be employed to insure a healthy start to the calf's life. Reducing contact amongst calves along with the calves' removal from the cow area greatly decreases spread of many problems. (Often the solution to pollution is dilution.) Respiratory problems can be virtually stopped by following these general principles. Diarrheal diseases are more difficult but can be lessened to a large extent through the same practices. The biggest point to remember in dealing with diarrhea is that 90-95% of the cases can be successfully treated with fluid therapy alone.

Producing a weaned heifer means managing through the neonatal period with as little disturbance as possible. It also entails successfully and rapidly transferring the calf from a milk-based diet to one consisting of solid, more economical feed. There are opportunities for the use of transitional milk in this situation, but also potential for trouble with its inappropriate use. Once the heifer is steadily consuming about 1.5 pounds solid feed per day, she is ready for weaning.

The key to successfully moving from an individual situation to group arrangements is managing group size and available feed and water space. Considerable research is being conducted on cow sociology and psychology. Social stresses stimulate release of hormones that adversely impact the immune system just as weather or other stress will. Small groups of similar sizes work best with group size growing larger as the animals grow. This is also the time to consider the effects of *all-in, all-out* procedures. Moving a few animals from one pen to the next simply insures you will continue to cycle pathogens through with each new calf. Bovine respiratory syncitial virus (**BRSV**) often is found as a primary pathogen involved in ongoing respiratory problems in youngstock managed in this way. Following these guides will also decrease the instances of poor intake and subsequent poor performance, coccidial outbreaks, over-fat heifers, and other management related problems. Typically during this time frame, immunization should be attempted. It should also be repeated to ensure the animal actually is stimulated and responds appropriately, at least to the extent of her genetic and nutritional potential.

Past this point, heifer management is simply attention to the detail of weight and height gain. This relates not only to diet formulation, but as mentioned earlier, the delivery of the diet. Appropriately sized and situated feeding and watering areas are a must along with proper housing to provide shelter, adequate ventilation, and secure footing to ensure the heifer will grow at the desired rate, will reach puberty early, and will ultimately conceive in time to deliver her first calf by 24 months of age. As breeding and calving time nears, management needs to ensure proper immunization so as to maximize the chance for a healthy pregnancy and production of high quality colostrum to insure another healthy, productive generation.

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