DIETARY APPROACHES TO KEEPING CALVES HEALTHY

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INTRODUCTION

Calf disease—particularly diarrhea and respiratory disease—has significant effect on the profitability of every calf raising enterprise. Calf raisers, including dairy farmers, veal growers, calf ranchers and others all deal with calves that are particularly susceptible to disease and then are exposed to disease-causing pathogens (especially viruses and bacteria) when they are transported from farm to farm. Underlying most of these strategies is the assumption that most calves will begin life with inadequate passive immunity. Studies continue to show that >50% of shipped calves (calves that leave one farm to be raised at another) arrive at the final facility with <10 g of IgG/L of serum within the first few days of life. Therefore, many calf raisers have begun looking for means of supplementing the immune system until it is strong enough to protect the calf from pathogens in the environment. Traditionally, we have relied on the use of antibiotics to reduce the effects of disease in calves. It is still quite common (in some parts of the U.S.) to include chlortetracycline or oxytetracycline/neomycin in the milk replacer and to aggressively treat outbreaks of respiratory disease or diarrhea with one or more antibiotic preparations.

We assume that the availability of antibiotics for subtherapeutic treatment (i.e., feeding) will be much more limited in the future. Therefore, alternatives to feeding antibiotics are required. It is important to note the difference between feeding antibiotics to improve growth and feed efficiency (subtherapeutic) and the treatment of disease. Antibiotics will continue to be available to treat disease. Their availability may be more limited, however.

Traditionally, most CMR in certain areas of the U.S. have contained antibiotics (AB) to prevent or treat bacterial scours (Heinrichs et al., 1995). Use of AB in CMR has recently been criticized, however, due to increasing evidence that such AB use may contribute to increased transfer of antimicrobial resistance to pathogens of medical importance. Although the efficacy of AB in CMR applications has been established (Morrel et al., 1977; Tomkins and Jaster, 1991; Quigley et al., 1997), a need exists for viable alternatives to AB in the diet of young calves.

We evaluated the use of oxytetracycline/neomycin in milk replacers with a group of 120 purchased bull calves in 2001 (Quigley, unpublished). Calves were assigned randomly to receive experimental CMR (Table 1) containing 0 or 200 g/ton (0.22 mg/kg) of oxytetracycline plus 400 g/ton of neomycin base (0.44 mg/kg). All CMR were formulated to contain
22% CP, 20% fat, 0.8% Ca, 0.7% P (air-dry basis) and to meet or exceed NRC requirements for vitamins and minerals.

Table 1. Least squares means of animal performance.

<table>
<thead>
<tr>
<th>N</th>
<th>Treatments³</th>
<th>SE</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Begin</td>
<td>Control</td>
<td>Medicated</td>
<td>—</td>
</tr>
<tr>
<td>End</td>
<td>60</td>
<td>60</td>
<td>—</td>
</tr>
<tr>
<td>Mortality, %</td>
<td>3.3</td>
<td>3.3</td>
<td>2.4</td>
</tr>
<tr>
<td>BW, kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d 0</td>
<td>44.9</td>
<td>44.5</td>
<td>0.5</td>
</tr>
<tr>
<td>d 28</td>
<td>49.1</td>
<td>50.8</td>
<td>0.7</td>
</tr>
<tr>
<td>d 56</td>
<td>68.8</td>
<td>73.5</td>
<td>1.3</td>
</tr>
<tr>
<td>ADG, g/d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d 0–28</td>
<td>149</td>
<td>221</td>
<td>20</td>
</tr>
<tr>
<td>d 29–56</td>
<td>699</td>
<td>813</td>
<td>28</td>
</tr>
<tr>
<td>d 0–56</td>
<td>424</td>
<td>517</td>
<td>22</td>
</tr>
<tr>
<td>DMI, g/d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CMR³</td>
<td>460</td>
<td>461</td>
<td>1</td>
</tr>
<tr>
<td>Starter³</td>
<td>543</td>
<td>674</td>
<td>36</td>
</tr>
<tr>
<td>ADG: DMI, g/kg³</td>
<td>340</td>
<td>394</td>
<td>16</td>
</tr>
</tbody>
</table>

³Treatments: Control = no additives; Medicated = CMR containing oxytetracycline + neomycin.
²P = Probability of a significant effect of CMR formulation.
³Significant effect of week (P < 0.01).
⁴Significant week × CMR interaction (P < 0.01).

Calves were fed CMR twice daily at approximately 0700 and 1600 h using individual nipple bottles. Calves were offered 454 g of CMR/d reconstituted in 3.8 L of water during weeks 1 to 8. The CMR was mixed in hot water (approximately 50°C) to disperse fat. Cool water was then added to bring temperature to approximately 39°C and the appropriate DM prior to feeding. Commercial textured calf starter (CS; Cargill Herd Builder, Cargill, Inc., Minnetonka, MN) was offered once daily for ad libitum consumption, and feed refusals were measured daily. Water was offered once daily for ad libitum consumption. Refusals of water were measured, and water intake was assumed to equal water offered minus water refused. No hay was fed. Hutches were bedded with straw throughout the study.

Data in Table 1 shows that the inclusion of antibiotics in CMR improved animal performance. This is particularly interesting because overall mortality was very low in the study.
(2 calves in each treatment) and overall morbidity (number of veterinary treatments) was also quite low. Nonetheless, calves fed the diet containing antibiotics grew faster, were heavier at 56 days of the study, consumed more calf starter and were more efficient than calves fed control CMR.

We have to balance the benefits of including antibiotics in the diets of animals with the potential harm that widespread use of antibiotics might cause to others. If the use of antibiotics can spread antibiotic resistance to other pathogens (including important medical pathogens), then it is in everyone’s best interest to limit or eliminate the unnecessary use of these drugs. It is noteworthy that some recent research suggests that inclusion of antibiotics in calf milk replacers may increase the probability of shedding of pathogens (e.g., Escherichia coli O157:H7), but the increased probability is of short duration (Alali et al., 2004).

In many parts of the world, subtherapeutic antibiotic use has been restricted or eliminated. Other legislatures (including those in the United States) are considering significant restrictions as well. Therefore, producers are facing the loss of a significant management tool with the restriction in use of antibiotics.

It is in this context that researchers have been looking for alternatives to antibiotics and new methods of feeding calves to reduce the potential for calves to get sick. What is a reasonable strategy in this effort? Well, consider that there are two primary sites of infection in young calves—enteric and respiratory. Other systems of the animal (reproductive, mammary, etc.) are not usually major sites of infection and disease in young calves. Considering enteric and respiratory disease, the most common source of disease is enteric infection. This is also the site where dietary intervention is most effective. Therefore, our focus will be on feeding practices to minimize the risk of enteric disease in calves.

Of course, proper nutrition is essential in keeping calves healthy. Formulation of diets to provide sufficient amounts of protein (including ruminally available and escape protein), energy (as fat and carbohydrates), vitamins, minerals and water is essential. However, in our current context, we will be focusing on “non-nutritional” or “extra-nutritional” strategies. These concepts must be incorporated into a feeding program in addition to the proper nutrition that is essential to the young animal.

Compounds that can be fed and have a non-nutritional effect on an animal have been called “nutraceuticals” or “functional foods”. There is considerable debate in the regulatory community regarding the proper classification of these compounds. Are they foods? Are they drugs? There is a lot of confusion about this point and the Food and Drug Administration has attempted to clarify the differences as it relates to human and animal “nutraceuticals”. With the passing of the “DSHEA” (dietary supplement health and education act), there is greater confusion, because dietary supplements that are sold for people with many claims related to health cannot be sold for use in animals for the same purposes.

The Food and Drug Administration has taken a strong stand related to the promotion and sale of nutraceuticals for animals. The following is an excerpt from an FDA publication that describes the position of FDA related to the use of “nutraceuticals” for animals. The specific references are to pets, but they are relevant to all animals. For the complete FDA publication, go to http://www.fda.gov/cvm/index/fdavet/1999/jan.html.
“Nutritional supplements for pets have been available for many years. These are products that provide a source of a recognized essential nutrient, such as calcium or vitamin A, and are intended to augment and ensure nutritional completeness of the diet. Labeling for nutritional supplements must follow the same rules as for other pet foods. If it claims to be a vitamin or mineral supplement, the label must bear guarantees for each vitamin or mineral in the product.

“Dietary supplements” describe a much broader range of products. Some provide essential nutrients, such as vitamins and minerals, but others contain substances that are not recognized as essential for the intended species (for example, vitamin C for dogs and cats, omega-3 fatty acids). Herbs, plant or organ extracts, enzymes, and a host of other substances are also often marketed as dietary supplements. The market for dietary supplements was boosted by passage of DSHEA. This law changed the way FDA regulated these products. Briefly, it said that FDA could not call a substance a “drug” or “food additive” if it met the definition for a dietary supplement and was not already regulated as a drug or food additive. Thus, it shifted the burden of the manufacturer having to prove a product was safe before it went on the market to the FDA having to prove it was unsafe before it could be removed. This prompted a sizable increase in the number and range of dietary supplements available on the market today.”

It must be noted that DSHEA only applies to human products, not pet products. Thus, some of the substances allowed for sale as human dietary supplements may not be legally permitted to be sold for animals. There is good reason for this, though. Although some of the supplements, such as herbal products, may have “thousands of years of history of safe use,” this does not include history of use in animals. It is well known that animals may react very differently to substances than people, and even small doses can cause adverse effects. For example, aspirin and chocolate, both substances that are used by people every day without ill effect, can be toxic to pets and even cause death. Therefore, since it’s not known what the true effects an herb or other supplement may have on pets, it’s safest not to allow marketing for that use.

The term “nutraceuticals” was coined to describe the increasing number of products offered for the prevention or treatment of disease but marketed under the guise of dietary supplements. The promise of a “safe” and “natural” remedy for disease is very appealing. However, since the product has not undergone the same testing for safety and efficacy as required for approved drugs, it’s impossible to know whether the product works at all or is even unsafe.

Clearly, the FDA is taking a position that “nutraceuticals” considers that claims made to change “form or function”, then the product is a drug. Most, if not all of the “nutraceuticals” sold today that make claims to improve animal health, reduce disease, etc. are in vio-
lation of these rules. The FDA has published several articles related to their position on “nutraceueticals”—for example in the Nov/Dec 2000 issue of FDA veterinarian (http://www.fda.gov/cvm/index/fdavet/2000/november.pdf) and some information on regulatory activities in the March/April 2001 issue of FDA Veterinarian (http://www.fda.gov/cvm/index/fdavet/2001/Mar_Apr.pdf).

There are many classes of “nutraceueticals” available. Many are popular as human dietary supplements, for example St. John’s Wort, ginseng and condroitin. However, we will limit this discussion to those products/compounds that may have some utility in reducing the effects of disease in calves. Briefly, we can categorize these into:

- functional proteins
- iron binding antimicrobial proteins (lactoferrin, transferrin)
- immunoglobulins
- probiotics
- immune “stimulants”
- oligosaccharides
- yeast and yeast culture
- others

There are many different other classes of compounds that may be considered “nutraceueticals” that will not be considered here, as they are not thought to be related to enteric disease.

To achieve the goal of reducing enteric disease, any compound must possess several attributes:

- it must survive processing, storage and handling of animal feeds
- it must not be degraded by temperatures typical of storage and feeding
- it must survive the rumen and/or abomasum of the animal (the rumen and abomasum if fed in dry feed, abomasum if fed in the milk or milk replacer)
- it must not be degraded by intestinal enzymes
- it must act while in the intestinal tract

**FUNCTIONAL PROTEINS**

Most nutritionists view proteins simply as sources of amino acids. This traditional view assu-mes that proteins are consumed by the animal and the proteins are digested by stomach acid and intestinal enzymes to their component amino acids, which are then absorbed into the bloodstream. However, some proteins will retain biological activity in the animal after being consumed by the animal. These *functional proteins* have the ability to elicit a physiological response in the animal. Functional proteins may partially resist digestion or functional protein fragments are produced during the digestion process. Functional proteins can be obtained from either animal or vegetable sources. Indeed, some functional proteins
(e.g., trypsin inhibitors in soybeans) are deleterious to producers and must be destroyed prior to feeding. There are several classes of functional proteins that act to reduce the effects of microbial challenge in the animal. These include iron binding proteins, immunoglobulins, defensins and bacteriocins and others.

The methods of collection and processing of functional proteins is extremely important to maintaining functionality. Proteins have been used as a source of amino acids for many years. In the past, most proteins were dried using high temperatures with little consideration to the value (i.e., digestibility) of the amino acids. Improvements in processing resulted in improved digestibility of protein, but there was considerable variation in protein quality due to variation in drying temperatures and length of time which the protein was heated (Goedeken et al., 1990; Knabe et al., 1989). More recently, spray-drying technologies have been introduced to the feed industry. This method of drying reduces the effects of heat and time and maintains the concentration of bioactive proteins in the products.

IRON BINDING ANTIMICROBIAL PROTEINS

Iron is an essential nutrient for growth. However, free iron in the body may promote the production of free radicals, which can result in tissue damage. Therefore, the body utilizes several different kinds of iron carrying proteins to provide mechanisms for transporting iron while simultaneously keeping it from causing damage. Iron is also an essential nutrient for many different kinds of bacteria. If iron were removed from the bacterial environment, then growth of the bacteria might be impaired. Indeed, research has been conducted with two different iron binding compounds, lactoferrin and transferrin, to determine if they can contribute to the animal’s immune system and possibly replacing AB.

Lactoferrin (Lf) is an iron-binding glycoprotein found in milk with a molecular weight of 80 kD. Lactoferrin may serve as an antimicrobial in the gut of the animal (Arnold et al., 1977; Shin et al., 1998), and as a regulator of the immune system (Rejman et al., 1992; Smith and Oliver, 1981). The antimicrobial activities of LF may be especially effective against enteric pathogens such as \textit{E. coli} (Shin et al., 1998) and others (Arnold et al., 1977). In January, 2002, the USDA approved activated lactoferrin as an antimicrobial protein to be applied on fresh meat to reduce the growth of important disease causing pathogens, including \textit{E. coli} O157:H7.

Joslin et al. (2002) evaluated the addition of Lf to CMR (and colostrum) in calves housed in individual pens at the University of New Hampshire Experiment Station. Calves were fed 0, 1 or 10 g/d of purified Lf in the milk replacer. Intake of CMR and starter, BW and gain and fecal scores were measured during the 56-day study.

The authors reported improved ADG and starter DMI (Figure 1) when calves were supplemented with 1 or 10 g of Lf in the CMR. Improvements in BW gain and starter intake were particularly evident during the latter weeks of the study. The authors suggest that calves were healthier and, consequently, consumed more starter DM, which improved growth. Unfortunately, however, there were only seven calves per treatment, which makes firm conclu-
sions difficult based on the small number of animals. Further, although the authors hypothesize that calves were healthier, fecal scores measured during the study did not differ among treatments (2.51, 2.46 and 2.52 on a scale of 1 = normal to 5 = severe diarrhea, respectively) and the number of days the calves had diarrhea (fecal score > 3) also did not differ statistically. Based on these data, the question of whether Lf can contribute to animal health and potentially reduce the effects of an enteric challenge (i.e., replace AB) have not been completely addressed and more research is required.

Figure 1. Starter DM intake in calves fed 0, 1 or 10 g of lactoferrin/d. Adapted from Joslin et al., 2002.

Transferrin (Tf) is an iron-binding protein in blood that performs a similar function in blood as lactoferrin in milk. Transferrin has been proposed as a method of reducing growth of pathogenic bacteria (Brock, 1989; Fettman and Rollin, 1985); however, no on-farm trials have been conducted with Tf in calf milk replacers. In vitro work conducted in our laboratory indicates that apo-Tf can reduce growth of pathogenic bacteria including Salmonella typhi-murium and E. coli by up to 50%.
ANTIMICROBIAL PEPTIDES

Other antimicrobial peptides that may be used to reduce the risk of enteric infections include lysozyme, lactoperoxidase, bacteriosins and defensins. These peptides kill pathogens by direct killing of bacteria and viruses. To date, no studies have evaluated these antimicrobial peptides in diets of calves.

IMMUNOGLOBULINS

Introduction

The use of immunoglobulins (Ig) to reduce the effects of pathogenic challenge has been recognized for hundreds of years. To understand the role of Ig in replacing AB, it is important to understand that the intestinal tract is the largest immunological organ in the body. The total area of these mucosal surfaces, which cover these tube-like tissues are at least two hundred times larger than those of skin (Takahashi and Kiyono, 1999). The large amount of lymphoid tissue (primarily as Peyer’s patches) in the gut also contributes to the immunological capability of the intestine. These tissues appear to be particularly important in enteric disease caused by viruses and bacteria (Frost et al., 1997; Brodersen and Kelling, 1999). Therefore, in addition to providing critical digestive functions, the intestine must also prevent diseases from entering the body.

The gastrointestinal tract is constantly exposed to insults consumed by the animal. These may include pathogenic organisms, toxins, noxious chemicals, physical insults (e.g., hardware disease) and many others. Organs in the gastrointestinal tract have many methods to deal with these insults, including secretion of digestive enzymes and acid, harboring of commensal organisms, and other methods (Kruzel et al., 1998). Of particular interest, however, is the presence of Ig in the intestines. The second component involves functional immunological elements found in the mucosal and submucosal compartments, e.g., gut associated lymphoid tissue. When gut integrity is disrupted by invasive pathogens or by trauma, a myriad of pro-inflammatory mediators are released from cells in the gut wall that exert actions in the tissue or gut lumen. Immunoglobulin is an important defense mechanism in overall immune response in the intestinal and production of Ig by gut associated lymphoid tissue is a critical function of these tissues.

Traditionally, the only Ig considered important in the intestine was IgA, which is produced by epithelial cells. Indeed, researchers continue to focus on production of intestinal IgA as a means of controlling disease (Sagodira et al., 1999; Coffin et al., 1999). However, other recent evidence suggests that IgG may also play an important role in reducing the risk of disease in animals. The two primary sources of IgG in the gut is through secretion of IgG from the blood into the intestine and oral consumption of IgG from milk or colostrum (lacteal secretions), blood or eggs.
Movement of circulating IgG into the gut

Research done at Washington State University by Dr. Tom Besser and coworkers investigated the movement of circulating IgG into the intestinal tract and the role of IgG in reducing effects of microbial challenge (1988a, b). The researchers conducted two studies to determine the metabolic fate of IgG that entered the bloodstream. In the first study, calves were injected with a radioactive ($^{125}$I) labeled IgG directly into the blood. The calves (n = 24) were colostrum deprived and obtained from a commercial U.S. dairy. The excretion of the radioactive label was then monitored over time by collecting urine and fecal samples and determining the amount of radiation they contained. The excretion of total radiation and the total radiation still bound to protein (an estimate of the “intact” IgG) were measured.

An average of 2.52% of the $^{125}$I was excreted in the urine every day (Table 2). Most of this was not bound to protein (only about 3% of urinary excretion), indicating that the IgG excreted in urine had been previously catabolized. Also, 1.5% of injected $^{125}$I was excreted by way of the feces. Most of this (82%) was still bound to protein, indicating that these IgG were not degraded prior to excretion in the feces. The total excretion of $^{125}$I was 4.02% per day of the amount injected. Regression analysis indicated that the half-life of the injected $^{125}$I containing IgG was 17.9 days.

<table>
<thead>
<tr>
<th>Item</th>
<th>$^{125}$I Excretion (%)/day</th>
<th>Protein Bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine</td>
<td>2.52</td>
<td>0.008</td>
</tr>
<tr>
<td>Feces</td>
<td>1.50</td>
<td>1.23</td>
</tr>
<tr>
<td>Urine &amp; Feces</td>
<td>4.02</td>
<td>1.31</td>
</tr>
<tr>
<td>Moved to gi tract</td>
<td>2.60</td>
<td>—</td>
</tr>
</tbody>
</table>

Table 2. Excretion of $^{125}$I-labelled IgG in the urine and feces of calves intravenously injected with $^{125}$I-labelled IgG. From: Besser et al., 1988a.

Calves were euthanized and the amount of $^{125}$I was determined in various compartments of the intestine to estimate directly the amount of IgG that moved from the circulation into the intestine. The total values corresponded to a daily transfer of 2.60% of the total infused $^{125}$I into the gastrointestinal tract. Most of this IgG appears to be secreted into the intestine as intact IgG, but a portion apparently is degraded by intestinal enzymes. The authors estimated that if a calf were to consume and absorb 100 g of IgG from maternal colostrum within the first 24 hours, it would subsequently secrete 1 to 4 grams of IgG back into the intestine daily for the first two weeks of life.
In a second experiment, Besser and coworkers (Besser et al., 1988b) fed newborn calves colostrum containing antibodies against a specific strain of rotavirus. Dry cows were immunized with a vaccine against the rotavirus at 6 and 3 weeks prior to expected calving to produce colostrum containing the specific antibody. The amounts of specific antibody were then measured in the blood and gastrointestinal contents following sacrifice at 5 or 10 days of age.

The correlation between serum rotavirus antibody and intestinal rotavirus antibody (Figure 2) showed a close correlation. This means that calves 1) absorbed the specific antibody from the colostrum consumed within the first 24 hours, 2) the specific antibodies then moved from the circulation into the lumen of the intestine, and 3) the movement of specific antibodies into the intestine occurred in proportion to concentrations in the blood.

**Figure 2.** Relationship of serum and intestinal rotavirus antibody titers. From: Besser et al., 1988b.

The value of intestinal IgG

Many bacteria and viruses that infect calves are enteric—typically causing intestinal damage and signs of disease (diarrhea, dehydration). Immunoglobulins in the intestine could
assist the animal to mount an effective immune response when they attach to the antigenic binding sites on the specific pathogen. Therefore, movement of IgG from the circulation into the intestinal lumen would be one way to provide immunity in response to the pathogens that infect the animal by the fecal-oral route.

To determine if there is any value to circulating IgG in dealing with intestinal pathogens, Besser and coworkers injected calves subcutaneously with 1.25 liters of whey extracted from the colostrum of cows immunized against rotavirus or colostrum from non-immunized cows. The control group was fed colostrum from non-immunized cows. These calves were then challenged with enteropathogenic strain of rotavirus at 72 and 96 hours after birth.

Administration of IgG by subcutaneous injection protected calves against rotavirus infection (Table 3). Calves treated with subcutaneous “immune” whey (whey containing rotavirus antibody) had higher serum antibody titers against rotavirus and were more protected against oral rotavirus challenge than calves that were injected with “non-immune” whey. Presumably, the mode of action for the immune whey was via movement of the IgG from the circulation into the intestinal lumen, where the rotavirus was present. It is important to note that these calves were fed no colostrum, so the only source of antibody was through subcutaneous injection.

Table 2. Excretion of 125I-labelled IgG in the urine and feces of calves intravenously injected with 125I-labelled IgG. From: Besser et al., 1988a.

<table>
<thead>
<tr>
<th>Item</th>
<th>Immune Whey</th>
<th>Non-Immune Whey</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotavirus Ab titer (1/log2)</td>
<td>14.85</td>
<td>9.10</td>
</tr>
<tr>
<td>% of calves infected</td>
<td>20.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Incubation time (hr)</td>
<td>72.0</td>
<td>32.0</td>
</tr>
<tr>
<td>Duration time (hr)</td>
<td>64</td>
<td>135</td>
</tr>
<tr>
<td>Days with Diarrhea</td>
<td>0.10</td>
<td>2.83</td>
</tr>
</tbody>
</table>

Ward et al. (1996) measured serum levels of rotavirus-specific maternally derived antibodies in neonatal pigs. Pigs were grouped into non-detectable, low, or high serum titers. Pigs were then challenged with virulent rotavirus at 3 days of age and monitored for infection and disease. All inoculated pigs shed rotavirus and developed diarrhea, and pigs with highest levels of circulating antibody to rotavirus developed less severe diarrhea and shed rotavirus for fewer days than pigs with lower antibody titers. The researchers concluded that circulating maternal antibody plays a significant role in mitigating clinical disease and movement of antibodies from the circulation into the lumen of the intestine is important in this response.
These studies indicate that:

- Ig in the intestine play an active role in the resistance to pathogenic organisms that infect calves via the oral route, such as rotavirus.
- Ig in the intestine are sufficiently resistant to digestion to provide immune response. Studies have documented the relative resistance of IgG to proteolytic degradation in the gut.
- A major source of IgG in the intestine of newborn calves is from circulating IgG that are absorbed from ingestion of colostrum within the first 24 hours.
- Larger concentrations of IgG in the serum generally produce larger concentrations of IgG in the lumen of the intestine.

**Reduced digestibility of Ig**

Immunoglobulins are more resistant to proteolysis than many other proteins. This is necessary for IgG to provide local response in the intestine of the animal. Roos et al. (1995) reported that the recoveries of N of ingested IgG and IgM still immunologically active were 19±3% and 19±4%, respectively in human patients consuming $^{15}$N labeled preparations of Ig. According to the data of Roos et al., the ileal digestibility of IgG in healthy humans was 79%. Interestingly, much of the immunological activity was associated with the F(ab’)$_2$ fragments, which are produced by pepsin and trypsin activity on IgG. The F(ab’)$_2$ fragments contain a molecular weight of ~100 kDa.

**IgG from milk/colostrum**

The role of IgG in milk and colostrum in supporting the health of young calves is very well defined. Dairy professionals have long recommended feeding transition milk (which contains from 2 to 4 g of total IgG/100 ml) to “bathe” the gut and reduce the effects of enteric challenge. The role of colostrum or milk derived antibody (which is a combination of IgA and IgG) has been evaluated in many species.

Ebina (1996) reported that colostrum from cows hyperimmunized against human rotavirus MO strain contained neutralizing antibody to four different G serotypes of human rotavirus. The colostrum was effective in protecting suckling mice against rotavirus infection. Further, purified IgG obtained from colostrum protected against infection with the homologous virus. After randomly grouping 20 infants from a baby care center, 10 infants received 20 ml of colostrum for 2 weeks and 10 control infants received none. Rotavirus-associated diarrhea developed in 7 of the 10 infants in the control group. None of the three infants in the group daily receiving the colostrum had such symptoms, and one of three infants in the group receiving treatment, every other day developed rotavirus-induced diarrhea. Oral administration of rotavirus-antibody colostrum seems to be an effective and safe means of preventing diarrhea caused by human rotavirus infection. Recently, the immunized cows
were boosted by reinjection of 4 serotypes of human rotavirus into a superficial cervical lymph node two weeks after delivery, resulting in mass production of cow’s milk containing a high-titered antibody to human rotavirus.

Fowler et al. (1995) obtained colostrum from cows immunized against rotavirus during the dry period. Colostrum fed colostrum to calves for 14 days after birth reduced shedding of rotavirus after oral challenge and improved fecal scores and rate of BW gain. Other researchers (Drew, 1994) have reported similar results. Clearly, there is a compelling reason to explore the potential for supplementation of liquid feeds with colostrum.

Challenges with commercial use of colostrum/milk derived antibodies are limited production of colostrum, a lack of facilities to process colostrum, very low concentrations of Ig in whole milk and expensive processes needed to extract Ig from milk, and competition with human IgG markets. Products utilizing milk/colostrum IgG are available for use as colostrum supplements, but no products are currently available for continued feeding as a source of intestinal IgG.

IgG from plasma.

The utilization of plasma in diets of young ruminants has been evaluated scientifically and on the farm. As early as the late 1800’s blood had been utilized in dietary formulations to replace cows’ milk, for both its nutritional value as well as improved health of calves. The advantages of IgG from plasma are their availability, low cost, and ease of collection and processing. Whole blood (primarily beef, pork or poultry) is collected from government inspected abattoirs, centrifuged to remove cellular components (red and white blood cells, platelets) and the resulting plasma is then spray-dried to produce a light-tan powder. Spray-dried animal plasma (SDAP) contains about 78% CP and contains approximately 16% IgG. Remaining nutrients in plasma include moisture (9%) and ash (10%). Plasma is not a significant source of fat or carbohydrate.

The value of the functional proteins in SDAP was first recognized in young pigs in the 1990’s (Gatnau and Zimmerman, 1990, 1992; Hansen et al., 1993; Kats et al., 1994; Sohn et al., 1991). These studies reported dramatic improvements in intake, body weight gain and efficiency when pigs were fed diets containing spray-dried animal plasma. Subsequent experiments reported that the response was primarily associated with the IgG fraction, although others indicated a beneficial effect of other fractions of plasma. Today, nearly 90% of starter diets fed to early weaned pigs in the U.S. contain SDAP. The rapid acceptance of SDAP in pig diets occurred even though the cost of the overall diets increased significantly.

The value of SDAP in the diets of herd replacement calves has been evaluated experimentally. Morrill et al. (1995) reported improved body weight gain in calves fed plasma (25% of protein) compared to control (whey protein concentrate). All diets in this study were medicated with neomycin/oxytetracycline. Animals in this study were housed on a commercial calf ranch in Kansas. All calves were purchased and transported to the research facility. Amount of stress in these calves was significant, as was shown by loss of body weight for the
first two weeks of the study. Body weight gains (Figure 3) approached 700 g/d by week 5, then were depressed with the outbreak of disease (Salmonella infection) on the farm. Under these conditions, plasma (bovine or porcine) resulted in significantly greater BW at 6 wk of age compared to calves fed control. By the end of 6 wk, calves fed milk replacer containing plasma had consumed 4.15 kg more calf starter than calves on control.

Figure 3. Body weight gain in calves fed milk replacer containing bovine or porcine plasma. From: Morrill et al. 1995.

Data by Quigley and Bernard (1996) showed no significant effect of bovine plasma (25% of protein) on animal growth, intake, or efficiency. Mean feed efficiency in the study was 469 and 442 g BW gain/kg of DM intake for calves fed control and plasma containing milk replacers, respectively. Mean body weight gains from 0 to 56 d of age were 523 and 469 g/d, respectively. Animals in this study were derived from dairy farms, raised under excellent management conditions and exposed to little stress. Rates of body weight gain in this study were greater than the study by Morrill et al. (1995) and were indicative of excellent management conditions.

Quigley et al. (2002) reported the effects of feeding SDAP or a product containing
bovine serum, fructooligosaccharides and minerals/vitamins (Gammulin®, APC, Inc.) in two studies utilizing 240 Holstein bull calves purchased from sale barns and dairy farms. Calves were usually within one week of age and in various stages of failure of passive transfer. In experiment 1, calves fed additive containing bovine serum tended to have fewer days with diarrhea, lower use of electrolytes, and improved BW gain from d 29 to 56 (Table 4). Addition of SDAP to milk replacer did not influence any parameter measured. In experiment 2, calves fed additive containing bovine serum or milk replacer containing spray-dried bovine plasma had lower mortality (4.4 vs. 20%) and tended to have improved fecal scores and fewer days with scours (Table 5). Antibiotic use was lower when calves were fed the additive. Indices of enteric health (incidence of scours and treatment with antibiotics and electrolytes) were improved when plasma was added to milk replacer throughout the milk feeding period or as an additive during the first 15 d of the milk feeding period, when calves were most susceptible to enteric pathogens. The primary difference between experiments 1 and 2 was the overall level of stress. More calves in experiment 1 were purchased from dairy farms than sale barns, and the experiment was conducted at an optimal time of the year (i.e., weather closest to the thermoneutral zone). CMR contained all milk protein and there was a general lack of enteric challenge. Conversely, Experiment 2 was conducted during a cold period of the year, the calves were fed CMR containing soy protein and an outbreak of ente-ric and respiratory pathogens occurred during the trial. Generally, these data suggest that calves fed SDAP—whether as SDAP in the CMR or as an additive such as Gammulin—will respond to the products, particularly when the overall level of challenge is significant.

Table 4. Least squares means of animal performance, Experiment I. From: Quigley et al., 2002.

<table>
<thead>
<tr>
<th></th>
<th>Treatments¹</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P-A-</td>
<td>P-A+</td>
<td>P+A-</td>
<td>P+A+</td>
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<td>P</td>
<td>A</td>
<td>I</td>
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<tr>
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<td>30</td>
<td>30</td>
<td>30</td>
<td>30</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Mortality, %</td>
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<td>0</td>
<td>0</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>IgG, g/L</td>
<td>9.0</td>
<td>10.3</td>
<td>8.5</td>
<td>11.1</td>
<td>1.0</td>
<td>NS</td>
<td>0.06</td>
<td>NS</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>35.0</td>
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<td>36.0</td>
<td>34.9</td>
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<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Age, d</td>
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<td>8.9</td>
<td>9.1</td>
<td>9.0</td>
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<tr>
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<td>1.6</td>
<td>1.6</td>
<td>1.6</td>
<td>0.03</td>
<td>NS</td>
<td>NS</td>
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</tr>
<tr>
<td>Scours, days³</td>
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<td>4.9</td>
<td>7.3</td>
<td>6.1</td>
<td>0.9</td>
<td>NS</td>
<td>0.09</td>
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<tr>
<td>Electrolytes, days³</td>
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<td>1.6</td>
<td>3.0</td>
<td>1.4</td>
<td>0.6</td>
<td>NS</td>
<td>0.10</td>
<td>NS</td>
</tr>
<tr>
<td>Antibiotics, days³</td>
<td>1.1</td>
<td>0.9</td>
<td>1.3</td>
<td>0.4</td>
<td>0.4</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

¹Treatment: P = CMR containing 0 (-) or 20% (+) of CP as spray-dried bovine plasma; A = addition of placebo (-) or supplement (+) containing bovine Ig and fructooligosaccharide.

²Contrasts: P = effects of P- vs. P+; A = effects of A- vs. A+; I = interaction of P and A.

³Significant effect of week (P < 0.01).
Quigley and Wolfe (2003) also recently reported that bovine or porcine derived SDAP added to CMR. Experimental milk replacers were formulated to contain whey protein concentrate (WPC) as the primary protein source or WPC plus 5% spray-dried bovine plasma (SDBP) or spray-dried porcine plasma (SDPP). The SDPP was heated to remove heat insoluble materials and provide products with similar IgG content. Calves were also fed commercial calf starter and water for ad libitum consumption. Intake, change in body weight, feed efficiency, morbidity and mortality were determined. Mortality was 10, 3, and 2 in calves fed WPC, SDBP and SDPP treatments, respectively (Table 6). Morbidity, measured as the number of days that calves had diarrhea was reduced by 30% when SDBP or SDPP were fed. Calves had diarrhea for 6.9, 3.9 and 4.7 d during the 42-d study when fed CMR containing WPC, SDBP and SDPP, respectively. Fecal scores tended \( (P < 0.10) \) to be reduced and feed efficiency tended to be improved when SDBP or SDPP were fed. Mean intakes of total dry matter during the 42-d study were greater when calves were fed SDBP or SDPP and were 661, 710 and 684 g/d for calves fed WPC, SDBP and SDPP, respectively. Mean BW gains from d 0 to 42 were 231, 261 and 218 g/d, respectively. Calves fed SDPP tended \( (P < 0.10) \) to have lower body weight gain during the first 28-d of the study. However, difference in daily body weight gain from d 1 to 28 was only 39 g/d. Inclusion of SDBP or SDPP in milk replacer reduced morbidity and mortality of milk-fed dairy calves.

Researchers at Virginia Tech (Mowry et al., 2001) recently compared CMR containing WPC vs. WPC plus 4% of the total protein as NutraPro (APC, Inc., Ankeny, IA). Holstein and Jersey calves \( (n = 78) \) were fed milk replacers between June and December, 2000

<table>
<thead>
<tr>
<th>Treatments(^1)</th>
<th>End</th>
<th>Mortality, %</th>
<th>IgG, g/L</th>
<th>Hematocrit, %</th>
<th>Plasma protein, g/L</th>
<th>Fecal Scores(^3)</th>
<th>Scours, days(^3)</th>
<th>Electrolytes, days(^3)</th>
<th>Antibiotics, days</th>
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<tbody>
<tr>
<td>P-A-</td>
<td>24</td>
<td>20.0</td>
<td>8.6</td>
<td>33.4</td>
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<td>1.49</td>
<td>5.0</td>
<td>2.2</td>
<td>4.2</td>
</tr>
<tr>
<td>P-A+</td>
<td>29</td>
<td>3.3</td>
<td>9.3</td>
<td>32.9</td>
<td>55.6</td>
<td>1.44</td>
<td>3.5</td>
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<td>P+A-</td>
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<td>3.3</td>
<td>9.3</td>
<td>32.9</td>
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<td>1.45</td>
<td>3.5</td>
<td>1.4</td>
<td>2.0</td>
</tr>
<tr>
<td>P+A+</td>
<td>28</td>
<td>6.7</td>
<td>10.1</td>
<td>32.4</td>
<td>55.6</td>
<td>0.03</td>
<td>4.0</td>
<td>1.4</td>
<td>0.6</td>
</tr>
</tbody>
</table>

1\(^{t}\)Treatments: CMR containing 0% (P-) or 4% (P+) spray-dried bovine plasma; A = addition of 0 (-) or 30 to 60 (+) g of additive/d for the first 15 d

2\(^{t}\)Contrasts: P = main effect of P; A = main effect of A; I = interaction of P and A.

3\(^{t}\)Significant effect of week \((P < 0.01)\).
and were fed for 28 d. Bull and heifer calves were used. There was no difference in survival, growth, intake or health of calves fed either WPC or NutraPro in this study. Calves were raised under excellent management and had minimal stress. Mean DMI were 14.7 and 14.8 kg during the 28-d study for calves fed WPC and NutraPro, respectively ($P > 0.10$). Mean BW gain during the trial were 193 and 174 g/d for calves fed WPC and NutraPro, respectively ($P > 0.10$).

The use of SDAP to reduce the effects of enteric challenges has been evaluated by several researchers. Quigley and Drew (2000) fed 21 Holstein bull calves fed CMR containing no additives, bovine serum or neomycin/oxytetracycline for 21 d. Calves were colostrum deprived and were challenged with $E. coli$ on d 3. Health, mortality, intake and BW gain were improved when either SDAP or AB were included in the CMR. Arthington et al. (2002) challenged 12 colostrum deprived, purchased Holstein bull calves (approximately 21 d of age) with coronavirus and measured intake, fecal scores and recovery from the challenge. Calves fed bovine serum recovered more quickly than calves that were not. The authors concluded that the addition of bovine serum increased the rate recovery of calves, including improved intake and fecal scores.

Finally, Hunt et al. (2002) fed 24 Holstein bull calves milk replacer supplemented with bovine serum or soy protein. Calves were orally infected with an $Cryptosporidium$ par-
vum \((10^8\) oocysts) of d 8 of life. Health, intake, intestinal integrity and oocyst shedding was measured for 10 days. Cryptosporidiosis induced diarrhea lasting more than 9 d and produced a 25% increase in intestinal permeability, a 33% decrease in villous surface area, and a 40% reduction in mucosal lactase specific activity. Animals receiving bovine serum had lower peak diarrheal volume and intestinal permeability (-33%), fewer oocysts shed, intestinal crypts were significantly deeper, and villous surface area returned to normal by 9 d after infection (all \(P < 0.05\)).

IgG from eggs.

Another source of IgG used in animal agriculture is chicken IgY. IgY is similar to IgG, and layers can be hyperimmunized against enteric pathogens (e.g., rotavirus) to produce specific IgY in their eggs. The eggs can then be processed to remove the white (most IgY is found in yolks) and spray-dried to produce a product containing specific antibodies. Commercially available products are available to provide IgY as a source of antibodies prior to gut closure (in the first 24 hours of life) or in a post-gut closure application (as a source of IgG to bathe the gut).

German researchers (Erhard et al., 1997) reported that newborn calves fed chicken egg IgY in the first day of life (20 g of egg powder containing 15 mg of IgY/g) absorbed the IgY and the half-life of the IgY was approximately 5 days. Due to the short half-life of heterologous Ig, the researchers recommended that egg powder, when fed, should be fed after the first 48 hours of life. The researchers also concluded “Most important for the prophylactic effect of specific antibodies on infectious diarrhea is not their systemic but their local intestinal availability”.

Ikemori et al. (1997) fed dairy calves CMR supplemented with IgG from bovine colostrum or IgY from spray-dried eggs. Both the cows and birds were vaccinated to produce antibodies against bovine coronavirus. One day after feeding CMR + experimental products (colostrum was fed at three different doses and egg powder at 2 doses), calves were orally challenged with bovine coronavirus \((10^9\) TCID\(_{50}\)). All calves fed no supplemental product developed severe diarrhea and died. Calves fed the egg or colostrum survived, except calves fed the low levels of colostrum. These data suggest that specific antibodies can in indeed protect animals against specific challenges, if the specific challenges on the farm are known.

Egg yolk antibodies are prone to variability of results under field conditions, however. Kuroki et al. (1997) conducted three field trials using egg yolk IgY from layers hyperimmunized against bovine rotavirus. In only one of the three trials was there an improvement in rates of mortality and growth rate. The authors concluded that the high health status of calves and low overall challenge in the two studies was responsible for the lack of response.

Immunoglobulins are important to the health, growth and profitability of dairy calves. It is important that calves are fed sufficient Ig within the first 24 hours of life. These research trials indicated above show that Ig (especially IgG) play an active role in all areas of the body—including the intestine, where many pathogens cause disease. The use of IgG from
milk/colostrum, eggs and plasma is a scientifically sound approach to replacing AB in animal diets. A tremendous body of research indicates the value of these proteins in reducing the effects of microbial challenge.

**PROBIOTICS**

Intestinal bacteria are an integral component of the intestinal immune system. Intestinal homeostasis relies upon the equilibrium between absorption (nutrients, ions), secretion (ions, IgA) and barrier capacity to pathogens and macromolecules of the digestive epithelium. The intestine, particularly the large intestine, is inhabited by a diverse population of bacteria that perform a variety of functions which contributes to many of these functions. When this homeostatic control is disturbed, chronic inflammation, diarrhea and disease may occur. A normal intestinal bacterial flora is a critical to maintaining health. A key part of their function is to “out compete” the pathogenic bacteria and keep them from becoming established in the gut. When an animal is exposed to significant stress, it is possible for the growth of these normal enteric bacteria to become impaired. This allows for the growth of potential pathogens, thereby increasing the risk of disease.

The theory related to the usefulness of probiotic bacteria is simple—the balance of the intestine becomes upset due to some insult. Growth of normal “commensal” bacteria (particularly lactic acid bacteria) is impaired. By providing an exogenous source of bacteria, it is possible that these exogenous bacteria can become established in the gut, thereby reducing the chance for pathogens to become established. Probiotic products are relatively inexpensive and readily available, therefore, they are included in many different types and kinds of combination products (e.g., Donovan et al., 2002).

Research results with probiotics added to diets of young calves have been equivocal. In some experiments, improvements in animal performance have been reported, in others, no effect of the inclusion of probiotics has been reported. It is probable that, like other potential AB replacements, effects are dependent on environmental conditions. In addition, the selection of specific bacteria may be important. Bacteria typical to the intestine (especially Lactobacilli and Bifidobacterium) have shown improved responses compared to other bacteria (e.g., Bacillus subtilis).

Abe et al. (1995) reported improved performance (decreased scours scores, improved growth) when probiotic bacteria (*Lactobacillus acidophilus* and *Bifidobacterium pseudolongum*). On the other hand, Harp et al. (1996) reported that feeding probiotics to calves challenged with *Cryptosporidium parvum* had no effects on fecal scores or oocyst shedding in dairy calves. Morrill et al. (1995) also reported no effect of adding probiotics on health or growth of calves. Some researchers have suggested that probiotics may reduce the shedding of zoonotic pathogens such as E. coli 0157:H7 (Ohya et al., 2000; Zhao et al., 1998).

Probiotics are often misused on the farm. Because probiotics are living bacteria, they must be handled carefully to maintain viability. The expiration date is very important to ensure viability. In addition, storage temperatures can influence the viability of the bacteria. Fi-
nally, it is important to remember that probiotics are bacteria—adding probiotics to medica-
ted milk replacers will defeat the purpose of including the probiotic in the first place!

**IMMUNE STIMULANTS**

A novel approach to increasing the resistance of animals to disease is to increase the
animal’s immune response. This approach is termed “immunotherapy” or “immunomodu-
lation”. There are several products that, when administered to animals (usually by injection)
will non-specifically stimulate the animal’s immune system and prepare it to meet the chal-
 lenges of any type of enteric infection. One such product, ImmunoBoost®, (Bioniche Animal
Health USA, Inc., Bogart, GA) is advertised as a USDA approved immune stimulant. Re-
 sults of the company’s technical evaluations in a challenge study with 22 Holstein bull calves
this product on a large California calf ranch using 200 newborn Holstein bull calves that were
fed either control CMR without or with an IV injection of the test product. Calves used in the
study were those that were purchased and transported to the calf ranch. Calves were
enrolled when they showed clinical signs of sickness (diarrhea, depression, anorexia). Calves were
monitored for five days. There was no effect of the product on any clinical score or in the
number of calves that were clinically ill. The authors indicated that the stress on the animals
was significant. They were colostrum deprived calves that were purchased and transported,
and the study was conducted in the summer, when the ambient temperature often exceeded
40 C (105 F). However, such stressors are not unusual in many parts of the world, and such
stressors are often imposed to increase the differences between treatments.

Portions of the yeast cell wall—specifically the β-glucan fraction of the cell wall—
has been shown to stimulate the immune system in many species of animals, including hu-
mans. For example, Hetland et al. (2002) reported that addition of β-glucans inhibited the
growth of *Mycobacterium tuberculosis* in vitro. Others have reported that immune stimula-
tion occurs primarily at the site of the macrophage in the intestine (Cleary et al., 1999; Olson
et al., 1996), although resistance to respiratory diseases have been observed in pigs fed β-
glucan (Jung et al., 2004).

The role of β-glucan in improving health of young calves has been reported (Cary et
al., 2004; Eicher and Johnson, 2002), although the exact nature of the response in young
calves and formulation (composition of β-glucan preparation and presence of additives such
as ascorbic acid) has not been optimized.

The idea of immune stimulants is interesting—“jump start” the immune system so it
can react to the inevitable pathogenic challenges. This may be a costly strategy, however. Up
regulating the immune response will increase energy and protein utilization. If pro-inflamma-
tory cytokines (IL-1β, IL-6 and TNF-α) in response to immune stimulants, energy and pro-
tein metabolism may be affected and appetite can be suppressed. However, this approach will
be appropriate in situations where immune compromise occurs.

Another approach to immune stimulation or immunomodulation is administration
of peptides that are directly involved in immune stimulation. Japanese researchers recently
reported that administration (oral or parenteral) of interferon did not significantly affect morbidity or mortality of Japanese Black cattle prior to weaning. Apparently, the administration of peptides such as interferon (a potent immunostimulatory cytokine) depends not only on the physiological state of the animal but also the site, dosage and length of administration of the peptide.

Muscato et al. (2002) recently reported the effects of feeding autoclaved rumen fluid to young milk-fed dairy calves. Calves were fed 8 ml of rumen fluid daily to weaning; these calves gained more body weight and had fewer scours than controls not receiving rumen fluid. The reason for improved response is not clear, but could potentially be due to the presence of antibacterial proteins used by bacteria to inhibit the growth of others.

**OLIGOSACCHARIDES**

Oligosaccharides are a class of carbohydrates that are not absorbed or digested in the small intestine of man and animals, and thus reach the colon unaltered. In the colon, oligosaccharides are readily fermented by the intestinal microflora. This may result in changes in this flora, thereby increasing the number of (potential) beneficial microorganisms, while repressing the number of (potential) harmful bacteria. This possible change in the intestinal flora may be beneficial to the health of man and animal. In addition, the production of VFA by bacteria fermenting oligosaccharides in animals may improve energy efficiency and alter (improve) intestinal morphology.

Several classes of oligosaccharides are found in nature: fructooligosaccharides, mannanoligosaccharides, galactooligosaccharides, glucooligosaccharides and others. Others are produced chemically and are used as functional foods, or prebiotics. These oligosaccharides are available for inclusion in milk replacer or dry feed diets. Most commonly available oligosaccharides are fructooligosaccharide (FOS) and mannanoligosaccharide (MOS). Products are available and have been tested in a wide number of animals species, including calves. Fairchild et al. (2001) reported improved health and growth of poultry when challenged with *E. coli* and fed Bio-Mos (Alltech, Inc., Nicholasville, KY). Heinrichs et al. (2003) recently reported that addition of Bio-Mos to milk replacer improved intake and reduced scours in calves. Another potential product includes galactosyl-lactose, which has been shown to reduce scours and improve growth in calves (Quigley et al., 1997).

Oligosaccharides have been added to calf milk replacers to reduce the potential growth of enteric pathogens and to promote the growth of “beneficial” bacteria. While data with milk-fed calves is generally scarce, results in other species (pigs, humans, pets) suggests that inclusion of oligosaccharides can alter populations of bacteria and improve or stabilize enteric health of calves.

**OTHER PRODUCTS**

Studies of a number of other ingredients/products are available that provide data to suggest that they can replace AB. Results of some of these trials are listed below.
GARLIC AND DERIVATIVES

Allicin (thio-2-propene-1-sulfenic acid S-allyl ester), a component of garlic, inhibits growth of bacteria by binding to the enzyme, alcohol dehydrogenase and pathogenic microorganisms such as *Thermoanerobium brockii* (Rabinkov et al., 1998). Allicin may also have antioxidant effects. Some researchers have reported that allicin can reduce the effects of fungal and viral diseases (Josling, 2001; Weber et al., 1992). A product containing FOS, allicin, and probiotic organisms (Enteroguard®, Pharmax Biologicals, Inc. W. Des Moines, IA) was evaluated (Donovan et al., 2002) in milk-fed calves (n = 45) fed CMR containing the experimental product or AB (neomycin and oxytetracycline) for five weeks. Calves were born and raised on an experimental farm and were fed colostrum immediately after birth. They were not transported. The authors reported no differences in fecal scores, incidence of diarrhea or electrolyte treatments when either treatment was fed. Unfortunately, this trial did not utilize a negative control, so it is not possible to know if the lack of difference between the experimental product and AB was because there was no response to the AB. Since calves had adequate passive transfer (minimum total serum protein > 5.1 g/dl) and were not exposed to challenges such as transport or movement through a sale barn, it is possible that the level of challenge in the study was insufficient to observe a difference between the experimental product and antibiotic treatment.

Olson et al. (1998) also evaluated an allicin-based product in calves challenged with Cryptosporidium parvum. Calves were dairy calves fed colostrum and not transported. A total of 24 calves used in the study. Calves were fed 3.8 L (4 quarts) of reconstituted milk replacer per day and had ad libitum access to starter and water. On arrival, 20 calves were orally inoculated with $1.5 \times 10^6$ C. parvum oocysts. Fecal scores were monitored for the next 21 days. There was no effect of the product on fecal scores or BW changes in calves to 21 days.

ESSENTIAL OILS AND BOTANICALS

Essential oils are compounds of plants that are known to provide aromatic (odor) characteristics to plants and are thought to serve as attractants, among other potential purposes. However, the actual role of many of these compounds is not well understood. Many essential oils, however, have been shown experimentally to reduce or inhibit the growth of bacteria and viruses. Therefore, they have and are being evaluated as potential replacements for antimicrobials. To date, no published studies are available evaluating essential oils in reducing effects of disease in young calves.

Recent work by Hill et al. (2004) suggest that some combinations of botanicals and oils (Apex) may improve intake of calf starter; however, no data are available to suggest that increased intake is mediated by improved intestinal health. Conversely, data by Manzanilla et al. (2004) indicated that addition of 5% (wt/wt) carvacrol (Origanum spp.), 3% cinnamaldehyde (Cinnamomum spp.) and 2% capsicum oleoresin (Capsicum annum) to the diets of weanling pigs changed stomach outflow rates, decreased ileal microbial mass and changed
the VFA profile in cecum and colon of pigs by increasing the proportion of acetate produced. Such changes could certainly indicate changes in intestinal microbiota, which can, in turn, affect the animal’s immune response.

**SUMMARY**

A number of viable alternatives exist for replacing AB use in animal diets. The use of functional proteins, oligosaccharides, probiotics and essential oils have all been tested alone or in combination with other ingredients. It is likely that combinations of products will be most effective. It is important to remember that each category of product has special requirements for processing, storage, handling and feeding to maximize the response. Our management will have to change and adapt to these new requirements.

**REFERENCES**


