

# Gut Health and How to Improve it

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## ■ Take Home Messages

- ▶ Gut health has three facets: contents, tissues, and microorganisms.
- ▶ Subacute ruminal acidosis (SARA) can affect one or more of these facets at the same time, especially when high grain diets are fed.
- ▶ Feeding programs employing high grain and low coarse fibre can risk gut health.
- ▶ In order to diagnose gut health problems accurately, we must run tests on both the diet and the cow.
- ▶ The use of buffers and yeast products can reduce the problems caused by high grain feeding.

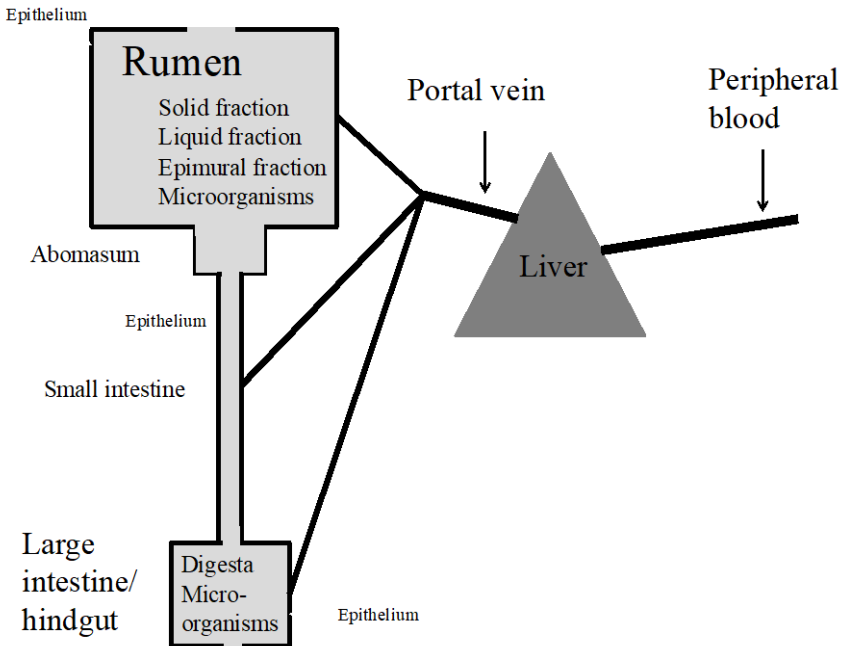
## ■ Introduction

Because of their high energy requirements, milking dairy cows need high grain diets. However, feeding these diets can cause gut health problems. These problems reduce how efficiently cows use their feed, how well the microbes and tissues of the gut function, and the general health and welfare of cows (Kleen et al., 2003; Plaizier et al., 2012; Plaizier et al., 2018). A common gut disease is subacute ruminal acidosis (SARA). This disease is characterized by high acidity and low pH in the rumen. Symptoms that have been related to SARA include reduced and variable feed intake, milk fat depression, diarrhea, inflammation, laminitis, reduced rumen contractions and reduced fibre utilization (Kleen et al., 2003; Plaizier et al., 2008). These symptoms are caused by many factors, and not only by low rumen pH and SARA (Kleen et al., 2003; Plaizier et al., 2008; Plaizier et al., 2018). As a result, diagnosing SARA based on these symptoms can result in inaccuracies in diagnosis (Kleen et al., 2003; Plaizier et al., 2008). The challenge that nutritionists face is meeting the nutrient requirements of high producing dairy cows without adding too much grain to the diet. SARA occurs in about 20% of early and peak lactation dairy cows (Plaizier et al., 2012; Plaizier et al., 2018).

It is, therefore, important that strategies for the prevention of SARA in dairy cows are developed.

## ■ Healthy Digesta

Digestion of feed in the rumen and the hindgut (Figure 1) involves the breakdown of feed by microbes (fermentation) and the production of acids, such as volatile fatty acids (VFA) and lactate. Grains contain more fermentable carbohydrates than fibre. Feeding high grain diets, therefore, results in the production of more acids in the rumen and hindgut than the feeding of high forage diets. When the production of these acids in the rumen and hindgut is greater than the removal of these acids from these compartments, these acids will accumulate (Plaizier et al., 2008). The rumen, but not the hindgut, is buffered by buffers from saliva. Saliva production is stimulated by chewing, which is stimulated by coarse fibre, also called physical effective fibre, peNDF) in the diet. When the peNDF content of the diet decreases, for example, due to the replacement of forage with grain, then the production of saliva and rumen buffering drop (Kleen et al., 2003; Plaizier et al., 2008). Another reason why rumen pH drops when grain feeding is increased is that grain feeding favours the production of lactate in the rumen and hindgut, and lactate is more acidic than VFA (Russell and Rychlik, 2001).



**Figure 1. Diagram of digestive tract and liver in cattle.**

There is no general agreement on how much rumen pH must drop before cows get sick (Kleen et al., 2003). Rumen pH cut-offs of 5.5, 5.6, and 5.8 have been suggested, based on the technique of rumen fluid sampling and the symptoms that are observed. These cut-offs are based on the sensitivity of many rumen bacteria to a low pH (Russell and Rychlik, 2001). However, a short duration drop in pH will not harm bacteria as much as a long duration drop in pH (Plaizier et al., 2008). The duration of the low pH, such as the daily duration below pH 5.6 or 5.8, may give a better indication of the severity of SARA and the stress on the cows than the lowest pH value that is reached.

It has long been believed that the symptoms of SARA are caused by low rumen pH (Kleen et al., 2003; Plaizier et al., 2008). However, more factors are involved. Khafipour et al. (2009a,b), and Li et al. (2012) induced low rumen pH and SARA by feeding a high grain diet and by feeding ground forages. Only the grain-induced SARA reduced feed intake and caused inflammation. Also, only the grain-induced SARA increased the contents of starch and bacterial toxins (lipopolysaccharides, LPS) in the rumen and hindgut, and caused inflammation. These results show that conditions in the hindgut may also be a factor in the symptoms of SARA, and that rumen pH depression alone does not cause these symptoms. Ametaj et al. (2010) also found that grain-induced SARA greatly increased the concentrations of several toxins in the rumen, such as bioamines. Many of these compounds may not be toxic as long as they stay in the digestive tract, but become harmful after they enter the blood circulation (Plaizier et al., 2012; Penner et al., 2014). Karmin et al. (2011) showed that grain-induced SARA causes oxidative stress. This stress can also cause inflammation and harm the cow. Grain-induced SARA, therefore, results in many changes in the cow other than a low rumen pH. The causes of SARA are, therefore, complex, which makes the diagnosis and treatment of this disease difficult. On commercial farms, SARA is likely caused by a combination of high grain and low coarse-fibre diets. The studies on experimentally induced SARA may, therefore, not be fully representative for naturally occurring SARA. More studies are needed to determine the impact of this type of SARA (Kleen et al., 2003; Plaizier et al., 2018).

## ■ Healthy Tissues

The tissues of the digestive tract, especially the epithelia (Figure 1), must support the passage of nutrients (absorption), while preventing the passage of microorganisms and toxins (translocation) into the blood circulation (Penner et al., 2009; Steele et al., 2011; Penner et al., 2014). Hence, the functionality of these tissues is critical for efficient milk production and the health of dairy cows. The anatomy of the rumen is different from that of hindgut. The rumen epithelium is multilayered without protective mucus, but the hindgut epithelium is a single layer with protective mucus.

Poor functionality of the epithelia in the compartments where fermentation takes place, i.e., the rumen and the hindgut, reduces the absorption of acids that are produced during fermentation and increases the translocation of toxins out of the digestive tract (Penner et al., 2009; Steele et al., 2011; Penner et al., 2014). High grain feeding, resulting in a low digesta pH, and high LPS content of digesta have been shown to reduce the functionality of rumen and hindgut epithelia.

As described earlier, feeding high grain diets increases the contents of toxins, including endotoxins from bacterial origin such as LPS, in digesta in the rumen and hindgut (Ametaj et al., 2010; Gressley et al., 2011; Plaizier et al., 2012). These increases, combined with reduced barrier function of the epithelia (Penner et al., 2014), heighten the risk of passage (translocation) of these toxins from the gut to the blood circulation. We believe that the systemic inflammation and laminitis commonly observed during high grain feeding are the result of the translocation of immunogenic compounds, such as LPS (Plaizier et al., 2012). Because of the differences in anatomy of rumen and hindgut epithelia, the risk of these translocations may be higher in the hindgut than in the rumen (Plaizier et al., 2012). Increases in grain feeding increase the ability of the rumen epithelia to absorb fermentation acids, most likely because of an increased availability of VFA. Hence, producers should increase grain feeding slowly, rather than abruptly, to allow the rumen epithelia to adapt. One of the most common VFA, butyrate, is the major energy source for rumen epithelia. Boosting the functionality of the rumen and hindgut epithelia has been attempted by the provision of more butyrate (Dionissopoulos et al., 2013). This has, however, only achieved limited success.

## ■ Healthy Microbiota

Cows rely on the microorganisms in their gut, and especially in the rumen and hindgut, for the use of their feed and their health. The functions of these microorganisms include fermenting feed, especially fibre, producing microbial protein and vitamins, breaking down toxins, and fighting off disease-causing microorganisms (pathogens) (Russell and Rychlik, 2001). The most common of these microorganisms are bacteria, but protozoa, fungi, archaea, and viruses are also present. Within each of these groups, large differences in what they utilize and produce, and how sensitive they are to acidity, oxygen and other environmental factors exist (Russell and Rychlik, 2001). The functions of many groups of microorganisms overlap (Weimer et al., 2015). This means that changes in the composition of microbial populations do not always cause major changes in the functionality of these populations (Weimer, 2015). In order for these microorganisms to function effectively, they must be able to withstand (robustness) or recover quickly (resilience) from stresses, such as SARA (Plaizier et al., 2017; Plaizier et al., 2018; Tun et al., 2018). The more varied the populations of microorganisms are, in terms of the

number of groups of considerable sizes (richness and diversity), the more robust and resilient these populations generally are (Plaizier et al., 2017; Plaizier et al., 2018; Tun et al., 2018). Grain-induced SARA increases acidity and the availability of starch, and decreases the availability of fibre both in the rumen and hindgut. This favours several microbial groups, such as utilizers of starch and lactate, over other microbial groups, such as utilizers of fibre (Russell and Rychlik, 2001; Plaizier et al., 2017; Tun et al., 2018). Generally, this dietary change reduces the richness, diversity, and functionality of the microbial populations in the rumen and hindgut, and creates opportunities for pathogenic microorganisms, such as *E. coli*, to increase their numbers in the digestive tract and feces (Plaizier et al., 2017; Tun et al., 2018).

## ■ Diagnosis

The current diagnosis of SARA, which is based on rumen pH values, is inaccurate. An accurate diagnosis requires a combination of clinical examinations, including blood, milk, urine, and feces parameters, rumen contractions, and rumination activity, as well as analyses of herd management and feed quality, including the dietary contents of neutral detergent fibre (NDF), starch and peNDF (Lean et al., 2014).

Chemical and physical analysis of the diet is key for the assessment of the risk for gut disorders, including SARA. The Penn State Particle Separator is a useful tool for the physical composition of the diet, including its peNDF content (Plaizier et al., 2008). Prior to interpreting the composition of the diet, we must consider that the composition of the diet that is consumed may differ from that of diet that was prepared because of sorting by cows.

Although low rumen pH is not the sole cause of gut health disorders such as SARA, the monitoring of rumen pH remains important. The method of rumen fluid collection and the time of collection relative to feeding are both important factors for the correct interpretation of pH values (Plaizier et al., 2008; Plaizier et al., 2018). Rumen boluses are used to monitor rumen pH continuously. These boluses can be administered through the esophagus, and most likely end up in the reticulum. With this technique, the variation in pH among sites in the rumen must be considered, because some studies have reported that the pH in the reticulum is relatively high (Plaizier et al., 2008; Plaizier et al., 2018). Short battery life and lifespan of only 100 days of these boluses have been reported. This implies that the use of these boluses may be costly. Another reason why rumen pH values must not be over-interpreted is that cows vary in their sensitivity to a low rumen pH and in their susceptibility to the symptoms of SARA and grain-overload. Reasons for this variation in “gut health robustness” are likely many-fold, and include variation in feeding behaviour, absorption of VFA, rumination behaviour, epithelial barrier function, and liver function (DeVries et al., 2005; Plaizier et al., 2018). Many of these factors

may have genetic components. Once these components are better understood, genetic progress in “gut health robustness” may be possible.

Measurements of the feces and urinary pH have also been considered for the diagnosis of SARA. However, the correlations between rumen pH, urinary pH, and fecal pH in many studies have been poor (Plaizier et al., 2008; Plaizier et al., 2018). Several measurements in whole blood and blood plasma have also been considered for diagnosis of SARA; these include PCO<sub>2</sub>, glucose, calcium, LPS, and acute phase proteins (Plaizier et al., 2008; Plaizier et al., 2017). Most of these are only indirectly related to gut health and the acidity of the rumen and hindgut, and many other factors affect the values of these measures. Hence, the diagnostic value of these measures may be limited.

Erratic feed intake is commonly considered to be a sign of poor gut health, including SARA (Kleen et al., 2003; Plaizier et al., 2008; Plaizier et al., 2018). However, as feed intakes of individual cows are commonly not recorded, this measure is not suitable for the diagnosis of gut health problems. Sensors for activity and chewing have, however, become available. Because poor gut health (including a low rumen pH), high grain feeding, and low feed intake have all been associated with a reduction in rumination, the monitoring of rumination activity could function as one of the tools to diagnose gut health problems (Kleen et al., 2003; Plaizier et al., 2018). Rumen stasis and reduction in the frequency of rumen contractions have also been associated with excessive grain feeding and rumen acidosis. However, only acute ruminal acidosis causes rumen stasis, and the effects of SARA on rumen contractions have been variable (Plaizier et al., 2018). The frequency of rumen contractions is easy to determine, e.g., with a stethoscope. Hence, the use of this measurement as part of the combination of diagnostic tests for gut health disorders is highly recommended.

Milk fat depression and changes in the milk fatty acid profile, including reductions in short chain fatty acids, increases in certain trans fatty acids (e.g. trans-10 cis 1C18:2), and changes in the concentrations of odd- and branch-chain fatty acids have been proposed to result from SARA (Colman et al., 2013). This concept needs to be evaluated in field surveys. When this concept has been proven, and the fatty acids can be measured by infrared technology, real time sensors for the analysis in milk may offer prospects for the early diagnosis of gut health problems.

## ■ Inflammation

High grain feeding increases the concentration of inflammatory proteins, known as acute phase proteins, in blood. These increases are part of the cow’s immune response. However, other signs of inflammation, such as fever and an increase in white blood cells are generally not observed during SARA (Plaizier et al., 2012; Plaizier et al., 2018). This shows that the inflammation

during SARA is moderate; however, that does not mean that the inflammation does not affect the cow because this moderate inflammation may use nutrients that could otherwise have been used for milk production and may reduce how well the cows can fight off infectious diseases. The inflammation during SARA may be located in rumen tissues (rumenitis), but this is not common during SARA (Kleen et al., 2003; Plaizier et al., 2008). This inflammation is, therefore, most likely systemic, meaning that it is located outside of the gut. The likely cause of this systemic inflammation is the passage of toxins from the gut to the blood circulation. Grain-induced SARA increases the content of these toxins in the rumen and the hindgut greatly (Ametaj et al., 2010; Plaizier et al., 2012; Plaizier et al., 2018). It also reduces how well the rumen and hindgut can prevent the passage of these toxins to the blood circulation (Penner et al., 2014; Plaizier et al., 2018). These factors combined are the reason why grain-induced SARA increases the concentrations of inflammatory toxins in the blood. The liver can detoxify these compounds, but SARA and other diseases that are common in early and peak-lactation cows reduce this function of the liver (Plaizier et al., 2012; Plaizier et al., 2018). This means that poor liver function increases the risk of problems caused by high grain feeding.

## ■ Treatment and Prevention

In addition to producers feeding balanced diets, the risk of rumen acidosis can be reduced by the inclusion of rumen modifiers, including antibiotics, buffers and neutralizing agents, yeasts, direct-fed microbials, and enzymes (Golder, 2014; Tun et al., 2018).

Diets are commonly formulated to contain sufficient peNDF and to not exceed the maximal inclusion rates of non-fibre carbohydrates and starch. Unfortunately, the composition of the diet consumed can differ from that of the formulated diet due to errors in the mixing of the diet and sorting by cows. Errors in mixing can be made when weighing equipment is not calibrated, or if the assumed dry matter (DM) contents of forages, especially silages, differ from the real DM contents of these feeds. Hence, regular calibration of this equipment and testing of the DM content of forages are recommended. Cows generally sort against long feed particles in favour of small feed particles. This reduces their intake of peNDF, even when the dietary inclusion rate of this fibre is sufficient. Sorting is often stimulated by high DM content of the diet and a large variation in dietary particle size (DeVries et al., 2005). The large variation in dietary particle size can be prevented by taking dietary particle size into account in the diet formulation, and by appropriately selecting forage chop lengths. A high dietary DM content can increase sorting behaviour because feed particles stick less to each other (DeVries et al., 2005). As a result, total mixed rations with a DM content higher than 50% may be prone to sorting. Adding water to the diet is an easy way to reduce its DM content.

Adding buffers to the diet is a common and cost-effective way to limit the rumen pH depression following the intake of a high grain diet. The most common buffer used is sodium bicarbonate. This buffer can be fed up to 0.8–1% of dietary DM. Another method of preventing the effects of high grain diets is to reduce the impact that these diets have on gut microbiota. Several products of *Saccharomyces cerevisiae* yeast have this potential (Golder, 2004; Plaizier et al., 2018; Tun et al., 2018). Most yeasts used in the livestock industry contain or are derived from *Saccharomyces cerevisiae* and *Aspergillus oryzae* strains (Plaizier et al., 2018). These products include live yeasts, dead yeasts and yeast culture fermentation products. The latter consist of dead yeasts, culture medium, and fermentation products. Li et al. (2016) found that a *Saccharomyces cerevisiae* fermentation product (Diamond V XPC, Diamond V Mills Inc, Cedar Rapids, Iowa) stabilized rumen pH in dairy cows during moderate and high grain feeding. Tun et al. (2018) observed that supplementation with another *Saccharomyces cerevisiae* fermentation product attenuated the reductions in microbial richness and diversity resulting from high grain feeding. Other actions of yeasts include increasing fibre digestion and increasing microbial protein production, which may be significant factors that could reduce the risk of acidosis.

Antibiotics that are used in the cattle industries to prevent rumen acidosis include tylosin and virginiamycin (Golder, 2014). However, it is likely that less of these antibiotics will be available in the future because of concerns related to antibiotic resistance and the move away from antibiotics for non-therapeutic use. Antibiotics that are not used in human medicine, such as ionophores and bambarmycin, may have more potential for use in livestock (Golder, 2014; Plaizier et al., 2018). However, results of prolonged supplementation with these compounds on gut health have been variable (Plaizier et al., 2018). In order to improve the efficacy of products used to prevent rumen acidosis, an improved understanding of the mechanisms by which these strategies affect the functionality of gastrointestinal microbiota and epithelia, and the immunity, inflammation and “gastrointestinal-health robustness” of cows is needed.

## ■ Conclusions

Gut health disorders in high yielding dairy cows are common. One such disorder that is well recognized is SARA. The term “SARA” is confusing, because several of its symptoms are not only caused by conditions in the rumen and by low rumen pH. Also, many of these symptoms can be caused by problems other than SARA. The diagnosis of SARA is complex and needs chemical and physical analysis of the diet, checking if cows sort their feed, and a combination of measures made on the cow, such as rumen pH, chewing behaviour, rumination, and milk fat. The fatty acid profile of milk may offer promise as a diagnostic tool. The monitoring of feed intake is useful, but not practical on most farms. The accuracy of measurements in urine, feces, and blood are likely too low to contribute to an accurate diagnosis of SARA.



Adequate formulation and mixing of diets and the prevention of sorting are key to the prevention of SARA. Dietary supplements such as buffers and yeast products can reduce the risk of SARA. However, the effects of buffers are less variable than those of yeast products, and more research on how buffers affect conditions in the rumen and hindgut are needed.

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