Invited review: abomasal damage in veal calves

Bus, J. D., Stockhofe, N., & Webb, L. E.

INTERPRETIVE SUMMARY

Invited review: The ins and outs of abomasal damage in veal calves. *By Bus et al*. A common finding in veal calves at slaughter is abomasal damage in the form of ulcers, erosions and scars, with current prevalence ranging from 70% to 93%. To date, there is however no clear etiology for this problem, and it is hence difficult for the veal industry to address it. This review synthesizes all current knowledge on abomasal damage in veal calves, taking from research in other species when evidence in calves is lacking. Thereby, it identifies for which risk factors further research is required, and proposes ways through which abomasal damage may be minimized in the future.

INVITED REVIEW: ABOMASAL DAMAGE IN VEAL CALVES

The ins and outs of abomasal damage in veal calves

Bus, J.D.*, Stockhofe, N.†, Webb, L.E.*[1]

*Animal Production Systems group, Wageningen University & Research, PO Box 338, 6700 AH Wageningen, Netherlands

†Wageningen Bioveterinary Research, Wageningen University & research, PO Box 65, 8200 AB Lelystad, Netherlands

[1] Laura E, Webb, P.O. Postal address: P.O. Box 338, 6700 AH Wageningen, the Netherlands

Landline: +31(0)317481911. Email: laura.webb@wur.nl

ABSTRACT

Of all cattle production systems, veal calves are most severely affected by abomasal damage, with current prevalence at slaughter ranging from 70% to 93% of animals affected. Though most damage is found in the pyloric region of the abomasum, fundic lesions are also found. Despite past research into the etiology of abomasal damage and despite many risk factors being put forward, no agreement on the causal factors of abomasal damage in veal calves has yet been achieved. The aim of this review was to integrate and analyze available information on the etiology of, and possible risk factors for, abomasal damage in veal calves. The review describes various proposed pathways through which risk factors may contribute to damage

formation. We conclude that the etiology of abomasal damage is most likely multifactorial, with diet being a main contributor. Pyloric lesions, the most common type of damage in veal calves, are likely the result of large and infrequent milk and solid feed meals, while fundic lesions may be caused by stress, though the evidence for this is inconclusive. Providing calves with multiple smaller milk and solid feed meals (or ad libitum provision) may decrease abomasal damage. In future research, ulcers, erosions and scars as well as fundic and pyloric lesions should be recorded separately, since etiologies of these may differ. Further research is required to understand the exact pathway(s) by which milk replacer causes abomasal damage in veal calves – i.e. whether low abomasal pH and/or overloading are important. Further research is also required to elucidate whether rapid intake of milk replacer and solid feed, which is influenced by restricted amounts fed, inter-calf competition and calf breed, increases abomasal damage. Finally, research is needed into the impact of medication and nutrient deficiencies other than iron. The types of experimental designs that can be used for future research could be enhanced if some way to assess abomasal damage *ante mortem* is developed. Finally, we conclude that it is unlikely that abomasal or ruminal hairballs, iron deficiency, water provision and various infections and diseases are significant contributors to abomasal damage in veal calves.

Keywords: abomasal damage, veal calf, etiology, risk factor

INTRODUCTION

Abomasal damage constitutes lesions of the inner wall of the ruminant abomasum, which include minor perturbations or more severe damage causing bleeding or perforation of the wall and subsequent peritonitis. Abomasal damage is a problem in cattle of all ages and all production systems, with (white) veal calves (hereafter veal calves) being most affected (e.g. Jelinski et al., 1996; Brscic et al., 2011; Kureljušić et al., 2013; Hund et al., 2016). Abomasal damage in the form of lesions can cause high mortality rates of, for example, between 0.53 and 0.11% in veal calves in Switzerland and Belgium (Bähler et al., 2012; Pardon et al., 2012a). The mortality rates only reflect the most extreme forms of abomasal damage – perforating ulcers – and hence only represent the tip of the iceberg. Average reported prevalence of non-fatal damage at slaughter ranged from 70 to 93% of veal calves in Europe (Bähler et al., 2010; Brscic et al., 2011). Certain veal farms in Europe were even reported to have 100% prevalence for abomasal damage (Brscic et al., 2011). Veal calves are reared on a diet made up of milk replacer (**MR**), supplemented by moderate amounts of solid feed (**SF**)

with a high percentage of concentrate (at least in Europe since 1997), until a slaughter age of approximately 6 months and a body weight of approximately 200-250 kg. The MR is typically fed in buckets or troughs twice a day, although some farms use automated milk dispensers, which allow for more frequent feedings (typically three meals per day) (Bokkers and Koene, 2001; Brscic et al., 2011). The SF is generally only fed after the morning MR meal, in the same container as the MR once the MR has been consumed. This diet of mostly iron-poor MR and concentrate ensures low blood hemoglobin levels and the pale color of the veal.

The exact implications of abomasal damage for calf welfare are not fully understood. Whether calves experience pain due to non-perforating abomasal damage has not been determined. In most cases, the presence of abomasal damage was not associated with clinical signs (Veissier et al., 1998; Marshall, 2009; Hund et al., 2016), unless the lesions were severe enough to perforate the abomasal wall or cause hemorrhage (Smith et al., 1983, 1986). Commonly, affected veal calves are found dead in the stable or lesions are only identified at slaughter (Marshall, 2009). Mortality following abomasal perforation, naturally, does present a welfare issue. Although it has been proposed that (non-perforating) abomasal damage may cause reduced feed intake and thus lead to decreased growth and economical losses (Tajik et al., 2012), most studies have been unable to identify a reduction in growth (Welchman and Baust, 1987; Breukink et al., 1989; Bähler et al., 2010).

Many articles address the causes and predisposing factors of abomasal damage in veal calves but no consensus has yet been reached, though it is generally accepted that the etiology is multifactorial. The aim of this systematic review was to integrate and analyze the available information on the etiology of, and possible risk factors for, abomasal damage in veal calves. The literature search was conducted from January to April 2017 using the search engine Web of Science, and included the following search terms: Abomas* AND damage/ulcer*/lesion*/scar*. In addition, the technique of snowballing references was applied. Titles and abstracts were scanned, during which papers referring to non-cattle species or not in English or Dutch were discarded. When no articles on cattle could be identified on specific mechanism, other ruminant and monogastric articles were used. These other articles were selected based on relevance to the mechanisms of interest only, given that often very few papers were written on the topics we sought, with a preference for ruminant species over monograstric species.. Because the fourth stomach compartment of the ruminant, the abomasum, is functionally similar to the monogastric stomach, it may be that knowledge of gastric ulcers extends to abomasal ulcers, though this should be approached cautiously. For

some articles, only the abstract could be obtained. This led to a total of *123* articles read for this review. Despite the fact that veal production systems have changed substantially over the past decades, older literature was included, because experimental studies from that time are often still relevant. This review is divided in four parts: association between abomasal damage in veal calves and 1) nutritional factors, 2) stress, 3) diseases, and 4) other miscellaneous factors such as breed and season. We start with an overview of lesion type and localization and end this review by proposing paths for future research.

ANATOMICAL LOCALIZATION AND LESION TYPE

In veal calves, abomasal damage has been commonly described as consisting of three types of lesions: ulcers, erosions and scars (e.g. Wiepkema et al., 1987; Veissier et al., 1998; Webb et al., 2013), though recently other methods, such as estimated surface area, have also been applied to record lesion severity (Berends et al., 2014). In this manuscript, we use the distinction between erosions, ulcers and scars, as these may have slightly different etiologies due to differences in location. Erosions are local defects of the mucosal layer that have not yet penetrated the lamina muscularis mucosae, the thin layer of smooth muscle that separates the lamina propria from the submucosa (Mattiello et al., 2002; Marshall, 2009; Webb et al., 2013). They are small in size compared to ulcers: usually only 1 to 20 mm in diameter (Smith et al., 1983), though sizes of up to 0.7 cm have been found (Webb et al., 2013). In addition, erosions are likely to have a lower prevalence than ulcers (Webb et al., 2013). Ulcers are lesions of the abomasal mucosa that penetrate into the submucosa and range from a few millimeters to several centimeters in size (Mattiello et al., 2002; Marshall, 2009; Webb et al., 2013). Ulcers can cause perforation of the abomasal wall, which can lead to inflammation and infection of the peritoneum (peritonitis), the membrane that forms the lining of the abdominal cavity (Jensen et al., 1976; Tanwar et al., 2009). Ulcers have been classified into four types. Type 1 ulcers are non-perforating ulcers that come without extensive bleeding, whereas Type 2 ulcers are non-perforating and involve (severe) blood loss. Type 3 ulcers are perforating with local peritonitis, and Type 4 ulcers are perforating with diffuse peritonitis (Smith et al., 1983; Van Immerseel et al., 2010; Marshall, 2009). Most experimental studies, however, did not use the latter classification to distinguish between ulcer types. Scars are proposed to be healed ulcers, partially because they are found in a similar location and are fibrous contractions of the mucosa (Degen, 1982 as cited by Wiepkema et al., 1987; Webb et al., 2013). When abomasal ulcers heal, this occurs via wound contraction and synthesis of new scar tissue (Smith et al., 1983). No scar tissue is formed in the healing process of erosions

because erosions heal using epithelial regeneration, which does not involve the formation of scar tissue (Smith et al., 1983). In veal calves, abomasal damage is mostly found in the pyloric region of the abomasum (Veissier et al., 1998; Breukink et al., 1989; Hemmingsen, 1966 and Pearson et al., 1987 as cited by Marshall, 2009; Lourens et al., 1985; De Wilt, 1985; Welchman, 1986). Nevertheless, erosions can also be found scattered throughout the abomasum (Wiepkema et al., 1987) and in the fundic region, though with lower prevalence and/or severity (Bähler et al., 2010a; Valgaeren et al., 2013; Groth & Berner, 1971 as cited by Welchman & Baust, 1987).

FACTORS ASSOCIATED WITH NUTRITION

A complete overview of all factors associated with nutrition and their possible role in the development of abomasal damage in veal calves is presented in Table 1.

Milk replacer

In the past, European veal calves were fed only MR, until European legislation mandated the provision of fibrous feed in addition to MR in 1997 (directive 97/2/EC). At slaughter, it appeared that many of the calves fed only MR were suffering from abomasal lesions, with a prevalence of up to 70% (Wensing et al., 1986; Wiepkema et al., 1987). An MR-only diet was typically fed in two meals per day, and increased linearly in volume throughout the fattening period ending with a provision of approximately 3kg of MR powder per day (Prevedello et al., 2012; Webb et al., 2013). The provision of MR has now decreased due to the mandatory provision of SF, the latter being generally provided above the EU requirement of 50 to 250g/d (Brscic et al., 2011). The theory is that an MR-only diet causes abomasal lesions via abomasal overloading and low abomasal pH; yet this has never been studied experimentally and hence without further research it is impossible to know whether these pathways are indeed accurate. Below we present the proposed mechanisms behind these two theories, and some indirect evidence in support of, or contradicting, these theories. The term ‘milk’ will be used when both MR and whole milk are discussed together, or when the distinction is not important. Although overloading and pH are the most mentioned theories in relation to the impact of MR on abomasal damage, the specific milk composition might also affect abomasal damage. No research could be found on the impact of MR composition on abomasal damage, nonetheless composition will impact the clotting potential of the MR, which may in some way impact abomasal damage. This area warrants future attention.

Abomasal Overloading. As explained above, most lesions in milk-fed calves are found near the torus pylorus, which controls the passage of abomasal contents into the duodenum, and which is a site of peristalsis and segmentation. Overloading of the abomasum could, hypothetically, cause localized hypoxia in the pyloric region (Lourens et al., 1985; Breukink et al., 1991): the pathway is proposed to start with an increase in the tonus of the abomasal muscles, leading to the occurrence of peristaltic contractions that are strongest around the pylorus. Both these contractions and direct pressure exerted on the abomasal wall by a large milk volume could lead to compression of the mucosa and blood vessels, and subsequent oxygen shortage. Over time, damaged sites could develop into erosions and ulcers, although the exact pathway for this is unclear. Current evidence is insufficient to support this theory. The only findings in favor of the overloading theory are three articles providing some indirect evidence: Veissier et al. (1998) found that group-housed calves that (probably) drank their MR meal faster had more pyloric lesions than individually-housed calves that (probably) drank their MR slower; and Bähler et al. (2010) and Welchman and Baust (1987) found that the heaviest calves, hence possibly dominant, faster-drinking calves, developed most pyloric (but not fundic) lesions. Two articles opposing the overloading theory are Berends et al. (2014), who found that decreasing milk meal size while simultaneously increasing the concentrate part of the diet causes worse damage (experimental study), and Brscic et al. (2011), who found that calves receiving, relatively speaking, low amounts of MR had a higher risk for lesions (risk assessment study).

Low Abomasal pH. In rats, horses and humans a low gastric pH has been associated with a higher frequency of gastric ulceration or eroding (Nagamachi and Skoryna, 1977; Murray, 1999; Uchida et al., 1999), and in adult beef cattle a lower pH has been associated with more abomasal erosion (Jensen et al., 1992), which has led to the proposition that pH may also be an important factor in abomasal damage in calves (Ahmed et al., 2002; Marshall, 2009).There is however currently no direct evidence for this. In fact, Hund et al. (2016) reported no difference in lumen pH between damaged and intact abomasa of slaughtered bulls, cows and (non-veal) calves. Pathways explaining the possible relationship between low abomasal pH and abomasal damage are: 1) excessive activation of the proenzyme pepsinogen into pepsin, whereby the proteolytic activity of pepsin may break through the barriers protecting the abomasal wall and cause lesion of mucosal proteins (Nagamachi and Skoryna, 1977; Ahmed et al., 2002; Mesarič et al., 2002); and 2) compromised functioning of the mucus layer that protects the abomasal mucosa, which leads to decreased hydrogen carbonate production and

192 increased back-diffusion of hydrogen ions into the abomasal wall, since fewer ions are
193 neutralized by hydrogen carbonate before coming into contact with the wall (Nagamachi and
194 Skoryna, 1977; Lourens et al., 1985; Yandrapu and Sarosiek, 2015). In support of the latter,
195 mucin concentration was reported to be lower at damaged sites (Pearson et al., 1987;
196 Breukink et al., 1991) and in the pyloric region (Lourens et al., 1985), the region in which
197 most damage occurs in veal calves.

198 Indirect evidence that pH may play a role in the development of abomasal damage is the
199 successful treatment of abomasal and gastric ulcers using medication that increases abomasal
200 pH, either by neutralizing secreted HCl or by decreasing HCl secretion, in other mammals
201 (Adult cattle: Tharwat and Ahmed, 2012; Sheep: Morgado et al., 2014; Musk-ox, moose, deer
202 and wapiti: Haigh, 1982; Humans: Maton and Burton, 1999; Holle, 2010). Though medication
203 can be used in the treatment of ulcers, lack of knowledge on their long-term (health)
204 consequences limits its application as a preventive measure. Moreover, preventive
205 administration of medication could be considered unethical. It should be noted that the HCl-
206 secretory cells, whose secretions cause abomasal acidity, only develop after a few days of life,
207 possibly to prevent colostral antigens from being broken down (Lourens et al., 1985; Weiner,
208 1996; Guilloteau et al., 2009).

209 Abomasal luminal pH in calves depends on meal volume, sucking rate, abomasal emptying
210 rate, acidity of the milk and the buffering and clotting capacity of the milk (Woodford et al.,
211 1987; Ahmed et al., 2002; Constable et al., 2005, 2006). Smaller milk volumes provided
212 multiple times a day maintain a higher and more stable abomasal pH than infrequent large
213 meals (Woodford et al., 1987; Ahmed et al., 2002). Normally, acidified MR would lead to a
214 decreased abomasal pH compared to normal MR (Vajda et al., 2007), however, acidified MR
215 can be provided ad libitum, leading to more frequent consumption (Webb et al., 2014), though
216 not all studies support this (Hill et al., 2013). The clotting properties of the milk can affect
217 abomasal pH, as whole milk, which has a fast clotting capacity, allows for a lower pH than
218 non-clotting MR (Constable et al., 2005). Hence, adjusting the milk regime can affect
219 abomasal pH, and potentially abomasal damage, though for the latter part no direct evidence
220 has yet been presented.

221 ***Solid feed***

222 If SF is supplemented to an MR diet, the incidence of abomasal lesions is often observed to
223 worsen (Wensing et al., 1986; Welchman and Baust, 1987; Breukink et al., 1991; Veissier et

al., 2001; Mattiello et al., 2002; Cozzi et al., 2010; Berends et al., 2012; Prevedello et al., 2012; Webb et al., 2013). However, such an effect has not been found with all roughage types, quantities and particle sizes. The current theory is that SF can exacerbate damage that has already been caused by large quantities of MR in two ways. The first pathway is by causing trauma, in literature often referred to as abrasion, to the abomasal wall. The second pathway is by blocking the pylorus, thereby delaying digesta from leaving the abomasum and exacerbating abomasal overloading by extending the time during which large quantities remain in the abomasum (Welchman and Baust, 1987; Mattiello et al., 2002; Webb et al., 2013). The traumatizing capacity of SF has been theorized to be enhanced by the earlier mentioned increased peristaltic contractions caused by abomasal overloading (with MR), since those contractions lead to increased contact between the coarse SF and the abomasal wall (Lourens et al., 1985). The effects of SF on abomasal damage may depend on the SF type provided, its physical form, and the amount of SF fed.

Solid Feed Type. Roughage types fed to veal calves include wheat and barley straw, lucerne (or alfalfa), beet pulp, maize silage and maize cob silage, although the high starch content of maize cob silage makes it similar to concentrate rather than roughage. With the exception of lucerne, these roughage types are chosen because they have a low iron content and hence minimally affect the hemoglobin level of the blood, which helps to preserve the pale color of veal. In research hay is sometimes fed to veal calves, but this is rarely done on farms, since hay, with its high iron content, will cause the meat to be darker (Blokhuis and ID-Lelystad, 2000). The effects of roughage on abomasal damage are not entirely clear. Studies have generally found that the feeding of straw, which is considered a very coarse roughage, exacerbates abomasal lesions (Van der Mei, 1985; Welchman and Baust, 1987; Breukink et al., 1991; Webb et al., 2013), although five studies do not support this (Van Putten, 1982; De Wilt, 1985; Veissier et al., 1998; Prevedello et al., 2012; Webb et al., 2015). The order of roughages from least to most deleterious appears to be: hay, maize cob silage/beet pulp, lucerne, maize silage and straw (Wensing et al., 1986; Breukink et al., 1991; Mattiello et al., 2002; Räber et al., 2013b; Webb et al., 2013). However, comparison between studies is difficult due to different amounts and particle sizes of roughage being fed. Interestingly, Räber et al. (2013a;b) found no significant difference in the pylorus between maize silage and straw, but did find more lesions in the fundus of straw-fed calves.

Cereal grains, barley grains, whole plant maize pellets and pellet mixes (containing for example oat hulls, maize or barley grain, soy flakes or plant oils, and a pellet binder) are the

types of concentrate that have been researched in veal calves for their effects on abomasal damage. However, most studies combined both concentrate and roughages in the diet. Only one study added solely concentrate to an MR diet, and found a decreasing trend for lesion incidence compared to straw (Räber et al., 2013a). In addition, one study compared two concentrate types, and found no difference in lesion incidence between the two (Räber et al., 2013b). Furthermore, feeding pellets of roughage and concentrate with four different compositions (differences were in the starch, fiber, crude protein and ash content) did not affect lesions larger than 0.5 cm (Morisse et al., 2000). A combination of both roughage and concentrate added to an MR diet is what is most commonly fed on European veal farms nowadays. Adding concentrate to roughage may prevent an increase in lesion incidence which would normally happen with roughage (Morisse et al., 1999). However, other studies found no improvement or even a worsening of the damage with a combination of roughage and concentrate versus only roughage (Berends et al., 2012; Prevedello et al., 2012). Very high levels of concentrate (concentrate:roughage ≥ 80:20) have been seen to lead to acute ulceration in beef calves (Tharwat and Ahmed, 2012) and can increase abomasal damage in veal calves as the amount fed increases, even when MR is decreased simultaneously (Berends et al., 2014). It should be noted that no studies used a larger relative proportion of roughage than concentrate, and therefore no general conclusion on all combinations of roughage and concentrate can be made.

The addition of specific feedstuffs, such as extruded pea, extruded soybean, or urea, has been researched to determine their value in adding protein or nitrogen to the diet without compromising veal color and quality. For all three, no effect on the incidence or severity of abomasal lesions was found (Prevedello et al., 2012; Brscic et al., 2014).

Physical Form of Solid Feed. A feedstuff can be provided in various physical forms. Roughage can be fed as large particles, chopped to a smaller particle size, be ground or be included in a pellet. Different physical forms may have different traumatizing or blocking effects, and one might expect that larger particles are more blocking than shorter ones and therefore cause more abomasal lesions. Shorter particles, however, may be sharper and may get stuck in the abomasal wall more easily. Chopping wheat straw to particle sizes equal to those of barley grain lowered lesion incidence to approximately equal levels for the two, supporting the theory that longer particles cause more damage, though the severity of the lesions was higher for barley grain (Cozzi et al., 2002b). This implies that both the size and

type of feed have an impact on abomasal damage. In contrast, Webb et al. (2013) found no effect of providing roughages in long-chopped, short-chopped or ground form.

For pelleted feeds, it would be expected that their finer particles would have a smaller traumatizing or blocking effect on the abomasal mucosa or pyloric sphincter, respectively, and thereby cause less damage to the abomasum. However, a difference in abomasal damage was not found between straw and straw pellets (Van Putten, 1982), which contradicts this hypothesis. In addition, pelleted maize silage was observed to cause more lesions than short-chopped or ground maize (cob) silage (Breukink et al., 1991; Wensing et al., 1986). Whether this difference is actually due to the pelleted form or due to the different roughage types cannot be determined from these studies. Nevertheless, the lack of difference between straw and pelleted straw implies that roughage type is the main determinant here.

Amount of Solid Feed. In addition to type and physical form of roughage, the amount of SF fed may impact abomasal damage. Larger amounts are expected to increase trauma to the abomasal wall and worsen blocking of the pyloric sphincter, thereby increasing abomasal damage. Indeed, it has been found that larger, but still restricted, amounts of roughage increase the prevalence and size of ulcers (Brscic et al., 2011; Webb et al., 2013). However, increasing amounts of cereal grains and straw were not seen to increase lesion incidence (Morisse et al., 1999). This may be linked to the inclusion of concentrate in the diet, as theorized before. In contrast, inclusion of a high level of concentrate (concentrate:roughage 80:20) does increase abomasal damage when the amount fed increases (Berends et al., 2014). For some roughage sources an interaction between the amount fed and the type of roughage was found, where the source was only severely damaging when fed in larger amounts. For example, maize (cob) silage caused fewer lesions than straw at small amounts (250g/d) and more lesions than straw in larger amounts (500g/d) (Webb et al., 2013). A finding that contradicts the hypothesis that larger amounts of SF lead to more abomasal damage is that provision of straw or hay ad libitum does not exacerbate lesions caused by MR (Webb et al., 2013, 2015). We may speculate that ad libitum provision allows the individual calf to select a diet that is quantitatively optimal for its body, including its abomasum. Furthermore, it minimizes competition between pen mates and allows meals throughout the day, likely reducing feeding rate and meal size. Alternatively, rumen development may play a role (see ”Rumen Development”). Finally, Prevedello et al. (2012) proposed that the moment at which the SF is consumed may matter. Consumption of SF just after the abomasum has been filled with a large quantity of MR may exacerbate overloading and increase abomasal damage.

Rumen Development

Before entering the abomasum, SF must pass the three other stomach compartments. In the first one, the rumen, SF will be fermented. It has been hypothesized that feed will be less coarse when it enters the abomasum if this fermentation occurs well (Berends et al., 2012). In addition, due to the smaller particle size SF should also block the pylorus less frequently than when fermented incompletely. Since calves are born with a non-functional rumen, its development affects the extent to which SF is fermented. Beef calves and lambs are more susceptible to abomasal perforation caused by ulcers during the development from pre-ruminant to ruminant, which is approximately at the age of four to eight weeks (Jelinski et al., 1996a; Dirksen et al., 1997; Vatn and Ulvund, 2000). Stimulating rumen fermentation and development at an early age has been proposed as a way of minimizing abomasal damage (Berends et al., 2012). This can be realized using a feeding regime aimed at early rumen development (**ERD**), which includes feeding both roughage and concentrate from an early age onwards. An increase in rumen volume and weight is stimulated by the feeding of fibrous feeds, whilst the development of rumen papillae is stimulated by volatile fatty acids and therefore by less fibrous feeds (Berends et al., 2014; Suarez-Mena et al., 2016).

In support of this theory, one study has found that calves with better developed rumens had fewer abomasal lesions than calves with less developed rumens (Webb et al., 2013), and others have found that stimulating early development with concentrate or hay meant that future feeding of coarse straw did not exacerbate damage (Veissier et al., 1998; Webb et al., 2015 (unpublished data)). However, when the ERD-theory was tested by adjusting calf diet before an age of twelve weeks, it was found that ERD only decreases the incidence of scars (Berends et al., 2012). These findings suggest that ERD protects calves from developing abomasal ulcers during the early weeks of life, leading to less scarring later on, but that it has no effect on ulcer or erosion development in later life. Two years later the same authors confirmed that better rumen development does not protect against abomasal damage at a later age (Berends et al., 2014), based on the finding that both rumen development score and abomasal damage increased for increasing SF amounts (when the proportion of concentrate was high).

Hairballs

Hairballs (or trichobezoars) are round masses composed of ingested hair (Çatik et al., 2015), which develop in the rumen (Osborne, 1976). Webb et al. (2013) proposed that ruminal

hairballs may prevent proper digestion in the rumen, which would allow large feed particles to pass through the first three stomach compartments into the abomasum. These under-fermented particles may cause trauma to the abomasal mucosa or block the pyloric exit. Rumen motility, which can be improved by feeding SF in addition to MR, aids in the removal of hair from the rumen, thereby preventing the development of hairballs (Morisse et al., 1999, 2000; Cozzi et al., 2002a). Alternatively, calves fed SF may ingest less hair than calves fed MR only, as they display fewer abnormal oral behaviors (Veissier et al., 1998; Mattiello et al., 2002), during which hair can be ingested. Calves fed straw or hay have less hair in their rumen than calves fed maize (cob) silage, with maize silage being the intermediate, and the amount of hair was further reduced as the roughage particle size was increased (Webb et al., 2010, 2013). Nevertheless, Webb et al. (2013) found that calves fed only milk had more ruminal hairballs and fewer abomasal lesions than calves fed additional roughage (with the exception of ad libitum hay, for which ulcer incidence was not increased). This implies that ruminal hairballs are at least not a prerequisite for the development of abomasal lesions.

Hairballs can also be found inside the abomasum, although this is only true in veal calves fed only MR. They have been hypothesized to cause trauma to the abomasal mucosa or to block the pylorus, both of which may lead to abomasal damage (Jelinski et al., 1996b; Marshall, 2009; Sasaki et al., 2012). Especially during abomasal surgeries performed on suckling calves, large amounts of hair were found in the ulcerated or perforated abomasa (Tulleners and Hamilton, 1980; Katchuik, 1992; Çatik et al., 2015). Only one study on veal calves measured the presence of both hairballs and lesions in the abomasum, but the two were not checked for a relationship (Osborne, 1976). Studies in beef calves suggest that hairballs are neither causing trauma to the abomasal mucosa nor blocking the pylorus enough to cause ulceration (Katchuik, 1992; Jelinski et al., 1996b). In lambs, significantly more bezoars were found in lambs with abomasal ulcers (Vatn and Ulvund, 2000). Despite these inconclusive results, veterinarians and researchers tend to assume a relationship between hairball presence in the abomasum and abomasal lesions (Stokka and Perino, 2000; Marshall, 2009; Çatik et al., 2015).

Nutrient deficiencies

Though it is often suggested that nutrients, most often mineral, deficiencies can cause or facilitate the formation of abomasal ulcers (Jelinski et al., 1996b; Stokka and Perino, 2000; Ahmed et al., 2002; Marshall, 2009; Van Immerseel et al., 2010), only one study on veal

386 calves was found to have researched part of this relationship. This study found no impact of
387 iron supplementation on abomasal damage, in MR-only fed calves (Webb et al., 2013). When
388 beef calves were supplied with a free choice mineral mix, a non-significant trend for
389 decreased need for abomasal surgery due to ulceration was observed (Katchuik, 1992). This
390 implies a role for nutrient deficiencies in abomasal ulceration (composition of the mineral mix
391 is unknown but can be assumed to differ between the farms the calves originated from). In
392 another study, deficiencies in copper and/or selenium occurred more often in beef calves with
393 (perforating) abomasal damage (Mills et al., 1990). Supplementation of copper to both cows
394 and their calves decreased the occurrence of ulceration to almost zero immediately (Lilley et
395 al., 1985).

396 It has been theorized that a low serum copper concentration can lead to a derangement of
397 elastin cross-linkages in the abomasal wall, compromising abomasal mucosa and
398 microvasculature and leaving the abomasal wall prone to damaging (Lilley et al., 1985;
399 Marshall, 2009). Besides this, copper deficiency can also lead to decreased neutrophil
400 function and subsequently to an increased risk of infection, as occurs when the abomasum is
401 damaged (Lilley et al., 1985; Mills et al., 1990; Marshall, 2009). Since a high concentration of
402 zinc, molybdenum or sulfur reduces the availability of copper, surplus of these minerals can
403 exacerbate the problem of copper shortage. Thus, in beef calves, nutrient deficiencies, at least
404 for copper and selenium, appear to affect abomasal damage. Whether the same occurs in veal
405 calves, has not yet been studied.

406 ***Water***

407 Veal calves receive fluids from milk, from other feeds provided, from the drinking of free
408 water, and from the oxidation of food and body tissue. Whereas water originating from feed
409 and free water is deposited in the rumen, water originating from milk generally bypasses the
410 rumen and is deposited in the abomasum (Hepola et al., 2008). Though some studies report
411 that calves fed MR ad libitum hardly drink any water (Hepola et al., 2008), others found that
412 calves may ingest large amounts of up to 36 liters, with an average consumption of 11.3 liters,
413 per day (Ruis-Heutinck and Van Reenen, 2000; Webb et al., 2014). Water intake increases
414 when calves start consuming SF (Kertz et al., 1984) and is higher in calves fed more SF
415 (Webb et al., 2014). Supplying calves with an increasing amount of free water (from three to
416 eight liters) did not affect abomasal ulcers, erosions or inflammations (Gottardo et al., 2002).
417 However, one risk assessment showed that calves receiving water ad libitum were at higher

risk for lesions than those receiving none at all (Brscic et al., 2011). However, consumption of water was in this study strongly linked to the provision of SF and ruminal plaque, indicating that SF may have caused the damage here.

THE FACTOR OF STRESS

In many monogastric species, acute stress has been experimentally shown to cause ulceration of the stomach mucosa (Rat: Goldman and Rosoff, 1968; Weiner, 1996; Guinea pig: Ludwig and Lipkin, 1969; Piglet but not pig: Norton et al., 1972;). In ruminants, such as calves, the abomasum acts similarly to the monogastric stomach. In some cases, the stress-caused lesions of monogastrics bear resemblance to ulcers found in the calf fundus (Welchman and Baust, 1987). Therefore, many authors have mentioned that stress may be a predisposing or even causal factor for ulceration in calves as well (Tulleners and Hamilton, 1980; Wiepkema, 1985; Lourens et al., 1985; Welchman and Baust, 1987; Wiepkema et al., 1987; Breukink et al., 1989; Mills et al., 1990; Lallès and Toullec, 1998; Stokka and Perino, 2000; Ahmed et al., 2002; Constable et al., 2005; Marshall, 2009; Van Immerseel et al., 2010; Sasaki et al., 2012; Valgaeren et al., 2013; Webb et al., 2013; Berends et al., 2014; Çatik et al., 2015). Proposed pathways through which stress could cause abomasal damage have a common starting point, whose involvement has only been demonstrated in rats. In rats, ulcers caused by stress only develop after a drop in body temperature (Weiner, 1996), which initiates two main pathways: 1) an increased production of gastric acids, whose effects were described previously (see "Low Abomasal pH") and 2) a decrease in the rhythm of stomach contractions from 6-7 to only 0.5-2 times per minute, which leads to decreased mucosal blood flow and subsequent damage through local hypoxia, mechanical damage and decreased function of the mucosa-protecting mucus and cytoprotective prostaglandins (Weiner, 1996; Marshall, 2009; Kureljušić et al., 2013).

It has been proposed that abomasal ulcers in veal calves are not related to stress, since the location of these ulcers are not similar to those of ulcers caused by stress in adult cattle (Breukink et al., 1991). In veal calves, ulcers are predominantly found in the pyloric region, whereas in adult cattle they are predominantly found in the fundic region. It is unclear what the assumption of stress being a causal factor in adult cattle is based on. Bähler et al. (2010) found that calves in conventional veal systems had more fundic but not pyloric lesions than animals kept in a potentially less stressful system in which they had more square meters per individual, could go outdoors and received water and roughage ad libitum. The authors

proposed that stress may hence be involved in the development of fundic but not pyloric lesions. In this study, however, diet was also an important difference between these two rearing systems. Other studies did not identify links between stress and abomasal damage in veal calves, regardless of the treatments that were used: individual housing versus group housing (Veissier et al., 1997; Bokkers and Koene, 2001), repeated regrouping (Veissier et al., 2001), or environmental enrichment (Veissier et al., 1997). Furthermore, calves used to human-calf interactions (gentled calves), which involved the stockperson talking to and stroking the calves, and letting the calf suck the persons fingers for 90 sec following feeding, had fewer pyloric lesions at slaughter (Lensink et al., 2000). As human-calf interaction allowed calves to suck on the stockperson's fingers, enhanced saliva production might also have decreased abomasal acidity and consequently ulceration. In that case, the difference found would be unrelated to stress, as also suggested by the absence of differences in stress measurements (behavioral observations, response to ACTH challenge) between gentled and control calves.

Calves performing more of the abnormal oral behavior 'tongue rolling/playing' were found to have significantly fewer abomasal ulcers and scars, but not fewer erosions (Wiepkema et al., 1987). In addition, in a more recent study the same relationship was found between abomasal lesions and tongue playing as well as oral manipulation of the environment (Webb, 2014). Stereotypies, such as these abnormal oral behaviors, are defined as repetitive and invariant behavioral patterns that lack an obvious goal or function (Rushen and Mason, 2006), and may provide captive animals with a way to cope with a sub-optimal environment (Würbel et al., 2006). Calves that tongue roll may hence develop less abomasal damage due to reduced stress through better coping. Similarly, rats that were exposed to acute stress, in the form of electric shocks, developed more gastric ulcers when punished for attempting to escape these shocks, which denies the rats a way to cope with the acute stress (Weiner, 1996). Other mechanisms might be that extra saliva produced during performing abnormal oral behaviors would increase abomasal pH, although it could be argued that saliva produced during object manipulation may not enter the gastrointestinal tract, or that increased satisfaction of oral eating behaviors decreased milk intake and thereby abomasal overloading.

FACTORS ASSOCIATED WITH DISEASE

Micro-organisms. Infections caused by fungi, bacteria, parasites, and diseases caused by viruses, have been hypothesized to lead to the development of abomasal damage in calves

(Ross, 1963; Smith, 1966; Stokka and Perino, 2000; Marshall, 2009; Moeller et al., 2013) – see Table 2a, b, c and d for an overview of these studies. This is partially because in humans they are known to cause peptic ulcers (Overmier and Murison, 2013). In calves, fungi have been isolated from abomasal lesions, but the evidence for a causal role is currently insufficient (Table 2a). Studies investigating bacterial involvement are more abundant, however, bacteria isolated from lesions may originate from post-mortem colonization. Additionally, administration of bacteria leads to a different type of damage than commonly observed in veal calves, namely numerous small ulcers spread throughout the abomasum (Table 2b). Furthermore, although some parasites are capable of causing ulcers in calves (Ross, 1963; Ross and Dow, 1965; Snider et al., 1981, 1985; Taylor et al., 1989; Yang et al., 1993), cattle (Snider et al., 1985) and elk (Woodbury and Parry, 2009), it is unlikely and not reported that indoor housed calves, fed on concentrate and silages, are exposed to these parasites. Moreover, the type of abomasal damage caused by parasites, referred to as nodules, is quite different from that described most commonly in veal calves (Table 2c). Finally, though some viruses can cause lesions in several organs (amongst which the abomasum) in calves (Moeller et al., 2013), beef calves (Bianchi et al., 2017) and adult cattle (Assis et al., 2002), prevalence of viral diseases lies much lower than the prevalence of abomasal damage (2% compared to >70% (Brscic et al., 2011; Bianchi et al., 2017)). Viruses, although possibly causing some of the cases of abomasal damage found in veal calves (Table 2d), are hence unlikely to be a main factor in the majority of damage found. However, given the small amount of research in this area, we encourage further attention here. Non-infectious diseases, left abomasal displacement and certain types of tumors might also cause abomasal ulcers in adult cattle and in very rare cases in calves (Smith et al., 1983; Mueller et al., 1999; Sasaki et al., 2012), but are deemed irrelevant in veal calves.

Medication. Veal calves in Europe (Belgium and the Netherlands) have been reported to be the group of farm animals receiving the most antimicrobial (**AM**) treatments (Bondt et al., 2012; Pardon et al., 2012b), most likely as a direct consequence of the mixing of young, low-immunity calves from many different origins. In Belgium, over 40% of calves were found to be treated with AM every day of the production cycle (Pardon et al., 2012b). Although much less frequently used than AM drugs, (non-)steroid anti-inflammatory drugs (**[N]SAID**) are also given to veal calves - of all treatments in Belgium veal, 88% was AM and 12% was NSAID around 2009 (Pardon et al., 2012b). In comparison to the 40% use of AM drugs, NSAIDs were found to be given to 0.6% of veal calves per day of production in Belgium

(Pardon et al., 2012b). Most NSAIDs are likely given as part of the treatment for respiratory diseases, like AM drugs (Pardon et al., 2012b). Ibuprofen (Walsh et al., 2016) and other NSAIDs (Semrad and Dubielzig, 1994; Sasaki et al., 2012) have been found to cause abomasal lesions in calves. Additionally, NSAIDs are a known cause of peptic ulcers in humans (Yeomans and Næsdal, 2008). Medication is widely used in veal calves and could hence be an important factor in the development of abomasal damage, though the current evidence for this is non-existent and future research is warranted. However, the use of NSAIDs lies far below the prevalence of abomasal damage in veal calves, and is hence unlikely to be one of the main factors.

OTHER FACTORS

Breed

It has been proposed by some authors that the breed of the calf may affect abomasal damage. For example, Montbeliard calves develop more pyloric scars than Holstein Friesian calves when both are kept in similar systems (Veissier et al., 1997). However, it should be noted that Montbeliard calves are also capable of growing faster, which is accompanied by a higher MR and SF intake, hence possibly more severe overloading of the abomasum. This was confirmed by both Bähler et al. (2010) and Brscic et al. (2011), who found no effect of breed on pyloric lesions, though in these studies breeds were categorized in three groups (dairy breeds, cross-breeds and other breeds) and only those were compared, not individual breeds. It is possible that breed only has an important impact on abomasal lesions when a particular breed is able to consume more MR and SF more rapidly.

Seasonal Effects

In adult cattle and in beef cattle, occurrence of abomasal damage differs between seasons. In adult dairy cattle, this could be related to the seasonality of milk production, since most ulcers develop around parturition, a period marked by stress and a severe change in diet (Smith et al., 1983; Sanford and Josephson, 1988; Ok et al., 2001; Tharwat and Ahmed, 2012). In beef calves, bad weather has also often been proposed as a contributing factor (Jensen et al., 1976; Lilley et al., 1985; Mills et al., 1990; Marshall, 2009). It is theorized that calves do not nurse when the weather is bad, which leads to a drop in abomasal pH, leaving the abomasum vulnerable to ulceration. When the weather has gotten less aversive, calves overconsume milk, which leads to abomasal overloading. In one study, the seasonal effect was fully

546 explained by the use of a seasonal beef production system, indicating that other season-related
547 effects, such as pasture growth, were not of causal value (Jelinski et al., 1996a).

548 Since veal calves originate mostly from a non-seasonal dairy system, are kept inside and do
549 not nurse their dams, bad weather should not have a large effect on abomasal damage.
550 Nevertheless, a risk assessment conducted by Brscic et al. (2011) showed that veal calves
551 have a higher risk of developing pyloric lesions when they are raised in the summer or
552 autumn and the lowest risk when reared in spring, both compared to winter. Why this effect
553 exists, is unknown. We may speculate that it correlates with other yet unidentified factors that
554 differ seasonally, or that differences in living conditions between seasons on the dairy farms
555 the veal calves originate from have a predisposing effect. Also temperature fluctuations in the
556 stable that can occur if temperature is not perfectly regulated year-round might have an effect,
557 for example through cold or heat stress. As mentioned before, it has been seen in rats that
558 fluctuations in body temperature can lead to the development of stomach ulcers (Weiner,
559 1996). Alternatively, calves may be fed more or ingest feed faster in certain seasons.

560 ***Housing and Management***

561 Certain aspects of housing and management have also been associated with lesion prevalence
562 via surveys. Absence of a heating system and regular visits of a veterinarian appear to be
563 linked to the occurrence of pyloric lesions (Brscic et al., 2011). Also, calves living in a stable
564 with an open-front building had fewer pyloric lesions than those in stables with manual
565 ventilation (Bähler et al., 2010). It is unlikely that these factors have a direct effect on
566 abomasal lesions, instead, they likely correlate with other factors that do have a direct effect,
567 such as stress or fluctuations in temperature.

568 ***Individual Susceptibility***

569 Finally, it has been proposed that calves differ in individual susceptibility to abomasal lesions,
570 since calves kept in similar systems, either on the same or on another farm, show very
571 different degrees of abomasal lesions. This is also observed within pens (Wensing et al., 1986;
572 Wiepkema et al., 1987), though contradictory findings exist (Räber et al., 2013b). Where
573 some calves show severe ulceration, other calves kept under the same conditions may have
574 completely undamaged abomasa. This means that calves are not all equally susceptible to
575 abomasal ulceration (Welchman and Baust, 1987), possibly due to different mechanisms with
576 which calves cope with stress (and stress is likely associated with fundic lesions). In addition,

it was seen that faster growing calves were more susceptible to damage (Bähler et al., 2010), though this was not seen in fattening bulls, in which carcass weight and fat distribution were not found to affect abomasal ulceration (Hund et al., 2016). This implies that the difference is not due to individual susceptibility, but possibly to more abomasal overloading in faster growing calves. It has previously been suggested that only by offering calves free choice of diet an appropriate diet can be provided for each individual calf (Webb et al., 2014).

In humans, it has been proposed that stomach ulcers have a heritable component (Holle, 2010). Whether this is also the case in calves, has to our knowledge never been studied. Nevertheless, if abomasal damage in calves indeed has a heritable component, the application of this finding is likely limited, because veal calves originate from the dairy sector, in which other breeding factors are considered.

CONCLUSION

The aim of this review was to integrate the information currently available on the etiology of, and risk factors for, abomasal damage, in the form of ulcers, erosions and scars. Some information may not have been included because it was not found or written in a (for us) foreign language (articles included were in Dutch, German or English). In addition, extrapolation of results from older literature may not be fully accurate, since the growing system in which veal calves are kept has changed substantially over time. Nevertheless, experimental studies from these periods can still provide useful information. An overview of all proposed factors and associated literature support/evidence is presented in Table 3. An overview of the most likely factors and the associated mechanisms is presented in Figure 1. Although a clear effect on the development of abomasal damage was not identified for all proposed factors, it is clear that the etiology is multifactorial, with various dietary factors contributing to pyloric lesion formation extensively and fundic lesions probably being linked to stress. Pyloric lesion incidence can likely be reduced by feeding smaller quantities of milk replacer in more frequent meals, which should already from an early age be combined with SF in the form of both concentrate and roughages. In addition, decreasing the level of stress experienced by veal calves may decrease the occurrence of fundic lesions improve overall animal welfare by minimizing negative experiences.

In future research, pyloric and fundic lesions as well as lesion types (ulcer (types 1-4), erosion or scar) should be scored separately. More research is required to understand the precise

608 pathways by which MR causes such a high prevalence of abomasal lesions in veal calves.
609 Further research is also warranted on the impact of rapid intake of MR and SF due to
610 restricted amounts, competition and breed. More research is also needed into the impact of
611 medication, the chemical composition of the MR, and into deficiencies of other nutrients than
612 iron, especially copper and selenium. Finally, no studies have yet focused on the effects of the
613 abomasal emptying rate on abomasal damage, whilst in adult cattle delayed abomasal
614 emptying has been proposed as a risk (Constable et al., 2006) and in humans peptic ulcer
615 disease has been associated with delayed gastric emptying (Minami and Mccallum, 1984).
616 Another important path of research would be to develop a method that can assess abomasal
617 damage ante mortem. Currently, calves must be sacrificed for the measurements of abomasal
618 damage, which limits the experimental design options. Possibly, the finding that calves that
619 grow fastest develop most abomasal lesions (Bähler et al., 2010) can be used for this purpose.
620 Finally, the link between abomasal damage and animal welfare, or more specifically pain, is
621 not well understood and has received no research attention as far as we can tell. Whether these
622 lesions are painful, and if so which types and the severity of the pain, is of crucial importance
623 because this health problem is widespread in the veal industry. One complication here is that
624 commonly used pain indicators in calves, such as growth rate and feeding rate, are in fact
625 factors linked to the etiology of the problem at hand. Other indicators of pain, for example
626 facial expressions, will have to be investigated.

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Table 1. Nutritional factors put forward as likely to worsen abomasal damage in veal calves, and associated number of studies in support (for) or not in support (against) of these proposed factors. The bold typeface here is used to visually emphasize which factors may contribute most to abomasal damage.

Factors	For	Against	Summary of findings	Conclusion
Milk replacer				
Abomasal overloading	4	2	No direct evidence, except that potentially faster drinking calves have worse damage.	Unknown
Low abomasal pH	0	0	No study has assessed this link.	Unknown
Solid feed				
Roughages vs. only MR	9	2	Roughages tend to exacerbate existing damage caused by MR, except when provided ad libitum.	**Yes, in restricted amounts**
Coarse vs. less coarse roughages	6	5	In restricted amounts, straw tends to worsen damage compared to only MR or other types of roughage.	**Yes, in restricted amounts**
Roughages vs. concentrate	2	3	Concentrate cause less damage when small amounts are provided. In large amounts, concentrate are worse than roughage.	**Yes, in small amounts**
Larger particles of roughage	1*	4	This is not supported by experimental evidence.	No
Increasing amounts of solid feed	2	3	Larger amounts of solid feed worsen damage when amounts relatively low (500 g/d) or when a large portion is concentrate (80:20). However, when roughage is provided ad libitum, existing damage is not exacerbated.	No, if ad libitum roughage **Yes, if mostly concentrate**
Poor rumen development	3	1**	Rumen development may protect against abomasal damage when large quantities of concentrate are not provided.	Probably
Ruminal hairballs	0	1	This is not supported by experimental evidence.	No
Abomasal hairballs	0	0	No study has assessed this link in veal calves.	Unknown
Nutrient deficiency				
Iron deficiency	0	1	This is not supported by experimental evidence.	No
Copper deficiency	0	0	No study has assessed this link in veal calves.	Unknown
Water				
Water provision	1	1	Evidence is inconclusive, but only experimental study is against.	Unlikely

**Larger particles = more but less severe lesions; **Large quantities of concentrate led to better rumen development but worse damage.*

Table 2a. Fungi have been isolated from abomasal ulcers, but there is insufficient evidence for a causal role

FUNGI					
Study conclusion	Lesion type	Fungus species	Number of calves	Reference	Study type
Isolation of fungal hyphae from damage	Numerous ulcers, edema	Not identified	3 out of 5	(Wray and Thomlinson, 1968)	O
Isolation of fungus from damage	Ulcerative abomasitis	*Saksenaea erythrospora*	1	(Lawhon et al., 2012)	O
Isolation of fungal hyphae from damage	Ulcers	*Absidia remosa* *Absidia corymbifera* *Mucor pusillus*	7	(Gitter and Austwick, 1957)	O

(O = observational; E = experimental)

Table 2b. Bacteria can cause a different type of abomasal damage than usually found in veal calves, and most studies have not been able to isolate bacteria from abomasal lesions

BACTERIA					
Study conclusion	Lesion type	Bacterium species	Number of calves*	Reference	Study type
Isolation of bacterium from six calves	Many small (1-2 mm) ulcers: ulcerative abomasitis	*Clostridium perfringens* type D *Escherichia coli* (likely post-mortem infection)	6	(Assis et al., 2002)	O
No difference in bacteria incidence between damaged and intact abomasa	Type 1 ulcer	All	215 fattening bulls, cows and calves	(Hund et al., 2015)	O
No relation between bacteria and damage	Fundic type 1 ulcers	*Clostridium perfringens* *Helicobacter* spp.	604	(Valgaeren et al., 2013)	O
No relation between bacteria and damage	Fundic and pyloric ulcers and erosions	*Escherichia coli* *Streptococcus faecalis* *Streptococcus bovis* *Bacillus* spp. *Corynebacterium* spp. *Moraxella* spp. *Acinetobacter* spp.	304	(Welchman and Baust, 1987)	O
Bacterium likely post-mortem contaminant	Fatal ulcers	*Clostridium perfringens* type A	30 beef calves	(Jelinski et al., 1995)	O
Isolation of bacterium from one calf	Hundreds of small type 1 ulcers	*Clostridium perfringens*	1	(Van Immerseel et al., 2010)	O
Isolation of bacterium from one calf	Many small ulcers: ulcerative abomasitis	*Clostridium perfringens* type A	1 Asian gaur calf	(Songer and Miskimins, 2005)	O
Administration of bacterium caused damage	Ulcerative abomasitis	*Clostridium perfringens* type A	10 bull calves	(Roeder et al., 1988)	E
Administration of bacterium caused damage	Gross lesions, abomasitis and sometimes peritonitis	*Salmonella enterica*	6	(Carlson et al., 2002)	E
Administration of bacterium caused damage	Gross lesions throughout the GI tract	*Chlamydiae* strain LW-613	12	(Doughri et al., 1974)	E

(O = observational; E = experimental)
**When not specified, calves were veal calves*

Table 2c. Some parasites can cause a different type of abomasal damage than commonly seen in veal calves

PARASITES Study conclusion	Lesion type	Parasite species	Number of calves	Reference	Study type
Administration of parasite caused damage	Abomasitis with ulcers	*Ostertagia ostertagi*	27	(Ross, 1963)	E
Administration of parasite caused damage	Larvae-containing nodules, edema	*Ostertagia ostertagi*	10	(Ross and Dow, 1965)	E
Administration of parasite caused damage	Small nodules	*Ostertagia ostertagi*	10	(Snider et al., 1981)	E
Administration of parasite caused damage	Small nodules	*Ostertagia ostertagi* and/or *Trichostrongylus axei*	20	(Snider et al., 1985)	E
Administration of parasite caused damage	Fundic and pyloric nodules	*Ostertagia ostertagi*	25	(Taylor et al., 1989)	E
Administration of parasite caused damage	Nodules	*Ostertagia ostertagi* and *Cooperia oncophora*	24	(Yang et al., 1993)	E

(O = observational; E = Experimental)

Table 2d. Some viruses may cause ulcers in various organs, among which the abomasum, but the evidence for this is limited

VIRUSES Study conclusion	Lesion type	Virus species	Number of calves	Reference	Study type
Viral infection caused lesions in various organs, among which the abomasum	Ulcers, edema	Bovine herpesvirus 1	2 out of 62 calves showed ulcers in the abomasum	(Moeller et al., 2013)	O
Viral infection caused lesions in various organs, among which the abomasum	Ulcers	Bovine viral diarrhea virus	1 out of 7 calves showed ulcers in the abomasum	(Bianchi et al., 2017)	O

(O = observational; E = experimental)

Table 3. Overview of current knowledge on all proposed risk factors of abomasal damage in veal calves, with associated number of studies in support (for) or not in support (against) of these proposed factors. Only studies specifically studying veal calves are included here.

Factor	For	Against	Summary of findings	Important
Milk replacer	4	2	Despite little actual experimental study in this field, MR is likely to play an important role. The exact pathways are unknown.	Yes
Solid feed	9	2	Solid feed provision on top of MR is likely to have an impact of the level of damage, unless roughage is provided ad libitum.	Yes
Rumen development	3	1	The evidence for rumen development protecting against abomasal damage is limited, but studies showing that ad libitum provision of roughage does not exacerbate damage support this hypothesis.	Probably
Hairballs	0	1	Both hairballs in the rumen and abomasum do not show a clear association with abomasal lesions.	No
Nutrients	0	1	Only iron was tested in veal calves.	No
Water	1*	1	The experimental study against has stronger findings than the observational study, which involves confounders.	Unlikely
Stress	1**	4	Despite studies showing a link between stereotypies and lower damage (not included here), the link with stress is not strong in veal calves, except for fundic lesions which are not the most common in this group of animals.	Unlikely
Bacteria	3***	3	Studies that found a link between bacteria and abomasal damage found very different patterns of damage, i.e. many small lesions widespread across the abomasum.	Unlikely
Virus	0	0	No research in veal calves. The prevalence of viruses that cause abomasal damage is much lower than the prevalence of abomasal damage, making a viral factor unlikely to be a main contributor to lesions veal calves.	Unlikely
Fungi	0	0	No research in veal calves.	Unknown
Parasites	0	0	No research in veal calves. In dairy calves, damage caused by parasites are nodules, which are very different from damage commonly observed in veal calves.	No
Breed	1	2	Breed is probably only relevant when it affects growth rate: hence feeding speed and amounts ingested.	Unknown
Medication	0	1	Too little medication specifically tested. Medication is widespread enough to be linked to damage.	Unknown
Season	1	0	Too little work on this. Probably only has an indirect effect.	Unknown
Housing	2	0	Too little work on this. Probably only has an indirect effect.	Unknown
Growth rate	1	0	Although there is little work on this, our own unpublished work also suggests that calves that grow faster have more damage.	Yes
Genetics	0	0	No study.	Unknown

**A cross-country survey by Brscic et al. (2011), where water provision was correlated with solid feed provision; **Big confounding factor of nutrition (Bahler et al., 2010); ***Two of these three studies found damage very different from that commonly found in veal calf abomasa.*

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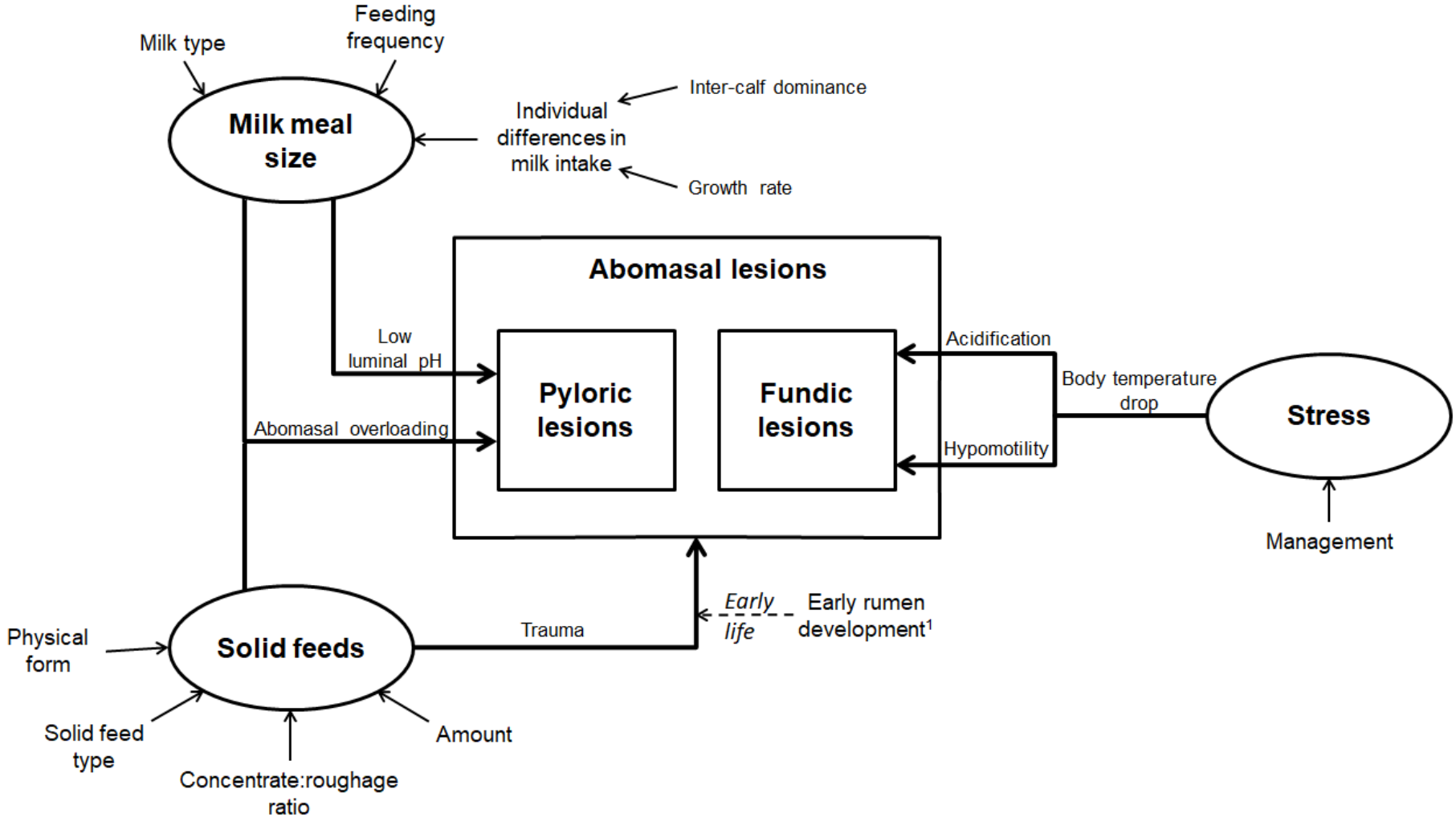
11 **Bus Figure 1**



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14 # Figure captions

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16 Figure 1. Schematic overview of the most likely risk factors for abomasal damage and the pathways through which these operate. [1] Can mitigate

17 trauma at least during early life