

Use of non-steroidal anti-inflammatory drugs at calving

Abstract

In recent years farmers, veterinary surgeons, and consumers have all shown increasing awareness of pain in cattle (and its associated negative welfare impacts), and accordingly there is increased focus on the use of analgesia following painful procedures such as disbudding and castration. Calving is a necessary event for cows and their calves, and is painful; however, pain-relief is not routinely provided, particularly to calves. This article reviews the literature regarding non-steroidal anti-inflammatory drug usage around calving to aid practitioners in making evidence-based decisions regarding management of calving-related pain in cows and calves.

Key words

Calving; cow; calf; analgesia; NSAID; welfare

Key points

- Analgesia is under-used around calving, particularly for treatment of calves.
- There is increasing evidence that calving is painful for both cow and calf. Available data strongly suggest that NSAID pain-relief leads to improved welfare of both cows and calves in the postpartum period.
- Postpartum treatment of cows with NSAIDs has the potential to result in productivity gains, which may incentivise use.
- Evidence for adverse effects is limited and appears to be NSAID specific.
- Administration of NSAIDs at calving is recommended for veterinary practitioners and farmers seeking to optimise the care of parturient cattle and newborn calves.

1 **Introduction**

2 Calving is a necessary event for productive cows; assisted parturition is common and is most
3 frequently performed by farmers (Egan *et al.*, 2001). Whilst difficult calving is believed to be painful
4 and stressful for cows and their calves, data to support this view are limited. Previous studies have
5 found that veterinary surgeons and farmers often administer analgesia to cows, and less commonly
6 calves, following assisted parturition (Laven *et al.*, 2009; Moggy *et al.*, 2017; Remnant *et al.*, 2017).
7 However, results of existing studies investigating analgesia administration after calving are
8 conflicting and very few studies report analgesia effects in newborn calves. As such, whilst it is well
9 described that cattle experiencing painful conditions, or following surgery, benefit from provision of
10 analgesia (Coetzee, 2013; Herskin *et al.*, 2018), the benefits of analgesic usage at calving are less
11 clear. This article aims to review the literature regarding analgesia usage around calving to aid
12 practitioners in making evidence-based decisions regarding management of calving-related pain in
13 cows and calves. For a more general overview of bovine analgesia, readers are referred to relevant
14 reviews in this journal and elsewhere (e.g. Orr *et al.*, 2014; Laven, 2020; Reader *et al.*, 2020; Steagall
15 *et al.*, 2021).

16 **Calving and pain**

17 Calving is a complex process with three recognised stages [Figures 1 and 2], each associated with
18 different sources of pain. Pain is a subjective experience defined by the International Association for
19 the Study of Pain as “*an unpleasant sensory and emotional experience associated with, or resembling*
20 *that associated with, actual or potential tissue damage*” (Loeser *et al.*, 2008). In human medicine
21 childbirth is recognised to be very painful, and it is known that women experience postpartum pain
22 related to normal uterine involution (Deussen *et al.*, 2020). By contrast, calving pain is poorly

Stage 1: Myometrial contraction, together with relaxation and dilation of the cervix, results in positioning of the foetus ready for expulsion, visceral pain predominates (Mainau *et al.*, 2011). This stage often presents as restlessness or isolation-seeking in cattle and may last for several hours (Mee, 2004; Proudfoot *et al.*, 2014).

Stage 2: Abdominal contractions are observed and the amniotic sac ruptures, followed by expulsion of the foetus. Somatic pain predominates during this stage and completion is typically achieved within two hours, although this may be longer (Mainau *et al.*, 2011; Kovács *et al.*, 2016). Animals are typically in stage 2 when veterinary assistance is sought.

Stage 3: Following expulsion of the foetus myometrial contractions reduce in intensity and frequency and placental membranes are expelled (Mainau *et al.*, 2011). Stage 3 is usually completed within 6 hours but retention of foetal membranes is not typically considered abnormal until 24 h have elapsed (Sheldon *et al.*, 2008).

1
2 Figure 1: The three stages of parturition

3



4
5 Figure 2: Cow and calf following successful completion of stage 2 parturition. Image: K. Ellis, reproduced with permission.

6

1 researched in cattle and it is unclear if cattle also experience postpartum pain in normal
2 circumstances, or only following calving injury; although recent research suggests that discomfort
3 following calving is experienced by all cattle, regardless of calving experience (Gladden *et al.*, 2021).
4 Moreover, pain experienced by calves during (or immediately after) birth is rarely studied (Laven *et al.*,
5 2012). Interestingly, veterinary surgeons typically consider neonatal calves to experience less
6 pain than adult cattle, even following dystocia (Huxley *et al.*, 2007; Laven *et al.*, 2009; Remnant *et al.*,
7 2017), and accordingly analgesic use following painful procedures is more common in adult cattle
8 than calves (Andrighetto Canozzi *et al.*, 2020); however, data to support this belief are absent.
9 Moreover, newborn babies have been found to experience pain similarly to adults (Goksan *et al.*,
10 2015), and substantial forces are applied to calves during assisted birth (Pearson *et al.*, 2020);
11 therefore, it is likely that newborn calves experience pain at birth (in particular if assisted), and this
12 needs to be considered by practitioners.

13 ***Bovine analgesia***

14 Bovine pain has been subject to increased interest in recent decades, and it is now well-recognised
15 by farmers and veterinary surgeons that cattle experience pain (Whay *et al.*, 2005; Huxley *et al.*,
16 2007; Laven *et al.*, 2009; Thomsen *et al.*, 2012; Remnant *et al.*, 2017). The most commonly used
17 analgesic drugs used in cattle practice are non-steroidal anti-inflammatory drugs (NSAIDs); only this
18 category of analgesic drugs have been investigated in the peri-partum period, therefore this article
19 focuses on this type of analgesia. As well as providing analgesia, NSAIDs have anti-inflammatory and
20 antipyretic properties, and share a common mechanism of action: cyclo-oxygenase (COX) enzyme
21 inhibition, resulting in prostaglandin and thromboxane inhibition (Smith *et al.*, 1971; Vane, 1971).
22 Detailed discussion of NSAIDs is outwith the scope of this article but can be found elsewhere (e.g.
23 Laven, 2020), and a selection of products licensed for use in cattle in the UK are summarised in Table
24 1.

25

1 Table 1: NSAIDs available for use in UK cattle practice¹

NSAID	Commercial products	Licensed route	Dose rate	Withdrawal period	
				Milk	Meat
Carprofen	Carprieve (Norbrook) Rimadyl (Zoetis)	IV, SC	1.4 mg/kg (1 ml/35 kg)	0 h	21 d
Flunixin²	Allewinix (Ceva)	IV, IM	2mg/kg (2ml/50kg)	24 h (IV)/ 36 h (IM)	10 d (IV)/ 31 d (IM)
	Cronyxin (Bimeda)	IV	2.2mg/kg (2ml/45kg)	12 h	8 d
	Finadyne transdermal (MSD)	Transdermal (pour-on)	3.33mg/kg (1ml/15kg)	36 h	7 d
	Finadyne (MSD)	IV	2.2mg/kg (2ml/45kg)	24 h	5 d
	Pyroflam (Norbrook)	IV	2.2mg/kg (2ml/45kg)	24 h	10 d
Ketoprofen²	Dinalgen (Elanco)	IV, IM	3mg/kg (1ml/50kg)	0 h	2 d
	Ketofen (Ceva) Ketodolor (Virbac)	IV, IM	3mg/kg (3ml/100kg)	0 h	1 d (IV)/ 4 d (IM)
	Nefotek (Bimeda) Rifen (Chanelle Pharma)	IV, IM	3mg/kg (3ml/100kg)	0 h	4 d
Meloxicam²	Inflacam (Virbac) Loxicom (Norbrook) Meloxidyl (Ceva) Metacam 20mg/ml (Boehringer Ingelheim) Rheumocam (Chanelle Pharma)	IV, SC	0.5mg/kg (2.5ml/100kg)	5 d	15 d
	Metacam 40mg/ml (Boehringer Ingelheim)	IV, SC	0.5mg/kg (1.25ml/100kg)	120 h	15 d
	Meloxidolor (Dechra)	IV, SC	0.5mg/kg (2.5ml/100kg)	Not available	15 d
Sodium salicylate	Solacyl (Dechra)	PO (in milk or water)	40mg/kg	Not licensed for use in lactating cows	0 d

2 IV = intravenous. IM = intramuscular. SC = subcutaneous. PO = *per os*.3 Information correct at the time of writing – the authors accept no responsibility regarding the use of these products. Readers are
4 recommended to refer to relevant product datasheets.5 1. List is restricted to products appearing in the NOAH compendium (National Office of Animal Health, 2022) and is not
6 exhaustive.

7 2. Available antibiotic/NSAID combination products are not included

8

1 ***Health and productivity effects of NSAID administration at calving***

2 Although an inflammatory response is a normal finding in postpartum cattle, this response is greater
3 in cattle that subsequently go on to develop postpartum disease (Humblet *et al.*, 2006; Qu *et al.*,
4 2014). Accordingly, there has been interest in the potential for NSAIDs to reduce the risk of
5 postpartum disease. Findings at a biochemical level have been promising with postpartum NSAID
6 administration being associated with reduced serum haptoglobin and β -hydroxybutyrate
7 concentration (Barragan *et al.*, 2020b; Pascottini *et al.*, 2020), but a consistent improvement in
8 clinical disease outcomes has not been shown. Use of different NSAIDs in various studies may be
9 one factor contributing to the inconsistent findings reported. For example, Barragan *et al.* (2021)
10 administered two doses of acetylsalicylic acid (Aspirin) to cows 12 and 24 hours after calving and
11 found that NSAID treated cows had a lower risk of developing metritis, but this finding was not
12 supported by the results of Richards *et al.* (2009), who found no effect of ketoprofen on postpartum
13 disease status.

14 There has been concern over the possible negative effects of NSAID administration around calving,
15 with particular focus on the increased risk of retained foetal membranes (RFM). As prostaglandins
16 are important in the postpartum period for placental expulsion, these concerns are not unfounded.
17 Different NSAIDs appear to have variable effects on placental retention. More than twenty years
18 ago a study associated flunixin administration with increased RFM risk following caesarean-section
19 (Waelchli *et al.*, 1999), but did not include animals that calved *per vaginam*. More recently, this
20 finding has been supported by a study of unassisted calvings that found flunixin administration was
21 associated with not just an increased risk of RFM, but also an increased risk of stillbirth (Newby *et*
22 *al.*, 2017). However an absence of negative effects of other NSAIDs has been reported, with studies
23 investigating effects of ketoprofen, meloxicam and acetylsalicylic acid all finding no difference
24 between NSAID-treated and untreated or placebo-treated animals (Richards *et al.*, 2009; Swartz *et*
25 *al.*, 2018; Barragan *et al.*, 2021).

1 Results of studies investigating the effects of NSAID administration (at calving) on subsequent
2 productivity are mixed; however, the different NSAIDs used, and different measures of milk
3 production analysed, makes comparisons between studies difficult. Most studies analysing the
4 effects of meloxicam, carprofen, flunixin and ketoprofen have found that milk production is not
5 affected by NSAID administration (Richards *et al.*, 2009; Schwartz *et al.*, 2009; Newby *et al.*, 2013;
6 Mainau *et al.*, 2014; Meier *et al.*, 2014); however, these studies are restricted to short-term
7 measures. Studies analysing longer-term measures of milk production (such as 305-d yield) are
8 fewer, but provide more promising results — suggesting NSAID treatment may be associated with
9 improvements in milk production (Farney *et al.*, 2013; Stilwell *et al.*, 2014) — a finding supported by
10 our recent work (Gladden, 2021). Milk production is affected by many factors and some studies
11 have found that NSAID administration interacts with other factors affecting milk yield. For example,
12 Farney *et al.* (2013) found that sodium salicylate treatment at calving was associated with increased
13 305-d yield of cows in the 3rd lactation and over, but not younger cows. By contrast, Stilwell *et al.*
14 (2014) found that milk yield at 305 days in milk (DIM) was increased in heifers treated with
15 carprofen (compared to untreated heifers), but milk yield of carprofen-treated multiparous cows at
16 305 DIM was no different to untreated cows.

17 Persistent postpartum inflammation is associated with delayed ovarian resumption (Cheong *et al.*,
18 2017), therefore it is possible that NSAID treatment at calving may be associated with improved
19 reproductive performance in the subsequent lactation. Few studies have analysed the effects of
20 NSAID treatment at calving on subsequent lactation performance; however, the limited available
21 data are promising. Acetylsalicylic acid treatment has been associated with improved reproductive
22 performance, with treated cows conceiving sooner and needing fewer insemination attempts to
23 conceive than placebo-treated cows (Barragan *et al.*, 2020a, 2021). Acetylsalicylic acid is not
24 licensed for use in adult cattle in the UK, but the results of our study suggest that ketoprofen
25 treatment has a similar beneficial effect (Gladden, 2021).

1 ***Welfare effects of NSAID administration at calving***

2 The limited number of studies on NSAID treatment at calving suggest welfare is improved if NSAIDs
3 are administered. For example, we recently observed that ketoprofen-treated cattle engaged in
4 lying postures consistent with improved comfort more than placebo-treated cattle (Gladden *et al.*,
5 2021). Additionally, previous studies have found NSAID-treated cows are more active, and engage in
6 feeding directed behaviours more frequently, than untreated or placebo-treated cows (Newby *et al.*,
7 2013; Mainau *et al.*, 2014; Stilwell *et al.*, 2014; Barragan *et al.*, 2020a). Furthermore, a recent study
8 has found that, although NSAID treatment was provided 24 h after calving, behavioural signs of
9 postpartum pain (such as back-arching and tail lifting) of NSAID-treated cows were reduced
10 compared to placebo-treated cows (Schmitt *et al.*, 2022). Collectively, these results strongly suggest
11 NSAID administration at, or soon after, calving has a positive impact on postpartum welfare of cattle,
12 and routine use should be considered by farmers and veterinary surgeons seeking to optimise
13 postpartum welfare.

14 ***Difficult calving***

15 It is often thought that dystocia is more painful than unassisted calving, but data to support this view
16 are limited. A factorial study design including analgesia-treated and placebo-treated animals, as well
17 as animals affected by a painful experience and unaffected control animals, in a 2 x 2 design [Figure
18 3], is considered optimal for assessment of animal pain (Weary *et al.*, 2006). This type of study
19 design allows determination of whether an observed difference in measured outcomes is a) related
20 to the painful experience and b) ameliorated by analgesia (suggesting that pain is the source of the
21 change in outcome). However, this type of study design is rarely used in studies of postpartum pain
22 in cattle, with only three studies (reported across five publications) employing a factorial design
23 (Gladden *et al.*, 2018, 2021; Swartz *et al.*, 2018; Barragan *et al.*, 2020a, 2020b). We did not identify
24 any effects of the interaction between calving assistance and NSAID treatment on biomarkers of
25 stress and inflammation or postpartum behaviour (Gladden *et al.*, 2018, 2021), although an

1 interaction effect on some measures of productivity were identified (Gladden *et al.* unpublished
 2 data). Swartz *et al.* (2018) found that the daily milk yield of cows experiencing eutocia
 3 (unconventionally defined as calving lasting ≤ 70 min) that were treated with a NSAID before calving
 4 was nearly 7 kg/d higher than cows in other calving type x NSAID treatment groups. By contrast,
 5 Barragan *et al.* (2020a) measured daily milk yield for 30 d postpartum and found that milk yield on
 6 some days was higher for NSAID-treated cows in the dystocia group but there was no treatment
 7 effect on unassisted cows. Similar to our study (Gladden *et al.*, 2018), Barragan *et al.* (2020b) did not
 8 identify any assistance x treatment interaction effects on biomarkers of stress, inflammation, or
 9 nociception. As such, it is unclear whether assisted cows (or cows experiencing dystocia) experience
 10 different effects of NSAID administration to unassisted cows, and further work is needed.

		Condition group	
		Painful condition present (P)	Painful condition absent (p)
Treatment group	Analgesia treatment (A)	PA	pA
	Placebo treatment (σ)	$P\sigma$	$p\sigma$

11

12 *Figure 3: Illustration of a 2 x 2 factorial study design (Modified from: Weary et al., 2006)*13 *PA, Pa, pA, pa each represent the pain x analgesia interaction group determined by the presence/absence of a painful*
 14 *condition (e.g. dystocia) and the (randomly) allocated treatment group*

15

16

17 **Administration of NSAIDs to newborn calves**

18 Few studies have investigated the effects of post-birth analgesic treatment of newborn calves;
 19 however, the available data suggest that NSAIDs show promise as an additional tool for improving
 20 calf health and welfare. Post-birth meloxicam treatment has been associated with increased vigour
 21 (Murray *et al.*, 2016), improved feed consumption (Murray *et al.*, 2016; Clark *et al.*, 2020), and
 22 improved early-life growth rate (Pearson *et al.*, 2019). Similarly, ketoprofen administration
 23 immediately after birth was associated with increased engagement in behaviours consistent with
 24 improved welfare (Gladden *et al.*, 2019).

1 The use of NSAIDs in newborn calves is off-licence for all products available in the UK and
2 consideration needs to be paid to potential risks of use in such young animals. The effects of NSAIDs
3 on renal development of young calves has not been studied; however, although COX-2 selective
4 inhibitors have been found to affect renal development of mouse pups, COX-1 inhibitors have not
5 been found to have the same effect (Kömhoff *et al.*, 2000). At birth, bovine renal function is thought
6 to be similar to that of adults (Dalton, 1968), which may reduce the nephrotoxic associated risks
7 posed by NSAIDs. This hypothesis is supported by Pearson *et al.* (2019), who did not find any
8 differences in renal and hepatic parameters of meloxicam and placebo-treated calves. Additionally,
9 in our work we did not identify any clinically adverse effects of ketoprofen administration to
10 newborn calves compared to a saline treatment (Gladden, 2021). Nevertheless, cattle practitioners
11 should adopt a risk-based approach when administering NSAIDs to young, potentially compromised
12 calves after a dystocia event as, although no studies report adverse effects, all studies only include
13 clinically healthy calves.

14 **Conclusion**

15 This article provides an overview of the currently available evidence for administration of NSAIDs to
16 parturient cows and newborn calves. Although results of different studies are sometimes
17 conflicting, when assessed collectively the data generally support NSAID treatment of cows at
18 calving — particularly from a welfare perspective, where the evidence supporting use is most
19 consistent. Furthermore, there is evidence that newborn calf welfare is also improved by NSAID
20 administration.

21 Non-steroidal anti-inflammatory drugs are widely available to bovine practitioners in the UK and are
22 a cost-effective tool with the capacity to aid improvements in the welfare of postpartum cattle.
23 Additionally, there is the potential for productivity gains to be made, which may incentivise use. The
24 wide availability, overall beneficial impact, and limited adverse effects reported, mean that
25 administration of NSAIDs at calving (with the exception of flunixin) can be recommended to

- 1 veterinary practitioners and farmers seeking to optimise the care of parturient cattle and newborn
- 2 calves.

References

Andrighetto Canozzi, M. E., Rossi Borges, J. A. and Jardim Barcellos, J. O. (2020) 'Attitudes of cattle veterinarians and animal scientists to pain and painful procedures in Brazil', *Preventive Veterinary Medicine*, 177, p. 104909.

Barragan, A. A., Bauman, L., da Costa, L., Velez, J., Gonzalez, J. D. R., Schuenemann, G. M., Menichetti, B., Piñeiro, J. and Bas, S. (2020a) 'Administration of acetylsalicylic acid after parturition in lactating dairy cows under certified organic management: Part I. Milk yield, milk components, activity patterns, fertility, and health', *Journal of Dairy Science*, 103(12), pp. 11697–11712.

Barragan, A. A., Bauman, L. M., Schuenemann, G. M., Velez, J., Lakritz, J., Coetzee, J. F., Gonzalez, J. D. R., Piñeiro, J. M., Menichetti, B. and Bas, S. (2020b) 'Administration of acetylsalicylic acid after parturition in lactating dairy cows under certified organic management: Part II. Biomarkers of nociception, inflammation, and stress', *Journal of Dairy Science*, 103(12), pp. 11713–11722.

Barragan, A. A., Bas, S., Hovingh, E. and Byler, L. (2021) 'Effects of postpartum acetylsalicylic acid on uterine diseases and reproductive performance in dairy cattle', *JDS Communications*, 2, pp. 67–72.

Cheong, S. H., Filho, O. G. S., Absalon-Medina, V. A., Schneider, A., Butler, W. R. and Gilbert, R. O. (2017) 'Uterine and systemic inflammation influences ovarian follicular function in postpartum dairy cows', *PLoS ONE*, 12(5), pp. 1–16.

Clark, M. O. C., Stahl, T. C. and Erickson, P. S. (2020) 'The effect of meloxicam on neonatal dairy calves: Immunoglobulin G uptake and preweaning performance', *Journal of Dairy Science*, 103(12), pp. 11363–11374.

Coetzee, J. F. (2013) 'Assessment and Management of Pain Associated with Castration in Cattle', *Veterinary Clinics of North America: Food Animal Practice*, 29(1), pp. 75–101.

Dalton, R. G. (1968) 'Renal Function In Neonatal Calves-Diuresis', *British Veterinary Journal*, 124(9), pp. 371–381.

Deussen, A. R., Ashwood, P., Martis, R., Stewart, F. and Grzeskowiak, L. E. (2020) 'Relief of pain due to uterine cramping/involution after birth (Review)', *Cochrane Database of Systematic Reviews*, 10(CD004908).

Egan, J., Leonard, N., Griffin, J., Hanlon, A. and Poole, D. (2001) 'A survey of some factors relevant to animal welfare on 249 dairy farms in the Republic of Ireland. Part 1. Data on housing, calving and calf husbandry', *Irish Veterinary Journal*, 54(8), pp. 388–392.

Farney, J. K., Mamedova, L. K., Coetzee, J. F., Minton, J. E., Hollis, L. C. and Bradford, B. J. (2013) 'Sodium salicylate treatment in early lactation increases whole-lactation milk and milk fat yield in mature dairy cows', *Journal of Dairy Science*, 96(12), pp. 7709–7718.

Gladden, N., McKeegan, D., Viora, L. and Ellis, K. (2018) 'Postpartum ketoprofen treatment does not alter stress biomarkers in cows and calves experiencing assisted and unassisted parturition: A randomised controlled trial', *The Veterinary Record*, 183, p. 414.

Gladden, N., Ellis, K., Martin, J., Viora, L. and McKeegan, D. (2019) 'A single dose of ketoprofen in the immediate postpartum period has the potential to improve dairy calf welfare in the first 48h of life',

Applied Animal Behaviour Science, 212, pp. 19–29.

Gladden, N., Ellis, K., Martin, J. and McKeegan, D. (2021) 'Administration of ketoprofen affects postpartum lying behaviours of Holstein dairy cows regardless of whether parturition is assisted', *The Veterinary Record*, e300.

Gladden, N. L. (2021) *Bovine parturition: welfare and production implications of assistance and ketoprofen analgesia (PhD Thesis)*. University of Glasgow.

Goksan, S., Hartley, C., Emery, F., Cockrill, N., Poorun, R., Moultrie, F., Rogers, R., Campbell, J., Sanders, M., Adams, E., Clare, S., Jenkinson, M., Tracey, I. and Slater, R. (2015) 'fMRI reveals neural activity overlap between adult and infant pain', *eLife*, 4, pp. 1–13.

Herskin, M. S. and Nielsen, B. H. (2018) 'Welfare effects of the use of a combination of Local Anesthesia and NSAID for disbudding analgesia in dairy Calves-Reviewed across different welfare concerns', *Frontiers in Veterinary Science*, 5(JUN), pp. 1–16.

Humblet, M. F., Guyot, H., Boudry, B., Mbayahi, F., Hanzen, C., Rollin, F. and Godeau, J. M. (2006) 'Relationship between haptoglobin, serum amyloid A, and clinical status in a survey of dairy herds during a 6-month period', *Veterinary Clinical Pathology*, 35(2), pp. 188–193.

Huxley, J. N. and Whay, H. R. (2007) 'Attitudes of UK veterinary surgeons and cattle farmers to pain and the use of analgesics in cattle', *Cattle Practice*, 15(2), pp. 189–193.

Kömhoff, M., Wang, J.-L., Cheng, H.-F., Langenbach, R., McKanna, J. A., Harris, R. C. and Breyer, M. D. (2000) 'Cyclooxygenase-2-selective inhibitors impair glomerulogenesis and renal cortical development', *Kidney International*, 57(2), pp. 414–422.

Kovács, L., Kézér, F. L. and Szenci, O. (2016) 'Effect of calving process on the outcomes of delivery and postpartum health of dairy cows with unassisted and assisted calvings', *Journal of Dairy Science*, 99(9), pp. 7568–7573.

Laven, R. (2020) 'An introduction to NSAIDs for cattle: recommendations for the veterinary surgeon', *Livestock*, 25(4), pp. 174–177.

Laven, R. A., Huxley, J. N., Whay, H. R. and Stafford, K. J. (2009) 'Results of a survey of attitudes of dairy veterinarians in New Zealand regarding painful procedures and conditions in cattle.', *New Zealand Veterinary Journal*, 57(4), pp. 215–220.

Laven, R., Chambers, P. and Stafford, K. (2012) 'Using non-steroidal anti-inflammatory drugs around calving: maximizing comfort, productivity and fertility.', *The Veterinary Journal*, 192(1), pp. 8–12.

Loeser, J. D. and Treede, R. D. (2008) 'The Kyoto protocol of IASP Basic Pain Terminology', *Pain*, 137(3), pp. 473–477.

Mainau, E., Cuevas, A., Ruiz-de-la-Torre, J. L., Abbeloos, E. and Manteca, X. (2014) 'Effect of meloxicam administration after calving on milk production, acute phase proteins, and behavior in dairy cows', *Journal of Veterinary Behavior: Clinical Applications and Research*, 9(6), pp. 357–363.

Mainau, E. and Manteca, X. (2011) 'Pain and discomfort caused by parturition in cows and sows', *Applied Animal Behaviour Science*, 135(3), pp. 241–251.

Mee, J. F. (2004) 'Managing the dairy cow at calving time', *Veterinary Clinics of North America: Food Animal Practice*, 20(3), pp. 521–546.

Meier, S., Priest, N. V., Burke, C. R., Kay, J. K., McDougall, S., Mitchell, M. D., Walker, C. G., Heiser, A., Loor, J. J. and Roche, J. R. (2014) 'Treatment with a nonsteroidal antiinflammatory drug after calving did not improve milk production, health, or reproduction parameters in pasture-grazed dairy cows',

Journal of Dairy Science, 97(5), pp. 2932–2943.

Moggy, M. A., Pajor, E. A., Thurston, W. E., Parker, S., Greter, A. M., Schwartzkopf-Genswein, K. S., Campbell, J. R. and Windeyer, M. C. (2017) 'Management practices associated with pain in cattle on western Canadian cow-calf operations: A mixed methods study', *Journal of Animal Science*, 95(2), pp. 958–969.

Murray, C., Duffield, T., Haley, D., Pearl, D., Veira, D., Deelen, S. and Leslie, K. (2016) 'The Effect of Meloxicam NSAID Therapy on the Change in Vigor, Suckling Reflex, Blood Gas Measures, Milk Intake and Other Variables in Newborn Dairy Calves', *Journal of Veterinary Science and Animal Husbandry*, 4(1).

National Office of Animal Health (2022) *NOAH Compendium*, Available at: <https://www.noahcompendium.co.uk> (Accessed: 23rd February 2022).

Newby, N. C., Pearl, D. L., LeBlanc, S. J., Leslie, K. E., von Keyserlingk, M. A. G. and Duffield, T. F. (2013) 'Effects of meloxicam on milk production, behavior, and feed intake in dairy cows following assisted calving', *Journal of Dairy Science*, 96(6), pp. 3682–3688.

Newby, N. C., Leslie, K. E., Dingwell, H. D. P., Kelton, D. F., Weary, D. M., Neuder, L., Millman, S. T. and Duffield, T. F. (2017) 'The effects of periparturient administration of flunixin meglumine on the health and production of dairy cattle', *Journal of Dairy Science*, 100(1), pp. 582–587.

Orr, J., Geraghty, T. and Ellis, K. (2014) 'Anti-inflammatories in cattle medicine', *Livestock*, 19(6), pp. 322–328.

Pascottini, O. B., Van Schyndel, S. J., Spricigo, J. F. W., Carvalho, M. R., Mion, B., Ribeiro, E. S. and LeBlanc, S. J. (2020) 'Effect of anti-inflammatory treatment on systemic inflammation, immune function, and endometrial health in postpartum dairy cows', *Scientific Reports*, 10(1), pp. 1–9.

Pearson, J. M., Pajor, E. A., Campbell, J. R., Caulkett, N. A., Levy, M., Dorin, C. and Windeyer, M. C. (2019) 'Clinical impacts of administering a non-steroidal anti-inflammatory drug to beef calves after assisted calving on pain and inflammation, passive immunity, health, and growth', *Journal of Animal Science*, 97, pp. 1996–2008.

Pearson, J. M., Thomsen, C., Kusler, A., Pajor, E. A., Gurdita, A., Ungrin, M. D. and Windeyer, M. C. (2020) 'Quantifying the Forces Applied During Manually and Mechanically Assisted Calvings in Beef Cattle', *Frontiers in Veterinary Science*, 7, pp. 5–12.

Proudfoot, K. L., Jensen, M. B., Weary, D. M. and von Keyserlingk, M. A. G. (2014) 'Dairy cows seek isolation at calving and when ill', *Journal of Dairy Science*, 97(5), pp. 2731–2739.

Qu, Y., Fadden, A. N., Traber, M. G. and Bobe, G. (2014) 'Potential risk indicators of retained placenta and other diseases in multiparous cows', *Journal of Dairy Science*, 97(7), pp. 4151–4165.

Reader, J., Angel, T. and Rogers, I. (2020) 'Practical use of non-steroidal anti-inflammatory drugs in farm practice', *Livestock*, 25(5), pp. 202–209.

Remnant, J. G., Tremlett, A., Huxley, J. N. and Hudson, C. D. (2017) 'Clinician attitudes to pain and use of analgesia in cattle: where are we 10 years on?', *The Veterinary Record*, 181, p. 400.

Richards, B. D., Black, D. H., Christley, R. M., Royal, D., Smith, R. F. and Dobson, H. (2009) 'Effects of the administration of ketoprofen at parturition on the milk yield and fertility of Holstein–Friesian cattle', *The Veterinary Record*, 165(4), pp. 102–106.

Schmitt, R., Pieper, L., Borchardt, S., Swinkels, J. M., Gelfert, C. C. and Staufenbiel, R. (2022) 'Effects of a single transdermal administration of flunixin meglumine in early postpartum Holstein Friesian

dairy cows: Part 1. Inflammatory and metabolic markers, uterine health, and indicators of pain', *Journal of Dairy Science*. American Dairy Science Association, 105(3), p. In Press.

Sheldon, I. M., Williams, E. J., Miller, A. N. A., Nash, D. M. and Herath, S. (2008) 'Uterine diseases in cattle after parturition.', *The Veterinary Journal*, 176(1), pp. 115–21.

Shwartz, G., Hill, K. L., VanBaale, M. J. and Baumgard, L. H. (2009) 'Effects of flunixin meglumine on pyrexia and bioenergetic variables in postparturient dairy cows', *Journal of Dairy Science*, 92(5), pp. 1963–1970.

Smith, J. B. and Willis, A. L. (1971) 'Aspirin selectively inhibits prostaglandin production in human platelets', *Nature: New biology*, 231(25), pp. 235–237.

Steagall, P. V., Bustamante, H., Johnson, C. B. and Turner, P. V. (2021) 'Pain Management in Farm Animals : Focus on Cattle , Sheep and Pigs', *Animals*, 11(6), p. 1483.

Stilwell, G., Schubert, H. and Broom, D. M. (2014) 'Short communication: Effects of analgesic use postcalving on cow welfare and production', *Journal of Dairy Science*, 97(2), pp. 888–891.

Swartz, T. H., Schramm, H. H., Bewley, J. M., Wood, C. M., Leslie, K. E. and Petersson-Wolfe, C. S. (2018) 'Meloxicam administration either prior to or after parturition: Effects on behavior, health, and production in dairy cows', *Journal of Dairy Science*, 101(11), pp. 10151–10167.

Thomsen, P. T., Anneberg, I. and Herskin, M. S. (2012) 'Differences in attitudes of farmers and veterinarians towards pain in dairy cows.', *The Veterinary Journal*, 194, pp. 94–97.

Vane, J. R. (1971) 'Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs.', *Nature: New Biology*, 231(25), pp. 232–235.

Waelchli, R., Thun, R. and Stocker, H. (1999) 'Effect of flunixin meglumine on placental expulsion in dairy cattle after a caesarean', *The Veterinary Record*, 144, pp. 702–703.

Weary, D. M., Niel, L., Flower, F. C. and Fraser, D. (2006) 'Identifying and preventing pain in animals', *Applied Animal Behaviour Science*, 100(1–2), pp. 64–76.

Whay, H. R. and Huxley, J. N. (2005) 'Pain relief in cattle: A practitioners perspective', *Cattle Practice*, 13(2), pp. 81–85.