

## PAIN RELIEF IN NZ DAIRY COWS

Veterinarians have the opportunity to improve wellbeing and reduce inflammation and pain in dairy cows by using and authorising non-steroidal anti-inflammatories (NSAIDs).

The desired outcomes from the use of NSAIDs are:

1. Pain relief (analgesia)
2. Anti-inflammatory effect
3. Anti-pyretic (reducing fever)

The most common NSAIDs used in New Zealand dairy cows are ketoprofen and meloxicam. Both of these inhibit the COX-1 and COX-2 enzymes in the inflammatory cascade although meloxicam is more selective towards COX-2. Ketoprofen also has a direct pain relief (analgesic) action by inhibiting the inflammatory mediator bradykinin. Refer Figure 1.

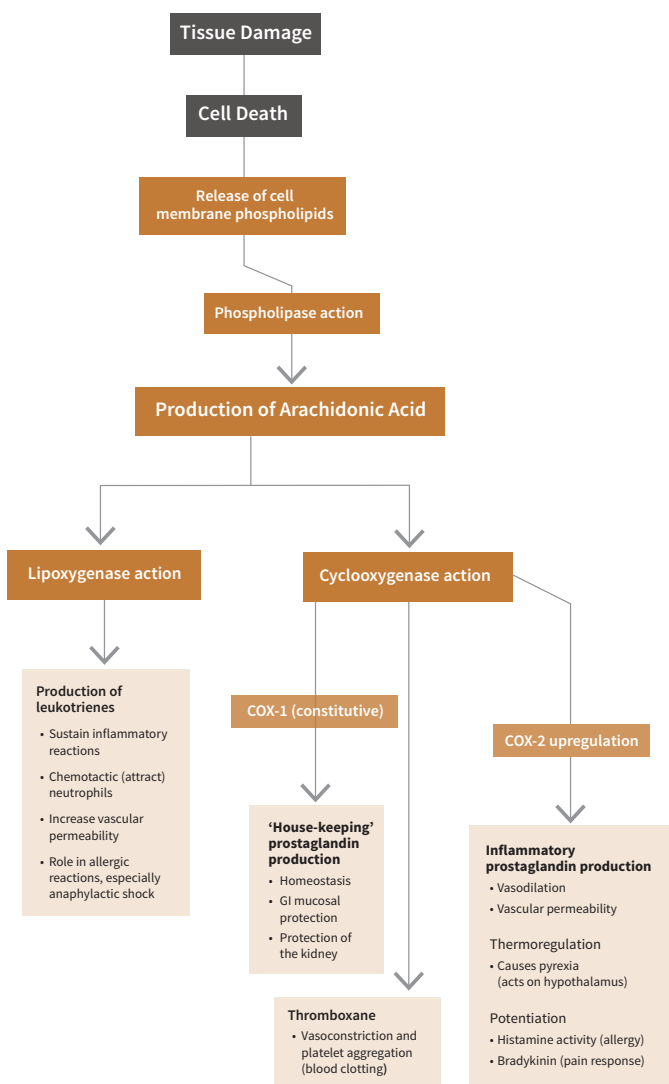


Figure 1. The inflammatory cascade

It is likely that for all available NSAIDs, the effective pain relief duration will be shorter than the anti-inflammatory effects. For example, meloxicam in cattle has an anti-endotoxin effect that lasts at least 50 hours<sup>1</sup> but post-surgical analgesia (e.g. following claw amputation) may not last longer than 24 hours<sup>2</sup>. This could be accounted for with different treatment frequency, for example, repeat daily dosing. When analgesic effects are important for animal well-being, daily NSAIDs such as ketoprofen may be advantageous as cattle can be treated on several consecutive days whereas meloxicam is only registered for a single dose.

### Measuring pain in cows

There is no standardised pain model for cows. Both the physiological effects of pain (e.g. increased temperature, increased heart rate, swelling, loss of function) and the psychological effects (e.g. a lame cow has reduced feed intake due to reluctance in walking to access feed due to pain) need to be considered.

The physiological effects are easier to measure but have limitations. While indicators including cortisol levels have been used to indicate a pain response, this measurement is not always appropriate as an indicator of pain because increased cortisol can also be associated with stress of being handled or discomfort.<sup>2,3</sup>

It is becoming more common for researchers to measure the psychological effects of pain using behavioural observations, even though measuring this can be difficult due to the stoic nature of cows. As an example, cows with a clinical diagnosis that may be painful (e.g. mastitis, lameness) had a significantly higher score for ‘attention towards the surroundings’, ‘head position’, ‘ear position’, ‘facial expressions’, ‘response to approach’ and ‘back position’ than cows in a healthy control group, and treatment with ketoprofen significantly reduced these scores.<sup>4</sup>

### Pain relief after surgery

Surgeries performed by veterinarians, such as claw removal, caesarean section or correction of a displaced abomasum, are painful procedures. While local anaesthetic improves animal welfare, and makes the procedure safer, the use of NSAIDs help manage pain during the recovery period. When an NSAID was administered to cows after abdominal surgery, cows flicked their tail less, spent more time lying on the side of the surgical site and had increased feed intake.<sup>16</sup>

### Pain relief at calving

Pain relief (ketoprofen or meloxicam) administered to cows with dystocia at the time of calving has been shown to increase activity, increase feeding time and increase milk yield.<sup>17,18,19</sup>

Alongside pain incurred as a result of the calving process, it is widely believed that all cows experience some degree of systemic inflammation in the several days after parturition. The magnitude and persistence of the inflammatory state varies widely among cows. Several studies have linked the degree of postpartum inflammation to increased disease risk and decreased whole-lactation milk production.<sup>20</sup> Targeted use of NSAIDs during this window of time has enhanced whole-lactation productivity in several studies. In a Canadian study, cows treated with a single dose of oral meloxicam at calving produced 0.64 L/day more milk over the first 90–120 days in lactation, had 0.75 times the odds of subclinical mastitis at first herd test, and were culled or died at 0.46 times the rate before 60 days in milk relative to untreated controls.<sup>21</sup> These results are consistent with other research indicating that parturition is a painful and risky event for cows.

The choice of NSAIDs used at calving is very important. Flunixin meglumine is COX-1 selective and can significantly increase the risk of retained foetal membranes (RFM).<sup>22</sup> Meloxicam is known to be a preferential COX-2 inhibitor thus having a targeted action against inflammatory processes.<sup>23</sup> Meloxicam however incurs an 84-hour milk withholding period for treated cows, which can make it less desirable for dairy cows compared with NSAIDs that have a nil milk withholding period. Ketoprofen inhibits both COX-1 and COX-2, showing greater activity as a COX-1 inhibitor. A study in the UK looked at the effects of ketoprofen treatment of dairy cows at calving.<sup>24</sup> Cows treated with ketoprofen at calving and again 24 hours later were 1.7 times less likely to incur an RFM compared to the untreated cows.



### Pain relief for mastitis

Mastitis is inflammation of the udder, usually caused by a bacterial infection. The clinical signs of mastitis depend on the bacteria involved and the cow's immune response. Symptoms of acute clinical mastitis may include a hot, swollen udder and reduced appetite, while for mild to moderate mastitis the only symptom may be clots in the milk.

### Mastitis caused by Gram positive bacteria

Most mastitis in NZ is caused by Gram positive bacteria (*Strep. uberis*, *CNS*, *Staph. aureus*). Treatment of acute mastitis with NSAIDs is clearly indicated from an animal wellbeing perspective.

There is increasing evidence that even mild to moderate mastitis can be painful and that the use of NSAIDs has benefits. Cows with moderate mastitis have elevated temperatures, and greater hock distances when standing, indicating that it is painful.<sup>6</sup>

Treatment of NZ dairy cows with mild to moderate clinical mastitis (as diagnosed by the farmer) and treated with a combination of meloxicam and penethamate resulted in a lower SCC and a reduced risk of removal from the herd (culling) compared to those cows treated only with penethamate.<sup>8</sup> In a European study the use of meloxicam in conjunction with antimicrobial therapy, for mild to moderate cases of clinical mastitis, resulted in a higher probability of bacteriological cure, an increased probability of conception to first artificial insemination, fewer artificial inseminations per pregnancy, and a greater proportion of cows pregnant by 120 days in milk.<sup>9</sup>

It is also important to consider the psychological effects of mastitis. Automated measures of activity, such as step count and lying down time are now being used as predictors of clinical problems and provide potential for early intervention with NSAID therapy.<sup>10</sup> These measurements indicate the administration of an NSAID to cows with mild or moderate clinical mastitis is important for cow wellbeing and pain relief, as well as benefits related to the clinical mastitis, SCC or culling for mastitis.<sup>11</sup>

### Mastitis caused by Gram negative bacteria

Coliform / Gram negative bacteria account for approximately 11% of clinical mastitis cases in New Zealand, and 99% of bacteria from these cases have an MIC >4 for common intramammary antibiotics tested.<sup>5</sup>

All NSAIDs have an anti-endotoxic effect. Gram negative endotoxin challenge studies show the administration of ketoprofen or meloxicam reduced rectal temperature and udder oedema, and increased ruminal contractions when compared with control animals.<sup>6</sup>

In a study of high-producing cows with acute clinical mastitis, ketoprofen in addition to antibiotic treatment for up to 5 days significantly increased the chance of cows recovering to >75% of pre-mastitis daily milk production, and these cows were less likely to be culled during that lactation compared to cows that did not receive ketoprofen treatment.<sup>26</sup>

For mild to moderate cases of clinical mastitis caused by *E. coli*, a non-antimicrobial approach with NSAID treatment with frequent milking is recommended. In cases of acute / severe *E. coli* mastitis, parenteral administration of fluoroquinolones, or third- or fourth-generation cephalosporins may be used. However, the evidence for the efficacy of intramammary-administered antimicrobial treatment for *E. coli* mastitis is very limited and hence cannot be recommended.<sup>7</sup>

## Pain relief for lame cows

Lameness has serious negative consequences on animal wellbeing, and has the potential to reduce the overall lifetime performance of dairy cows due to milk production loss and culling.<sup>12</sup>

Most lameness results from damage to the corium and the subsequent inflammation. Depending on the site of the corium damage this may be seen clinically as sole haemorrhage, sole ulcers, toe abscesses or white line disease. It is visually evident that moderate to severe lameness is painful for cows. For mild to moderate lameness the signs are more subtle, with lame cows spending more time lying down and less time eating. Locomotion scoring has been adopted by vets and farmers to assess and monitor lameness in cows and assist with management decisions including early intervention.<sup>13</sup>

Following a clinical case of lameness, there can be permanent changes to the hoof structure, including the corium, digital cushion and the pedal bone.<sup>25</sup> Refer Figure 2.

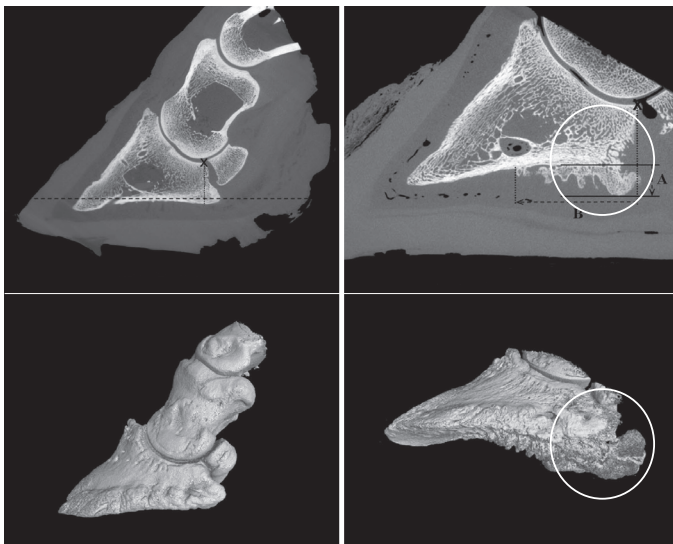


Figure 2. Sagittal x-ray views (top) and 3-dimensional images of normal (left) and diseased (right) bovine digits showing extensive exostosis (in circles)<sup>25</sup>

These changes may become irreversible, and increase the risk of a cow becoming lame again in the future. The aim of trimming the hoof of a lame cow is to remove underrun horn and redistribute weight in the foot to improve cow comfort, allowing time for the corium to generate new horn tissue to cover the sole. It is not possible to repair the pedal bone, the digital cushion or corium.

### Timely effective lameness treatment with ketoprofen

Because lameness is an inflammatory process, NSAIDs are indicated for all cases of lameness. As meloxicam has an 84 hour withholding period for milk, NSAIDs with nil withholding period such as ketoprofen are more popular with dairy farmers.

In a UK study, dairy cows with claw horn lesions that were treated with a therapeutic trim, a block on the sound claw, and a 3-day course of ketoprofen were less likely to be lame five weeks after treatment than a trim alone.<sup>14</sup> Refer Figure 3.

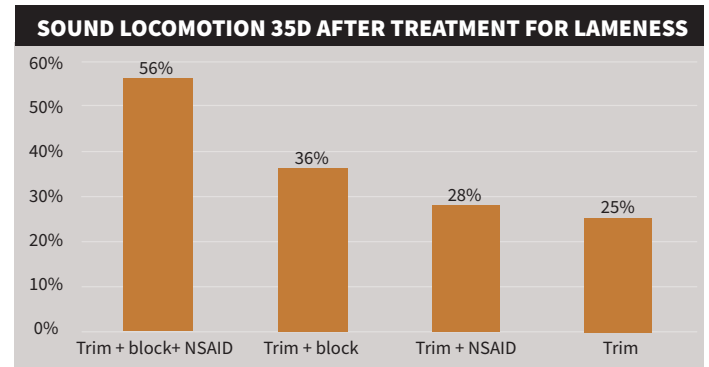


Figure 3. Lameness cure is maximised when ketoprofen is administered along with therapeutic trimming and elevation of the diseased claw using a block<sup>14</sup>

Whilst cows may gradually recover, they remain at higher risk of recurrent future lameness and earlier culling from the herd. Consequently, it is paramount to reduce the incidence and duration of any initial 'lifetime lameness' events.

A recent 3 year longitudinal randomised controlled UK Study<sup>15</sup> assessed the role of ketoprofen (sold as KetoMax brand in NZ) in lameness treatment. Treatment Group 1 included routine lameness identification via fortnightly locomotion scoring, and a subsequent corrective trim and block for lame animals. Treatment Group 3 was the same as Group 1 and also included treatment with ketoprofen on 3 consecutive days following the first and subsequent calvings, and ketoprofen on 3 consecutive days following identification of each lameness event.

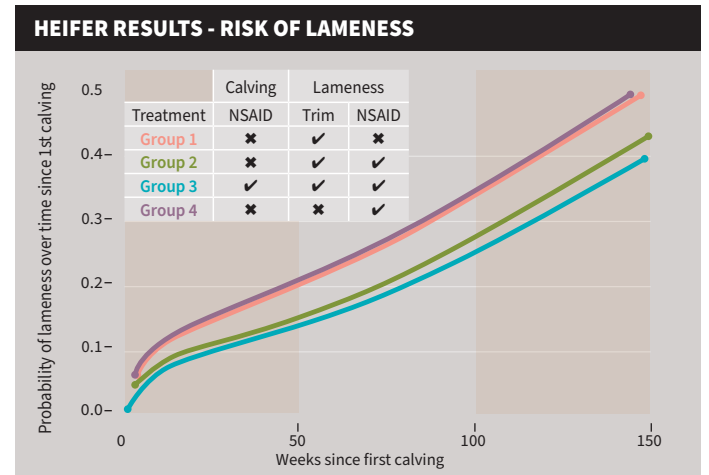


Figure 4. Reducing lameness with targeted use of NSAIDs - setting up heifers & cows for success and longevity<sup>25</sup>

The study outcomes were very compelling. Animals recruited as first calving heifers in Group 1 had twice as many animals lost from the herd (culled for any reason) during the study, compared with their treatment Group 3 herdmates. Also, during the 3 year study these same Group 3 animals had substantially reduced a) overall lameness prevalence and b) severe lameness prevalence, when compared to their Group 1 herdmates. The study illustrates the role inflammation close to calving may play in predisposing young cows to lameness, and highlights the opportunity to reduce lameness in dairy herds via routinely identifying and treating lame heifers and younger cows.

### Summary and take-home messages:

NSAIDs reduce both the physiological and psychological effects of pain, so that cows can return to normal function and behaviour, and production, faster.

- NSAIDs are indicated for mastitis, lameness, dystocia and after surgery.
- Ketoprofen and meloxicam are safe to use at all stages of lactation, although meloxicam has a 84 hour withholding period for milk.
- There is growing evidence that treating heifers and young cows with ketoprofen at calving, and when lameness is identified, reduces lameness in dairy herds.
- Consumer demand for optimal animal wellbeing and increased scrutiny of farming are factors to consider for increased use of NSAIDs as pain relief in cattle.
- Demonstrating improved cow care contributes to NZ dairy farming sustainability.

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