

Literature Review on the Welfare Implications of

Castration of Cattle

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THE ISSUE

Castration of male cattle is common practice throughout the world. Although castration inflicts pain on the animal and causes a period of slow growth rate and poorer feed efficiency there are benefits as well. Castration reduces aggressiveness^{1,2} and sexual activity by lowering testosterone levels, and modifies carcass characteristics by decreasing the number of animals with a high muscle pH ("dark cutters"). Intact male cattle (bulls) tend to produce lower quality grade, less consistent, less marbled, and less tender meat. In addition, carcasses from bulls command lower prices at market when compared with carcasses from steers.

There are several different methods of castration; however, they can be classified into three major groups: physical, chemical, and hormonal. These groups can be divided further by technique but overall, castration is achieved by removing the testicles surgically, damaging them irreparably, or causing them to atrophy by stricture of the blood supply.⁵

A survey of US members of the American Association of Bovine Practitioners (AABP) and the Academy of Veterinary Consultants (AVC) regarding castration methods has shown that surgical castration is the most common method used, and that one in five veterinarians reported using an analgesic or local anesthetic at the time of castration.¹⁰ In another survey of US members of the AABP, respondents indicated that they believed castration of dairy calves younger than 6 months old caused the least pain among a list of common procedures and medical conditions.¹¹ Correspondingly, survey participants reported providing analgesic drugs to approximately 30% of calves castrated at less than 6 months of age.¹¹

Physical Methods—Physical castration methods that are frequently used are those that involve surgical removal of the testicles, application of a constricting elastic band (rubber ring) at the base of the scrotum, and bloodless castration by the use of external clamping with an appropriate device (i.e. Burdizzo clamp). ¹² Combinations of physical methods can also be used, such as application of a Burdizzo clamp followed by rubber ring placement ^{13,14} and surgical removal of scrotal tissue 9 days after application of a rubber ring ^{15.}

Chemical Methods—Chemical castration includes injection of sclerosing or toxic agents (e.g. 88% lactic acid) into the testicular parenchyma to cause irreparable damage and loss of function. ¹⁶ Chemical

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castration requires additional procedural time and technical skill, and almost twice the healing time compared with surgical castration. ¹⁶

Hormonal Methods—Hormonal castration (immunocastration) typically involves injection of immuncontraceptives to induce antibody production against gonadotropin releasing hormone (GnRH), resulting in decreased production of endogenous hormones.¹⁷ Immunocastration has been shown to increase live weight, hot carcass weight, average daily gain, and dressing percentage following castration when compared with surgical methods.¹⁸ Although testosterone production is reduced for approximately 6 months after immunocastration, persistent mounting behavior, consumer concerns and the need for repeat injections have made the technique less effective and desirable than traditional, physical methods.²

PAIN

Acute pain—All physical methods of castration cause pain.^{2,13,19} Animals exhibit pain responses during and after castration; these responses include struggling, kicking the hind legs, tail swishing, foot stamping, head turning, restlessness, stilted gait, reduced activity, increased recumbency, abnormal standing posture, reduced interest in dams and each other and reduced grazing and feed intake.^{7,20,26} Pain response to tandem or simultaneous castration and dehorning has been found to be additive. Pain responses due to combining these procedures have been shown to last unabated, up to and more than four hours when performed without pain mitigation.²⁷ Pain associated with the surgical and Burdizzo clamp methods is relatively immediate, whereas pain resulting from elastrator ring/band placement is delayed due to interruption of the blood supply by the band/ring.^{24,25} Burdizzo castration also causes a more severe inflammatory response than band castration.²⁸ Three-to four-week-old calves castrated using rubber rings exhibited no signs of pain at the time of ring placement; in contrast, Burdizzo-castrated calves demonstrated marked signs of pain if not anesthetized, and mild to moderate pain if anesthetized prior to castration.²⁵

Application of a tight band around the scrotum and testes produces extraluminal compression of the arteries and veins, resulting in impeded arterial flow to and venous drainage of the tissues. Lack of perfusion compromises the supply of oxygen and metabolic substrates to the tissues and results in ischemia. Continued ischemia induces severe cellular damage and coagulation necrosis.²⁸⁻³⁰ Ischemic lesions of the intestinal tract or limbs are widely known to cause pain during the acute phase, followed by reduced pain as the lesion progresses. Blood pressures and heart rates of 2-month-old lambs remained high 4 hours after placement of rubber rings, suggesting the persistence of pain.³¹

Intratesticular injection of an 88% lactic acid solution in 50- to 128-kg calves resulted in similar or increased severity of behavioral responses compared with those following surgical castration. No significant differences were observed in scrotal swelling and pain for the first two days after surgery. In addition, healing was prolonged and unsatisfactory for chemically castrated calves compared to those surgically castrated.

Effect of age on response to castration has also been investigated.^{29,31} One- to seven-day old calves castrated using elastrator rings exhibited few behaviors associated with pain or distress, and plasma cortisol concentrations of castrated calves did not significantly differ from those of uncastrated controls.³² Although 6-day-old bull calves exhibited fewer violent pain responses than 21- or 42-day-old calves after castration, pain-associated behaviors were observed in all groups.²⁴ Forty-two-day-old calves exhibited a high incidence of pain-associated behaviors and a marked increase in plasma cortisol concentration, possibly indicating these animals experienced more pain than 6- or 21-day-old calves.²⁴ Supporting the value of early castration, it has been found that beef calves castrated before weaning ate more and had higher average daily gain (ADG) with lower inflammatory responses in the 14 days after

castration than calves that were castrated after weaning.³³ Additionally, desynchronized electroencephalogram (EEG) and electrodermal activity readings (both indicative of pain response) were greater in 6-month-old calves compared to 8-week-old calves after castration.³⁴ One author noted that similar cortisol concentrations were measured in castrated calves and those in which castration was simulated.³⁵ However, substance P was significantly increased in calves that were castrated.³⁵ This suggests that substance P is likely associated with nociception (pain) and may become a validated method of pain assessment in food-producing animals. More research in this area needs to be done as validated methods of pain assessment must be used for a drug to be indicated for pain relief in the target species.³⁶

Chronic pain—Persistent wounds were observed in 14-month-old bull calves castrated using emasculator bands; these wounds may produce chronic pain.⁷ Assessment of chronic pain has primarily been based on reduced weight gain and growth, but findings suggest that pain may persist for several weeks following castration.^{19,25} On the basis of behavioral parameters and the presence of inflammation and sepsis, it appears that castration with rubber rings produces both acute and chronic pain, whereas application of the Burdizzo clamp and surgical castration produce less chronic pain.¹⁹ Another author²⁵ reported similar observations in 21- to 28-week-old calves. Calves castrated with rubber rings developed purulent inflammation at the site of ring placement, as well as swelling and hardening of the issues, until the distal scrotum detached after a mean of 47 days.²⁵ Significantly more abnormal posturing was exhibited by rubber ring-castrated calves than by Burdizzo-castrated calves for the first week after castration.²⁵ In addition, calves castrated with rubber rings exhibited signs of pain in response to scrotal palpation for up to 4 weeks longer than those castrated using Burdizzo clamps.²⁵ So although banding may cause less immediate discomfort than surgery, the overall impact of banding may be greater (e.g. greater overall reduction in food intake and daily gain^{14,26}). Questions remain regarding the impact of chronic pain secondary to castration.²

SURGICAL COMPLICATIONS

Potential complications associated with castration include hemorrhage, excessive swelling or edema, infection, poor wound healing, and failure.⁴ Use of the Burdizzo clamp may be associated with a higher failure rate, most likely caused by operator error.^{2,4}

Hemorrhage—Risk of hemorrhage is greater after surgical castration.⁴ In a survey of New Zealand cattle producers, surgical castration was associated with reportedly higher complications, including bleeding, swelling, infection, and death.³⁷

Disease—Castration-associated immunosuppression may increase risks of local or systemic disease after the procedure. Murata³⁸ observed significant reductions in circulating white blood cells and T-lymphocyte function and significant increases in total white blood cell count and neutrophil count in 3-to 4-month-old bull calves castrated using a Burdizzo clamp; values returned to baseline by 7 days after surgery. Surgical castration causes increased haptoglobin and decreased gamma-interferon production. Haptoglobin exerts a suppressive effect on lymphocyte function, and reduction of gamma-interferon results in suppression of the immune system's cell-mediated immunity and response to antigens. Studies indicate that castration-associated leukocyte depression may be limited or eliminated by pre-surgical administration of a local anesthetic and a systemic analgesic. Administration of ketoprofen, either alone or in combination with local administration of lidocaine, decreased haptoglobin concentrations and prevented suppression associated with surgical castration. In contrast, administration of xylazine in combination with butorphanol had no effect on haptoglobin concentrations after surgical castration. Increased haptoglobin concentrations were not observed

following elastrator band castration of 14-month-old bull calves. 7 or ring castration of 6-month old bull calves when given flunixin meglumine in combination with local lidocaine use. 40

Necrotic tissue, such as ischemic scrotal tissues and testes after banding, is prone to infection with pathogens. Similarly, the wound associated with surgical castration is at risk of infection. Clostridial organisms, ubiquitous in soil, may enter the wound and result in local or systemic infection; clostridial vaccination prior to castration is recommended. Use of rubber rings in calves older than 6 months may be associated with increased risks of tetanus or other infection.

Performance—Cattle may demonstrate reduced feed intake and average daily gain (ADG) for a period of time after castration. ^{23,43,44} Many experiments failed to detect differences related to castration method. ⁴³⁻⁴⁶ Differences may be found in specific studies where band castration may produce either superior ⁴⁷ or inferior growth rates ^{7,48} when compared with surgically castrated animal or controls.

Delaying castration conveys no benefit in terms of carcass weight, ^{7,49} and taste panels suggest that consumers prefer beef from cattle that are castrated at an early age. ⁴⁹ A recent study found that bulls castrated at a later age were 3% more likely to require treatment for bovine respiratory disease (BRD) than bulls that were castrated early. ⁵⁰ This can cause profit loss due to an increase in the number of days to market, decrease in hot carcass weight and potential carcass value. Castrating beef calves immediately after transport, however, may compound the stress experienced by the calves and lead to increased losses due to illness. ⁵¹ Booker et al ⁴⁷ observed that delayed castration is beneficial in bull calves that were at high risk of developing fever in the feedlot.

Fisher et al³ observed that surgical castration of 5.5-month-old calves resulted in reduced ADG for the first 7 days after surgery, but calves to which local anesthetic had been administered before castration exhibited higher ADG for the same period when compared with calves undergoing surgery alone. Calves castrated using Burdizzo clamps exhibited ADG similar to control calves for the first 7 days, but ADG was reduced from the 15th to the 21st days after surgery.³ Surgical castration of 6- to 9-month-old bull calves reduced daily weight gain and feed intake.⁹ No effect of castration was observed on overall growth of 1.5- to 5.5-month-old calves for 42 days after castration using a Burdizzo clamp.⁵² Some producers may opt for a partial scrotal resection-type castration to retain some testosterone/androgen growth effects, but a potential side effect is that the bull may remain fertile.⁵³

Physiologic stress—Castration is considered to be one of the most stressful experiences for livestock. 7,22,54 Blood cortisol concentrations have been studied as indicators of physiologic stress in animals. Regardless of the means of castration, cortisol concentrations are increased following the procedure; however, onset, magnitude, and duration may vary with the procedure used. 4,13,19,43,54 Surgical castration appears to produce the most substantial rise in plasma cortisol concentration. 3,6,19,37,54 Application of the Burdizzo clamp may also be associated with a similar, rapid rise in cortisol concentration due to the barrage of afferent neural impulses during and after crushing of the spermatic cord and scrotal nerves. 13,19,55 Chase et al 43 observed that plasma cortisol concentrations increased immediately after surgical castration; animals that were banded had cortisol increases of less initial intensity, but the concentrations were similar for both procedures on the second postoperative day. Salivary cortisol concentrations observed between 15 minutes and 2 hours after castration in 4- to 11week-old calves undergoing surgery were much higher than those of calves castrated using rubber rings. 22 Stafford⁵⁴ observed similar overall cortisol responses for elastrator band, rubber ring, and surgical castration, but lower cortisol responses for castration using a Burdizzo clamp. Pieler et al. found that Burdizzo castration, surgical castration and partial scrotal resection do not cause significantly different levels of stress when the animal is administered xylazine and local anesthesia.⁵⁶

Placement of elastrator bands/rings without prior anesthesia produced a slightly lower cortisol increase than surgical castration.¹⁴ Immunocastration resulted in only transient increases in cortisol concentration, likely due to stress induced by handling and injection.³

Age of the animal at time of castration may affect the severity of the cortisol response. Plasma cortisol levels of calves castrated at less than one week of age did not differ significantly from those of uncastrated controls using elastrator bands,³⁴ although another study using a Burdizzo clamp did show behavioral and cortisol responses indicating pain and these were reduced with the use of a local anesthetic.⁵⁷ Following castration by surgical, Burdizzo clamp, or rubber ring methods, post-castration cortisol concentrations returned to baseline values more quickly in 6- and 21-day-old calves than in 42-day-old calves.²⁴ Use of a Burdizzo clamp or surgical castration produced a minimal response in 11-week-old calves, but a more profound response in 24-week-old calves.⁵⁸ Cortisol responses of 1.5-month-old and 4.5-month-old calves castrated using a Burdizzo clamp were approximately one-half and one-third, respectively, of the cortisol responses of 5.5-month-old calves castrated using the same method.⁵²

ANESTHESIA AND ANALGESIA

Local anesthetics—Application of local anesthesia prior to castration is mandated in some countries, and significantly reduces the cortisol response to castration. ^{13,25,54,57} Administration of lidocaine into the testicular parenchyma and distal scrotum virtually abolished the cortisol response to castration when elastrator bands or rubber rings were used on 3-month-old calves.⁵⁴ Serum cortisol concentrations returned to baseline values within one hour of castration, and remained at those levels for the remainder of the 72-hour sampling period following lidocaine injection into the spermatic cords and scrotal neck.²⁵ Local anesthesia had less effect on cortisol concentration when Burdizzo clamps were used, and a minimal effect with surgical castration.⁵⁴ In several studies, local anesthesia with lidocaine^{25,57} or bupivacaine⁵⁷ significantly attenuated the increase in plasma cortisol concentration after Burdizzo clamp castration. Lidocaine administered locally with flunixin meglumine may also be an effective method of analgesia and of cortisol tempering.⁵⁹ Lidocaine injected into the scrotal neck almost abolished the cortisol response to a combined clamp-ring castration approach in lambs, and injection into the spermatic cord reduced cortisol responses by 45% compared with animals castrated without local anesthesia.¹³ Similar results were obtained when lidocaine was administered before rubber ring placement in lambs, but no beneficial effects were observed from administration of local anesthesia prior to castration using a Burdizzo clamp. ^{13,54} Suppression of the cortisol increase by local anesthetics is short-lived, and cortisol concentrations increase once the pharmacologic effects of the anesthetic agent have ceased.^{3,6,21} Administration of local anesthetic prior to surgical castration of 5.5-month-old calves resulted in improved ADG for the first week after surgery as compared with surgery alone, suggesting a longer duration of benefit.³

Epidurals— Epidural anesthesia or local anesthesia (with lidocaine) prior to castration using a Burdizzo clamp did not significantly reduce the integrated (area under the curve) cortisol response in 13-month-old bull calves compared with use of the Burdizzo clamp alone. Although peak cortisol response was reduced approximately 30% by administration of an epidural, suppression was only observed for the one-hour duration of effect for the epidural. Xylazine epidurals combined with intravenous flunixin meglumine produced no significant differences in animal health or feedlot performance compared to animals that did not receive anesthesia/analgesia. 16,26

Sedation—Intravenous xylazine, alone or with ketamine, has been shown to reduce behavioral indications of distress and serum cortisol concentrations immediately after castration.⁶⁰ The addition of

ketamine to more traditional chemical restraint formulas ("ketamine stun") can increase patient cooperation, and has been shown to lower stress response to both dehorning and castration in calves. 61

Analgesia— Administration of NSAIDs results in prolonged postoperative analgesia. 62 Administration of ketoprofen, either alone or in conjunction with local anesthetic, significantly reduced the cortisol response associated with castration. ^{6,21,54} Cortisol responses of 22-week-old calves to which ketoprofen was administered prior to castration were similar to those of uncastrated controls, and the calves exhibited comparable growth rates for at least 7 days following castration.⁶ Administration of ketoprofen also reduced the postoperative rise in plasma fibrinogen concentrations; this increase was not attenuated by administration of local anesthetic alone. The combination of local anesthesia and preoperative ketoprofen virtually eliminated the cortisol response to castration in 3-month-old calves, regardless of method used.³⁵ Ketoprofen administered to 13-month-old bull calves reduced cortisol response by 52% compared with cattle to which local anesthesia was administered prior to castration, and by 58% compared with cattle to which epidural anesthesia was administered prior to castration.²¹ Calves to which ketoprofen was administered prior to castration exhibited increased feeding and rumination activities and fewer pain-associated behavioral responses than those castrated without ketoprofen.²¹ Intramuscular ketoprofen alone has not been shown to significantly limit post-castration pain. 63 Intravenous nalbuphine may reduce pain-related behaviors but does not significantly reduce physiologic signs of distress following castration.⁶⁴ Sodium salicylate administered either alone or in conjunction with sedation (intramuscular xylazine, ketamine, butorphanol - XKB), also significantly reduced the cortisol response associated with simultaneous castration and dehorning. ⁶⁵ In addition, sodium salicylate reduced the decrease in ADG from simultaneous castration and dehorning. 65 Sodium salicylate is also observed to increase the time animals spend lying down post-castration when administered with XKB.66 Administration of meloxicam prior to castration reduced the decrease in ADG in the first two weeks following castration.⁶⁷ Other studies have shown meloxicam to reduce but not eliminate pain-related behaviors following castration. Those same studies noted no significant effect on performance after castration when comparing calves treated with meloxicam to the control group. 68,69,70,71 Meloxicam also reduced the number of animals requiring treatment for bovine respiratory disease following castration.⁶⁷

Access—Obstacles to the provision of pain relief to cattle include limited availability of some pharmaceuticals and costs associated with their use. 72,73 The only NSAID approved for use in cattle in the United States is flunixin meglumine, and its approval is for control of fever associated with respiratory disease or mastitis, and fever and inflammation associated with endotoxemia, rather than for control of pain. Extralabel drug use in the United States is only permitted under certain conditions, among which is that the animal must undergo a prescribed meat and/or milk withdrawal period afterwards. ⁷⁴ Use of flunixin meglumine is complicated by its intravenous route of administration (significant tissue reactions have occurred after intramuscular administration). It would be useful to determine whether flunixin meglumine is an acceptable substitute for ketoprofen, or that ketoprofen is preferable and so supported for extra-label use under the Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA). Ketoprofen has a short half-life and a withdrawal time of 7 days is recommended.⁷⁵ Recently one author demonstrated that flunixin meglumine in combination with caudal epidural anesthesia appeared to improve stride length and visual pain assessment in calves.⁵ Improving the availability of approved, easily administered NSAIDs in the United States is necessary for safe and uniform use. 60,76 Many currently available research metrics and tools could be utilized to test anesthetics and analgesics for approval in the United States. 77 Little research has been done to show that pain management significantly increases production outcomes, furthermore, most of the studies in this area have been too short to adequately assess this.⁷⁸ Use of pharmaceuticals, which may be accompanied by a need for additional veterinary assistance, adds to production costs⁷⁸; however, research conducted in New Zealand suggests the associated increase is small in relation to overall farm costs. 44 A review of

pain assessment and pharmacological approaches to pain relief after castration suggests that the use of multimodal analgesic regimens (e.g., NSAID and a local anesthetic) are more effective at mitigating pain and distress associated with castration than using one modality on its own.⁷⁸

SUMMARY

Castration is considered to be a necessary management practice for cattle. Although younger cattle exhibit less pain, stress, and distress in response to the procedure, all methods of castration induce pain and physiologic stress in animals of all ages. Pain and physiologic stress resulting from castration should be minimized to provide for the overall welfare of the animal. Although obstacles to immediate implementation exist, research results suggest that application of local anesthesia and the administration of analgesics have the potential to minimize or eliminate pain and stress associated with castration.

REFERENCES

- ^{1.} Kent JE, Thrusfield MV, Robertson IS, et al. Castration of calves: a study of methods used by farmers in the United Kingdom. *Vet Rec* 1996;138:384-387.
- ² Stafford KJ. Alleviating the pain caused by the castration of cattle. Vet J 2007;173:333-342.
- ^{3.} Fisher AD, Crowe MA, Alonso de la Varga ME, et al. Effect of castration method and the provision of local anesthesia on plasma cortisol, scrotal circumference, growth, and feed intake of bull calves. *J Anim Sci* 1996;74:2336-2343.
- ⁴ Stafford KJ, Mellor DJ. The welfare significance of the castration of cattle: a review. NZ Vet J 2005;53:271-278.
- ^{5.} Currah, JM, Hendrick SH, and Stookey JM. The behavioral assessment and alleviation of pain associated with castration in beef calves treated with flunixin meglumine and caudal lidocaine epidural anesthesia with epinephrine. *Can Vet Journ* 2009: 50:375-382.
- ^{6.} Earley B, Crowe MA. Effects of ketoprofen alone or in combination with local anesthesia during the castration of bull calves on plasma cortisol, immunological, and inflammatory responses. *J Anim Sci* 2002;80:1044-1052.
- ^{7.} Fisher AD, Knight TW, Cosgrove GP, et al. Effects of surgical or banding castration on stress responses and behaviour of bulls. *Aust Vet J* 2001;79:279-284.
- 8. Important Farm Techniques and Management Procedures. Available at: http://www.fao.org/ag/AGP/AGPC/doc/publicat/PUB6/P609.htm Accessed October 9, 2006
- ^{9.} Faulkner PM, Eurell T, Tranquili WJ, et al. Performance and health of weanling bulls after butorphanol and xylazine administration at castration. *J Anim Sci* 1992;70:2970-2974.
- ^{10.} Coetzee JF, Nutsch AL, Barbur LA and Bradburn RM. A survey of castration metholds and associated livestock management practices performed by bovine veterinarians in the United States. *BMC Vet Res* 2010;6:12.
- ^{11.} Fajt VR, Wagner SA, and Norby B. Analgesic drug administration and attitudes about analgesia in cattle among bovine practitioners in the United States. *JAVMA* 2011;238(6):755-767.
- ¹² Stilwell G, Lima, MS, and Broom DM. Effects of nonsteroidal anti-inflammatory drugs on long-term pain in calves castrated by use of an external clamping technique following epidural anesthesia. *Amer Journ Vet Res* 2008:69(6):744-750.
- ^{13.} Dinniss AS, Mellor DJ, Stafford KJ, et al. Acute cortisol responses of lambs to castration using a rubber ring and/or a castration clamp with or without local anaesthetic. NZ Vet J 1997;45:114-121.
- ^{14.} Mellor DJ, Stafford KJ, Todd SE, et al. A comparison of catecholamine and cortisol responses of young lambs and calves to painful husbandry procedures. *Aust Vet J* 2002;80:228-233.
- ¹⁵. Becker J, Doherr MG, Bruckmaier RM et al. Acute and chronic pain in calves after different methods of rubber-ring castration. The Veterinary Journal 2012;194:380-385.
- ^{16.} Fordyce G, Hodge PB, Beaman NJ, et al. An evaluation of calf castration by intra-testicular injection of a lactic acid solution. *Aust Vet J* 1989;66:272-276.
- ^{17.} Fisher AD, Crowe MA, Alonso de la Varga ME, et al. Effect of castration method and the provision of local anesthesia on plasma cortisol, scrotal circumference, growth, and feed intake of bull calves. *J Anim Sci* 1996;74:2336-2343.
- ^{18.} Amatayakul-Chantler S, Hoe F, Jackson JA et al. Effects on performance and carcass and meat quality attributes following immunocastration with the gonadotropin releasing factor vaccine Bopriva or surgical castration of Bos indicus bulls raised on pasture in Brazil. Meat Science 2013;95:78-84.
- ^{19.} Molony V, Kent JE, Robertson IS. Assessment of acute and chronic pain after different methods of castration of calves. *App An Beh Sci* 1995;46:33-48.
- ^{20.} Fordyce G, Hodge PB, Beaman NJ, et al. An evaluation of calf castration by intra-testicular injection of a lactic acid solution. *Aust Vet J* 1989;66:272-276.
- ^{21.} Ting STL, Earley B, Hughes JML, et al. Effect of ketoprofen, lidocaine local anesthesia, and combined xylazine and lidocaine caudal epidural anesthesia during castration of beef cattle on stress responses, immunity, growth, and behavior. *J Anim Sci* 2003;81:1281-1293.
- ^{22.} Fell LR, Wells R, Shutt DA. Stress in calves castrated surgically or by the application of rubber rings. *Aust Vet J* 1986;63:16-18.

- ^{23.} Fisher AD, Crowe MA, O'Nuallain EM, et al. Effects of cortisol on in vitro interferon-γ production, acute-phase proteins, growth, and feed intake in a calf castration model. *J Anim Sci* 1997;75:1041-1047.
- ^{24.} Robertson IS, Kent JE, Molony V. Effect of different methods of castration on behaviour and plasma cortisol in calves of three ages. Res Vet Sci 1994;56:8-17.
- ^{25.} Thuer S, Mellema S, Doherr MG, et al. Effect of local anaesthesia on short- and long-term pain induced by two bloodless castration methods in calves. *Vet J* 2007;173:333-342
- ^{26.} Gonzalez LA, Schwartkopf-Genswein KS, Caulkett NA et al. Pain mitigation after band castration of beef calves and its effects on performance, behavior, Escherichia coli, and salivary cortisol. J Anim Sci 2010;88:802-810.
- ^{27.} Sutherland MA, Ballou MA, Davis BL et al. Effect of castration and dehorning singularly or combined on the behavior and physiology of Holstein calves. Journal of Animal Science 2013;91:935-942.
- ^{28.} Pang W, Earley B, Sweeney T et al. Temporal patterns of inflammatory gene expression in local tissues after banding or burdizzo castration in cattle. *BMC Vet Res* 2009;5:36.
- ^{29.} Kumar V, Abbas AK, Fausto N. Cellular adaptations, cell injury, and cell death. In: Kumar V, Abbas AK, Fausto N. Robbins and Cotran Pathologic Basis of Disease. 7th ed. Philadelphia: Elsevier, 2005;3-46.
- ^{30.} Mitchell RN. Hemodynamic disorders, thromboembolic disease, and shock. In: Robbins and Cotran Pathologic Basis of Disease. 7th ed. Philadelphia: Elsevier, 2005;119-144.
- ^{31.} Peers A, Mellor DJ, Wintour EM, et al. Blood pressure, heart rate, hormonal and other acute responses to rubber-ring castration and tail docking of lambs. NZ Vet J 2002;50:56-62.
- ^{32.} Mellor DJ. Effects of castration on behaviour and plasma cortisol concentrations in young lambs, kids, and calves. *Res Vet Sci* 1991;51:149-154.
- ³³. Warnock TM, Thrift TA, Irsik M et al. Effect of castration on beef calf performance, feed efficiency, and inflammatory response. Journal of Animal Science 2012;90:2345-2352.
- ^{34.} Dockweiler JC, Coetzee JF, Edwards-Callaway LN et al. Effect of castration method on neurohormonal and electroencephalographic stress indicators in Holstein calves of different ages. Journal of Dairy Science 2013;96:4340-4354.
- ^{35.} Coetzee JF, Lubbers BV, Toerber, SE, Gehring R, Thomson DU, White BJ, and Apley MD. Plasma concentrations of substance P and cortisol in beef calves after castration or simulated castration. *Amer Journ Vet Res.* 2008:69(6):751-762.
- ^{36.} US FDA, Center for Veterinary Medicine. Guideline No. 123. Development of target animal safety and effectiveness data to support approval of no-steroidal anti-inflammatory drugs (NSAID's) for use in animals. Available at

http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm052663.pdf. Accessed Jun 23, 2009.

- 37. Stafford KJ, Mellor DJ, McMeekan CM. A survey of the methods used by farmers to castrate calves in New Zealand. NZ Vet J 2000;48:16-19.
- 38. Murata H. Effects of Burdizzo castration on peripheral blood lymphocyte parameters in calves. Vet J 1997;153:229-231.
- ³⁹. Ballou MA, Sutherland MA, Brooks TA et al. Administration of anesthetic and analgesic prevent the suppression of many leukocyte responses following surgical castration and physical dehorning. Veterinary Immunology and Immunopathology 2013;151:285-293.
- ⁴⁰ Marti S, Velarde A, de la Torre JL, Bach A et al. Effects of ring castration with local anesthesia and analgesia in Holstein calves at 3 months of age on welfare indicators. *J Anim Sci* 2010;88:2789-2796.
- 41. Magrath LA, Magrath JM. Tetanus in calves from elastration. J Am Vet Med Assoc 1954;125:451.
- 42 La Fontaine D. Dehorning and castration of calves under six months of age. Agnote, Australia. Available at: <a href="https://transact.nt.gov.au/ebiz/dbird/TechPublications.nsf/C5AF1480C26CC23269256EFE004F648E/\$file/804.pdf?OpenElement#search=%22Dehorning%20and%20castration%20of%20calves%20under%20six%20months%20of%20age%22Accessed October 9, 2006.
- 43. Chase CC, Larsen RE, Randel RD, et al. Plasma cortisol and white blood cell responses in different breeds of bulls: a comparison of two methods of castration. *J Anim Sci* 1995;73:975-980.
- 44. Stafford KJ, Mellor DJ, Dooley AE et al. The cost of alleviating the pain caused by the castration of beef calves. *Proc N.Z. Soc Anim Prod.* 2005;65.
- 45. Griffin D, Perino LJ. Banding and surgical castration techniques influence on average daily gain and feed intake of yearling feedlot bulls. Pers. com.
- 46. Kreikemeier KK, Stokka GL, Blasi DA et al. A Comparison of Surgical vs Banding Castration Methods in Nonstressed Stockers. Kansas State University, Cattle Feeder's Day 1995 Available at:
- http://www.beefstockerusa.org/research/kansas/ComparisonSurgical.pdf Accessed September 6, 2007
- ⁴⁷. Booker, CW, Abutarbush SM, Schunict OC, et al. Effect of castration timing, technique, and pain management on health and performance of young feedlot bulls in Alberta. *Bovine Practitioner* 2009: 43:1-11.
- 48. Berry BA, Choat WT, Gill DR. Effect of castration on health and performance of newly received stressed feedlot calves. 2001 Animal Science Research Report Beef and Dairy Cattle, Swine, Poultry, Sheep, Horses and Animal Products August 2001, Publication: P986, Oklahoma Agricultural Experiment Station, Divison of Agricultural Science and Natural Resources, Oklahoma State University. Available at: http://www.ansi.okstate.edu/research/research-reports-1/2001/2001%20Berry%20Research%20Report.pdf Accessed November 24, 2015.

- ^{49.} Heaton K, ZoBell DR, Cornforth D. Effects of delayed castration of British cross-bred cattle on weight gain, carcass traits, and consumer acceptability. Proceedings, Western Section, American Society of Animal Science, Vol 55. 2004.
- ^{50.} Massey C, Dhuyvetter KC, Llewelyn et al. Castration and morbidity and their effects on performance, carcass quality, and price differentials for bulls and steers. The Professional Animal Scientist 2011;27:19-28.
- ^{51.} Wagner S. Pain control in food animals. Available at:
- http://www.michvma.org/documents/MVC%20Proceedings/Wagner2.pdf Accessed September 10, 2007.
- ⁵² Ting STL, Earley B, Veissier I, et al. Effects of age of Holstein-Friesian calves on plasma cortisol, acute-phase proteins, immunological function, scrotal measurements and growth in response to Burdizzo castration. *An Sci* 2005;80:377-386.
- ^{53.} Pieler D, Wohlsein P, Peinhopf W et al. Endocrine testicular function and spermatogenesis persist in calves after partial scrotal resection but not Burdizzo castration. Theriogenology 2014;81:1300-1306.
- ^{54.} Stafford KJ, Mellor DJ, Todd SE, et al. Effects of local anaesthesia or local anaesthesia plus a non-steroidal antiinflammatory drug on the acute cortisol response of calves to five different methods of castration. Res Vet Sci 2002;73:61-70.
- ^{55.} Obritzhauser W, Deutz A, Kofer J. [Comparison of two castration methods in cattle: plasma cortisol levels, leukocyte count and behavioral changes] *Tierarztl Prax Ausg G Grosstiere Nutztiere* 1998;26:119-126.
- ⁵⁶. Pieler D, Peinhopf W, Becher AC et al. Physiological and behavioral stress parameters in calves in response to partial scrotal resection, orchidectomy, and Burdizzo castration. Journal of Dairy Science 2013;96:6378-6389.
- ^{57.} Boesch D, Steiner A, Gygax L et al. Burdizzo castration of calves less than 1-week old with and without local anesthesia: short-term behavioural responses and plasma cortisol levels. *Appl Anim Behv Sci* in press.
- ^{58.} King BD, Cohen RDH, Guenther CL, et al. The effects of age and method of castration on plasma cortisol in beef calves. *Can J Anim Sci* 1991;71:257-263.
- ^{59.} Webster HB, Morin D, Jarrell V et al. Effects of local anesthesia and flunixin meglumine on the acute cortisol response, behavior, and performance of young dairy calves undergoing surgical castration. Journal of Dairy Science 2013;96:6285-6300.
- ^{60.} Coetzee JF, Gehring R, Tarus-Sanf J, Anderson DE. Effect of sub-anesthetic xylazine and ketamine ('ketamine stun') administered to calves immediately prior to castration. *Veterinary Anaesthesia and Analgesia* 2010;37:566-578.
- ⁶¹ Abrahamsen EJ. Chemical restraint and injectable anesthesia of ruminants. Veterinary Clinics of North America: Food Animal Practice 2013;29:209-227.
- 62. Anderson DE, Muir WW. Pain management in ruminants. Vet Clin Food Anim 2005;21:19-31.
- ^{63.} Moya D, Gonzales LA, Janzen E et al. Effects of castration and frequency of intramuscular injections of ketoprofen on behavioral and physiological indicators of pain in beef cattle. Journal of Animal Science 2014;92:1684-1695.
- ^{64.} Coetzee JF, Lechtenberg KF, Stock ML et al. Pharmacokinetics and effect of intravenous nalbuphine in weaned Holstein calves after surgical castration. Journal of Veterinary Pharmacology and Therapeutics 2013;37:169-177.
- ⁶⁵. Baldridge SL, Coetzee JF, Dritz SS et al. Pharmacokinetics and physiologic effects of intramuscularly administered xylazine hydrochloride-ketamine hydrochloride-butoprphanol tartrate alone or in combination with orally administered sodium salicylate on biomarkers of pain in Holstein calves following castration and dehorning. *AJVR*. 2011;72(10):1305-1317.
- ^{66.} Pauly C, White BJ, Coetzee JF et al. Evaluation of analgesic protocol effect on calf behavior after concurrent castration and dehorning. International Journal of Applied Research in Veterinary Medicine 2012;10:54-61.
- ^{67.} Coetzee JF, Edwards LN, Mosher RA et al. Effect of oral meloxicam on health and performance of beef steers relative to bulls castrated on arrival at the feedlot. *J Anim Sci.* 2012;90:1026-1039.
- ⁶⁸ Daniel JA, Krawczel PD, Whitlock BK et al. Effect of meloxicam on gain and behavior of calves castrated by banding preweaning. ADSA-ASAS Joint Annual Meeting. Indianapolis, IN. Jul. 2013. Available at: http://works.bepress.com/brian whitlock/47
- ⁶⁹ Krawczel PD, Carroll JA, Burdick Sanchez NC et al. Meloxicam mediates short-term behavioral changes of castrated calves. ADSA-ASAS Joint Annual Meeting. Indianapolis, IN. Jul. 2013. Available at: http://works.bepress.com/brian_whitlock/48
- ^{70.} Whitlock BK, Krawczel PD, Carroll JA et al. Effect of meloxicam on gain and inflammatory response of calves castrated by banding post-weaning. ADSA-ASAS Joint Annual Meeting. Indianapolis, IN. Jul. 2013. Available at: http://works.bepress.com/brian_whitlock/46
- 71. Repenning PE, Ahola JK, Callan RJ et al. Impact of oral meloxicam administration before and after band castration on feedlot performance and behavioral response in weanling beef bulls. Journal of Animal Science 2013;91:4965-4974.
- 72. Wagner S. Pain control in food animals. Available at:
- http://www.michyma.org/documents/MVC%20Proceedings/Wagner2.pdf Accessed September 10, 2007.
- ^{73.} Watts JM. The welfare of cattle: review of recent literature. Available at: http://www.prairieswine.usask.ca/pdf/welfare/cattle.pdf Accessed July 10, 2005.
- ^{74.} Smith G. Extralabel use of anesthetic and analgesic compounds in cattle. Veterinary Clinics of North America: Food Animal Practice 2013;29:29-45.
- ^{75.} George LW. Pain control in Food animals In: Recent Advances in Anesthetic Management of Large Domestic Animals. Steffey EP (Ed.) International Veterinary Information Service: Ithaca NY.
- ^{76.} Gehring R, Baynes RE, Riviere, E. Application of risk assessment and management principles to the extralabel use of drugs in food-producing animals. *J Vet Pharm Ther* 2006;29:5-14.

^{77.} Coetzee JF. Assessment and management of pain associated with castration in cattle. Veterinary Clinics of North America: Food Animal Practice 2013;29:75-101.

^{78.} Coetzee JF. A review of pain assessment techniques and pharmacological approaches to pain relief after bovine castration: practical implications for cattle production within the United State. *Appl. Anim Behav Sci.* 2011;135(3):192-213.