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Review of literature on the relief of pain in livestock undergoing husbandry procedures

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Abstract

The objective of this project was to review the current scientific knowledge and literature regarding the relief of pain in livestock undergoing husbandry procedures. A large range of husbandry procedures and recommendations for pain relief are addressed. Pain is a complex phenomenon involving pathophysiological and psychological components that are frequently difficult to recognise and interpret in animals. Pain is an aversive sensory and emotional experience associated with an awareness of damage or threat to the integrity of the animal's tissues, normally changing its physiology and behaviour to reduce or avoid damage, reducing the likelihood of recurrence and promoting recovery. In the scientific assessment of pain the optimum approach is to select multiple independent measurements. The options include the hypothalamic-pituitary-adrenal axis (cortisol response in most cases), behaviour, immune responsiveness, health and performance.

Pain management aims to alleviate the pain and inflammatory responses following tissue trauma, to improve the animal's ability to cope with the trauma; and to improve wound healing and help regain normal bodily functions. The absence of pain in the presence of stimuli that would normally be painful is termed "analgesia". "Anaesthesia" is a term that refers to the loss of sensation, and anaesthetic substances operate by either blocking the nociceptive activity from reaching the brain (e.g., local anaesthesia), or preventing the brain from registering sensations (e.g., general anaesthesia). Analgesic / anaesthetic drugs are usually from the following classes of drugs: opioids; non-steroidal anti-inflammatory drugs (NSAIDs); α_2-adrenergic agonists; local anaesthetics; and miscellaneous drugs – e.g., glutamate system antagonists (ketamine). In practice the most useful of these for application to the relief of pain during husbandry procedures include NSAIDs and local anaesthetics, due to their modes of action, administration methods and degree of efficacy.

Routine husbandry procedures in cattle and sheep production include castration, dehorning and spaying in cattle, and castration and tail-docking in sheep. In relation to castration in sheep, rubber rings are the preferred method used by Australian producers (45% of sheep producers). Improvements in pain relief and wellbeing can be achieved by combining rubber ring and clamp castration. Similarly for tail docking, significant improvements in pain relief may be achieved by combining rubber rings with the use of a clamp device. Pain may also be reduced by the use of NSAIDs as analgesic agents during castration and tail-docking. However, there are no NSAIDs registered for use in sheep. In cattle, horn removal is achieved by various methods. Pre-emptive use of NSAIDs is effective at reducing pain but further work is required to optimise the timing of such treatments. For castration of cattle, either closed (burdizzo or rubber ring methods) or open (surgical) approaches are used. Pain relief can be achieved by local anaesthesia (LA), or NSAIDs which have greater effectiveness than the use of LA. Combinations of LA and NSAIDs have shown increased effectiveness of pain relief for many of these procedures. However the need for pre-emptive treatments with NSAIDs up to 20 minutes before the procedure can limit their practical application. Where ovariectomy of heifers is necessary as the only method to control unwanted pregnancies in extensive "range" type beef production, then steps to control mortality due to haemorrhage, and efforts to reduce the associated pain should be used. Immuno-castration as an alternative strategy to spaying and castration in cattle has been developed, but it has practical difficulties that limit its commercial uptake. These difficulties revolve around variability in immune responses and therefore biological efficacy.

Executive summary

The objective of this project was to review the current scientific knowledge and literature to provide sound data on which to base choices in drug selection and patterns of use in husbandry and in future research into alleviating pain associated with husbandry procedures. A large range of husbandry procedures and recommendations for pain relief are addressed. Pain is a complex phenomenon involving pathophysiological and psychological components that are frequently difficult to recognise and interpret in animals. Pain assessment in farm animals can only be inferred indirectly from measurement of changes in behaviour and physiological functions in response to pain (Rutherford, 2002). These changes reflect the degree of noxiousness of the tissue damaging procedure and give an indication of the animal's attempts at coping with the pain. In the scientific assessment of pain relief the optimum approach is to select multiple (probably at least 3) independent measurements such as:

- the HPA axis, ie cortisol which is generally a good indicator, but suffers the limitation that it can reach a maximum (or ceiling-effect) which may interfer in its value as an index of pain (especially during the peak in secretion);
- behavioural responses, although care must be taken in regard to which behaviours are selected and how they may be accumulated into an index or score as well as experience of the observer;
- immune responsiveness, the options here include suppression in lymphocyte blastogenic responses, suppression of in-vitro culture responsiveness of lymphocytes to secrete IFN-γ in response to stimulation by a novel mitogen or recall antigen, or suppression of immune response to a novel antigen or vaccine;
- health and performance.

Generally it can be concluded that pain is perceived when these indicators are altered simultaneously.

The objectives of pain management are: 1) to alleviate the pain and inflammatory responses elicited following tissue trauma from potentially causing overt physiological reactions and psychological distress to the animal; 2) to improve the animal's ability to cope with the trauma; and 3) to improve wound healing and aid the animal to regain normal bodily functions more rapidly. The absence of pain in the presence of stimuli that would normally be painful is termed "analgesia" (Shafford et al., 2001), and analgesics are substances, which induce analgesia (Nolan, 2000). "Anaesthesia" is a term that refers to the loss of sensation, and anaesthetic substances operate by either blocking the nociceptive activity from reaching the brain (e.g., local anaesthesia), or preventing the brain from registering sensations (e.g., general anaesthesia) (Nolan, 2000; Dobromylskyj et al., 2000). Anaesthesia does not necessarily equate with analgesia.

Pain treatment can be directed at the periphery, at sensory axons, or at central neurons (Otto and Short, 1998). Analgesic / anaesthetic drugs may be divided into the following main classes:
(1) Opioids;
(2) non-steroidal anti-inflammatory drugs (NSAIDs);
(3) α_2-adrenergic agonists;
(4) local anaesthetics;
(5) Miscellaneous drugs – e.g., glutamate system antagonists (ketamine).

The most useful of these for application to the relief of pain during husbandry procedures include NSAIDs and local anaesthetics. Typically local anaesthesia requires treatment 5 – 10 minutes before the procedure, while pre-emptive use of NSAIDs as analgesic agents are thought to require 15 to 20 min before they are effective. This time requirement restricts the practical widespread usage of these agents. Further research could focus on combining the use of these drugs and determining if effective analgesia can be obtained by reducing the pre-treatment time-lag required for analgesia.

The legal requirement for the use of pain relief during husbandry procedures varies considerably between different countries depending on the method involved and the age of animals. However, the precise scientific basis for setting the requirements are unclear, but it may in part be due to public or consumer-driven demand for improved farm animal welfare by reducing the pain caused by routine husbandry procedures such as castration. For example, in Ireland use of anaesthesia is required for surgical/Burdizzo castration of cattle over six months of age. In contrast, castration of calves without use of anaesthesia must be done before they reach two months of age in the UK. Also in Ireland and the UK, rubber ring castration (or use of other devices for constricting the flow of blood to the scrotum) without use of anaesthesia can only be performed in calves less than seven days of age. In New Zealand, cattle should be castrated as young as possible, but when carried out on animals over six months of age pain relief must be used. Furthermore, if the technique of tightened latex bands (banding) is used then pain relief must be provided irrespective of age. In Germany, castration of cattle without use of anaesthesia is allowed only in animals less than four weeks of age. While in Switzerland, castration of male cattle has been prohibited without anaesthesia since September 2001. Furthermore, the use of elastic rings for castration of animals is forbidden in Germany and Switzerland. By contrast, there is no legal requirement for the use of anaesthesia for castration in the US (Capucille et al., 2002). In Australia, the model code of practice for the welfare of animals requires that castration of cattle without the use of local or general anaesthesia should be confined to calves at their first muster prior to weaning and preferably to calves under the age of six months, and only in exceptional circumstances should castration be left to greater than 6 months of age. At this point it is preferable if the procedure is performed by a veterinarian. It is recommended that castration in calves by rubber rings be restricted to those less than 2 weeks of age, and use of the burdizzo method should be performed on bulls as young as possible. In all of the countries mentioned above, where the administration of anaesthesia is required for castration, the procedure must be done either by a veterinarian or under veterinary supervision. In the case of cattle dehorning, the Australian code of practice is similar to that of castration. Dehorning without local anaesthetics should be confined to animals at the first muster and preferable under 6 months of age. In older cattle tipping (removal of horn tips without cutting into sensitive tissues) is permitted without anaesthesia. Dehorning of calves is recommended by either scoop dehorners, gouging knife or heat cautery as soon as the horn buds are detectable. In sheep tail docking up to 6 months of age is permitted without anaesthesia, and is preferably conducted between 2 and 12 weeks of age. Castration of sheep, when required, is preferably conducted before 12 weeks of age, and again beyond 6 months of age anaesthesia is recommended.

In relation to castration in sheep, rubber rings are the preferred method used by Australian producers (45% of sheep farmers). Research indicates that improvements in pain relief and therefore wellbeing can be achieved by combining rubber ring and clamp castration. Combined rubber ring and clamp castration appears more effective at moderating the cortisol response following castration of lambs than the use of local anaesthesia where cortisol usually rebounds once the anaesthesia effects subside.

Similarly for tail docking in sheep significant improvements in terms of reduced pain may be achieved by combining rubber rings with the use of a clamp device. Data also suggest that pain may be reduced by the use of non-steroidal anti-inflammatory drugs (NSAID's) as analgesic agents during castration and tail-docking. However, further work is required to evaluate all options fully, address practicalities of use for industry and lead to product registration of appropropriate NSAIDs for use in sheep.

In cattle, horn removal may be carried out in young calves by debudding with a scoop or hot cauterization device; and de-horning of older cattle is achieved by sawing, cutting with foetotomy wire or a “crange” device. Pre-emptive use of NSAIDs is effective at reducing pain, more so than local anaesthsia, although further work is required to optimise the timing of such treatments and address practicialities of use by industry.

For castration of cattle either burdizzo (clamp), banding or surgical approaches are the main methods of choice. Reduction in pain can be achieved by use of local anaesthesia, although NSAIDs have proven to have greater effectiveness over a longer period than that achieved by use of local anaesthesia.

Combinations of local anaesthsia and pre-emptive NSAID treatments have shown increased effectiveness of pain relief for many of these procedures. However due to the different rates of action the timing of treatment with local anaesthsia and the NSAID may be different which reduces the practical applications of such approaches.

Where ovariectomy of beef heifers is the only method to control unwanted pregnancies in extensive “range” type beef production then steps to control mortality and efforts to reduce the associated pain (eg use of epidural anaesthesia, intra-peritoneal anaesthesia and / or NSAIDs) should be considered.

While immuno-castration as an alternative strategy to spaying and castration in cattle has been developed, it has been bedeviled with practical difficulties that have limited its commercial uptake. These difficulties revolve around variability in immune responses between individual animals that affects the precise timing of onset of oestrous suppression and return to cyclicity in heifers, and affects the efficacy of castration in bulls. Improved consistency in immune responsiveness following at most 2 immunizations (ie primary and booster) without using potentially toxic adjuvant preparations is required.

In writing this review a number of deficiencies were identified in the relevant literature. These are categorized into those relevant to i) assessment of pain, ii) alleviation of pain, iii) husbandry procedures, and iv) pharmaceutical industry / licensing issues:

i) Pain assessment:

- In the assessment of pain further improvements in the development of objective scoring of behavioural indicators are required (e.g., improved use of VAS scores or other systems of pain scoring).
- The precise role of β-endorphin in modulating the response to pain remains to be elucidated in cattle.

ii) Pain alleviation:

- Despite the beneficial effects of combined rubber ring and clamp castration in lambs, only one study on a similar approach has been reported for cattle. Further attempts to alleviate the pain of castration in cattle by combining rubber ring / banding with burdizzo clamp devices are warranted.
- Studies are required to develop effective anaesthesia and analgesia during spaying of heifers. Possible approaches include epidural anaesthesia, intraperitoneal anaesthesia, pethidine and/or NSAIDs.
- Substantial work on combining analgesic / anaesthesic agents is required to develop better pain alleviation options for many of the procedures that are performed on cattle and sheep.
- Ketoprofen is the most effective NSAID studied to date for alleviation of pain during husbandry procedures in cattle. Further work is required to determine its usefulness for a greater variety of husbandry procedures. However, it is one of the more expensive NSAIDs available, and the effectiveness of alternative NSAIDs also needs to be determined.

- Timing of administration of NSAIDs, particularly when combining their use with local anaesthesia, needs further study to allow development of practical regimes of pain relief that will be easily implemented at farm level, particularly when large numbers of animals are undergoing acute husbandry procedures.
- Work is required to assess the potential of NSAIDs during castration and tail docking in sheep, either on their own or in combinations with local anaesthesia.

iii) Husbandry procedures:

- Studies on the prolonged health status following tail docking of lambs by various procedures are required to determine what, if any, effects on the incidence of joint-ill disease and fly-strike are associated with tail docking by various methods in addition to the acute stress responses.
- Detailed epidemiological studies evaluating health of animals following acute husbandry procedures are also warranted to establish health / morbidity issues.
- Further work is required to look at other amputation dehorning methods and associated pain relief options.
- If chemical castration is to be considered as a serious option in cattle (and sheep) then comprehensive studies looking at the associated pain are required.
- To overcome existing practical difficulties with immunoneutralization approaches to spaying and castration, improvements in achieving a more consistent immune response following at most 2 immunizations (ie primary and booster), without using potentially toxic adjuvant preparations, are required.
- Immunocastration as an option for commercial sheep meat production has not been addressed to any extent. This is an area that has potential.

iv) Pharmaceutical industry / drug licensing:

- The lack of registered NSAIDs for use in sheep needs to be addressed, but in many cases commercial reality may prevent the pharmaceutical industry from following through with registration for this species.
- In all cases where new drugs or new licensing of existing drugs (for pain relief or as an alternative approach to a procedure) are required in animals destined for human consumption due care regarding residues and appropriate withdrawal periods is a necessity.

It is envisaged that a number of benefits from this work should flow to industry, policy makers / legislators, veterinarians and farmers. Regulations and codes of practice that require use of local or general anaesthesia as a means of pain relief should be updated to encourage the use of analgesic agents where they have shown to have increased efficacy at achieving pain relief. Veterinarians need to acknowledge these alternative methods of achieving pain relief for use during many of the necessary husbandry procedures that are carried out. Producers need to be informed that there are alternative and more effective means of achieving pain relief other than just local anaesthesia. Finally, efforts are required by industry to obtain regulatory approval for drugs that lead to improved pain relief in ruminants used in our food industries.

Contents

1. Introduction

Routine husbandry procedures (such as castration: cattle and sheep; dehorning: cattle; and tail-docking: sheep) are carried out in most countries. In some countries spaying (ovariectomy) of beef heifers is carried out as a means of suppression of oestrous behaviour, thus preventing unwanted pregnancies. They are performed to avoid the undesirable consequences of intact bulls or rams being used in meat production (castration), to reduce risk of injury to herd mates and human operatives (castration and dehorning), to prevent unwanted pregnancies (ovariectomy in heifers) and to prevent fly strike in sheep (tail docking). This review sets out to discuss the various options used for these procedures, pain perception and its relief, and possible alternative strategies.

2. Methodology

This review is based on a thorough search of the authors' personal database of papers, a search of Pubmed, CAB and Science Direct using appropriate search terms (e.g., "cattle and castration", "sheep and castration", "cattle and dehorning", "sheep and tail-docking", "sheep and analgesia", "cattle and analgesia"). Additional searching of literature from other species was included when sufficient literature on cattle and sheep proved to be lacking. From the list of unique articles generated, those relevant to the topics of the review were selected. On reading the articles further selections were made and articles ruled out when they proved to be i) irrelevant to the topic, ii) poorly designed (leading to poor or misleading conclusions), or iii) inappropriate at addressing the hypothesis(es) posed. A total of 336 unique, predominantly scientific peer reviewed papers, chapters or technical articles form the basis of the review.

3. Routine husbandry practices in sheep and cattle

3.1. Castration

The necessity for the castration of male cattle intended for beef production varies depending on the management and rearing systems employed by the producers, and the intended beef market supply. While the majority of cattle are fattened as young bulls in mainland Europe, male cattle are predominantly castrated and fattened as steers in the UK, Ireland, Australia and the US (SCAHAW, 2001; NAHMS, 1998). Castration is considered an essential husbandry procedure in order to:
(1) Aid stock control and management on extensive properties.
(2) Reduce sexual and aggressive behaviours.
(3) Minimise risk of physical injury to other animals and the handlers.
(4) Manage genetic selection.
(5) Prevent indiscriminate mating when both sexes are mixed in feedlots or at pasture.
(6) Reduce the incidence of meat quality problems associated with bruised or dark cutting meat.
(7) Satisfy consumer preferences regarding taste and tenderness of meat.
(Robertson, 1966; Price and Tennessen, 1981; Seideman et al., 1982; Kenny and Tarrant, 1984; Tennessen et al., 1985)

However, the practice of castration is recognized as an animal welfare concern in the European Union (SCAHAW, 2001) and in many other countries (Stookey, 1996; AWC, 2002; Capucille et al., 2002). Castration procedures have been shown to elicit varying degrees of distress in several species of production animals, including the pig (Robertson, 1966; McGlone et al., 1993; White et al., 1995; Weary et al., 1998; Taylor and Weary, 2000; Taylor et al., 2001; Lessard et al., 2002; Cronin et al., 2003; Hay et al., 2003), sheep (Robertson, 1966; Cottrell and Molony, 1995; Dinniss et al., 1997a, b; Kent et al., 1998; Mellor and Stafford, 1999; Molony et al., 1993, 1997, 2002; Thornton and Waterman-Pearson, 1999, 2002) and cattle (Robertson, 1966; Zweiacher et al., 1979; Macaulay, 1989; Robertson et al., 1994; Molony et al., 1995; Murata, 1997; Fisher et al., 1996, 1997a,b, 2001; Capucille et al., 2002; Earley and Crowe, 2002). The degrees of stress are depicted by inferences from the severity of the stress (neuroendocrine) response, tissue inflammation and wound healing rate, pain-associated behaviours, suppression of immune function, and acute reduction in growth. The nature and duration of an animal's response to castration are dependent on a number of factors, including the method employed, the age of animals, the post-castration management, and whether or not pain relief is provided with the surgical procedure.

3.2. Castration of cattle

3.2.1. Open castration methods (orchidectomy)

3.2.1.1. Surgical castration

There are two principal surgical techniques for castrating male cattle (Jennings, 1984; Cox, 1987; St. Jean, 1995; Baird and Wolfe, 1999). The first technique involves excision of the distal one-third of the scrotum with a scalpel or sharp castration knife, to expose the testicles by allowing them to descend through the scrotal incision. In the second technique, the lateral scrotal walls are incised with a scalpel or a Newberry knife to expose the testicles. The advantage of using the Newberry knife is that both the lateral walls and the median septum are simultaneously incised, thereby enhancing wound drainage (Figures 1 a and g). Traction is then applied manually to the exposed testes and spermatic vasculature to allow complete removal of the testicles. Manual traction (also called the "surgical pull" method; Stafford et al., 2002) usually provides adequate haemostasis for small calves. However, the application of an emasculator ("surgical cut" method; Stafford et al., 2002) for thirty seconds is recommended. This crushes and cuts the spermatic vessels for all ages and improves haemostasis (Figures 1 b and h). Alternatively, a ligature (e.g., Zweiacher et al., 1979) can be placed proximally around the tunica vaginalis and the spermatic cord is then cut below the ligature. This approach is rare or absent in Australia as this increases the potential for foreign material in the open wound which increases the risk of secondary infection. The wounds are then left to close by second intention healing. Proper surgical hygiene must be observed during the castration procedure to avoid any unnecessary cross-contamination, infection or sepsis. Concurrent clostridial immunisation is recommended. The animals should be observed for haemorrhage in the first 24 hours, and if practicable then allowed unrestricted exercise to reduce oedema (St. Jean, 1995; Baird and Wolfe, 1999). Amputation of the distal one-third of the scrotum is not recommended for castrating calves weighing over 150 kg, as contraction of the tunica dartos following surgery reduces the diameter of the surgical incision with subsequent risk of inadequate wound drainage (Baird and Wolfe, 1999).

3.2.1.2. Russian castration

The Russian castration or Baiburcjan method reported in 1961 involves an almost total expression of the testicular parenchyma from the capsules of both testes through a stab incision made laterally to exclude the blood supply to the testes and epididymis. Spermatogenesis is inhibited, but the outer hormone (testosterone) producing part is left intact (Robertson, 1966; Hardy and Meadowcroft, 1986). Russian castrates showed improved growth rate over steers, but they differed from bulls in that there was absence of agonistic behaviours (Hardy and Meadowcroft, 1986). However, the scarcity of this method in the literature indicates that the method is uncommon, and is presumably related to the impractical complexity and cost of surgery required to perform the castration procedure.

3.2.2. Closed or bloodless castration methods

Several techniques are available for castrating cattle without incision of the scrotum. These "bloodless" techniques induce either: 1) ischaemia of the testicles with subsequent atrophy or necrosis (Baird and Wolfe, 1999), 2) chemical sclerosis of the testicular tissues (Skarda, 1986), or 3) cryptorchidism (Hardy and Meadowcroft, 1986).

3.2.2.1. Emasculatome – Burdizzo castration
A "Burdizzo" emasculatome or clamp is used to crush the spermatic cord, but the blood supply to the scrotum remains preserved. The burdizzo is typically applied once or twice (the second crush is repeated distally with about one cm gap) to each spermatic cord along the neck of the scrotum, where the spermatic cord is pulled to the side of the scrotum to facilitate clamping with the instrument. The jaws of the instrument must remain closed long enough to ensure that both the blood supply and nerves to the testis are irreversibly destroyed (Figures 1 c and i). The application of a single 10 second crush on each spermatic cord has been used in calves up to 42 days of age (Robertson et al., 1994), and two 10 second crushes have been used in 5.5 month old calves (Fisher et al., 1996). The latter is consistent with Muldoon (n.d.) who recommended two 10 second crushes. However, the practice is highly variable among different farmers (Hosie et al., 1996; Kent et al., 1996). Cox (1987) recommended a much longer crushing time of 30 to 60 seconds. With this technique, the testicle is left to atrophy in the scrotum and because of the lack of open wounds, the potential for haemorrhage or infection is minimised. However, crushing of the median raphe of the scrotum must be avoided to prevent the complete occlusion of the blood supply that would lead to necrosis, open wounds or sloughing of the entire scrotum. Animals should receive tetanus prophylaxis (St. Jean, 1995; Kent et al., 1996; Baird and Wolfe, 1999). Burdizzo instruments ranging from 15 cm to 45 cm in length are available for lambs and calves of variable ages.

3.2.2.2. Elastration – Rubber ring castration or banding
This procedure involves the application of a specially designed elastic band (Figures 1 d and e) with the aid of an applicator around the neck of the scrotum, proximal to the testicles. This will cause ischemic necrosis of the testicles, and eventually lead to testicular atrophy and sloughing of the scrotum. Small rubber rings are used for calves less than one month of age and lambs up to 1 week (rubber ring castration), and for older calves heavy wall latex bands are used along with a grommet to securely fasten the mechanically tightened tubing at the appropriate tension (Figures 1 f and j; a technique called "banding"). Tetanus has been reported in banded calves and therefore animals should receive tetanus prophylaxis to minimise the risk (Baird and Wolfe, 1999; Capucille *et al.*, 2002).

3.2.2.3. Chemical castration
This procedure involves injection of a sclerosing agent, lactic acid (Fordyce et al., 1989; 88% w/w; Chem-Cast, Bio-Ceutic Laboratories, Inc., MO, US), directly into the testicles. This leads to the atrophy of the germinal tissues (reviewed in Capucille et al., 2002). The method is claimed to cause less pain and complications than surgical or Burdizzo methods, but is recommended only for calves less than 70 kg (cited in Skarda, 1986). This has been confirmed by Hill et al. (1985) who showed that chemically castrated calves (using Chem-Cast) at 15 d of age (50 kg BW) had significantly lower scrotal oedema scores and a trend toward increased rate of live weight gain at day 28 compared with surgical castration. The overall 196 day rate of live weight gain and weaning weights were not different among the castration methods. However, Fordyce et al. (1989) reported that pain was apparent (based on the degree of struggling and vocalisation) following insertion of the needle and during injection, particularly during injection of the final 25% of the prescribed dose. Twenty five percent of the chemically castrated calves had scrotal necrosis caused by the high pressure of injection and drug leakage from the testes; 18% of the animals were only unilaterally castrated, and the healing time was about twice that of surgical castrates (Fordyce et al., 1989). From a practical perspective the Chem-Cast procedure took 3 times longer than surgical castration (58 sec vs 20 sec; Fordyce et al., 1989). Intra testicular pressure was very large to the point where the authors considered that it would be impossible to inject any more than the prescribed dose (Fordyce et al., 1989). If chemical castration is to be considered as a serious option then comphrensive studies looking at the associated pain are required.

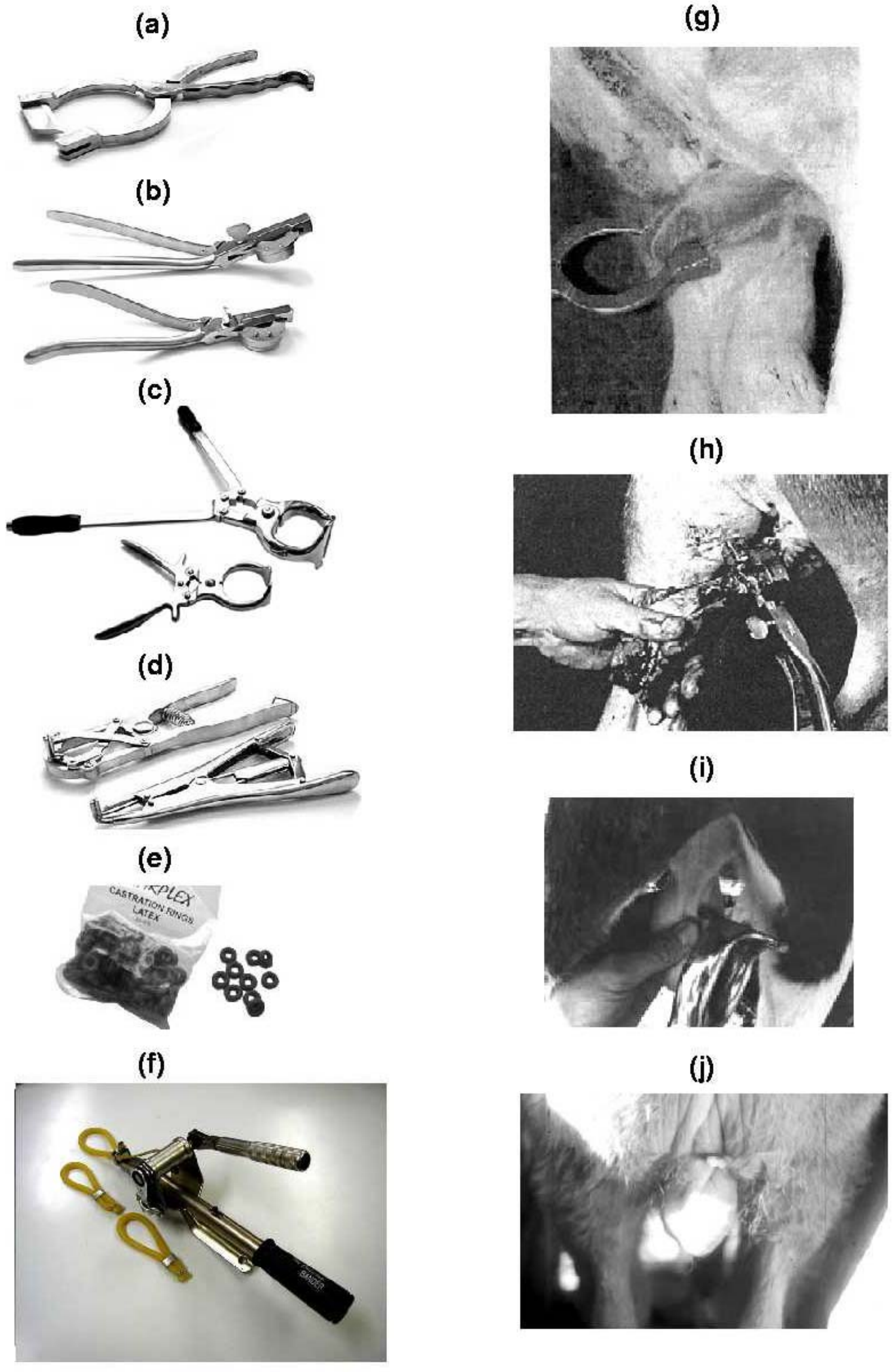

Figure 1 Castration instruments and methods. (a) Newberry knife, (b) emasculator, (c) emasculatome (Burdizzo), (d) rubber ring castrator, (e) latex rings, (f) Callicrate bander, (g) application of a Newberry knife (Baird and Wolfe, 1999), (h) application of an emasculator used to crush and cut the spermatic cord following surgery (St. Jean, 1995), (i) application of a Burdizzo to crush

the spermatic cord but leaving the scrotal skin intact (Seykora, 2000), and (j) application of a latex band with a grommet to fasten the rubber band using the calicrate bander (f) (Lents et al., 2001).

3.2.2.4. Induced cryptorchidism (Short scrotum castration)
Cryptorchidism is a condition in which one or both testicles fail to descend to their normal position in the scrotum (St. Jean, 1995). This condition can be artificially induced by pushing the testes to the top of the scrotum into the inguinal region where they are retained by placing an elastrator ring immediately below the testes (Hardy and Meadowcroft, 1986). Dinniss et al. (1997a) remarked this technique has been mistakenly called "cryptorchidism" instead of "short-scrotum" castration in sheep. Liveweight gain is improved in cryptorchids compared with steers. However, studies showed the cryptorchids to be as restless and aggressive as bulls, but they are almost completely sterile (Hardy and Meadowcroft, 1986).

3.2.3. Effect of age and method at castration
There is a general perception among producers that delaying castration could extend the production advantages of keeping animals as bulls until weaning or beyond puberty (Keane and Drennan, 1998). However, a number of studies have shown that there is no advantage in delaying castration of bulls from birth up to 17 months of age in terms of liveweight, growth rate, or carcass weight at slaughter (Worrell et al., 1987; Bagley et al., 1989; Parrassin et al., 1999; Keane, 1999; Knight et al., 1999a,b). Use of anabolic steroids as growth enhancing implants has been shown to counteract the loss in performance of castrated calves so that growth rate is comparable with that of intact calves (e.g., Baker et al., 2000). However, the use of anabolic agents for beef production is prohibited in some countries (e.g., the European Union since the late 1980s; Directive 88/146/EEC; Keane, 1999).

Keane (1999) reported that Burdizzo castration of spring-born calves in their first autumn (complete castration) at five to six months of age did not significantly affect the overall 347 day liveweight gain compared with: 1) delayed unilateral castration – the right testicle removed in autumn and left testicle the following spring with ~178 days apart, or 2) split castration in spring with about one month interval between removal of each testicle. Furthermore, the author reported no interaction between castration treatment and breed type (Friesian versus Charolais x Friesian). Knight et al. (1999a,b) reported that the age at surgical castration (range: 7 to 15 months versus 17 months) of post-pubertal bulls had no effect on either liveweight or carcass weight when the animals were slaughtered at the same age of 22 months.

Gregory and Ford (1983) showed that castration by surgical or emasculatome method did not differ in terms of their long-term effects (141 days) on the growth rates of 12 month old cattle. In contrast, Fisher et al. (1996) reported that surgical castration of 5.5 month old calves resulted in lower 35 day growth rates compared with Burdizzo castration, and the depressive effect occurred mainly during the first week after castration. However, the animals used in the latter study were maintained in individual tie stalls which may influence their growth compared with animals raised in the feedlot environment in the former study. ZoBell et al. (1993) found no difference between surgical castration and banding on the growth rates of zeranol implanted (Ralgro, Pittman-Moore, Inc., Terre Haute, IN, US) 8 to 9 month-old cattle over 112 days. However, banded animals had higher growth rates during the first 28 days after castration compared with surgical castrates (ZoBell et al., 1993) and the use of zeranol implant likely masked any possible effects of castration. In mature animals, Chase et al. (1995) reported no differences between banding and surgical castration of 20 to 21 month old cattle (395 to 465 kg) in terms of liveweight gain over 35 days compared with intact bulls. By contrast, Knight et al. (2000) reported that bulls castrated by banding or surgery lost their liveweight advantage over steers within 1 to 3 weeks. Fisher et al. (2001) reported that surgical castrates grew faster than banded castrates over a 56 day period and both castration treatments resulted in slower growth rates than intact bulls when the procedures were performed at either 9 or 14 months of age. However, the banding of 14 month old bulls (400 kg) resulted in large open wounds that persisted for several weeks until after the scrota had dropped off, but this did not occur in 8 to 9 month-old bulls. This led the authors to recommend against the use of banding in 14 month old cattle. Mixed results have been reported for animals castrated at younger ages. King et al. (1991) found no effect of either surgical or Burdizzo castration on the liveweight or daily gain of 76 day old calves (118 kg) compared with bulls over a three month period after castration. By contrast, Fenton et al. (1958) found no difference in either surgical, Burdizzo, or elastrator castration procedures in 7 week old (47.6 kg) calves in terms of liveweight gain five weeks after castration, but the control calves had higher gains than castrates. However, the authors reported a significant retardation of growth for the elastrator group on the 28th day after castration due to chronic pain and sepsis (based on visual assessement and palpation of the scrotum) proximal to the ring. This is supported by the findings of Molony et al. (1995) who showed trends for lower 36 day growth rates in rubber ring, and combined rubber ring plus Burdizzo castrated week-old calves compared with intact, surgical or Burdizzo castrated calves. Mullen (1964) reported that the effects of surgical versus Burdizzo castration procedure on growth depended on the initial weight of the calves. Calves castrated by either method between 102 to 152 kg body weight did not differ in weight changes over 24 weeks. In contrast, calves surgically castrated between 76 to 102 kg body weight suffered less severe weight loss than by Burdizzo method (Mullen, 1964). In a study looking at physiological parameters (cortisol), inflammation markers and immune function following burdizzo castration of calves at 1.5, 2.5, 3.5, 4.5, and 5.5 months of age (Ting et al., 2005), it was clearly demonstrated that castration at the older age (5.5 months) induced considerable stress and inflammation. Castration at the younger end of the age spectrum (1.5 months) resulted in significantly reduced cortisol and inflammatory responses, but it did not influence the suppression of immune function. In a systematic review (Bretschneider, 2005), the effects of age and castration method (surgical vs banding) were evaluated based on 19 peer-reviewed original studies. This work clearly demonstrated that weight loss increased (quadratically), and stress response increased as the age of castration increased. While surgical and banding methods of castration were not different in terms of the degree to which they affected either growth rate or stress response.

Overall the evidence regarding age of castration suggests that where castration is required it should be conducted at ≤ 6 months of age and ideally closer to 1.5 months of age. In terms of method of castration, there are inconsistencies in the literature as to which castration approach is better from a welfare perspective. Generally at lower ages there is little difference between the methods, but at older ages there appears to be inconsistencies as to which is the optimal method.

3.2.4. On-farm castration practices in cattle

A postal survey conducted by Kent et al. (1996) in the UK revealed that the majority of farmers (n = 1000 questionnaires with 28% respondents) preferred to use Burdizzo (43%), followed closely by surgical and rubber ring methods (39% and 32%, respectively) for the castration of bovines. Some farmers (10%) used more than one method. However, the age at castration tended to dictate which method was used by the farmers. Rubber ring castration was the preferred method (72%) over Burdizzo or surgical castration for calves in their first week of life. Burdizzo castration (46%) was preferred for calves aged from one week to two months, and surgical castration (45%) for calves greater than three months (Table 1). Overall, 62% of calves were castrated up to three months, and less than 5% of calves were castrated greater than 6 months of age. In Ireland, the Burdizzo method is considered the most popular procedure used by Irish farmers (Muldoon, n.d.). Keane and Drennan (1998) indicated that the general practice in Ireland is to castrate calves at five to six months, although some producers may delay the procedure until 12 to 14 months of age. This is comparable with the practice of delaying castration of cattle between 9 and 14 months of age in France (SCAHAW, 2001). By contrast, Stafford et al. (2000) reported in a large survey (n = 14,000 questionnaires with 27% respondents) that the rubber ring method (85%) was the most popular procedure carried out on farms in New Zealand. This was followed by the surgical method (18%), and only a few (0.07%; 25 respondents) used the clamp (Burdizzo) method. Rubber ring

(93%) and surgical (54%) castration methods were performed in calves in their first 3 months of life, and only a small proportion of calves were castrated by either methods after 6 months of age (0.4% and 7%, respectively). Clamp castration was performed in animals between 6 and 12 months (mean age = 4.7 months) of age. Overall, the majority of farmers (60%) in New Zealand castrated calves before three months of age, whilst only a few (2%) castrated calves above six months of age. These figures compare favourably with that previously reported by Kent et al. (1996) for the data from the UK. The 'National Animal Health Monitoring System (NAHMS) Beef 97' study in the US (n = 1,190 producers with five or more beef cows, representing 77.6% of US beef producers across 23 States) indicated that surgical castration is the preferred method, followed by the use of rubber bands, and emasculatome by the beef cow-calf producers (55.4%, 37.8%, and 5.6%, respectively). However, the herd size dictated which castration method is preferred. In larger herds, surgical castration was predominant (80.5% of animals) compared with the smallest herds (49.4%). In small herds, producers were almost as likely to use elastrator bands as surgical castration (49.4 and 43.7%, respectively). The majority of producers castrated their animals in the first month of life (39%), and in the following two months (36.7%). A small proportion of the producers castrated calves between three and four months of age (8%), and a greater number of the producers castrated calves above four months of age (16.3%). Most cow-calf producers (74.5%) castrated male calves prior to sale (NAHMS, 1998).

It is of interest to note that many farmers in both the UK and New Zealand performed other routine husbandry practices concomitantly with the castration procedure. Kent et al. (1996) reported that 54% of farmers carried out procedures such as ear tagging, dehorning, and vaccination at the same time as the castration procedure took place. Similarly, Stafford et al. (2000) reported that calves were ear-marked (50.6%), drenched (27.3%), vaccinated (19.5%), treated for lice (9.8%), disbubbed or dehorned (9.1%), or weaned (2.6%) at the same time as castration.

The UK survey data indicated that the overall incidence of failures, complications and deaths associated with the castration procedures were in each case less than 1% of the total number of calves involved in the survey, but the latter two were more frequently observed after surgical castration than by other methods (Kent et al., 1996; Table 1). Furthermore, Burdizzo method was associated with higher castration failure rates, likely due to the incorrect application or maintenance of the instrument (Kent et al., 1996). A few farmers applied the Burdizzo only once (29%), or for less than 5 seconds (15%), which was substantially shorter than the recommendation of 30 to 60 seconds by Cox (1987). In Australia, knife / surgical castration is the most common method used, with rubber rings and some banding also being practiced (AD Fisher, CSIRO, Armidale; personal communication). Burdizzo castration in cattle is almost never used (AD Fisher, CSIRO, Armidale; personal communication).

3.3. Castration of sheep

Castration of male lambs destined for slaughter is conducted to avoid ram taints in post-pubertal rams at slaughter, eases the ability to achieve an acceptable degree of finish on male lambs when slaughtered in late summer and eases pelt removal (Andersen et al., 1991). It also prevents unwanted pregnancies in female lambs destined for slaughter or indiscriminate matings when mature male lambs and adult ewes are grazed together. Conventional castration of ram lambs involves the use of either rubber rings (generally at young ages) or application of a burdizzo clamp (often at much older ages 3 weeks to 12 weeks). Rubber ring methods have been widely adopted in the sheep industries worldwide. Early work reporting their use suggested that they did not cause pain to lambs of about 1 week of age (Barrowman et al., 1953, 1954). However, several studies using rubber rings for castration (and tail docking) demonstrate that considerable pain (indicated by both abnormal behavioural changes and physiological changes) is induced following application of rubber rings in lambs aged from 4 hours up to 42 days (eg Mellor and Murray, 1989a, b; Mellor et al., 1991, Lester et al., 1991, 1996; Wood et al., 1991, Kent et al. 1993; Moloney et al., 1993, Kent et al., 1995).

The clamp (burdizzo) method appears to have considerable potential for improvement. It can be very effective and safe, but for some operators, it can be difficult to apply and may have considerable variation in its effectiveness (Hosie et al., 1993). New more easily applied and reliable instruments (some with powered assistance and timers) have been developed for use in older lambs (Hosie et al., 1993). Interestingly, a novel strategy of application of rubber rings followed by application of a burdizzo clamp or powered castration clamp applied completely across the top of the scrotum in a single operation has been shown to markedly decrease the incidence of abnormal behaviours and cortisol in lambs after castration and as a method of tail-docking (Kent et al., 1998, 2001). The basis for reduced pain associated with the combined rubber ring and burdizzo methods of castration and tail-docking in lambs is that crushing the nerves in the spermatic cord or tail would reduce neural transmission from ischemic tissue distal to the crush and ring (Kent et al., 1993). Healing times for chronic leasions produced by rubber rings were also reduced by using the combined method (Kent et al., 2000; Sutherland et al., 2000). The benefits of combined use of the burdizzo following application of rubber rings may be somewhat better if the burdizzo is clamped on the scrotum proximal to the rubber ring as opposed to the distal position (Kent et al., 1995). However, the greater risk of occluding and damaging the urethra when trying to place the clamp at the proximal side of a previously applied ring is greater (Kent et al., 1995).

Table 1. (a) Percentage of farmers using each method of castration and the age at which calves were castrated; and (b) percentage of problems reported by farmers after castration of calves during a three-year period in the United Kingdom

	Method of castration			
	Rubber ring	Burdizzo	Surgery	Overall
Number of farmers	53	72	60	166
(a) Age at castration, %				
<1 week	72	3	2	22
1 week to 2 months	21	46	25	30
>2 to 3 months	2	13	12	10
>3 months	0	24	45	18
Mixed ages	6	15	17	14
(b) Problems reported by farmers, %				
Deaths	0	3	9	4
Complications	7	13	28	16
Failures	5	35	0	16

Source: Kent *et al.* (1996)

Use of combined rubber ring castration with conventional application of a castration clamp (little nipper, Ritchey Tagg, UK) where each spermatic cord was clamped separately, leaving an area of scrotal tissue unclamped, either before (Dinniss et al., 1997a) or after (Dinniss et al., 1997b) ring application was not successful at reducing the associated cortisol rise. This was likely due to a number of differences between the studies reported by Dinniss et al. (1997 a,b) and those of Kent et al. (1995, 1998, 2001) and Moloney et al. (1997). In all the studies of Kent et al. (1995, 1998, 2001) and Moloney et al. (1997) generally the age of the lambs was 5 to 20 days where as those in the studies of Dinniss et al. (1997a, b) were substantially older (45 to 55 days), there were also breed differences and differences in the clamp devices used (Little Nipper vs Burdizzo or powered clamps). In addition the Kent studies (Kent et al., 1995; 1998; 2001; Moloney et al., 1997) applied the clamp completely across the top of the scrotum in a single operation as opposed to the approach of Dinniss et al. (1997a, b) where each spermatic cord was clamped separately leaving an area of unclamped scrotal skin in between.

Therefore to date the only conclusions that can be made regarding combined ring and clamp castration are that combined castration of young lambs (5 to 21 days) results in substantially reduced cortisol and abnormal behaviour responses than either conventional burdizzo use or use of rubber rings alone. The lowered response in cortisol, following combined rubber ring and clamp castration, was somewhat more prolonged than that associated with the use of local anaesthesia where cortisol usually rebounds in castrated lambs once the anaesthesia effects wears off.

In Australia, historically cutting techniques were most common for castration of sheep, where the scrotum was completely cut followed by either cutting or stretching of the spermatic cords. Currently the most common methods are with a lamb-marking knife or by rubber rings (AD Fisher, CSIRO, Armidale; personal communication). The burdizzo method is rarely used in Australia, partly due to the perception that precision is difficult with large numbers of sheep (AD Fisher, CSIRO, Armidale; personal communication).

3.4. Tail docking – Sheep

Tail docking in sheep is carried out as a preventive method against “Blow-fly strike”. It ensures that the hind-quarters of the sheep are cleaner than in sheep that are not tail docked. It is also thought that with some breeds of sheep in some parts of the world (eg Norduz sheep in Turkey which are described as a fat-tailed breed) that fat deposition in the tail has an adverse effect on carcass quality, and that tail docking increases carcass leanness (Bingol et al., 2006).
The options for tail docking reported in the literature include:

i) Hot docking knife:
During this procedure a clean cut and cauterization of the tail is made with a docking iron / knife heated with a gas flame.
ii) Rubber rings:
This involves application of small latex rubber rings of approximately 5 mm diameter on the tail at the docking point, following which the tail undergoes atresia and falls off over a period of 1 to 2 weeks.
iii) Tail docking with a knife.
iv) Burdizzo with a knife distal to the burdizzo clamp.
v) Combination of burdizzo and rubber rings:
In this approach the rubber ring is placed on the tail and then the burdizzo clamp is placed on the tail either immediately distal or proximal to the rubber ring (Molony and Kent 1993; Kent et al., 1998, 2001).

However other techniques (personal communication with sheep producers and personal experience) are also used in Europe, and likely elsewhere, which are not available in a descriptive form in the scientific literature. These include:

i) Hand wringing of the tail:
During this procedure one hand of the operator holds the tail, just posterior to the tail head, while the other hand grips the tail behind this point and wrings the tail off.
ii) Burdizzo and hand ringing of the tail:
This involves clamping the tail at the point of tail docking with a Burdizzo and then pulling the tail posterior to the clamp by a rapid hand movement.

The rubber ring and hot docking knife methods have been compared in terms of the lambs behavioural response (Grant, 2004). In behavioural terms hot docking and rubber ring docking produced only short-lived alterations and pain (< 90 min). However when the procedure of tail docking was combined with other husbandry procedures such as rubber ring castration or mulesing and ear tagging then the abnormal behaviour postures used to assess pain responses continued beyond 90 minutes (Grant 2004). Various studies comparing the usage of various docking techniques (burdizzo and knife, or hot docking knife with rubber rings and rubber rings followed by application of a burdizzo) have been described (Molony et al., 1993; Kent et al., 1993, Kent et al., 1998; Kent et al., 2001). A limitation of many of the studies on tail docking in lambs is that it has been looked at in combination with castration and in many papers it is difficult to discern the specific effects of tail docking or castration per se (eg Dinniss et al., 1997b; Molony and Kent, 1993; Kent et al., 1995).

Survey results of industry practice of tail-docking in sheep in Australia from 2001 show that 45% of farmers used rubber rings, 27% a gas knife, 14% a sharp knife and 8% a mulesing shears (Cicerone 2002). In 1983 the results from a national survey showed that 45% were docked at the 2nd joint, 30% at the 3rd joint and 15% at the 1st joint (Presser, 1983). In the survey by Cicerone, 2001, the tail cut was made at the recommended 3rd joint by 52% of producers, while 10% docked at the 1st joint, which is not recommended. So although the adoption of best practice has increased between 1983 and 2001, there is further scope for improvement.

The rubber ring technique for tail docking is commonly used in practice due to its ease of use, however on its own, it appears to induce more pain than the other techniques (based on behavioural and cortisol indicies). Use of a knife for tail docking induces a large cortisol response that may last up to 8 hours. Alternatively the use of the gas heated docking iron (knife) consistently resulted in the lowest elevation in cortisol and abnormal behaviours following tail docking compared with either rubber ring or rubber ring combined with burdizzo (Kent et al., 2001; Graham et al., 1997; Lester et al., 1991, 1996). This difference was attributed to the cauterising action of the docking iron, which destroys the nociceptors adjacent to the cutting wound compared with an absence of cautery when the tail was removed using a sharp knife. However farmers in Ireland report greater incidences of subsequent joint-ill infections following tail docking with a gas heated docking iron (personal communications with numerous Irish sheep farmers) than with rubber ring or burdizzo clamp with a knife. The early literature describing studies of different docking methods (Garner and Sanders, 1936; Filmer 1938; Ewer, 1942) found no differences in bodyweight gain between lambs docked with a knife, Burdizzo or with a not iron. However, wounds of lambs docked with the hot iron took longer to heal and a greater proportion of wounds were considered potentially attractive to fly strike, though no fly strike was observed. Such open wounds may be a contributor to increased joint-ill disease as observed in some practical situations by Irish sheep producers (especially in a housed environment), but should not generally be an issue under extensive (Australian) management systems with lambs outdoors.

The novel, but little used, strategy of application of rubber rings followed by application of a burdizzo clamp or powered castration clamp has been shown to markedly decrease the incidence of abnormal behaviours and cortisol in lambs both after tail docking and castration (Kent et al., 1993, 1995, 1998, 2001; Molony et al., 1993) compared with rubber rings alone. Indeed, the optimum method appeared to be a combination of the rubber ring and a powered clamp device (Kent et al., 2001).

Strategic studies designed to look at prolonged health status following tail docking by various procedures are still warranted and required to determine what if any adverse health effects (such as joint-ill disease and fly strike) are associated with tail docking by various methods in addition to the acute stress responses.

3.5. Disbudding / Dehorning - Cattle

Dehorning or disbudding of horned cattle is a mandatory requirement in many countries to reduce the risk of injuries to humans or other animals (Marshall, 1977, Vowles, 1976), and having polled cattle is considered important to minimize bruising and enhance animal welfare in Australia (Primary Industries Standing Committee, 2004). Surprisingly the Australian model code for cattle welfare does not specify if this should be ideally achieved by breeding for genetically polled animals or by conventional dehorning / disbudding practices (Primary Industries Standing Committee, 2004). Various options are employed to prevent horn growth (disbudding) including heat cauterization and chemical cauterization (caustic paste; a method that should not be used in Australia; Primary Industries Standing Committee, 2004). Heat is often the method of choice for younger calves (up to 8 weeks of age; when horn buds are 5 to 10 mm long). When horns become longer and a disbudding iron is not effective, they have to be removed by amputation (dehorning; Weaver, 1986). There is considerable variation both between breeds and within breeds and between individuals within breeds in the age at which disbudding becomes impossible and amputation (dehorning) becomes the necessary method. Dehorning of older cattle is carried out by various methods and includes:

- Dehorning scoop that consists of two interlocking semicircular blades attached to handles that amputate the horn close to the underlying bone.
- Guillotine shears / crange device.
- Saw -where the horn is cut close to the skull bone using a tenon saw
- Foetotomy wire – where the horn is cut close to the skull bones by repeated sawing with a foetotomy wire.
- Cryosurgery (Bengtsson et al., 1996) - however this method was unreliable (60% effective at best) and too difficult to implement in practice and has not been published on since.

The cortisol responses of male Friesian calves (5 to 6 months of age) to amputation dehorning by each of the first 4 methods listed were similar, suggesting that the degree of distress and pain caused by the different methods of dehorning are similar (Sylvester et al., 1998a). With scoop dehorning (which may cause either shallow or deep impact on the underlying bone and surrounding skin), the depth of the wound did not affect the cortisol response (McMeekan et al., 1997).

3.6. Spaying of heifers

In many beef management systems it is desirable to suppress oestrous behaviour in heifers in order to avoid unwanted pregnancies. Heifers become pubertal between 9 (Glencross, 1984) and 24 (Robinson, 1977) months of age. Recurrent oestrus (every 18 to 21 days) results in increased disturbance, stress, risk of injury and unwanted pregnancies in the herd (Curran et al., 1965; Roche and Crowley, 1973). Slaughter of heifers during oestrus increases the incidence of bruising and dark cutting meat (Kenny and Tarrant, 1988). Surgical approaches to suppress oestrus include ovariectomy (Dinusson et al., 1950; Ray et al., 1969; Horstman et al., 1982; Zinn et al., 1989) and hysterectomy (Wiltbank and Casida, 1956, Hamernik et al., 1985). Hysterectomy involves major surgery and is not practiced in extensive beef units. Ovariectomy can be carried out by flank incision or per vagina by colpotomy. In the flank method, a small and rapid incision is made in the musculature of the flank of the animal, and both ovaries are removed through the one incision. In the colpotomy procedure an ecraseur is passed through a stab incision in the dorsal wall of the anterior vagina (near the cervix; Drost et al., 1992). The ecraseur is hooked around the ovarian pedicle and cuts and crushes the ovarian ligament and blood supply to allow removal of each ovary through the vaginal incision. Alternatively the ovaries are excised with a Willis ovariotome and dropped into the abdominal cavity (known as the Willis dropped ovary technique; WDOT; Jubb et al., 2003).

In Australia, flank spaying without analgesia, is only permissible in the Northern Territory and Western Australia. The WDOT is the only method not included in the Queensland Veterinary Surgeons regulation as an act of veterinary science. The WDOT is performed only by veterinarians and lay persons with a high degree of technical ability. Currently, anaesthesia/analgesia is not generally used for either the flank spay procedure (in Western Australia and the Northern Territory) or the WDOT (in all states). Operating speeds of 30-50 animals per hour are achieved. Ovariectomy results in reduced growth rate due to removal of the source of steroid secretion and for this reason can be undesirable. However, in extensive beef farms in northern Australia where complete bull control is impossible, ovariectomy is still the only permanent and practical solution to prevent unwanted pregnancies and to minimize breeder cow mortalities. Losses due to haemorrhage and infection are variable depending on the operator and management but are usually less than 1%. Publications from the USA and Canada report that mortality and morbidity following ovariectomy are generally associated with fatal haemorrhage, peritonitis and adhesions between the reproductive tract and other pelvic and abdominal organs (Drost et al., 1992; Habermehl, 1993). The use of umbilical clamps placed on the stumps of the ovarian vein and artery before cutting with the ecraseur, significantly reduces losses from bleeding (Youngquist et al., 1995). However, this procedure takes considerable time and would pose practical difficulties in range conditions where large numbers of animals are to be spayed.

Little if any work has been done to quantify the degree of pain associated with ovariectomy or looking at the effectiveness of pain relief during ovariectomy in heifers. Widespread ovariectomy is no longer practiced in most beef production units worldwide, except in extensive range management systems. Alternatives to spaying are briefly discussed later in this review. There are no apparent reports of pain relief for spaying of heifers in the scientific literature. However it is reasonable to suggest that analgesic approaches such as epidural anaesthesia (which is used in many research situations where ovariectomy is required), intra-peritoneal anaesthesia (such as that used for abdominal surgery), pethidine injection or NSAIDs could be used. However, suitable drugs and adoption of appropriate withdrawal periods would be required when treating animals destined for human consumption. Furthermore practical limitations for use in commercial and sometimes extensive conditions also need to be considered.

4. Pain, injury, behaviour and ‘pain markers’

4.1. Definition and function of pain

The International Association for the Study of Pain has defined pain in human beings as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (IASP, 2003). However, this definition emphasises the human ability to verbally communicate their subjective pain experiences (Rutherford, 2002). In the absence of language in animals, the following definitions have been proposed:

(1) “Pain in animals is an aversive sensory experience caused by actual or potential injury that elicits protective motor and vegetative reactions, results in learned avoidance behaviour, and may modify species specific behaviour, including social behaviour” (Zimmermann, 1986).

(2) “Animal pain is an aversive sensory and emotional experience representing an awareness by the animal of damage or threat to the integrity of its tissues (note that there might not be any damage); it changes the animal’s physiology and behaviour to reduce or avoid the damage, to reduce the likelihood of recurrence and to promote recovery” (Molony, 1997).

Pain is a component of the sensory–emotional system in highly evolved animals that is a part of an overall set of controls responsible for homeostasis; it constitutes an alarm that ultimately has a role to protect the organism (Le Bars et al., 2001; Craig, 2003). In humans, pain is recognised as: “a multidimensional experience, composed of: 1) a sensory-discriminative component represented by the ability to identify the stimulus within spatiotemporal and intensive domains; 2) a hedonic component through which the aversive and unpleasant qualities of pain are experienced; and 3) a cognitive component that reflects the ability to evaluate the significance of the pain in terms of its meaning for survival and threat to well-being” (Casey, 1996). Due to the anatomical and physiological similarities between humans and higher animals (Zimmermann, 1986; Flecknell, 2000), it is generally considered that animals are also capable of experiencing pain in a “plurimodal” way (Serviére, 2001; Figure 2).

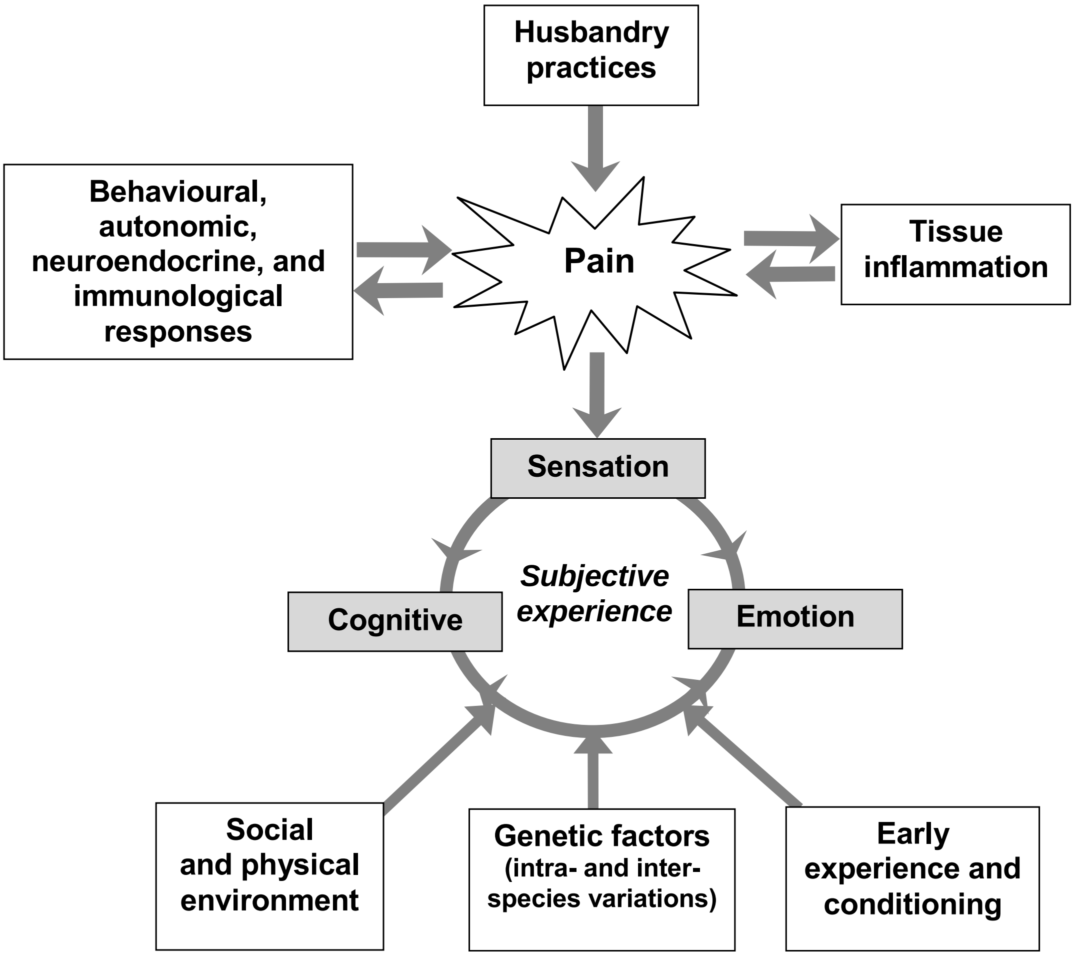

Figure 2 A model for the response of animals to pain caused by husbandry practices. Pain is shown as a plurimodal experience (adapted from Servière, 2001).

4.2. Classification of pain and injury

Pain can be classified into: 1) transient, 2) acute or 3) chronic pain based on its origin, character, and duration (Kitchell and Johnson, 1985; Woolf, 1995; Loeser and Melzack, 1999; Rutherford, 2002). Transient pain (equivalent to "physiological pain"; Woolf, 1989) is elicited by the activation of nociceptors in the skin or other tissues of the body in the absence of any significant tissue damage. This type of pain is physiologically inconsequential due to its rapid onset and offset after the stimulation is applied, as can be seen during an incidental or procedural pain, for example during a venepuncture or injection for immunisation (Loeser and Melzack, 1999). Acute pain (also termed phasic pain) occurs immediately at the onset of injury, and the duration may be brief or last for several hours (sub-acute pain) or it may further develop into chronic pain. Acute pain serves as a warning of damage or potential damage and is likely to invoke withdrawal or avoidance behaviour, while sub-acute pain provokes protective behaviour that aids healing following injury. In contrast, chronic pain (also termed tonic pain) lasts longer (months or years) and usually is associated with inactivity and depression (Kitchell and Johnson, 1985; Rutherford, 2002). Chronic pain is viewed as a "maladaptive" or "non-functional" pain because the pain has lost its original adaptive function and has outlasted the healing time of injury (Woolf, 1995; Le Bars et al., 2001; Millan, 1999; Rutherford, 2002). "Non-functional pain" is defined by Molony (1997) as "the pain that occurs when the intensity or duration of the experience is not appropriate for the damage sustained (especially if none exists) and when physiological and behavioural responses are unsuccessful in alleviating it."

Pain can also be classified according to its origin within the body (Rutherford, 2002). The three main distinctions that have different neurophysiological and pathophysiological characteristics are: 1) visceral (internal organs in abdomen or thoracic regions), 2) somatic pain (generally well localised in the cutaneous, muscular or bone area), and 3) neuropathic pain (damaged or dysfunctional nervous system) (Woolf, 1995; McMahon, 1997). Pain arising from the internal organs can become localised distally, at superficial sites, known as "referred pain" (McMahon et al., 1995).

4.3. Hypersensitivity, inflammatory pain, and hyposensitivity – The opposing effects of an altered sensory function following injury

Tissue trauma results in a complex cascade of inflammatory events that leads to enhanced pain (i.e., a heightened response due to decreased sensory or pain thresholds) to noxious stimuli, termed "hyperalgesia" (Raja et al., 2000; Levine and Reichling, 2000). Algogenic substances (i.e., pain generating; see Dray, 1995) released from the injured tissue, damaged nerves and leukocytes mediate the response (Menefee and Katz, 2003). Peripheral nociceptors become hypersensitive to stimuli, creating a condition called "peripheral sensitisation", and previously innocuous stimuli (e.g., gentle pressure on the skin) may become noxious at the site of injury, a condition termed "allodynia" (Nolan, 2000). Repetitive C fibre input from the injured tissue evokes a state of spinal facilitation, referred to as "wind-up"; sequential stimuli evoke progressively greater responses in dorsal horn neurons, and increases in the size of their receptive fields (Woolf, 1989; Woolf and Thompson, 1991). Changes occurring at the injured site are known as "primary hyperalgesia." This may spread to the surrounding area termed "secondary hyperalgesia." The latter may be accompanied by "central sensitisation" of the CNS to the processing of sensory signals (Woolf, 1989; Raja et al., 2000; Fields and Basbaum, 2000; Menefee and Katz, 2003). Collectively, these events are the characteristic features of "inflammatory" or "pathological" pain (Woolf, 1989). While studies in animals and humans have established that nociception results in central, spinal sensitisation (Woolf and Wall, 1986; Wall, 1988; Woolf and Chong, 1993), exposure to more intense nociceptive stressors (see Le Bars et al., 1979; Termann et al., 1986) can cause sensory inhibition. These supraspinal phenomena are called 1) "stress-induced analgesia" (or more accurately termed hypoalgesia) that originate from higher CNS and/or humoral activities, or 2) "diffused noxious inhibitory control" which occurs from activation of the descending inhibitory mechanisms in the CNS (see Tricklebank and Curzon, 1984; Kelly, 1982, 1986; Grisel et al., 1993; Toates, 1995; Wilder-Smith et al., 1996; Thornton and Waterman-Pearson, 1999). These events are a consequence of the release of neurotransmitters from opioid and non-opioid mediated systems (Amit and Galina et al., 1986; Yamada and Nebeshima, 1995; Rubinstein et al., 1996; Zimmer et al., 1998). In summary, changes in sensory function following nociception may result in two distinct, opposing phenomena: 1) segmental or spinal sensitisation (hyperalgesia), and 2) generalised supraspinal inhibition or "hyposensitivity" to noxious stimulation (Wilder-Smith et al., 1996).

4.4. Assessment of pain in animals

Pain is a complex phenomenon involving pathophysiological and psychological components that are frequently difficult to recognise and interpret in animals (reviewed in Rutherford, 2002; ACVA, 2003). Since animals do not share a common verbal language with humans, the "subjective state" of pain in animals cannot be quantified directly. However, since higher animals and humans have similar neurological and physiological anatomy, it is generally considered that animals are capable of experiencing pain, which they will avoid given an opportunity, and which can dominate their behaviour and physiology in a similar (but not necessarily identical) way to the experience of pain in humans (Duncan and Molony, 1986; ACVA, 2003). Pain assessment in farm animals can only be inferred indirectly from measurement of changes in behaviour and physiological functions in response to pain (Rutherford, 2002). These changes reflect the degree of noxiousness of the tissue damaging procedure and give an indication of the animal's attempts at coping with the pain. Ideally, pain measurement should exclude the effects of stress, so that the degree of pain perceived can be assessed more accurately. However, since pain itself is a potent stressor, the effects of pain are often confounded with physiological stress and psychological factors.

4.5. Behavioural responses to pain

Noxious stimuli in animals evoke a class of pain behaviour, termed "nociceptive or nocifensive" behaviour (Zimmermann, 1986). These behavioural signals can be recognised as follows:

(1) *Active escape behaviours* – involuntary or spontaneous motor withdrawal reflexes (e.g., kicking, tail swishing) which protect parts or the whole animal; increased locomotory activities (e.g., restlessness) or specifically directed behaviour (termed "evoked behaviours") to escape or alleviate the pain (e.g., by licking the painful area).

(2) *Passive avoidance behaviours* – changes in gait or postures (e.g., lameness or guarding), and reduced locomotor activities (e.g., by standing still) to minimise the pain by avoiding stimulation of injured tissues and to assist healing. The animal may show reduced self-maintenance (feeding, rumination, drinking, grooming, and sleeping) as the time spent coping with the pain predominates, reduced play or exploratory behaviours, and reduced social interaction with conspecific or human handlers.

(3) *Communicative and aggressive behaviours* – designed to elicit help or to stop another animal or human from inflicting more pain by vocalisation, e.g., changes in facial expressions, postures, defensive aggression, or other means such as smell.

(4) *Avoidance learning* – the behaviour of the animal is modified by learning (memory) so as to avoid recurrence of the experience.

(5) *Behavioural responses to stimuli* – the animal in pain may develop hyperalgesia which can be assessed using acute noxious stimuli (e.g., response to thermal pain), and the injured tissue may become hypersensitive to gentle palpation and manipulation. The animal may also exhibit an "altered mental state", for instance by displaying "learned helplessness" and may become unresponsive and apathetic or depressed following unsuccessful attempts to relieve the pain. Their awareness and reactivity may be assessed by observing their reactions to visual and/or auditory stimuli, or humans.

(Adapted from Zimmermann, 1986; AVTRW, 1989; Molony and Kent, 1997; Dobromylskyj et al., 2000; Kent and Molony, 2003)

4.6. Pain coping strategies

The type of behavioural (i.e., passive versus active) coping strategies adapted by an animal in pain depend on numerous complex factors (see Figure 2), but the most important include: inter- and intra-species variations (Mellor et al., 1991; Koolhaas et al. 1999; Dobromylskyj et al., 2000; Anil et al., 2002), the age of the animal, and the nature and time course of the inciting stimulus (Robertson et al., 1994; Stafford et al., 2001; Lumb, 2004). The characteristics of emotional, behavioural and physiological responses to pain are determined to a large extent by: 1) the behavioural needs and significance of the pain and 2) the degree to which the pain can be escaped (Molony et al., 1995; Toates, 1995; Lumb, 2004). Activation of the different classes of nociceptors leads to distinct qualities of pain conveyed to the higher CNS. Inescapable nociceptive inputs (C-nociceptors), whether of deep or superficial origin, activate neurons in the ventrolateral columns of the periaqueductal grey matter (**PAG**) that coordinate appropriate patterns of autonomic and motor support, namely quiescence and symphatho-inhibition *(passive coping strategies)*. Escapable pain (Aδ-nociceptors) activates the lateral columns of the PAG and triggers active patterns of autonomic, motor, and sensory changes that enable an animal to escape or confront a transient threat (*active coping strategies*) (Figure 3; Lumb, 2004).

4.7. Measuring pain-associated behaviours

There are a number of pain measurement scales and observational methods available for assessing pain in animals (Dobromylskyj et al., 2000; Rutherford, 2002), and these can be broadly classified as follows:

(1) *Subjective pain scoring systems* – the assessment of acute and clinical pain in veterinary medicine has been largely confined to unidimensional rating scales (i.e., it describes only the pain intensity) developed for use in humans, namely the simple descriptive scale (**SDS**), numerical rating scale (**NRS**), and visual analogue scale (**VAS**) (reviewed in Dobromylskyj et al., 2000; Holton et al., 2001). The SDS consists of 4 to 5 expressions used to describe various levels of pain intensity (e.g., no pain, mild pain, moderate pain, or severe pain; see Steiner et al., 2003). Each expression is assigned an index value that becomes the pain score for the animal. However, the discrete differences in values between descriptions may not necessarily be equally spaced. In contrast, the VAS consists of a horizontal line which, for example, may be set at 100 mm, anchored to both ends are the two extremes of behaviours, e.g., “no pain” to the left and “worst possible pain” to the right end of the line. The observer places a cross marking on the line to indicate the amount of pain the animal is suffering. The distance from the “no pain” end of the line (measured in mm) is the pain score (e.g., Thornton and Waterman-Pearson, 1999). The NRS is similar to the VAS, except that the observer assigns a numerical score for pain intensity to each behavioural category that is weighted based on a description of behaviours (e.g., Pritchett et al., 2003). Multifactorial composite scales have been developed, for instance by Morton and Griffiths (1985) in “Guidelines on the recognition of pain, distress and discomfort in experimental animals” and by Sanford et al. (1986). However, the validity of these guidelines has been questioned

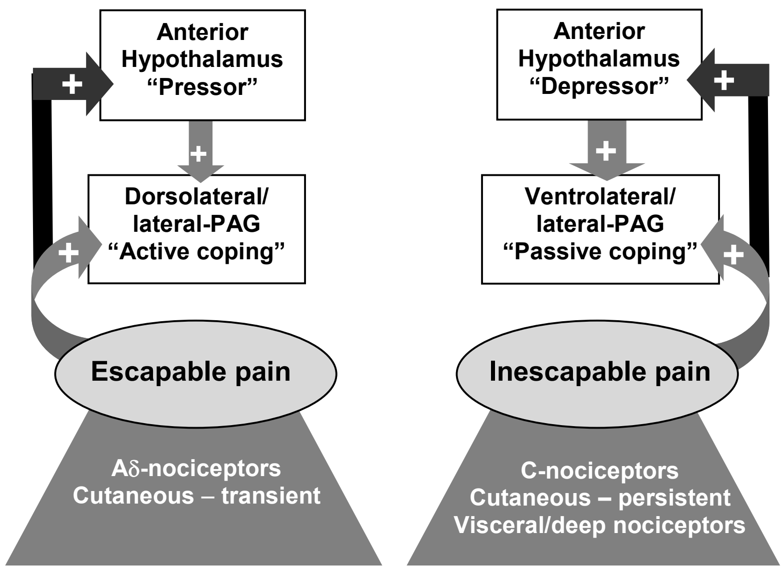

Figure 3 Activation of hypothalamic and midbrain circuits by escapable and inescapable pain. PAG, periaqueductal grey (Lumb, 2004).

since no information is provided on what criteria were used to select the pain indices and on how the weights were attributed to them (Holton et al., 2001). In common with the unidimensional scoring systems, these composite scales are based on developers' and observers' best estimates of weights that should be assigned to the behavioural categories, which is necessarily subjective, and the proper recognition of the selected criteria will depend on the knowledge and experience of the observer (Sanford, 1992), but may also be influenced by personality, mood and empathy towards the animal (Sanford et al., 1986). Therefore, these subjective pain scales vary considerably in their standards of reliability, sensitivity, and validity (reviewed in Rutherford, 2002). Holton et al. (1998) reported that the variations between the SDS, NRS and VAS for assessing pain in post-operative dogs were unacceptably large. Similar variations in performance between the NRS and VAS, and between different observers (veterinarians versus grooms) were found in the assessment of post-operative pain in horses (Price et al., 2003b). By contrast, good agreement has been found between the VAS and an NRS system when assessing lameness in sheep, but the VAS was more sensitive (Welsh et al., 1993). Furthermore, the authors reported that difference between observers using the VAS or NRS were not significant. Studies in horses using the NRS (Price et al., 2003c) and in lambs using VAS (Thornton and Waterman-Pearson, 1999) for assessing pain indicated that the results were in good agreement compared with those obtained from objective physiological (cortisol) or more detailed behaviour measurements. Collectively, while the pain scoring systems are subjective by their nature, the value of these methods for pain assessments in animals has been demonstrated in some studies, and they may provide useful information in addition to objective-based assessments.

(2) *Ethogram-based systems* – an ethogram is an exact and complete catalogue of behavioural patterns typically displayed by an animal belonging to a specific species (Banks, 1982). The value of the ethogram is to provide a benchmark against which one can measure behavioural deviations (Banks, 1982). Therefore, an ethogram-based system for observing behaviours is considered an objective method for assessing pain in animals (Rutherford, 2002). Changes in behavioural states (e.g., postures) or events (e.g., trembling, vocalisation) (see Martin and Bateson, 1986 for further definitions) of an animal in response to pain can be measured by either direct observation, or using a continuous real-time or time-lapse video recording. Detailed discussions on the sampling methods for behaviour are described elsewhere (Banks, 1982; Martin and Bateson, 1986). Often a simple, economical and representative approach called "scan sampling" or "point (instantaneous time) sampling" is used, if continuous recording is not feasible or too time consuming. The occurrence of a particular behaviour displayed by an animal in a group is recorded at the predefined time interval, and the result may be expressed either as the total incidence, or as the (proportion or percentage) total time spent in a particular behaviour per unit of sampling time (Martin and Bateson, 1986). An approximation to a continuous recording can be achieved if the sample interval is short relative to the average duration of the behavioural pattern (Martin and Bateson, 1986). Thus, certain behavioural events as well as behavioural states can be validly recorded by scan sampling and combined into a fewer summary categories (e.g., Molony and Kent, 1997; Molony et al., 2002). Although concern has been raised on the possibility that a bias or subjective classification of descriptors (Morrow-Tesch et al., 1998) may be introduced by the developer, this can be overcome by applying sound scientific principles based on 1) consensus professional experience in clinical pain assessment and management, and 2) validation using multivariate statistical (i.e., factor and discriminant) methods (e.g., Holton et al., 2001; Molony et al., 2002).

The observational methods for assessing pain in animals can be further classified as: 1) *non-invasive*, 2) *interactive*, and 3) *analgesic drug intervention* methods. The non-invasive method simply involves the observation of undisturbed behaviours of animals, and pain assessment is achieved using a subjective scoring or objective ethogram-based system, or both. The objectives of using the interactive methods are to assess the changes in sensory function or mental states of the animals in pain, and these methods include:

(1) *Aversion test* – to test the awareness, reactivity, flight and/or exploratory behaviours of the animal by exposure to a novel surrounding, a threatening visual (i.e., novel objects, human presence or approach) or auditory stimulus, such as in an open-field (arena) test (Macaulay and Friend, 1987; Macaulay, 1989; Fell and Shutt, 1989; Boissy and Bouissou, 1995; Thornton and Waterman-Pearson, 1999; Pritchett et al., 2003). Other objective tests of escape-avoidance behaviour include using a strain gauge to quantify the mechanical forces exerted by an animal restrained in a crush in response to a painful husbandry procedure (Schwartzkopf-Genswein et al., 1997).

(2) *Palpation test* – to test the reaction of the animal to gentle touch and pressure on the painful area i.e., allodynia; (Molony et al., 1995; Thornton and Waterman-Pearson, 1999; Steiner et al., 2003) or other parts of the body to determine its reaction to the handler (Eager et al., 2003).

(3) *Test of nociception* – quantification of stress or injury induced changes in nociception, a phenomenon characterised by the underlying changes in neurophysiological functions and behavioural expressions can be incorporated into acute stress research in farm animals in order to broaden our understanding of the potential integration between the peripheral and behavioural responses to stressors (reviewed by Herskin, 2004). Changes in sensitivity toward stimuli which are normally capable of producing pain (i.e., "hypoalgesia" for increased tolerance to pain, or "hyperalgesia" for reduced tolerance to pain) are fundamental, integrative components of physiological and behavioural responses to stressful events (Hayes et al., 1978; Kelly, 1982; Amit and Galina, 1986; Walters, 1994; Yamada and Nabeshima, 1995). Furthermore, such events facilitate the coordinated expression of adaptive, defensive, or maladaptive behaviours and have significance for the survival of the animal (Toates, 1995; Rutherford, 2002; Herskin, 2004). Therefore the degree of suffering in animals may be indirectly assessed by measuring the changes in sensory processing (nociception) in response to a specific noxious stimulus (Rutherford, 2002; Herskin et al., 2003). Measurements of nociception have been determined primarily in rodents by the application of noxious chemical, mechanical, electrical, or thermal stimuli, and the endpoint (i.e., the latency to response or the nociceptive threshold) is typically characterised by a display of simple spinal reflexive behaviours (e.g., kicking) or other more complex types of behaviours (reviewed by Chapman et al., 1985; Dubner and Ren, 2000; Le bars et al., 2001). In large farm animals, the use of mechanical stimulation has dominated and to a lesser extent the use of contact or remote thermal stimulation has been described (see reviews by Chambers et al., 1994; Herskin, 2004).

Finally, the degree of pain suffered by an animal can be assessed by its reversal using an analgesic drug treatment, termed "analgesiometry" (Dobromylskyj et al., 2000; Stafford et al., 2001). This can be done by comparing changes in behavioural pattern with or without drug treatment (e.g., Faulkner and Weary, 2000), and by the nociceptive test described above (e.g., see Welsh and Nolan, 1995a,b). A necessary precaution is to establish that the analgesic treatment does not have non-specific effects in normal animals that would influence the behavioural variables (e.g., sedation) examined (Dobromylskyj et al., 2000).

Which is the best behaviour-based method for pain assessment?

Since in practice the methods available for pain assessment in animals represent a continuum from subjective to objective measures (Rutherford, 2002), the best possible system is likely to be derived from using both methods. For example, Holton et al. (2001) developed a validated composite scale (modelled on one developed in human medicine by Melzack, 1975) for assessing pain in dogs using a comprehensive catalogue of 47 behavioural descriptors considered by veterinarians to be indicative of pain. Each descriptor was weighted with an intensity value using a 100 mm VAS score assigned by a large group (n = 75) of veterinarians. Statistical methods were then applied to examine the structure of the data to reduce the allocation of common descriptors into the seven most relevant behavioural categories: 1) demeanour and response to people, 2) posture, 3) mobility, 4) activity, 5) response to touch, 6) attention to painful area, and 7) vocalisation. Holton et al. (2001) reported that efforts are currently underway to evaluate the effectiveness of this recently developed composite scale for pain assessment under varied clinical settings.

4.8. Assessment of pain associated with husbandry procedures

Many of the good controlled studies evaluating pain associated with husbandry procedures in cattle and sheep use castration as a model. Some further papers regarding tail-docking in sheep and dehorning in cattle are also available, but most do not include a full array of pain indicators. Therefore much of the discussion in this section deals predominantly with castration.

4.8.1. Types of castration-induced pain.

Surgical castration causes injuries to the well innervated skin of the scrotum (i.e., somatic pain) and various internal structures associated with the testes (i.e., visceral pain). The traction, pulling and/or cutting of the cord to remove the exposed testes causes injury to the distal end of the structures that produce a diffused and poorly localised intra-abdominal pain (Thornton and Waterman-Pearson, 1999). This has been shown to be the most noxious stage of the procedure (Taylor and Weary, 2000). Although most nociceptive inputs from the testes are removed following surgery, noxious sensory barrages will continue to be emitted from the nerves remaining in the tissue, which are enhanced by the release of inflammatory mediators in the injured tissues to sustain the acute pain (Molony et al., 1995). Similarly, the crushing of afferent nerves from the testes and scrotal tissues following Burdizzo castration produces an irreversible conduction block, thus the acute pain produced is expected to be intense (Molony et al., 1995), but of brief duration. However, the nerves in the undamaged central part of the scrotal skin remain intact, which will continue to send noxious signals to the CNS (Molony et al., 1995; Dinniss et al., 1997b). By contrast, rubber ring castration is considered to produce a less intense, localised somatic pain due to 1) the lesser pressure exerted by the rubber ring on the scrotal neck compared with the application of a Burdizzo clamp, and 2) the slower onset of noxious sensory barrages from the development of ischemia in the scrotal tissues (Cottrell and Molony, 1995). However, a more prolonged chronic (inflammatory) pain may result proximal to the ring (Kent et al., 1995; Molony et al., 1995).

4.8.2. Neurophysiological assessment of castration-induced nociception.

Several neurophysiological studies on the peripheral afferent activity, and the changes in cerebro-cortical functions, have provided evidence for the existence of nociception induced during castration in farm animals. Using electrophysiological techniques, Cottrell and Molony (1995) showed that rubber ring castration in anaesthetised young lambs initiated afferent activity in the superior spermatic nerves that persisted for periods in excess of 90 min; a time course that was similar to the behavioural and physiological (cortisol) changes observed following castration in conscious lambs and calves (e.g., see Kent et al., 1993; Molony et al., 1995). Cottrell and Molony (1995) reported that the excitation of afferent activity following the application of a rubber ring was the result of 1) the compression of normally silent, high threshold mechanoreceptors in the pampiniform plexus, followed by 2) an increased sensitivity of the testicular and pampiniform mechanoreceptors, due to the temporally increased intratesticular pressure following the induction of ischaemia (i.e., ischaemic pain caused by the occlusion of lymphatic and blood vessels). Furthermore, the authors noted that the application of a rubber ring was insufficient to cause a complete neuronal pressure block on the slowly conducting unmyelinated afferent fibres that continued to show excitation for upwards of 90 min.

Changes in electroencephalographic activity (electroencephalogram; **EEG**) have been studied as a potential indicator of nociception in animals. The EEG consists of waveforms with an amplitude of a few tens of microvolts and a frequency spectrum from less than 0.1 Hertz (Hz) to about 30 Hz; most being in the low frequency range, and with some recognisably recurring frequencies such as the alpha-rhythm (8 to 13 Hz). The source of these waveforms is mainly in the cerebral cortex and they are produced by synchronous synaptic activity of the pyramidal cells and their apical dendrites (Molony, 1986). The pain assessment using EEG is based on the principle that in humans, specific changes in the EEG frequency spectra reflect the cortical electrical activity that is associated with the cognitive perception of pain, which can be correlated with patients' verbal reports on pain perception (Ong et al., 1997). Ong et al. (1997) demonstrated that graded temporal increase (for 4 seconds) in the absolute power values within the specific bandwidths of the EEG spectrum occurred in conscious adult sheep subjected to increasing intensity of electrical stimulation. Furthermore, the sheep showed increasing escape-avoidance behaviour with increasing intensity of the stimulus. However, in a subsequent study, Jongman et al. (2000) showed that lambs subjected to more painful husbandry procedures actually had consistently lower power values (relative treatment effects on power values for sham shearing = handling ≥ surgical castration = tail docking = formalin injection = mulesing = ear tagging) and the results were in the opposite direction to the previous study. More recently, Murrell et al. (2003) demonstrated that the nociception induced by closed castration in the horse under halothane anaesthesia was associated with an immediate shift towards higher EEG frequency activity. Specifically, there was an increased median frequency (**F50**), and decreased total amplitude (de-synchronization) of the EEG spectra. The authors commented that this corresponded with the increased activity in the middle frequency ranges of the EEG following electrical stimulation in anaesthetised sheep reported by Ong et al. (1997), and the change was not a mere reflection of the adequacy of anaesthesia. Murrell et al. (2003) proposed that an increase in F50 could be used as a specific marker for nociception in the horse. A similar result was found by Mellor in a study of anaesthetised young lambs subjected to rubber ring castration (MAF, 2003). Mellor noted that the advantage of conducting this type of study under general anaesthesia was to avoid contamination of the somatosensory EEG recordings by the somatomotor cortical activity caused by body movements in conscious animals. However, changes in EEG profiles have yet to be studied in the bovine during castration.

Since stressful events can modulate the nociceptive response to pain in animals (Tricklebank and Curzon, 1984; Amit and Galina et al., 1986; Kelly, 1982, 1986; Grisel et al., 1993; Toates, 1995), it would be interesting to determine what effects, if any, castration stress has on the nociception of cattle. However, such data are currently lacking in cattle. Changes in the nociceptive threshold response to a noxious stimulus following castration have been described in lambs (Thornton and Waterman-Pearson, 1999). Thornton and Waterman-Pearson (1999) reported that increased "mechanical nociceptive thresholds" (a behavioural threshold response to a noxious mechanical stimulation) occurred 4 to 7 h after rubber ring plus clamp castration or surgical castration in lambs compared with controls. However, the assessment of nociceptive threshold can give rise to different results depending on the time course and the type of stimulus (mechanical versus thermal) used (Welsh and Nolan, 1995b). Recently, Veissier et al. (2000) described a method using a radiant heat source produced by a CO_2 laser for testing thermal nociception in calves. Further study is required to investigate whether this method is appropriate for detecting changes in thermal nociception following castration in cattle.

4.8.3. Behavioural assessment following husbandry procedures.

Changes in behaviour in response to castration and other husbandry procedures have been investigated in the bovine (Macaulay and Friend, 1987; Macaulay, 1989; Mellor et al., 1991; Robertson et al. 1994; Molony et al., 1995; Fisher et al., 2001), ovine (e.g., Mellor and Murray 1989a; Mellor et al., 1991; Molony et al., 1993; Thornton and Waterman-Pearson, 1999; Molony et al., 2002) and pigs (e.g., Taylor et al., 2001; Hay et al., 2003). These studies have shown that different castration methods produce varying qualities and intensities of pain, which result in very specific, but also some common changes in behaviours across different species and age of animals. Table 2 shows an ethogram (characterisation of the complete catalogue of behaviour patterns displayed; see section 4.7) used for assessing castration pain in the bovine developed by a group at the University of Edinburgh, Scotland (see Robertson et al., 1994; Molony et al., 1995). A matrix of behavioural indices (i.e., activities and postures) was used to better encapsulate the multidimensional nature of pain response in animals. These behaviours are categorised into a set of "normal" against "abnormal" (pain related) behaviours. The latter is considered as such, because these behaviours are rarely seen in intact or control animals (Robertson et al., 1994; Molony et al., 1995) and are thus thought to be indicative of pain. These summations of behaviour categories as normal and abnormal (see Table 2) could be applied in future research that will use behaviour as an indicator of pain in farm animals.

Robertson et al. (1994) examined the effects of three methods of castration without analgesia using rubber rings, Burdizzo or surgery in Ayrshire bull calves at three different ages (6, 21, and 42 days) and observed their behaviours over a three-hour period post-castration (Table 2). The authors reported significantly higher frequencies of restlessness, tail wagging and foot stamping following rubber ring castration than with either surgical or Burdizzo castration across all ages. However these activities peaked more slowly and were prolonged by at least two hours in calves castrated by rubber rings than by surgical or Burdizzo methods. The 6 day old calves showed less tail wagging and foot stamping and more head turning, and they spent more time lying normally than the older calves. The total time spent in abnormal postures was increased following castration by all methods, and the 21 and 42 day old calves spent less time eating and suckling than untreated controls, indicating that the pain induced by castration temporarily dominated their behaviours. The time spent in abnormal standing postures increased immediately in the Burdizzo and surgical castrates and lasted for 24 min in the 6 day old calves, but were sustained for up to 120 min in the 21 and 42-day old calves. By contrast, there was a delayed onset of abnormal postures across all ages of calves castrated by rubber rings. The abnormal standing postures in these calves increased from 24 min after castration, followed by increased abnormal lying postures from 90 min to 180 min after castration. An interesting observation was that the Burdizzo castrated calves adopted an immobilised "statue" standing, whereas the rubber ring castrated calves displayed greater active behaviours. Robertson et al. (1994) concluded that 1) all methods of castration cause acute pain irrespective of age, and 2) Burdizzo castration produced the least pain, but the effect was more pronounced in younger calves. Molony et al. (1995) investigated the acute (first 3 hours) and chronic (over 48 days) component of pain produced by four different methods of castration using rubber rings, Burdizzo, surgery, or combined Burdizzo and rubber ring castration in one week old Ayrshire calves. In common with the previous study, calves castrated by rubber rings showed significantly greater active behaviours than either by surgical or Burdizzo castration, but the latter two methods produced greater statue standing posture, indicating that the pain elicited may be more intense, but may be of shorter duration than by the rubber rings. This was confirmed in calves castrated using the combined rubber ring and Burdizzo method, as these calves showed increased statue standing than by rubber ring castration alone. However, the significance of the two different coping strategies adopted by these calves following different methods of castration remains to be determined. Studies in mice suggest that the adaptation of different coping strategies to pain may be related to activation of different nociceptors and hypothalamic-midbrain pathways to induce different patterns (i.e., active versus passive) of behavioural responses (Lumb, 2004). Cottrell and Molony (1995) proposed that the individual behavioural and physiological responses to the acute pain suffered by an animal after castration may be examined by selective denervation to determine the relative contributions of individual nerves to the response. Molony et al. (1995) observed that there was a trend for the abnormal standing postures to persist for up to 9 and 15 days in the Burdizzo or surgically castrated calves, respectively, while the changes in postures were coupled with intermittent increases in the incidences of lesion licking that persisted for up to 42 days in the rubber ring, or combined rubber ring and Burdizzo castrated calves. These changes were supported by the similar trend shown in the clinical lesions scores (Figure 4). Molony et al. (1995) concluded that 1) Burdizzo castration, when correctly applied, produced the least pain in young calves, and 2) rubber ring castration was associated with chronic pain that lasts for at least 42 days. Furthermore, although the combined rubber ring and Burdizzo procedure did reduce the acute and chronic pain associated with rubber ring castration alone in calves, the reduction was less dramatic than that seen in young lambs.

Table 2. Definitions of behaviours, grouped by category, which are used for assessing castration pain in the bovine

Category	Behaviour	Abbreviation	Description	Reference[a]
Normal behaviours				
Activity (bouts/events)	Walking	WLK	• Forward movement at any rate, including running. This behaviour may not be applicable to confined or penned animals.	(1,2,3)*
	Eating	FED	• *Young calves*: suckling milk from a teat or drinking milk in a bucket, chewing hay or straw, eating concentrate. • *Cattle*: head facing feed bunk, chewing or gathering feed (silage or concentrates) in a feedlot, or grazing on pasture when outdoors.	(1,2,4,5)*
	Ruminating	RUM	• *Cattle*: regurgitating feed, chewing, then swallowing cud.	(1,2,4)*
	Drinking	DRK	• Nose inside water bucket.	(3)*
	Playing	PLY	• *Calves*: prancing or jumping.	(1,2,3)*
Postures (behavioural states)	Normal standing	SN	• Standing still supporting all body weight on four feet in a restful posture, with no movement or activity and no obvious signs of abnormality.	(1,2,3)*
	Normal ventral lying	LN (LHU + LHD)	• Lying in ventral (sternal) recumbency with all legs folded or tucked under the body and the head down (LHD), either round to one side or directly in front or head up (LHU).	(1,2)
Abnormal (pain-associated) behaviours				
Activity (bouts/events)	Restlessness	RES	• The number of times an animal partly or fully stood up and lay down. Each action is defined as the act of rising and subsequently lying down.	(1,2)
	Foot stamping and kicking	FSK	• Lifting of a front leg or hind leg and forcefully placing it onto the ground while standing, or kicking out while standing or lying.	(1,2)
	Easing quarters	ESQ	• Whole body shifted between each side of the front or hind legs while standing, with each movement counted as one action, including movements of the shoulder and hindquarters in a less forceful manner than foot stamping and kicking, or without moving from the place of rest.	(1,2,4)*
	Head turning	HDT	• Movement of the head beyond the shoulder, and looking back at the source of the pain, and including grooming.	(1,2,6)*
	Tail wagging	TW	• A single tail movement from side-to-side (>30^{o} from vertical), or a series of continuous tail movements without pausing is recorded as one action; the tail remains hanging down and without slapping back to indicate fly avoidance. Interference from flies or other biting insects must be kept to a minimum for this measure to be valid.	(1,2,4,5,6)*
	Stretching	STR	• Forward extension of the forelegs or backward extension of the hindlegs (stiffness), each recorded as one action; stretches associated with urination are excluded.	(2)

Table 2. (*Continued*)

Category	Behaviour	Abbreviation	Description	Reference[a]
	Trembling	TRB	• Shivering or skin rippling produced by the major muscles in the torso or limbs, but excluding twitching of the ears.	(1,2,6,7)*
	Vocalisation	VOC	• Occurrence of each vocal sound by an animal has been recorded in lambs following castration. The vocal characteristics of the (eg high and low frequency) calls emitted during a discrete period immediately following castration require further studies in cattle, but these have been studied in castrated pigs and in cattle following branding.	(1,2,6,7,8)*
	Facial expression(s)		• Lip curling has been observed in lambs after castration, but further research on facial expressions is required in cattle.	(6)
Postures (behavioural states)	Abnormal standing	SAB	• Standing or walking unsteadily (e.g., swaying) with an obvious abnormal posture or gait; sometimes associated with a hunched back and trembling, tail tucked between hindlegs, or frequent foot stamping, kicking and tail wagging; walking backwards or on knees; leaning on a support or falling over.	(1,2,4)*
	Statue standing	SS	• Standing still for more than 10 s (immobility), with the occasional head movement only.	(1,2)
	Abnormal ventral lying	LAB	• Lying in sternal recumbency with partial or full extension of one or both hind legs or lying with the scrotum kept off the ground.	(1,2)
	Lateral lying	LL	• Lateral recumbency; lying flat with one shoulder and hindquarter on the ground and two or more legs extended.	(1,2)
Summation of behavioural categories.				
Total active (abnormal) behaviours		TACT	Summation of RES, FSK, ESQ, HDT, TW, STR (TRB, VOC)	(1,2,6)*
Total normal behaviours		NORM	Summation of TSN, TLN	(1,2,6)*
Total normal standing		TSN	Summation of SN, WLK, FED, PLY (RUM and DRK)	(1,2)*
Total normal lying		TLN	Summation of LHU, LHD	(1,2)
Total abnormal postures		ABPOS	Summation of TSAB, TLAB	(1,2)
Total abnormal standing		TSAB	Summation of SS, SAB	(1,2)
Total abnormal lying		TLAB	Summation of LL, LAB	(1,2)
Total standing behaviours		TS	Summation of TSN, TSAB	(1,2)
Total lying behaviours		TL	Summation of TLN, TLAB	(1,2)

[a]References: adapted from (1) Robertson *et al.* (1994) and (2) Molony *et al.* (1995); an asterisk (*) indicates that the definition of behaviour from (1, 2) has been modified using the descriptions in (3) Eicher and Dailey (2002); (4) Schreiner and Ruegg (2002); (5) Fisher *et al.* (2001); (6) Molony *et al.* (2002); (7) Hay *et al.* (2003); (8) Watts and Stookey. (1999); Note that the abbreviations indicated above are modified from the original authors (1 and 2).

In contrast, Mellor et al. (1991) found that rubber ring castration in 1 to 7 day old Friesian calves did not cause them to display any significant abnormal behaviour. The castrated calves spent most of their time lying down or were asleep, similar to that observed in controls. However, these animals were kept in visually-isolated individual pens that may affect their behaviours (Warnick et al., 1977). Importantly, these calves showed subtle signs of abnormality such as head turning and licking of flanks and scrotum following castration (Mellor et al., 1991). Studies conducted by Robertson et al. (1994) and Molony et al. (1995) have shown that active behaviours such as restlessness, tail swishing and foot stamping could be used as sensitive indicators of castration pain since higher frequencies of these activities were found in castrated calves than controls. These findings have been confirmed by Carragher et al. (1997) who observed significantly higher rates of rear leg stamping and tail swishing in surgically castrated 17 month old Friesian cattle, which lay down for shorter periods and stood in different postures than controls for up to 21 hours post-treatment. Similarly, Fisher et al. (2001) found a greater incidence of leg stamping and tail swishing events in surgically castrated 14 month old cattle than in either banded castrates or controls. However, the authors postulated that these responses might not necessarily be indicative of severe pain per se, because grazing behaviours were only transiently affected in the castrates versus controls. McMeekan et al. (1999) noted that an animal's priority may change over time causing their behaviour to change even if the pain is still being perceived following tissue trauma.

Robertson et al. (1994) and Molony et al. (1995) reported that abnormal postures such as statue standing and hyperextension of the hind-legs while lying could be used as indicators of castration pain in calves. Similar types of active behaviours and abnormal postures have been observed following castration with or without tail docking in lambs (Molony et al., 1993; Kent et al., 1995; Molony et al., 1997, 2002), although lambs show more overt behavioural responses to castration than calves (Mellor et al., 1991; Robertson et al., 1994). A recent study in 5 day old piglets subjected to surgical castration also showed significantly greater occurrences of prostration (equivalent to statue standing), stiffness (lying with hyperextension of legs) and trembling during the first hour following treatment, and tail wagging for up to 2 days compared with untreated controls (Hay et al., 2003), which reaffirms the value of these behavioural indices for assessing castration pain in farm animals.

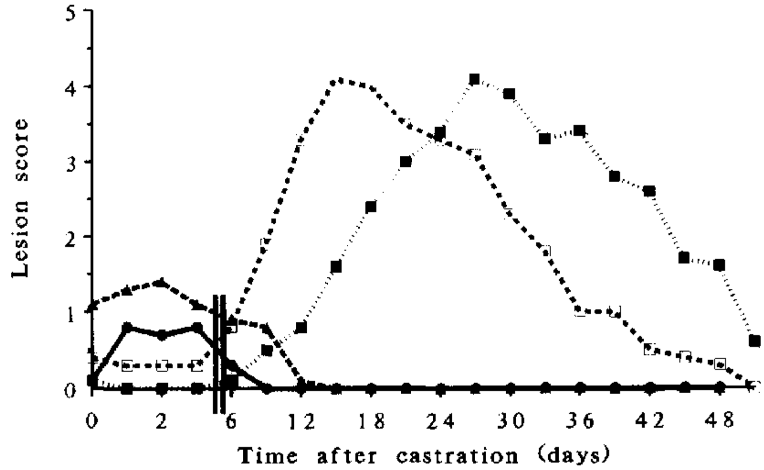

Figure 4 Mean lesion scores following castration of five to seven day-old calves by Burdizzo (σ---σ), surgical (●—●), combined Burdizzo rubber ring (□---□), and rubber ring (■IIIII■; n = 8/treatment) methods of castration. Lesions at the site of castration were visually scored based on the following 11-point scale: 0, no swelling, inflammation or infection visible; 0.5–2, increased degrees of swelling without obvious erythema, 2.5 and 3.0, swelling with

obvious erythema but without pus; and 3.5–5, presence of pus with increasing inflammatory response. (Molony *et al.* 1995).

The number or characteristics of vocal calls emitted by animals following castration have been studied in lambs (Molony et al., 1997, 2002) and pigs (White et al., 1995; Taylor et al., 2001; Taylor and Weary, 2000; Weary et al., 1998). Currently the only data available in cattle are on restraint and branding stressors (e.g., Schwartzkopf-Genswein et al., 1997a; Watts and Stookey, 1999). These studies have shown that castration in the pig or branding in cattle results in either a greater audio frequency spectrum or higher proportion of calls than restraint alone. Interestingly, Taylor and Weary (2000) found that the pulling and severing of the spermatic cord during surgical castration in piglets evoked a greater amount of calls than the initial stage of scrotal incision which led the authors to conclude that the former was associated with the most painful components of castration. Furthermore, the methods for severing the cord either by cutting the cord with a scalpel versus tearing the cord by manually pulling on the testicles did not result in any significant differences in terms of the vocal calls. It should be noted that although specific types of vocalisation are considered a sensitive characteristic of an animal experiencing pain (Morton and Griffiths, 1985; Watts and Stookey, 2000), the act of vocalisation itself is not unique to pain (Watts and Stookey, 2000; Molony et al., 2002). However, it may nonetheless signal a high degree of negative affective state to an unpleasant emotional experience (Watts and Stookey, 1999, 2000; Feinstein, 2003). Therefore the analysis of vocalisation by measuring 1) the propensity of a specific treatment group to vocalize, 2) the rate of vocalisation, and 3) other acoustical parameters of the calls should provide a reliable method for assessing acute distress in cattle (Watts and Stookey, 1999, 2000). Similarly in sheep, vocalisation increases with pain, however incidence alone is not unique to pain (Molony et al., 2002; Owens, 1984, Stevens et al., 1994). An assessment of the sound characteristics would be required to use vocalisation as an index of pain (Weary et al., 1998) in lambs.

Active pain behaviours, scrotal pain on palpation, and unresponsiveness behaviour have been studied in lambs following different methods of castration using subjective VAS (see section 4.7; Thornton and Waterman-Pearson, 1999). Thornton and Waterman-Pearson (1999) showed that the subjective VAS scores could provide valuable additional information that is comparable with that of objective behavioural assessment. Recently, a large-scale study in lambs has confirmed this finding, since significant correlations ($r = 0.69$, $P < 0.05$) were found between the objective behavioural data quantified for 30 min by trained personnel and the VAS scores assessed for only two min by untrained shepherds (Kent et al., 2004). However, this positive relationship was highly dependent on the skill and experience of the observer (Kent et al., 2004). Further research using VAS scores is warranted for the assessment of castration-induced pain in cattle.

An animals reaction to negative events, such as castration, is termed “emotionality” or “temperament” and such emotional responses are generally assessed by behavioural tests (see Désiré et al., 2002). However, suitable models for measurement of the emotional distress (e.g., see Désiré et al., 2002) associated with the perception of castration pain in cattle have yet to be fully developed. Furthermore, the behaviour-based approach is likely to be the most practical, non-invasive method for the assessment of castration stress and pain in cattle. The usefulness of a subjective pain scoring system based on objective ethological data should be further examined (e.g., see Kent et al., 2004 for sheep).

4.8.4. Effects of castration on acute phase proteins (APP)

Several castration studies in cattle have demonstrated the value of monitoring the elevation of plasma APP as sensitive markers of tissue inflammation (Faulkner et al., 1992; Fisher et al., 1997a,b; Earley and Crowe, 2002; Ting et al., 2003a; 2003b; 2004; 2005; Pang et al., 2006). The response typically reaches a peak within 3 days following castration. However, the presence of haematomata following castration may result in the rapid disappearance of the plasma APP (Kent and Goodall, 1991). Fisher et al. (2001) reported that whilst surgical castration resulted in elevation of the APP haptoglobin concentrations, there was a lack of detectable APP haptoglobin and fibrinogen concentrations in the plasma following banding castration of cattle.

4.8.5. Effects of husbandry procedures on catecholamine concentrations

Currently no data are available on the changes in sympathetic-adrenomedullary activity in response to castration in the bovine. Mellor et al. (2002) reported that in 8-week-old lambs subjected to rubber ring castration and tail docking, plasma noradrenaline concentrations peaked after 10 min and remained high for 30 min before returning to control values. In contrast, adrenaline concentrations in these animals did not differ significantly from untreated controls; the failure to detect treatment differences was likely due to large variations in adrenaline concentrations observed within groups, and the lack of blood sampling within the first 5 min following treatment which failed to capture the short plasma half-life of 1 to 2 min (Mellor et al., 2002). Furthermore, the authors showed that a similar pattern of changes in plasma noradrenaline concentrations occurred following scoop dehorning in 10-week-old calves. There was a significant increase in adrenaline concentrations 5 min after treatment in dehorned calves compared with controls. A similar effect on plasma adrenaline concentrations has been reported following either freeze or hot-iron branding in 257 day old calves, although the response occurred significantly only at 0.5 min after treatment, and no effect was found on noradrenaline concentrations (Lay et al., 1992). This observation may be due to the lesser degree of tissue trauma caused by branding compared with dehorning. Recent data from Hay et al. (2003) showed no clear effect of surgical castration on urinary free catecholamine concentrations in 5 d-old piglets taken (twice daily) over 4 days of sampling after surgery. However the authors admitted that samples were taken opportunistically, and not always from the same animal. Furthermore, they commented that maximal excretion of catecholamines might have been missed, because the first urinary samples were taken 2.5 to 4 hours after castration. The major limitation of catecholamines as inicators of pain responses is that the restraint and procedures to obtain blood or urine samples may also induce a catecholamine response thus confounding any interpretation that can be inferred.

4.8.6. The response of the HPA-axis to injury

In a classical study of “wound hormones” produced in injured tissue, Egdahl (1959) demonstrated that the adrenocortical response to limb injury in dogs is dependent on the stimulation of afferent sensory nerves. Plasma corticosteroid (cortisol) concentrations were measured in the adrenal vein in animals with 1) an intact sciatic nerve, 2) an operative injured nerve, and 3) after burn injury to the leg. In animals with an intact sciatic nerve, operative injury and burns to the limb resulted in immediate and sustained increased corticosteroid concentrations. Cutting the nerve after injury resulted in a rapid decline in the hormone response. In contrast, animals with their nerves transected before the injury had unchanged hormone concentrations after the trauma (Egdahl, 1959). Although Egdahl’s findings that the adrenocortical response to injury is dependent on the stimulation of afferent sensory nerves were observed in dogs, this physiological response is expected to apply generally to all mammalian species.

4.8.6.1. Effects of castration on glucocorticoid secretions

Although a number of routine husbandry stressors such as capture, handling and restraint can elicit glucocorticoid secretion (Grandin, 1997), several controlled studies in cattle have nevertheless successfully shown that the HPA-axis can be markedly stimulated to release excess cortisol in response to castration (Macaulay and Friend, 1987; Macaulay, 1989; King et al., 1991; Faulkner et al., 1992; Robertson et al., 1994; Chase et al., 1995; Molony et al., 1995; Fisher et al., 1996; 1997a,b;

Carragher et al., 1997; Earley and Crowe, 2002; Stafford et al., 2002). The magnitude of the cortisol secretion is generally correlated with the degree of surgical trauma (Weissman, 1990; Kehlet, 1991; Mellor et al., 2000). Cortisol secretions following surgical castration are substantially greater than that elicited by the Burdizzo or elastrator methods (Macaulay and Friend, 1987; Macaulay, 1989; Robertson et al., 1994; Molony et al., 1995; Fisher et al., 1996), indicating that this method caused the greatest trauma (Figure 5). Generally, the cortisol response to castration subsides by 24 h following treatment. However, Carragher et al. (1997) found that cortisol concentrations in surgically castrated 16-month-old bulls can continue to be elevated for up to 14 days after castration, but were normal by 28 days.

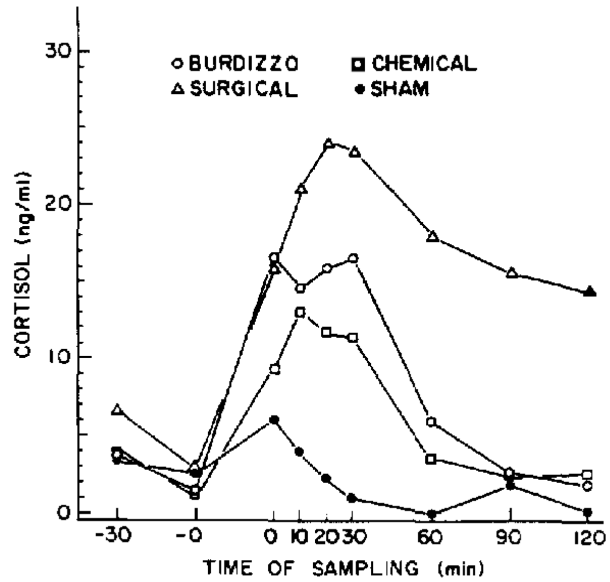

Figure 5 Cortisol concentrations in Holstein bull calves in response to surgical, Burdizzo, chemical, and sham castration (Macaulay, 1989).

Calves are capable of mounting a cortisol response to castration from when they reach between 5 to 7 days of age (Robertson et al., 1994; Molony et al., 1995). However, Mellor et al. (1991) found no cortisol response to rubber ring castration in 1 to 7 day-old calves. Compared with the surgical method, the use of Burdizzo castration (Molony et al., 1995; Fisher et al., 1996), coupled with reduction in the age at castration from 167 to 78 d of age (King et al., 1991) or from 42 to 21 days of age (Robertson et al., 1994) minimised the secretion of plasma cortisol elicited by the castration procedure in calves.

4.8.7. Effects of castration on β-endorphin production

No data are currently available on plasma β-endorphin secretion following castration in cattle. However, previous studies have reported that plasma β-endorphin is elevated in the blood from 15 min and up to 24 hours following surgical castration in lambs, when plasma cortisol has subsided (Shutt et al., 1987, 1988; Mears and Brown, 1997). Interestingly, in humans that have undergone surgery, plasma β-endorphin secretion is up-regulated, and can be positively correlated with postoperative pain severity (Matejec et al., 2003). However, the precise role of β-endorphin in modulating the response to pain remains to be elucidated in the bovine species.

4.8.8. Effects of castration on immunity and health

4.8.8.1. Castration effects on immunity

Several studies have established that castration in cattle causes the suppression of the adaptive immune function. Murata (1997) found that the suppression of Concanavalin A stimulated lymphocyte blastogenesis in whole blood culture occurred two days following Burdizzo castration in 3 to 4 month-old Holstein calves and the effect was accompanied by leukocytosis with neutrophilia. Similarly, Fisher et al. (1997a,b) and Earley and Crowe (2002) reported the suppression of *in vitro* IFN-γ production (stimulated with a novel mitogen Concanavalin A, or a recall antigen Keyhole Limpet haemocyanin) in cultured whole blood samples collected from surgically castrated 5 to 5.5 month-old Friesian calves at 24 and 72 hours after treatment. However, all of these studies showed that the temporal suppression of adaptive immune function was restored seven days after castration (Murata, 1997; Fisher et al., 1997b; Earley and Crowe, 2002).

4.8.8.2. Castration effects on animal health.

Although detailed epidemiological studies on the effects of castration per se on health are unavailable, earlier work by Addis and colleagues in the mid 1970s indicated that castration of calves causes adverse effects on animal health, particularly when it was performed at any time near weaning or shipment (cited in Zweiacher et al., 1979). This supports the theoretical framework developed by Moberg (Moberg, 1985, 1996, 2000) who postulated that exposure to multiple stressors leads to an adverse "cumulative" effect on the health and welfare of an animal. Zweiacher et al. (1979), in two separate studies, found that calves (mean BW = 180 kg) purchased as steers had less health problems than those purchased as bulls and subsequently castrated by surgical methods on arrival at a feedlot (mean percentage of animals requiring treatment for sickness = 17.5% for steers [n = 97] and 38.4% for surgical castrates [n = 104]). These health effects were not related to the time (castration on arrival versus after 1 week or after 2 weeks) or methods of castration (surgery with either use of an elastrator band for ligation, or crimping of testicular cords with an emasculator to prevent blood loss). However, the death losses were highest in bulls castrated on the day of arrival at the feedlot compared with bulls castrated one week, or two weeks after arrival (mean percentage death loss = 8.5% for bulls castrated on arrival [n = 35], 0.0% for bulls castrated after one week [n = 35], and 3% for bulls castrated after two weeks [n = 34]). These animals were also branded, dehorned, wormed and vaccinated on arrival at the feedlot. In their second study, surgical castration occurred on the day of arrival and the prophylactic treatment with oxytetracycline for the first three days appeared to reduce, but not prevent the higher occurrence of sickness in the castrates (mean percentage of animals requiring treatment for sickness = 2.6% for steers [n = 38] and 13.0% for surgical castrates [n = 85]; Zweiacher et al. [1979]). These findings are supported by Berry et al. (2001) who showed that calves (166 kg BW) purchased as bulls and subsequently castrated by a surgical method the day after arrival at a feedlot had greater incidences of sickness (requiring treatment for respiratory disease) than those calves purchased as steers (Table 3). However, in another study, these authors did not find any differences in terms of health response between steers, banded calves or surgically castrated calves on arrival. The main problems associated with the studies on the effects of castration on animal health reported so far are that there were numerous other confounding factors involved (e.g., transport, branding and dehorning). Thus more detailed and specific epidemiological studies may be warranted in order to draw a more definitive conclusion.

Table 3. Health status of crossbred male calves that were already castrated (steers) or castrated on the day after arrival at a feedlot (castrated bulls). All animals were ear-tagged, vaccinated, treated for parasites, and received a broad-spectrum antibiotic (Tilmicosin; Micotil, Elanco Animal Health) before the start of the experiment (Berry *et al.*, 2001)

	Treatments			
Item	Steers	Castrated bulls	SEM	P-value
Number of calves	24	81		
Number of treatments[a]	0.50	0.93	0.16	0.02
First medication rate[b]	0.33	0.59	0.10	0.03
Repeated treatment rate[c]	0.00	0.12	0.06	0.07
Second medication rate[d]	0.00	0.11	0.06	0.09
Treated, %				
at least once	33.3	59.3	–	–
greater than once	0.0	23.5	–	–

[a]Average number of times calves were removed from their pen for possible treatment.
[b]Average number of calves that received antibiotic treatment (florfenicol; Nuflor, Schering Plough).
[c]Average number of calves that received first treatment followed by second treatment within 7 days.
[d]Average number of calves that received a second treatment after recovery from initial sickness.

4.8.9. Conclusions regarding pain assessment

It is clear that there is an expansive array of literature regarding pain assessment in animals, although the majority of information for ruminants relates to castration. This involves a multitude of techniques associated with behaviour, physiological responses, immune responses, health and performance indicies, acute phase responses and changes in nociception. The scientific assessment of pain in animals is a complex and difficult task, and therefore in trying to come up with quick easily assessable indicators there is a risk of missing out on some key markers of pain response. Indeed there are a series of principals and caveats regarding the use of physiological and behavioural indices of pain that have been outlined in a recent review (Mellor and Stafford, 2004), that must be borne in mind. A suggested “Gold standard” approach is to select multiple (probably at least 3) independent measurements such as:

1. the HPA axis, ie cortisol which is generally a good indicator, but suffers the limitation that it can reach a maximum (or ceiling-effect) which may interfer in its value as an index of pain (especially during the peak in secretion);

2. behavioural responses, although care must be taken in regard to which behaviours are selected and how they may be accumulated into an index or score as well as experience of the observer;

3. immune responsiveness, the options here include suppression in lymphocyte blastogenic responses, suppression of in-vitro culture responsiveness of lymphocytes to secrete IFN-γ in response to stimulation by a novel mitogen or recall antigen, or suppression of immune response to a novel antigen or vaccine;

4. health and performance.

When using these indicators it is imperative to apply the guidelines, principals and caveats that have been outlined in detail by Mellor and Stafford (2004).

5. Pain management and therapeutics associated with husbandry procedures

5.1. The concept of pain management

The objectives of pain management are: 1) to alleviate the pain and inflammatory responses elicited following tissue trauma from potentially causing overt physiological reactions and psychological distress to the animal; 2) to improve the animal's ability to cope with the trauma; and 3) to improve wound healing and aid the animal to regain normal bodily functions more rapidly (Devey and Crowe, 1997; Otto and Short, 1998). Pain management for castration is achieved by pharmacological interventions. However, factors affecting the development of pain and inflammation, such as the age of animals, the techniques for the procedures (e.g., castration) and associated severity of injury, and the post-operative animal management may be optimised to reduce the adverse effects of castration.

5.2. The concept of analgesia and anaesthesia

The absence of pain in the presence of stimuli that would normally be painful is termed "analgesia" (Shafford et al., 2001), and analgesics are substances, which induce analgesia (Nolan, 2000). "Anaesthesia" is a term that refers to the loss of sensation, and anaesthetic substances operate by either blocking the nociceptive activity from reaching the brain (e.g., local anaesthesia), or preventing the brain from registering sensations (e.g., general anaesthesia) (Nolan, 2000; Dobromylskyj et al., 2000). Anaesthesia does not necessarily equate with analgesia. General anaesthesia produces loss of consciousness, so the animal cannot perceive pain, but in unconscious animals noxious stimuli will still be transmitted to and processed by the CNS (Dobromylskyj et al., 2000). However some anaesthetic agents also have analgesic properties (Dobromylskyj et al., 2000).

5.3. The concept of pre-emptive analgesia and multimodal pain therapy

Repeated stimulation from surgery or trauma and subsequent inflammation sensitises the peripheral nociceptors and spinal dorsal horn neurons. This leads to persistent pain and hypersensitivity. However this "wind-up" event can be minimised or prevented by pre-emptive administration of analgesia prior to injury. The benefits include reduced post-surgical pain and analgesic drug requirement (Shafford et al., 2001). Pain arises from a combination of peripheral and central hypersensitivity involving a multitude of pathways, mechanisms and transmitter systems, and it is unlikely that a single class of analgesic will optimally alleviate pain (Dobromylskyj et al., 2000). Therefore, a multimodal pain therapy involves use of two or more analgesic agents in combination to provide additive or synergistic analgesic effects to achieve a more "balanced" or optimum analgesia (Kehlet, 1994; Dobromylskyj et al., 2000). However, to date few studies addressing the alleviation of pain associated with husbandry procedures in cattle and sheep have adopted usage of combined analgesic agents.

6. The pharmacology of analgesic / anaesthetic drugs and their therapeutic uses for routine procedures in cattle and sheep

Pain treatment can be directed at the periphery, at sensory axons, or at central neurons (Otto and Short, 1998). Analgesic drugs may be divided into the following main classes (Otto and Short, 1998; Dahl and Ræder, 2000; Nolan, 2000):

1) Opioids

2) non-steroidal anti-inflammatory drugs
3) α_2-adrenergic agonists
4) local anaesthetics
5) Miscellaneous drugs – e.g., glutamate system antagonists (ketamine)

6.1. Opioids

Opioids may be referred to as narcotic analgesics because of their ability to induce narcosis, or a state of drowsiness in humans and some species of animals. Several distinct opioid receptors have been identified in the CNS, spinal cord, gastrointestinal tract, and various peripheral tissues. The three main opioid receptors identified include OP_3 or *mu* (μ), OP_2 or *kappa* (κ), and OP_1 or *delta* (δ). Opioid drugs may be classified according to their receptor selectivity, and may be active at one, two or all of the receptors. Thus opioids are categorised as either agonists, partial agonists, mixed agonist–antagonists, or antagonists. The activation of a receptor subtype is associated with a particular pharmacological profile; for instance, the activation of μ-receptors is associated with supraspinal analgesia, hypothermia, euphoria, miosis, bradycardia, respiratory depression, and physical dependence, whereas spinal analgesia, sedation, dysphoria, and miosis are mediated by κ-receptors. All opioid drugs displaying agonist activity at μ-receptors are analgesics. These include morphine, butophanol, buprenorphine (partial agonist), fentanyl, pethidine, methadone, and alfentanil. Systemically applied opioid analgesics hyperpolarize neurons and nerve terminals leading to 1) pre-synaptic inhibition of excitatory neurotransmitter release (voltage-gated calcium channels); and 2) desensitisation of post-synaptic membranes to neurotransmitters (reviewed by Otto and Short, 1998; Nolan, 2000; Twycross, 2000; George, 2003).

Morphine: While morphine has been used clinically in both sheep and pigs, it appears that relatively high doses are required. Even at these high doses effective analgesia is not always achieved in sheep (Chambers et al., 2002). In dogs it is widely distributed throughout the body and is rapidly cleared with a short elimination half-life (1-2 h; Merrell et al., 1990).

Butorphanol: Butorphanol is a mixed agonist/antagonist opioid drug, and is active at both the μ- and κ-receptors. Butorphanol is probably the most commonly used opioid in livestock (George, 2003). However the analgesic properties of butorphanol are poor and short-lived in many species. Indeed, licenced doses for dogs are often lower than those suggested from research studies (Sawyer et al., 1991).

Buprenorphine: After parenteral administration, buprenorphine has a slow onset to action and a long elimination half-life in dogs. In sheep its duration of action is about 3 hours (Nolan, 2000). The effectiveness of buphenorphine in ruminants appears dependent on the stimulus. Following orthopaedic surgery, it provided effective post-operative analgesia (0.01 mg buphenorphine / kg BW i.m.) in sheep (Otto et al., 2000). However it was ineffective against mechanical or electrical stimuli (0.005 mg / kg BW; Grant et al., 1996), but was effective against thermal stimuli (Nolan et al., 1987).

Fentanyl: Fentanyl is relatively short-acting, but generally highly potent, and is usually administered by an i.v. bolus injection. When administered to sheep at 10 µg/kg BW it provided analgesia against both mechanical and thermal stimuli for 0-60 minutes, but at a lower dose (5 µg/kg BW) it was only effective against thermal stimuli (Waterman at al., 1990). Again its short duration of action is a limitation on its use for pain relief in ruminants. More recently Fentanyl has been used by transdermal administration (via skin patches), these have been developed for human use and have been applied in animals (Kyles, 1998). Patches provide variable release rates, and are designed with resevoirs of fentanyl in an alcohol cellulose gel with a membrane controlling the rate of delivery of the drug to the skin. These have been applied in dogs, cats (Kyles et al., 1996; Scherk-Nixon, 1996), and pigs (Harvey-Clark et al., 2000) but not to ruminants.

Pethidine: Pethidine is less potent than morphine, and is rapidly cleared from the body (Waterman and Kalthun, 1989; 1990), and therefore has little potential use as an analgesic agent in ruminants. It is indicated to provide analgesia during parturition, and as a sedative. It is also indicated to relieve pain and discomfort following caesarian section and other major obstetric procedures.

Methadone: Similar in effect to morphine, although it may have a marginally longer duration of action (Nolan, 2000). However Grant et al. (1996), did not find methadone useful (0.6 mg/kg BW) in a model of acute pain in sheep.

Alfentanil: Alfentanil has a relatively short elimination half-life (0.4 to 2 hours), and achieves poor distribution within the body of horses and dogs (Pascoe et al., 1991; Hoke et al., 1997). It is predominantly used by i.v. infusion as a bolus before induction of anaesthesia, and although it does not appear to have been investigated it would not be expected to provide prolonged pain relief in ruminants.

While opioid analgesics have potential as pain relief agents during routine procedures they are not licensed for use in food animals under European Union legislation (Nolan, 2000). Of all the opoids, only pethidine is licenced in Australia for use in cattle. It is claimed to provide analgesia during parturition and to provide pain relief following caesarean section and other major obstetric procedures. Its dosage is in the range of 1-2 mg / kg BW by i.m. or slow i.v. routes. However it is listed in Poison Schedule 8 (i.e., it is a drug of addiction and is highly restricted to veterinary use only) and its use must be recorded in a register. In practice it is therefore not commonly used clinically in cattle.

6.2. Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs (**NSAIDs**) are non-narcotic agents, with anti-inflammatory, analgesic, and antipyretic properties of varying effectiveness depending on the particular drug and the clinical condition. The major categories of NSAID include: 1) salicylates (aspirin); 2) propionic acid derivatives (carprofen, fenoprofen, fenbufen, flurbiprofen, ibuprofen, indoprofen, naproxen, ketoprofen), 3) pyrazolon derivatives (phenylbutazone, oxyphenbutazone, antipyrine, aminopyrine); 4) anthranilic acids (meclofenamic acid), and 5) the aminonicotinic acid derivative (flunixin meglumine) (reviewed by Otto and Short, 1998; Nolan, 2000). However, only a limited list of these are licenced for use in ruminants (cattle). The licenced list includes: flunixin meglumine, carprofen, ketoprofen and meloxicam in the UK / Europe (Nolan, 2000). In Australia flunixin meglumine (Finadyne, and Flunix), tolfenamic acid (Tolfedine and Vetoquinol), ketoprofen (Ketofen) and meloxicam (Metacam) are licenced for use in cattle but no NSAIDs are approved for use in sheep. The basic mechanism of action of NSAIDs is the inhibition of the enzyme cyclooxygenase (**COX**), decreasing the production of prostaglandins at the peripheral site of tissue injury, and in the CNS. Prostaglandins are important mediators of inflammation, fever and pain, and they generally act as sensitising agents to enhance the activation of nociceptors, and facilitate the processing of nociceptive inputs in the CNS (Higgins et al., 1987; McCormack, 1994a; Vane and Botting, 1998; Dahl and Ræder, 2000). However, other centrally mediated, COX-independent pathways have also been identified (reviewed by McCormack, 1994a,b). For instance, the inhibitory mechanism of carprofen in calves appears to be independent of either COX or 12-lipoxygenase inhibition (Lees et al., 1996). Recent *in vitro* data indicated that the anti-inflammatory effects of carprofen and flunixin meglumine are mediated by the suppression of lipopolysaccharide-induction of inducible nitric oxide synthase, and nuclear factor κB activation (Bryant et al., 2003). NSAIDs have been shown to mediate their analgesic effect through interactions with the opioidergic and the α_2-adrenergic pain modulation systems (Chambers et al., 1995; Herrero and Headley, 1996). Chambers et al. (1995) reported that in healthy sheep administered flunixin or dipyrone, the rise in mechanical threshold was prevented by pre-treatment with naloxone (an opioid antagonist) or atipamezole (an α_2-adrenergic anatagonist). The COX enzyme is understood to exist as a number of isoforms, including COX-1 and COX-2. The COX-1 isoform is constitutively expressed in normal cells and is thought to be only involved in housekeeping functions (e.g., renal flow and protection of gastric mucosa) while COX-2 is thought to be inducible during pain and inflammation and does not usually exist constitutively in resting cells (e.g., Dahl and Ræder, 2000; Nolan, 2000). However, more recent data indicated that distinct genes for COX-1 and COX-2 may give rise to a number of constitutive as well as inducible COX proteins with overlapping functions (Chandrasekharan et al., 2002; Warner and Mitchell, 2002). A major drawback of some NSAIDs is the non-selective inhibition of COX involved in homeostasis, which can potentially cause gastrointestinal irritation resulting in ulcer formation (applies in particular to COX 1 inhibition), and nephrotoxicity (caused potentially by both COX1 and COX 2 inhibitors; Nolan, 2000). A further practical limitation on NSAIDs is the need for preemptive treatment 10 to 30 minutes before the procedure is carried out. The use of some of these NSAIDs as analgesic agents during husbandry procedures is discussed later.

Phenylbutazone: Phenylbutazone is a pyrazolone derivative. It has antipyretic, analgesic and antirheumatic effects. In cattle it is often used for the treatment of arthritis, laminitis, pyrexia, endotoxemia, viral respiratory disease and mastitis. It is no longer registered for use in cattle in Australia.

Aspirin: Aspirin (a salicylate) is an old well establlished NSAID used orally. However its use as an analgesic agent during husbandry procedures has not been investigated using appropriate doses.

Dipyrone: Dipyrone was one of the first NSAIDs to be developed. It is a pyrazolone derivative with a similar structure to phenylbutazone. Dipyrone (25 mg / kg BW i.v.) was effective as an analgesic agent both in healthy sheep challenged with a noxious mechanical stimuli and also increased pain thresholds in clinically lame sheep (Chambers et al., 1995). It is no longer registered for use in cattle in Australia.

Flunixin meglumine (Finadyne, and Flunix): Flunixin meglumine has very good analgesic, antipyretic and anti-inflammatory activity. It is a potent inhibitor of both COX 1 and COX 2 activity. In cattle it is indicated for respiratory disease, acute coliform mastitis, downer cows, calving paralysis, diarrhoea and pneumonia. It may be administered by the deep i.m or i.v. routes. With shallow i.m. injection it is excessively irritant. Flunixin meglumine (2.2 mg / kg BW i.v.) was effective as an analgesic agent both in healthy sheep challenged with a noxious mechanical stmuli and also increased pain thresholds in clinically lame sheep (Chambers et al., 1995). However, when used in a model detemining the response to electrical stimulation it was not effective (2 mg / kg BW i.m.; Grant et al., 1996).

Tolfenamic acid (Tolfedine and Vetoquinol): Tolfenamic acid is licenced for use as an analgesic to treat postoperative pain and to treat acute pain events associated with chronic musculoskeletal disease (i.e., it is an anti-inflammatory and antiarthritic agent). In cattle it is indicated for analgesia pain and inflammation associated with fever, lameness, mastitis, respiratory disease, downer cows, calving paralysis, post caesarian and parturition pain management. Administration is by i.m. or i.v. injection.

Ketoprofen (Ketofen): Ketoprofen is licenced for use in horses, cattle, dogs and cats. It is a potent, non-selective inhibitor of COX (1 and 2), and is a good anti-inflammatory, analgesic and antipyretic agent that is indicated for respiratory disease, musculoskeletal conditions, mastitis and peri / post operatively in cattle. It may be administered by both the i.v. and i.m. routes.

Meloxicam (Metacam): Meloxicam is more selective against the COX 2 rather than the COX 1 pathway. It exhibits anti-inflammatory, antiendotoxic, antiexudative, analgesic and antipyretic effects. It in indicated for use during acute respiratory infection, diarrhoea, and acute mastitis. Its route of administration is by either the i.v or the s.c route. Indeed it is one of the few NSAIDs that is non-irritant and can be tolerated with minimal if any adverse reactions when used by the s.c. route. As it is selective against COX 2, it generally has a lower propensity to cause gastrointestional irritation.

Carprofen: As metioned above, the action of carprofen may be independent of inhibition of COX enzymes at therapeutic doses, but yet it has good anti-inflammatory effects. It is not licenced in Australia for use in cattle, but it is in Europe, where it is indicated for the therapy of acute inflammation associated with respiratory disease.

6.3. α_2-adrenergic agonists

α_2-adrenergic agonists (e.g., xylazine, detomidine, medetomidine, and romifidine) are commonly used in veterinary medicine to induce sedation, analgesia and muscle relaxation by binding to α_2-adrenergic receptors present in the CNS. There are four different subtypes of α_2 receptors that are distributed within the brain, the spinal cord, and other tissues throughout the body. The dorsal horn neurons of the ruminant spinal cord contain a rich array of α_2-adrenergic receptors that bind to systemic or epidurally delivered agonists or antagonists. Ruminants are about 10 times more sensitive to the sedative effects of xylazine than horses and pigs. The usefulness of α_2-adrenergic agonists for inducing analgesia is limited by the profound effects of dose-dependent sedation and cardiovascular depression. Further, gut motility is inhibited, as α_2-adrenoceptors are located presynaptically on parasympathetic nerve terminals in intestinal smooth muscles. They also induce variable degrees of respiratory depression, and depress thermoregulation. Frequently used α_2-adrenergic agonists in large animals include xylazine and detomidine (reviewed by Otto and Short, 1998; Dart, 1999; Nolan, 2000; George, 2003). Xylazine is licensed for cattle in Europe and for both cattle and sheep in Australia. In sheep α_2-adrenergic agonists can induce dysponea and severe arterial hypoxaemia and should be used with considerable care (Waterman et al., 1987). Xylazine is indicated for sedation, analgesia and muscle relaxation. While these drugs are potent analgesics in most species (Nolan et al., 1987; in sheep see Grant et al., 1996 and Grant and Upton, 2001), their usefulness is restricted by their dose dependent sedation and cardiovascular depression (Khan et al., 1999). They may be administered im, s.c. or i.v. Xylazine may also be administered epidurally, although it has a relatively short effect.

6.4. Local anaesthetics

Local anaesthetics act by inhibiting the action potentials of any nervous fibre (peripheral or from CNS) responsible for nerve conduction, by the interaction of the drugs with the voltage-gated Na^+ channels (Arias, 1999). Thus, transmission of noxious signals along peripheral nerves is blocked in tissues exposed to a local anaesthetic, and the sensation of pain is abolished with complete analgesia. However, the duration of action is dependent on the time that the drug is in contact with the nerve, which is governed by the lipid solubility of the drug, the blood flow to the tissue, and the pH of the tissue. A vasoconstrictor (usually adrenaline) is frequently included in the preparation to prolong the effects (reviewed by Nolan, 2000). The large myelinated Aβ fibres and thin Aδ fibres are more susceptible to the local anaesthetic blockade than the unmyelinated C fibres (Huang et al., 1997). Amide-linked local anaesthetic drugs such as lignocaine, mepivacaine, and bupivacaine are commonly used in veterinary medicine. Lignocaine is a short acting drug with a rapid onset of action (5 to 10 min) and a maximum duration of action of 0.75 to 1 h that can be prolonged up to twice the normal length with adrenaline (Jones, 1997; Nolan, 2000). Longer acting drugs such as bupivacaine have a slow onset (reaching peak within 30 min) but prolonged duration of action varying from 2 to 6 h (Nolan, 2000). In Australia, lignocaine is registered for sheep and cattle, prolicaine is registered for cattle, while Bupivicaine is not registered.

6.5. Miscellaneous drugs - ketamine

Ketamine is a non-competitive antagonist of the N-methyl-D-aspartate (**NMDA**) receptor, one of the excitatory amino acid receptors at which glutamate acts. This receptor is intimately involved in the induction and maintenance of altered pain responses following trauma/inflammation (Woolf and Thompson, 1991; Nolan, 2000). Agonists of the receptor appear to have some analgesic and antihyperalgesic properties. However, the use of ketamine is restricted due to excitatory actions within the CNS (Nolan, 2000).

6.6. Epidural anaesthesia and analgesia

Epidural anaesthesia in large animals is frequently performed by administration of local anaesthetic agents (Otto and Short, 1998). Caudal epidural anaesthesia is induced by injection of a small volume (5 to 7 mL) of local anaesthetic into the epidural space of the spinal canal at either the sacrococcygeal space (S5-C1) or first intercoccygeal (C1-C2) space (Skarda, 1986; Caron and LeBlanc, 1989). Grubb et al. (2002) compared the efficacy of lignocaine and xylazine for inducing caudal epidural anaesthesia in dairy cattle weighing 520 to 613 kg. The authors reported that combined administration of lignocaine and xylazine (0.22 mg/kg and 0.05 mg/kg, respectively) produced a quicker onset (5 min) and longer duration (303 min) of analgesia (tested using the pinprick and haemostat pressure stimulation methods) than either drug given singly (Table 4). In all cattle, xylazine, administered either alone or with lignocaine, induced mild to moderate sedation and ataxia and cutaneous analgesia that ranged from the coccyx to approximately the T13 thoracic region. The cutaneous analgesia included the perineal region and was similar (but not always identical) in spread on both sides of the spine. Lignocaine alone produced mild ataxia and cutaneous analgesia limited to the perineal area in all cows. None of the cows experienced severe sedation or ataxia (Grubb et al., 2002).

Table 4. The dosage, time to onset and duration of action of analgesia after caudal epidural (sacrococcygeal space) administration of lignocaine, xylazine, or combined lignocaine-xylazine in nine adult (>4 year-old) dairy cows in a Latin square design (Grubb et al., 2002)

	Dose, mg/kg	Total volume, mL/500 kg	Time to onset of analgesia, min[a]	Duration of action, min[a,b]
Lignocaine[c]	0.22	5.5	4.8 ± 1.0[x]	81.8 ± 11.8[x]
Xylazine[d]	0.05	5.5	11.7 ± 1.0[y]	252.9 ± 18.9[y]
Lignocaine-xylazine	0.22/0.05	5.7	5.1 ± 0.9[x]	302.8 ± 11.0[z]

[a]Data are presented as mean ± SEM.

[b]Analgesia was defined as lack of a response to pin prick and haemostat pressure (closed to the first ratchet) applied first in the perineal area and then moved cranially toward the thoracic region until a response to either stimulation methods was observed.

[c]2% lignocaine hydrochloride without adrenaline (AmVet Pharmaceuticals, Fort Collins, CO, US).

[d]10% xylazine (AnaSed, Lloyd Laboratories, Shenandoah, IA, US) diluted with sterile water.
[xyz]Within column, values with a different superscript letter are different, $P < 0.05$.

The duration of analgesic effect of epidural drug is dependent on factors such as needle position, capacity of the epidural space, epidural fat, neural distance or cranial distribution, vascular or lymphatic absorption and the time required for elimination of the drug (De Rossi et al., 2003; Lee et al., 2003).

6.7. General anaesthesia

Generally, ruminants are considered poor subjects for general anaesthesia because of the hazards of tympany, regurgitation, and aspiration pneumonia (Reibold, 2003). The measures required to guard against hazards from general anaesthesia make it difficult to manage large numbers of animals (Mellor and Stafford, 1999). Therefore, it is unlikely that this technique will be of practical use for the castration or other routine husbandry procedures in large ruminants (Caulkett et al., 1993).

7. Application of anaesthesia / analgesia during husbandry procedures

The major local anaesthetic agents reported in the literature for use during husbandry procedures include lignocaine local anaesthesia (LA), bupivacaine LA and xylazine / lignocaine epidural. The main analgesic agents include the NSAIDs such as ketoprofen, carprofen, diclofenac, flunixin, meloxicam, tolfenamic acid, and aspirin. Generally there is little information available regarding dose titrations for use during castration, dehorning or tail docking. In the majority of cases the doses tested fall within the manufacturers recommended doses (Tables 5, 6, 7, 8) which are presumably arrived at based on clinical efficacy during studies for drug registration approval. Many reports on the use of NSAIDs relate to the treatment of respiratory disease, but generally there are limited scientific reports on their use and optimisation of dose rates for use as analgesic agents during husbandry procedures.

7.1. The legal requirement for the use of anaesthesia

7.1.1. Castration in cattle

The legal requirement for the use of anaesthesia for castration in cattle varies considerably between different countries depending on the method involved and the age of animals. However, the precise scientific basis for setting the requirements are unclear, but it may in part be due to public or consumer-driven demand for improved farm animal welfare by reducing the pain caused by routine husbandry procedures such as castration.

Table 5. Effectiveness of anaesthesia / analgesia agents during castration in cattle. Pain assessment is based on the more effective responses measured in each publication

Procedure	Age	Agent[a] (administration)	Dose rate	Route of Admin[b]	Pain assessment	Duration of effectiveness[c]	Author
Banding[d]	5.5 mo	Carprofen (-20 min)	1.4 mg/kg BW	IV	Cortisol	2 h	Pang et al., 2006
					Acute phase proteins	14 days	
Burdizzo	5.5 mo	Carprofen (-20 min)	1.4 mg/kg BW	IV	Cortisol	4 h	
					Acute phase proteins	None	
Burdizzo	< 1 mo	Lignocaine LA (-5 min)	10 ml 2%	Intra spermatic cord and SC	Behaviour	2-4h	Thuer et al., 2006
					Cortisol	2-4h	
Ring[e]		Lignocaine LA (-5 min)	10 ml 2%	Intra spermatic cord and SC	Behaviour	2-4h; but chronic pain	
					Cortisol	2-4h	
Burdizzo	13 mo	Ketoprofen (K; -20 min)	3 mg/kg BW	IV	Cortisol	12 h	Ting et al., 2003a
					Behaviour	6 h minimum	
		Lignocaine LA (-20 min)	18 mL 2%	Intra testes + SC	Cortisol	2 h	
					Behaviour	Not as effective as K	
		Epidural[f] (-10 min)	0.05 mg Xy + 0.4 mg L/ KG BW	Epidural	Cortisol	2 h	
					Behaviour	6 h minimum	
Surgical	11 mo	Ketoprofen	3 mg/kg BW	IV	Cortisol	8 h (prevented 2nd peak)	Ting et al., 2003b
					Immune function	24 h	
					Behaviour	6 h	
Ring	2-4 mo	Lignocaine LA	10 ml 2%	Intra testes + SC	Cortisol	3h: Effective	Stafford et al., 2002
		LA + Ketoprofen (-20 min)	LA + K 3mg/kgBW	IV	Cortisol	3h: Effective	
Banding	2-4 mo	Lignocaine LA	10 ml 2%	Intra testes + SC	Cortisol	3h: Effective	
		LA + Ketoprofen (-20 min)	LA + K 3mg/kgBW	IV	Cortisol	3h: Effective	
Surgical TR[f]	2-4 mo	Lignocaine LA	10 ml 2%	Intra testes + SC	Cortisol	None	
		LA + Ketoprofen (-20 min)	LA + K 3mg/kgBW	IV	Cortisol	3h: Effective	
Surgical EM[g]	2-4 mo	Lignocaine LA	10 ml 2%	Intra testes + SC	Cortisol	2.5 h Partial	
		LA + Ketoprofen (-20 min)	LA + K 3mg/kgBW	IV	Cortisol	2.5h: Effective	
Burdizzo	2-4 mo	Lignocaine LA	10 ml 2%	Intra testes + SC	Cortisol	None	
		LA + Ketoprofen (-20 min)	LA + K 3mg/kgBW	IV	Cortisol	1.5 h: Effective	
Surgical	5.5 mo	Ketoprofen (K; - 20 min)	3 mg/kg BW	IV	Cortisol	>12 h	Earley and Crowe, 2002
		Lignocaine LA (-20 min)	18 mL 2%	Intra testes + SC	Cortisol	1.5 h	
		K + LA (-20 min)	Combined	Combined	Cortisol	2.5 – 3 h	
Burdizzo	5.5 mo	Lignocaine LA (-15 min)	22ml 2%	Intra testes + SC	Cortisol	1.5 h	Fisher et al., 1996
					Testes size	Increased with LA	
Surgical	5.5 mo	Lignocaine LA (-15 min)	22ml 2%	Intra testes + SC	Cortisol	~1.5 h (not very effective	
Surgical	300-600k	Xylazine (-30 min)	0.07 mg / kg BW	Epidural	Behaviour reactivity	97% sedated effectively Analgesia in 80% of bulls	Caulkett et al., 1993
Surgical (Newbury)	6-9 mo	Butorphanol (-90 s) Xylazine	0.07mg/kg BW 0.02 mg/kg BW	IV	Cortisol, Haptoglobin	Not effective	Faulkner et al., 1992

[a]LA = local anaesthetic. [b]IV = Intra venous (jugular); SC = sub-cutaneous along burdizzo, ring or incision line. [c]Duration of effectiveness is based on the period during which reduction in the occurence of abnormal behaviour was observed or duration of suppression of cortisol as indicated in the pain

assessment column. [d]Banding with Callicrate bander, [e]Ring with Elastrator or equivalent, [f]Epidural with Lignocaine and Xylazine, [f]Surgical TR = cords broken by traction, [g]Surgical EM = cords cut with an emasculator

Table 6. Effectiveness of anaesthesia / analgesia agents during castration in sheep. Pain assessment is based on the more effective responses measured in each publication

Procedure[a]	Age	Agent[b](administration)	Dose rate	Route of Admin[c]	Pain assessment	Duration of effectiveness[d]	Author
Ring CX[e]	< 1 wk	Lignocaine LA (-5 min)	4 mg/kg BW in 5 ml	Intra spermatic	Behaviour	9 h	Mellema et al., 2006
				cord and SC	Cortisol	2 h	
Burdizzo CX	< 1 wk	Lignocaine LA (-5 min)	4 mg/kg BW in 5 ml	Intra spermatic	Behaviour	9 h	
				cord and SC	Cortisol	2 h (not as effective)	
Ring Cx plus ring TD	< 2 d	Lignocaine LA (0 s) -high pressure needleless	0.3 ml 2% each	Scrotal neck	Behaviour	Reduced abnormal activity score	Kent et al., 2004
Ring CX plus ring TD	Neonatal	Carprofen	0.5 mg/kg BW	SC	Behaviour / Haptoglobin	Not effective	Price and Nolan, 2001
Ring CX[e] Plus ring tail docking)	6 wk	Lignocaine LA (-5 to 10 s)	1.5 ml 2%	Scrotal neck	Cortisol	2.5h; partially effective	Sutherland et al., 1999
		Lignocaine LA (+5 to 10 s)	1 ml 2% per testis	Intra testes	Cortisol	2.5h; partially effective	
Ring CX and TD[e]	1 wk	Lignocaine LA (0 s) -high pressure needleless	0.4 ml 2% each	Scrotal neck & tail	Behaviour Cortisol	Effective 60% reduction in peak	Kent et al., 1998
		Lignocaine LA (0 s) - needle and syringe	0.4 ml 2% each	Scrotal neck & tail	Behaviour Cortisol	Effective	
		Lignocaine LA (0 s) -high pressure needleless		Intra testes	Behaviour Cortisol	Less effective than scrotal Neck	
		Powered clamp		Proximal to ring	Behaviour Cortisol	Effective [duration?] 44% reduction in peak	
None	~18 mo	Xylazine (2%)	0.2 mg/kg BW	Epidural	Pin prick test	72 to 99 min	Mohammed & Liman, 1998
Burdizzo CX		Diclofenac (-20 min)	1.5 mg/kg	IM	Behaviour Cortisol	Effective 2.2 h; Effective	Molony et al., 1997
		Bupivacaine LA (-1 to 2min)	0.5 ml (0.25 %)	Intra testes	Behaviour Cortisol	Not effective 1 h; partially effective	
Ring/Burdizzo CX		None			Behaviour Cortisol	Not effective Not effective	
		Bupivacaine LA (-1 to 2 min)	0.5 ml (0.25 %)	Intra testes	Behaviour Cortisol	Partially effective Not effective	
Surgical CX	8 mo	Lignocaine (-10 min)	0.6 - 1.0 mg/kg BW	Intrathecal	Analgesia scores	Effective in 10/11 rams	Scott et al., 1996
Ring CX/TD	< 1 wk	Lignocaine (-15 to 20 min)	0.3 ml (2%)	Coccygeal epidural	}		Wood et al., 1991
			3 ml (2%	Spermatic cord, scrotal neck & intra testes	Behaviour Cortisol	Effective Effective	
		Naloxone (-10 to 12 min	0.2 mg/kg BW	IV	Behaviour Cortisol	Not effective Not effective	

[a]CX = castration; TD = tail docking; Ring docking or castration was with an elastrator. [b]LA = local anasthesia; [c]IV = Intra venous (jugular); SC = sub-cutaneous along burdizzo, ring or incision line, IM = intramuscular. [d]Duration of effectiveness is based on the period during which reduction in the occurence of abnormal behaviour was observed or duration of suppression of cortisol as indicated in the pain assessment column. In most cases the behaviour indicator used was abnormal postures / behaviours. [e]Ring with Elastrator or equivalent

Table 7. Effectiveness of anaesthesia / analgesia agents during tail docking in sheep. Pain assessment is based on the more effective responses measured in each publication

Procedure[a]	Age	Agent[b](administration)	Dose rate	Route of Admin[c]	Pain assessment	Duration of effectiveness[d]	Author
Ring TD plus ring Cx	< 2 d	Lignocaine LA (0 s) -high pressure needleless	0.3 ml 2% each	Tail around ring	Behaviour	Reduced abnormal activity score	Kent et al., 2004
Ring CX plus ring TD[e]	Neonatal	Carprofen	0.5 mg/kg BW	SC	Behaviour / Haptoglobin	Not effective	Price and Nolan, 2001
Ring TD[e]	3-6 wks	Aspirin	26 mg / kg BW[f]	oral	Behaviour	Not effective	Pollard et al., 2001
Ring CX and TD[e]	1 wk	Lignocaine LA (0 s) -high pressure needleless	0.4 ml 2% each	Scrotal neck & tail	Behaviour Cortisol	Effective 60% reduction in peak	Kent et al., 1998
		Lignocaine LA (0 s) - needle and syringe	0.4 ml 2% each	Scrotal neck & tail	Behaviour Cortisol	Effective	
		Lignocaine LA (0 s) -high pressure needleless		Intra testes	Behaviour Cortisol	Less effective than scrotal neck	
		Powered clamp		Proximal to ring	Behaviour Cortisol	Effective 44% reduction in peak	
Ring TD[e]	3 wk	Bupivacaine LA (-1 to 2 min)	1.0 ml (0.25 %)	SC	Cortisol Behaviour	Effective Effective	Graham et al., 1997
		Bupivacaine (-1 to 2 min)	0.5 ml (0.25 %)	Epidural	Cortisol Behaviour	Effective Not effective	
		Ralgres freeze spray (- 3s)	~6 ml	Topical around tail	Cortisol Behaviour	Effective Not effective	
		Diclofenac (-20 min)	1.5 mg/kg	IM	Cortisol Behaviour	Effective Not effective	
Ring[e]/Burd TD		Bupivacaine LA (-1 to 2 min)	1.0 ml (0.25 %)	SC	Cortisol	Not effective	
		Bupivacaine (-1 to 2 min)	0.5 ml (0.25 %)	Epidural	Cortisol	Effective	
		Ralgres freeze spray (- 3s)	~6 ml	Topical around tail	Cortisol	Not effective	
Hot Iron TD		Bupivacaine LA (-1 to 2 min)	1.0 ml (0.25 %)	SC	Cortisol	Not effective	
		Bupivacaine (-1 to 2 min)	0.5 ml (0.25 %)	Epidural	Cortisol	Effective	
		Diclofenac (-20 min)	1.5 mg/kg	IM	Cortisol	Not effective	
Ring CX/TD	< 1 wk	Lignocaine (-15 to 20 min)	0.3 ml (2%)	Coccygeal epidural			Wood et al., 1991
			3 ml (2%	Spermatic cord, scrotal neck &intra testes	Behaviour Cortisol	Effective Effective	
		Naloxone (-10 to 12 min	0.2 mg/kg BW	IV	Behaviour Cortisol	Not effective Not effective	

[a]CX = castration; TD = tail docking; Ring docking or castration was with an elastrator. [b]LA = local anasthesia; [c]IV = Intra venous (jugular); SC = sub-cutaneous along burdizzo, ring or incision line, IM = intramuscular. [d]Duration of effectiveness is based on the period during which reduction in the occurence

of abnormal behaviour was observed or duration of suppression of cortisol as indicated in the pain assessment column. In most cases the behaviour indicator used was abnormal postures / behaviours. [e]Ring with Elastrator or equivalent. [f]Dose rate of Aspirin was inadequate.

Table 8. Effectiveness of anaesthesia / analgesia agents during dehorning in cattle. Pain assessment is based on the more effective responses measured in each publication

Procedure	Age	Agent[a] (administration)	Dose rate	Route of Admin[b]	Pain assessment	Duration of effectiveness[c]	Author
Caustic paste (+Xylazine sedative)	1-5wk	Lignocaine (-10 min)	4.5ml/horn (2%)	Cornual nerve	Behaviour	Not effective	Vickers et al., 2005
Cautery disbudding (+Xylazine sedative)	1-5wk	Lignocaine (-10 min)	4.5ml/horn (2%)	& around bud	Behaviour	Not effective	
Cautery disbudding (+Lignocaine LA)	< 2 wk	Ketoprofen (K) (-10 min)	3 mg/kg BW	IM	Behaviour Cortisol	Not effective Reduced peak?	Milligan et al., 2004
Amputation dehorning (Scoop)	12-14 wk	Lignocaine+K (-15 min)	5ml/horn; 3mg/kg	Cornual; IV	Cortisol	Effective	Stafford et al., 2003
		Xylazine (-20 min)	0.1 mg/kg BW	IV	Cortisol	Effective for 2h only	
		Xylazine (-20 min) + Lignocaine (-15 min)	0.1 mg/kg BW 5 ml/horn	IV Cornual nerve	Cortisol	Effective for 3 h only	
		Xylazine + LA + tolazoline reversa (+5min	As above; T at 2 mg/kg BW	As above; T IV	Cortisol	Not of additional benefit	
Amputation dehorning (Scoop)	12-16wk	Lignocaine (L; -15 min) + bupivacaine(B; +2h)LA	6 ml / horn (2%) 6 ml / horn (.25%	Cornual nerve Cornual nerve	Cortisol	5h effective, deferred peak	Sutherland et al., 2002b
		L + B LA +phenylbutazone (-15min	 4-5.3mg/kg BW	Cornual nerve IV	Cortisol	5h effective, deferred peak	
		L + B LA +ketoprofen (-15min)	 4-5.3mg/kg BW	Cornual nerve IV	Cortisol	5h effective, partially effective thereafter	
Amputation dehorning (Scoop)	12-16wk	Lignocaine (L; -15 min) + bupivacaine(B; +2h)LA	6 ml / horn (2%) 6 ml / horn (.25%	Cornual nerve Cornual nerve	Cortisol	5h effective, deferred peak	Sutherland et al., 2002a
		LA + cautery			Cortisol	>24h effective, no peak	
Cautery disbudding (+Xylazine sedative&Lignocaine LA)	4-8 wk	Ketroprofen (-2, +2, +7h)	3 mg/kg(anafen)	Oral	Behaviour	>24 h effective	Faulkner &Weary, 2000
Cautery disbudding	4-6wk	Lignocaine LA (-15 min)	(2%)	Cornual nerve	Co/Beh/HR*	Partially effective	Grondahl-Neilsen et al., 1999
		Lignocaine LA (-15 min) + xylazine/butorphanol (-20 mi	(2%) 0.2, 0.1 mg/kg	Cornual nerve IM	Co/Beh/HR	Partially effective	
		Xylazine/butorphanol (-20 mi	0.2, 0.1 mg/kg	IM	Co/ Beh/ HR	Partially effective	
Cautery disbudding	4-6wk	Lignocaine LA (–20 min)	13 ml (2%)	Cornual nerve & around bud	Behaviour Cortisol	2 h effective 1.5h effective	Graf & Senn, 1999
Amputation dehorning (Scoop)	12-16wk	Bupivacaine (B; -20min)	6 ml / horn (.25%	Cornual nerve	Cortisol	Effective 0.5-4h deferred peak	McMeekan et al., 1998b
		Ketoprofen (K; -20 min)	3 ml 10%	IV	Cortisol	Effective from 2 - 9 h	
		Lignocaine (L)+K (-20min)	6 ml 2% L + K	L: CN; K IV	Cortisol	Effective 0 – 9 h	
		B +K (-20min)	6ml .25% B + K	B: CN; K IV	Cortisol	Effective 0-6 h	
Amputation dehorning (Scoop)	12-16wk	Bupivacaine (B; -20min)	6 ml / horn (.25%	Cornual nerve	Cortisol	Effective 0.5-4h deferred peak	McMeekan et al., 1998a
		B (-20min, + 4h)	6 ml / horn (.25%	Cornual nerve	Cortisol	Effective 0.5-6.5 h,deferred peak	
Amputation dehorning (Scoop)	20-24 wk	Lignocaine LA (-30 min)	6 ml / horn (2%)	Cornual nerve	Cortisol	Effective 0.5-3h deferred peak	Sylvester et al., 1998b
		Cautery for 6 s		On wound	Cortisol	Reduced the 2nd peak	
		LA + Cautery		Combined	Cortisol	Effective 0.5 to 9 h	
Amputation dehorning (Scoop)	6-8 wk	Lignocaine LA (-20 min)	3 ml / horn (2%)	Cornual nerve	Cortisol	Effective 0-2 h deferred peak	Petrie et al., 1996
Cautery disbudding		Lignocaine LA (-20 min)	3 ml / horn (2%)	Cornual nerve	Cortisol	Marginal benefit 0.5-1h	
Caustic paste	4-8 wk	Lignocaine LA (-15 min)	4 ml / horn (2%)	Cornual nerve	Behaviour	Reduced adverse reactions	Morisse et al., 1995**
Cautery disbudding		Lignocaine LA (-15 min)	4 ml / horn (2%)	Cornual nerve	Behaviour	Reduced adverse reactions	

[a]LA = local anaesthesia; [a]IV = Intravenous, IM = intramuscular, CN = cornual nerve. [c]Duration of effectiveness is based on the period during which reduction in the occurence of abnormal behaviour was observed or duration of suppression of cortisol as indicated in the pain assessment column. *Co = cortisol, Beh = behaviour, HR = Heart rate.
**Cortisol was measured but with inadequate sample frequency.

In Ireland, use of anaesthesia is required for surgical/Burdizzo castration of cattle over six months of age (Protection of Animals [Amendment] Act 1965 [S.I. 10 of 1965]; Oireachtas, 1965). In contrast, castration of calves without use of anaesthesia must be done before they reach two months of age in the UK (Veterinary Surgeons Act 1966; DEFRA, 2003). In Ireland and the UK, rubber ring castration (or use of other devices for constricting the flow of blood to the scrotum) without use of anaesthesia can only be performed in calves less than seven days of age (Oireachtas, 1965; DEFRA, 2003). In New Zealand, cattle should be castrated as young as possible, but when carried out on animals over six months of age pain relief must be used (New Zealand National Animal Welfare Advisory Committee, 2005). Furthermore, if the technique of tightened latex bands (banding) is used then pain relief must be provided irrespective of age (NZ Animal Welfare; Painful Husbandry Procedures; Code of Welfare, 2005, issued under the Animal Welfare Act, 1999). In Germany, castration of cattle without use of anaesthesia is allowed only in animals less than four weeks of age (Animal Welfare Act 1998; cited by Animal Legal and Historical Centre, Michigan State University, 2003). In Switzerland, castration of male cattle has been prohibited without anaesthesia since September 2001 (Artikel 65 der Tierschutzverordnung vom 1 Septemeber 2001 [Article 65 of the Swiss Animal Protection Ordinance, Amendment 2001]; Steiner et al., 2002). Furthermore, the use of elastic rings for castration of animals is forbidden in Germany and Switzerland. By contrast, there is no legal requirement for the use of anaesthesia for castration in the US (Capucille et al., 2002). In Australia, the “Australian model code of practice for the welfare of animals – Cattle” (Primary Industries Standing Committee, 2004) requires that castration of cattle without the use of local or general anaesthesia should be confined to calves at their first muster prior to weaning and preferably to calves under the age of six months, and only in exceptional circumstances should castration be left to greater than 6 months of age. At this point it is preferable if the procedure is performed by a veterinarian. Castration greater than 6 months of age unless by a veterinarian is illegal under some state and territory legislation (Primary Industries Standing Committee, 2004, section 5.4). It is recommended that castration in calves by rubber rings be restricted to those less than 2 weeks of age, and use of the burdizzo method should be performed on bulls as young as possible. In all of the countries mentioned above, where the administration of anaesthesia is required for castration, the procedure must be done either by a veterinarian or under veterinary supervision.

7.1.2. Dehorning in cattle

In the case of cattle dehorning, the Australian code of practice is similar to that for castration. Dehorning without local anaesthetics should be confined to animals at the first muster and preferable under 6 months of age. In older cattle tipping (removal of horn tips without cutting into sensitive tissues) is permitted without anaesthesia. Dehorning of calves is recommended by either scoop dehorners, gouging knife or heat cautery as soon as the horn buds are detectable (Primary Industries Standing Committee, 2004). Dehorning in many European countries is achieved by heat cauterization of the young horn bud along with the use of local anaesthesia. Otherwise dehorning of older animals generally occurs by use of a saw or foetotomy wire along with the use of local anaesthesia.

7.1.3. Tail Docking and castration in Sheep

In sheep tail docking up to 6 months of age is permitted without anaesthesia, and is preferably conducted between 2 and 12 weeks of age (Primary Industries Standing Committee, 1991). Castration of sheep, when required, is preferably conducted before 12 weeks of age, and again beyond 6 months of age anaesthesia is recommended (Primary Industries Standing Committee, 1991). In many European countries tail-docking and castration of lambs with rubber rings occurs within the first 2 weeks of life, generally it is required by most codes of practice that rubber rings should not be used beyond 1 to 2 weeks of age.

7.2. Cattle

A number of studies have compared various pain management techniques for cattle subjected to castration procedures (Table 5) and where they have used a combination of pain assessment techniques (eg cortisol, behaviour and immune response measures), the effects are generally consistent across the range of measures used. Faulkner et al. (1992) showed that i.v. administration of butorphanol and xylazine (0.07 mg/kg and 0.02 mg/kg, respectively) in 6 to 9 month old cattle did not alleviate the post-castration increase in plasma cortisol and acute-phase protein, haptoglobin. However, the drug was administrated only 90 seconds before the restraint and castration procedure, which may have been insufficient to take effect. Effective sedation with xylazine requires 3 to 5 minutes when it is administered by the i.v. route. In a review, Steiner et al. (2002) concluded that the sedation with xylazine and injection of lignocaine into the base of the scrotum, followed by Burdizzo castration could provide a safe technique for "pain-free" castration of young calves less than one month of age. However, in a study by Fisher et al. (1996), the administration of lignocaine local anaesthesia before surgical or Burdizzo castration of 5.5 month-old calves reduced the cortisol response to the procedure for the first 0.25 to 1.5 h, but had no effect on the overall 12-h integrated cortisol response. This was due to a marked increase in cortisol concentrations that occured when the effect of the lignocaine wears off. This observation was consistent with the usage of lignocaine as a cornual nerve block administered 15 to 20 minutes before amputation dehorning in cattle (Petri et al., 1996; Sylvester et al., 1998b).

Use of the NSAID, ketoprofen, effectively suppressed the surgical castration-induced peak cortisol response, and the 12 hour integrated cortisol response by 56% relative to surgery alone and by 40% relative to surgery with local anaesthesia in both 5.5 month old (Earley and Crowe, 2002) and 11 month old (Ting et al., 2003b) Friesian bulls. Furthermore, a combined administration of ketoprofen and local anaesthesia delayed the peak cortisol (Earley and Crowe, 2002) response by 4 h relative to surgery alone. However the overall integrated cortisol response over 12 hours was greater than the ketoprofen treatment alone due to a delayed secondary peak in cortisol response (Table 9; Earley and Crowe, 2002). The reason for this was unclear. In contrast, Stafford et al. (2002) showed that a combined local anaesthetic and ketoprofen administration almost completely eliminated the peak and integrated plasma cortisol responses of 2 to 4 month old Friesian calves to surgical castration. With burdizzo castration of 13 month old bulls, ketoprofen was more effective at reducing the overall cortisol response than either local anaesthesia or epidural anaesthesia, it was also effective at minimizing pain-associated behaviours (Ting et al., 2003a). Further work with an alternative cheaper NSAID, carprofen (Rimadyl approximately 1/3 the cost of Ketofen, in Europe), was less effective at alleviating the pain markers following castration (banding or burdizzo; Pang et al., 2006), although it tended to reduce the integrated cortisol response and the acute phase protein response.

Caulkett et al. (1993) assessed the degree of sedation, ataxia and analgesia following caudal epidural xylazine (0.07 mg/kg in 7.5 mL) administrated at a mean time of 30 min before surgical castration of 300 to 600 kg bulls. They reported that adequate sedation was achieved in 97.4% of animals and good surgical analgesia was achieved in 80.5% of animals. However, their assessment was limited to behavioural reactivity. Only 16.9% of animals displayed ataxia. The authors concluded that the method provided sufficient sedation and analgesia for the castration of mature bulls. In a more comprehensive study Ting et al. (2003a) compared the effect of combined xylazine/lignocaine caudal epidural anaesthesia with both lignocaine local anaesthesia and ketoprofen NSAID when castrating by the burdizzo method. Consistent with earlier studies Fisher et al. (1996), LA reduced the peak cortisol concentrations following castration, there was a secondary rise in cortisol resulting in the total integrated (AUC) cortisol response being similar to that of castration without anaesthesia / analgesia. Xylazine / lignocaine caudal epidural anaesthesia was no better than local anaesthesia (similar suppression of the peak response, but had a secondary rebound effect), while Ketoprofen NSAID was effective at reducing both the peak and overall cortisol response (Figure 7).

Table 9. Mean ± SE area under the 12-h cortisol curve (AUC), peak cortisol, and interval to peak cortisol concentrations of 5.5 month old Friesian calves left untreated (C), surgically castrated (S), surgically castrated following ketoprofen (S + K), surgically castrated following local anaesthetic administration (S + LA), or surgically castrated following local anaesthetic and ketoprofen (S + LA + K; n = 8/treatment group).

Plasma cortisol	Treatment				
	C	S	S + K	S + LA	S + LA + K
AUC, $ng/mL^{-1} \cdot h$	56.8 ± 5.37^{a}	176.1 ± 27.68^{d}	78.1 ± 13.87^{ab}	130.8 ± 15.18^{cd}	117.6 ± 19.76^{bc}
Peak, ng/mL	19.0 ± 4.63^{a}	45.8 ± 6.16^{b}	24.7 ± 5.12^{a}	22.1 ± 2.69^{a}	28.8 ± 4.23^{a}
Interval to peak, h	–	0.31 ± 0.04^{a}	0.29 ± 0.04^{a}	2.63 ± 0.77^{b}	4.61 ± 1.75^{b}

[a,b,c,d] Means within a row without common superscripts are different ($P < 0.05$)
Source: Earley and Crowe (2002)

The effectiveness of local anaesthesia for castration seems to depend on the method of administration. Cottrell and Molony (1995) reported that intratesticular injection of local anaesthesia (0.1 mL of 2% lignocaine without adrenaline) abolishes the impulse activity of the superior spermatic nerve within two minutes of injection in lambs subjected to rubber ring castration. However, they commented that other nerves supplying the scrotal area may not be effectively blocked. These include nerves originating from the scrotal plexus – the distal cutaneous branch, the scrotal nerve, and the genitofemoral nerves, as well as other visceral afferent nerves from the epididymis, vas deferens, and mechanoreceptors in the parietal peritoneum of the vaginal ring (Cottrell and Molony, 1995).

When dehorning cattle (Table 8), lignocaine LA was somewhat effective at reducing cortisol rises and adverse behaviours during cautery or caustic paste disbudding for a period of 1.5 to 2 h (Morisse et al., 1995; Petri et al., 1996, Graf and Senn, 1999; Grondahl-Neilsen et al., 1999) in young calves (4-8 weeks). Although it produced no discernable benefit when used in conjunction with xylazine sedative (Vickers et al., 2005) in 1 to 5 week old calves. When ketoprofen (3 mg/kg BW orally in milk 2 hours pre, 2 hours post and 7 hours post dehorning) was used in conjunction with xylazine sedative and lignocaine LA an effective 24 hour period of pain alleviation was achieved (Faulkner and Weary, 2000).

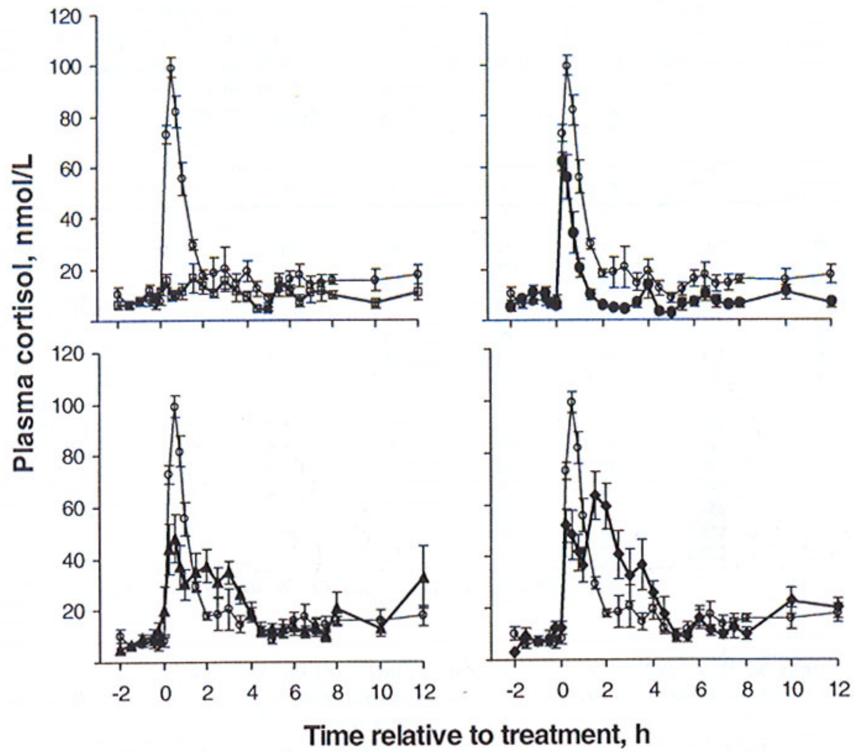

Figure 7: Mean ± SE plasma cortisol concentrations for bulls left untreated (□), burdizzo castration (**O**), burdizzo castration following ketoprofen administration (●), burdizzo castration following Lignocaine local anaeshesia (σ), or burdizzo castration following combined xylazine and Lignocaine caudal epidural anaesthesia (υ); n = 9 for untreated controls and n= 10 in other treatments. The integrated plasma cortisol responses (area under the curve) were greater (P < 0.05) in all castrated animals than in control bulls. The administration of ketoprofen, local or caudal epidural anaesthesia reduced (P < 0.05) the peak cortisol response to castration, but only ketoprofen decreased (P <0.05) the integrated cortisol response compared with castration alone or castration with local or caudal epidural anaesthesia (Ting et al., 2003a).

In the case of the more severe amputation dehorning (scoop) in older calves, local anaesthesia (Lignocaine or Bupivicaine) was only partially effective at alleviating pain for a period of 2 to 4 hours, respectively (Petri et a., 1996, Sylvester et al., 1998b, McMeekan et al., 1998a, b). When these two anaesthetic agents were administered sequentially (Lignocaine at –15 minutes relative to horn amputation, and bupivicaine 2 hour post amputation) a 5 hours period of pain alleviation was achieved (Sutherland et al., 2002 a, b). However prolonging the local anaesthesia effectively only deferred the rise in cortisol without completely preventing it (McMeekan et al, 1998b, Sutherland et al., 2002a,b). Use of the NSAID, ketoprofen, administered 15 to 20 min before de-horning had little effect on peak cortisol, but ensured a rapid reduction in cortisol to pre-treatment baseline concentrations (Table 8; McMeekan et al., 1998b). However, when phenylbutazone (a NSAID) was used, it failed to prevent the inflammation-related cortisol response, suggesting that as in other species it is mainly anti-inflammatory rather than analgesic (Chambers et al., 2002). In the calf dehorning model the combined use of pre-emptive ketoprofen and lignocaine together virtually eliminated the cortisol response to dehorning (McMeekan et al., 1998b; Sutherland et al., 2002b). Indeed the behaviour of calves receiving this combined ketoprofen and local anaesthesia was similar to that of controls over the acute and chronic period following dehorning (McMeekan et al., 1999). However where ketoprofen was used in conjunction with longer acting local anaesthetics (bupivacaine; 4 hours; or lignocaine followed by bupivacaine; 5 hours) there was a significant cortisol response once the local anaesthesia wore off (Sutherland et al., 2002b). Similarly the use of ketoprofen in combination with local anaesthesia during scoop amputation dehorning was effective at maintaining low cortisol up to 8 hours post dehorning (Stafford et al., 2003). In the same study Stafford et al. (2003), clearly demonstrated that xylazine sedation, or xlyazine sedation with local anaesthesia (lignocaine) were effective at alleviating pain for only 2 or 3 hours, respectively. Heat cauterization of the amputation wound in association with local anaesthesia was also very effective (Sutherland 1998a). Unfortunately there is a complete absence of literature available on other methods of amputation dehorning (foetotomy wire, saw, guillotine) and alleviation of the associated pain.

Therefore in cattle it can be concluded that the optimal and most practical methods for alleviation of prolonged pain following castration is the use of Ketoprofen NSAID administered IV (Earley and Crowe, 2002; Ting et al., 2003a, 2003b; Table 5), rather than local anaesthesia (contrary to most legislation in this area). Few other alternative NSAIDs have been tested yet, but certainly carprofen was less effective (Pang et al., 2006; Table 5). Likewise for the disbudding (cautery or caustic) of horns in young calves ketoprofen along with local anaesthesia is beneficial, however it needs to be examined both in the presence and absence of LA (Table 8). For horn amputation (scoop) the most effective option of achieving pain relief appears to be lignocaine LA in conjunction with Ketoprofen NSAID (Table 8; McMeekan et al., 1998b; Stafford et al., 2003). Unfortunately Ketoprofen is one of the more expensive NSAIDs available, and further work is required to determine if any cheaper alternatives are effective. With the use of ketoprofen, further work looking at i.m. and oral administration is required both for castration and dehorning procedures. Further work is also required to look at other amputation dehorning methods and associated pain relief options. Another practical limitation on NSAIDs is the need for preemptive treatment 10 to 30 minutes before the procedure is carried out. Detailed studies evaluating the timing of administration of NSAIDs before castration or dehorning are therefore required. Combined local anaesthesia with NSAID treatments will pose difficulty in practice where they are to be administered at somewhat different times relative to the procedure being performed. If the timings can coincide it will improve the practical application of combined anaesthesia / analgesia approaches.

7.3. Sheep

In sheep lignocaine LA is the most commonly assessed drug for pain relief during castration (Table 6). It has been administered either intra-spermatic cord and subcutaneously (Mellema et al., 2006), or intra-testes and subcutaneously (Molony et al., 1997; Kent et al., 1998; Sutherland et al., 1999), around the scrotal neck (Kent et al., 1998; Sutherland et al., 1999) or in a combination of caudal epidural, intratestes, scrotal neck and spermatic cord (Wood et al., 1991). This combined route of administration with Lignocaine was effective (Wood et al., 1991) but would be impractical for large scale application. Clearly the papers in Table 6 indicate that the scrotal neck or spermatic cord routes are more effective for lignocaine administration than intra-testicular. Use of bupivicaine has not been exhaustively tested and where it was used there was an inadequate wait for this long acting anaesthetic agent to achieve effective analgesia before castration (Molony et al., 1997), normally 10-20 min would be required for bupivicaine to take effect. Xylazine epidural has been assessed in older rams (18 months) as a means to achieving analgesia (determined by pin prick), but has not been tested as a means for pain relief during castration (Mohammed and Liman, 1988). The only NSAID tested for use during castration in sheep is Diclofenac, and it appeared to be effective (Molony et al., 1997). Combining rubber ring castration with a clamp (burdizzo or other) was also effective at reducing the perceived pain associated with castration of lambs (Kent et al., 1995, 1998, 2001; see earlier discussion on this in section 3.3). Administration of local anaesthetic (2 % lignocaine with adrenaline) under the rubber ring with a high-pressure jet injector when castrating (with simultaneous tail-docking) decreased abnormal limb and tail movement by 78% and also decreased the time spent in abnormal postures compared with rubber rings alone (Table 6; Kent et al., 2004).

Again for tail docking in sheep only limited attempts at pain alleviation are reported (Table 7). Lignocaine, Bupivacaine and Diclofenac (NSAID) use has been assessed (Wood et al., 1991; Graham et al., 997; Kent et al., 1998). However both the Wood et al. (1991) and Kent et al. (1998) studies are confounded with concurrent castration. Lignocaine and bupivacaine both appear to be effective (Graham et al., 1997; Kent et al., 1998). Additionally, administration of local anaesthetic (2 % lignocaine with adrenaline) under the rubber ring with a high-pressure jet injector when tail-docking (with simultaneous castration) decreased abnormal limb and tail movement by 78% and also decreased the time spent in abnormal postures compared with rubber rings alone (Table 7; Kent et al., 2004). Diclofenac NSAID reduced cortisol, but did not reduce abnormal behaviours associated with rubber ring tail docking. It was also not effective at alleviating pain with hot iron tail docking (Graham et al., 1997).

Other NSAIDs are available such as flunixin, meloxicam, tolfenamic acid, and aspirin, however they have not been tested for their effectiveness as analgesic agents during husbandry procedures. Pharmacokinetic studies in sheep have revealed that despite a relatively short plasma half-life (2.48 hours) for flunixin meglumine it maintained a prolonged therapeutic action (i.e., extended presence in inflamed tissue fluid; Cheng et al., 1998). Repeated injections of flunixin alleviated chronic pain associated with lameness in sheep (Welsh and Nolan, 1995a). Phenylbutazone maintained a longer plasma half-life of 17.9 hours and also had prolonged anti-inflammatory therapeutic action (Cheng et al., 1998). Similar to the castration work in cattle, Carprofen had no effect in lambs being castrated or tail docked (Price and Nolan, 2001). Oral aspirin was used in a recent tail docking study in lambs (Table 7; Pollard et al., 2001). However the dose tested (26 mg/kg BW) was inadequate based on known pharmacokinetic parameters, and not surprisingly it was ineffective at alleviating the abnormal behaviours post docking.

In summary, the data suggest that where castration of male lambs is required, either lignocaine LA (scrotal neck or spermatic cord route of administration along with some subcutaneous infiltration) or combined use of rubber rings and clamp rather than either rubber rings or clamps on their own is indicated. For tail docking either lignocaine or bupivacaine is effective as LA agents, while the NSAID diclofenac was variably effective. Again use of a powered clamp or burdizzo along with rubber rings was also reported at being effective at reducing abnormal behaviours and reducing cortisol. Further work is required to fully assess the potential of NSAIDs (e.g., ketoprofen, flunixin, carprofen and meloxicam) during castration and tail docking in sheep, either on their own or in combinations with LA.

8. Alternatives to conventional castration and spaying including immunoneutralisation and management options to avoid the need for these procedures where appropriate.

8.1. Raising intact bulls - advantages and disadvantages

Several studies have shown that intact male cattle grow more rapidly, utilise feed more efficiently and produce a higher-yielding carcass with less fat and more edible product (Seideman et al., 1982;

Worrell et al., 1987). These positive effects can be ascribed to the production of anabolic testicular hormones, and increased muscle protein accretion from reduced proteolytic capacity of muscles in bulls (Morgan et al., 1993). Bulls can grow up to 17% faster than steers, with up to 13% higher feed conversion efficiency (Field, 1971; Arthaud et al., 1977; Knight et al., 1999a), and the carcass gain of bulls can be up to 30% higher than that of steers for only a 3% increase in feed intake (Steen, 1995). However, the meat from bulls (12 to 18 months of age) tends to have lower tenderness, less fat, less marbling, a higher ultimate pH, and a higher incidence of undesirable dark cutting meat (Field at al., 1966; Cross et al., 1984; reviewed by Field, 1971; Seideman et al., 1982 and Purchas et al., 1995). Management problems (aggression and unwanted pregnancies in beef heifers) are also associated with intact males. For these reasons, the production of beef from castrated males is still preferred in most major cattle producing countries including Ireland, UK, US, South America, Australia and New Zealand and with the exception of niche markets bull beef is unlikely to be a main production option in these countries in the foreseeable future.

8.2. Alternative, non-invasive (immunocastration) castration method

“Immunocastration” involves the inhibition of hypothalamic gonadotrophin-releasing hormone (also known as luteinising hormone-releasing hormone) by antibodies induced by active immunisation. This technique was proposed by Robertson et al. (1979) as a practical alternative method for castrating cattle. The process results in reduced testosterone secretion, involution of the testes, arrested spermatogenesis, and a reduction in aggressive and sexual behaviours (Finnerty et al., 1994, 1996; Bonneau and Enright, 1995; Jago et al., 1997; Huxsoll et al., 1998; Price et al., 2003a). Immunocastration offers a welfare friendly means to castrate cattle (Fisher et al., 1996), requires less labour and equipment, and has less risk of complications (Zweiacher et al., 1979; Robertson et al., 1994) than conventional methods. A body of studies have shown that the non-invasive immunocastration procedure in cattle can effectively circumvent any reductions in growth rate and feed efficiency associated with traditional castration methods. In addition, immunocastration results in carcass quality that is comparable with that of steers, but is significantly higher than that of intact bulls (Finnerty et al., 1994, 1996; Huxsoll et al., 1998; Knight et al., 1999a; Cook et al., 2000; Aïssat et al., 2002). However, the main disadvantage with the method is that it requires repeated immunisation (typically with a primary followed by booster immunization 1 month later, with further boosters, at 2 to 6 month intervals, dependent on the vaccine/adjuvant formulation used) in order to achieve or maintain effective suppression of testosterone concentrations and aggressive behaviour (Finnerty et al., 1994, 1996; Jago et al., 1997; Huxsoll et al., 1998). Efforts are underway to improve the efficiency of the immunocastration formula and protocol (Cook et al., 2000; Aïssat et al., 2002; Price et al., 2003a).

8.3. Alternatives to spaying for suppression of oestrous behaviour in heifers

Various non-surgical options are reported for the suppression of oestrous behaviour in heifers. There include steroidal (synthetic progestagens) administration either orally (Bloss et al., 1966; Zimbelman and Smith, 1966) or by subcutaneous silastic implant (Roche and Crowley, 1973), GnRH agonist / antagonist approaches (Conn et al., 1987, 1988; Reiger et al., 1989; Peters et al., 1993) and immunoneutralization of endogenous hormones. The practical options for immunoneutralisation include GnRH immunization (Adams and Adams, 1990; D’Occhio et al., 1992, Stumpf et al., 1992; Prendiville et al., 1995a, 1995b; 1996) and prostaglandin $F_{2\alpha}$ immunization (Crowe et al., 1994a, 1994b, 1995a, 1995b, 1995c). Both these immunoneutralization approaches successfully suppress oestrous behaviour. Indeed GnRH immunization has been commercially developed as a vaccine to immunocastrate male cattle and to suppress oestrus in heifers (Hoskinson et al., 1990). Immunoneutralisation is an acceptable approach on welfare grounds as the pain / stress associated with the vaccination is negligible (Fisher et al., 1996). The main reason for immunoneutralisation not being adopted widely is due to variability between animals in the immune response and therefore the duration of suppression of oestrous (heifers) or aggressive (bulls) behaviours. Further improvements in achieving a more consistent immune response following at most 2 immunizations (ie primary and booster) without using potentially toxic adjuvant preparations are required.

9. Identification of any significant information gaps

In writing this review a number of deficiencies were identified in the relevant literature. These are categorized into those relevant to i) assessment of pain, ii) alleviation of pain, iii) husbandry procedures, and iv) pharmaceutical industry / licensing issues:

i) Pain assessment:

- In the assessment of pain further improvements in the development of objective scoring of behavioural indicators are required (e.g., improved use of VAS scores or other systems of pain scoring).
- The precise role of β-endorphin in modulating the response to pain remains to be elucidated in cattle.

ii) Pain alleviation:

- Despite the beneficial effects of combined rubber ring and clamp castration in lambs, only one study on a similar approach has been reported for cattle. Further attempts to alleviate the pain of castration in cattle by combining rubber ring / banding with burdizzo clamp devices are warranted.
- Studies are required to develop effective anaesthesia and analgesia during spaying of heifers. Possible approaches include epidural anaesthesia, intraperitoneal anaesthesia, pethidine and/or NSAIDs.
- Substantial work on combining analgesic / anaesthesic agents is required to develop better pain alleviation options for many of the procedures that are performed on cattle and sheep.
- Ketoprofen is the most effective NSAID studied to date for alleviation of pain during husbandry procedures in cattle. Further work is required to determine its usefulness for a greater variety of husbandry procedures. However, it is one of the more expensive NSAIDs available, and the effectiveness of alternative NSAIDs also needs to be determined.
- Timing of administration of NSAIDs, particularly when combining their use with local anaesthesia, needs further study to allow development of practical regimes of pain relief that will be easily implemented at farm level, particularly when large numbers of animals are undergoing acute husbandry procedures.
- Work is required to assess the potential of NSAIDs during castration and tail docking in sheep, either on their own or in combinations with local anaesthesia.

iii) Husbandry procedures:

- Studies on the prolonged health status following tail docking of lambs by various procedures are required to determine what, if any, effects on the incidence of joint-ill disease and fly-strike are associated with tail docking by various methods in addition to the acute stress responses.
- Detailed epidemiological studies evaluating health of animals following acute husbandry procedures are also warranted to establish health / morbidity issues.
- Further work is required to look at other amputation dehorning methods and associated pain relief options.
- If chemical castration is to be considered as a serious option in cattle (and sheep) then comprehensive studies looking at the associated pain are required.

- To overcome existing practical difficulties with immunoneutralization approaches to spaying and castration, improvements in achieving a more consistent immune response following at most 2 immunizations (ie primary and booster), without using potentially toxic adjuvant preparations, are required.
- Immunocastration as an option for commercial sheep meat production has not been addressed to any extent. This is an area that has potential.

iv) Pharmaceutical industry / drug licensing:
- The lack of registered NSAIDs for use in sheep needs to be addressed, but in many cases commercial reality may prevent the pharmaceutical industry from following through with registration for this species.
- In all cases where new drugs or new licensing of existing drugs (for pain relief or as an alternative approach to a procedure) are required in animals destined for human consumption due care regarding residues and appropriate withdrawal periods is a necessity.

10. Literature cited

ACVA. 2003. American College of Veterinary Anesthesiologists' position paper on the treatment of pain in animals. Available: http://www.acva.org/ professional/Position/pain.htm. Accessed 12 Dec. 2003.

Adams T. E., and B.M. Adams. 1990. Reproductive function and feedlot performance of beef heifers actively immunized against GnRH. J. Anim. Sci. 68:2793-2802.

Aïssat, D., J. M. Sosa, D. M. de Avila, K. P. Bertrand, and J. J. Reeves. 2002. Endocrine, growth, and carcass characteristics of bulls immunized against luteinizing hormone-releasing hormone fusion proteins. J. Anim. Sci. 80:2209–2213.

Amit, Z., and Z. H. Galina. 1986. Stress-induced analgesia: adaptive pain suppression. Physiol. Rev. 66:1091–1120.

Andersen M. K., R. A. Field, M.L. Riley, R. J. McCormick, G. D. Snowder and D. G. Bailey 1991. Effects of age, castration, and season on difficulty of pelt removal in lambs. J. Anim. Sci. 69: 3284-3291.

Anil, S. A., L. Anil, and J. Deen. 2002. Challenges of pain assessment in domestic animals. J. Am. Vet. Med. Assoc. 220:313–319.

Animal Legal and Historical Center. 2003. German Animal Welfare Act. Federal Law Gazette I. p. 1094 (English Translation). Detroit College of Law, Michigan State University. Available: http://www.animallaw.info/nonus/statutes/stdeawa 1998.htm. Accessed 12 Dec. 2003.

Arias, H. R. 1999. Role of local anesthetics on both cholinergic and serotonergic ionotropic receptors. Neurosci. Biobehav. Rev. 23:817–843.

Arthaud, V. H., R. W. Mandigo, R. M. Koch, and A. W. Kotula. 1977. Carcass composition, quality and palability attributes of bulls and streers fed different energy levels and killed at four ages. J. Anim. Sci. 44:53–64.

AVTRW. 1989. Guidelines for the Recognition and Assessment of Pain in Animals. Prepared by the Working Party of the Association of Veterinary Teachers and Research Workers (AVTRW). Universities Federation for Animal Welfare, Potters Bar, Herts, UK.

AWC. 2002. A workshop to identify animal welfare issues within animal industries. Animal Welfare Centre (AWC), Victorian Institute of Animal Science, Werribee, Australia. Available: http://www.animal-welfare.org.au/comm/ awissues.pdf. Accessed 15 Oct. 2003.

Bagley, C. P., D. G. Morrison, J. L. Feazel, and A. M. Saxton. 1989. Growth and sexual characteristics of suckling beef calves as influenced by age at castration and growth implants. J. Anim. Sci. 67:1258–1264.

Baird, A. N., and D. F. Wolfe. 1999. Castration of the normal male. Pages 295–312 in Large Animal

Urogenital Surgery. D. F. Wolfe and H. D. Moll, eds. 2nd Ed. Williams and Wilkins, Baltimore, Maryland, US.

Baker, J. F., J. E. Strickland, and R. C. Vann. 2000. Effect of castration on weight gain of beef calves. Bov. Pract. 34:124–126.

Banks, E. M. 1982. Behavioral research to answer questions about animal welfare. J. Anim. Sci. 54:434–446.

Barrowman, J. R., T. G. Boaz and K. G. Towers. 1953. Castration of lambs: comparison of the rubber ring ligature and crushing methods. Emp J. Exp. Agric 21: 192-205.

Barrowman, J. R., T. G. Boaz and K. G. Towers. 1954. Castration and docking of lambs: use of the rubber-ring ligature technique at different ages. Emp J. Exp. Agric 22: 189-202.

Bengtsson, B., A. Menzel, P. Holtenius, and S.-O. Jacobsson. 1996. Cryosurgical dehorning of calves: a preliminary study. Vet. Rec. 138: 234-237.

Berry, B. A., W. T. Choat, D. R. Gill, C. R. Krehbiel, R. A. Smith, and R. L. Ball. 2001. Effect of castration on health and performance of newly received stressed feedlot calves. Animal Science Research Report: Beef and Dairy Cattle, Swine, Poultry, Sheep, Horses and Animal Products. Online Publication P986. Oklahoma Agricultural Experiment Station, Division of Agricultural Science and Natural Resources, Oklahoma State University. Available: http://www.ansi.okstate.edu/ research/ 2001rr/. Accessed 26 May 2002.

Bingol, M., T. Aygun, O. Gokdal and A. Yilmaz. 2006. The effects of docking on fattening performance and carcass characteristics in fat-tailed Norduz male lambs. Small Ruminant Reearch, Available on line 17 May 2005.

Bloss R.E., J. I. Northam, L. W. Smith, and R. G. Zimbelman. 1966. Effects of oral melengestrol acetate on the performance of feedlot cattle. J. Anim. Sci. 25:1048-1053.

Boissy, A. and M.-F. Bouissou. 1995. Assessment of individual differences in behavioural reactions of heifers exposed to various fear-eliciting situations. Appl. Anim. Behav. Sci. 46:17–31.

Bonneau, M., and W. J. Enright. 1995. Immunocastration in cattle and pigs. Livest. Prod. Sci. 42:193–200.

Bretschneider, G. 2005. Effects of age and method of castration on performance and stress response of beef male cattle: a review. Livest. Prod. Sci. 97: 89-100.

Bryant, C. E., B. A. Farnfield, and H. J. Janicke. 2003. Evaluation of the ability of carprofen and flunixin meglumine to inhibit activation of nuclear factor kappa B. Am. J. Vet. Res. 64:211–215.

Capucille, D. J., M. H. Poore, and G. M. Rogers. 2002. Castration in cattle: techniques and animal welfare issues. Compend. Contin. Educ. Pract. Vet. 24:S66–S73.

Caron, J. P., and P. H. LeBlanc. 1989. Caudal epidural analgesia in cattle using xylazine. Can. J. Vet. Res. 53:486–489.

Carragher J. F., T. W. Knight, A. F. Death, J. R. Ingram, and L. R. Matthews. 1997. Stress of surgical castration in post-pubertal bulls. NZSAP 1997 Abstract Booklet No. 46. Available: http://www.rsnz.govt.nz/clan/nzsap/con97/1997/ab97032.html. Accessed 19 Sept. 2002.

Casey, K. L. 1996. Match and mismatch: identifying the neuronal determinants of pain. Ann. Intern. Med. 124:995–998.

Caulkett, N. A., D. G. MacDonald, E. D. Janzen, P. N. Cribb, and P. B. Fretz. 1993. Xylazine hydrochloride epidural analgesia: a method of providing sedation and analgesia to facilitate castration of mature bulls. Compend. Contin. Educ. Pract. Vet. 15:1155–1159.

Chambers, J. P., A. E. Waterman, and A. Livingston. 1994. Further development of equipment to measure nociceptive thresholds in large animals. J. Vet. Anaesth. 21:66–72.

Chambers, J. P., A. E. Waterman, and A. Livingston. 1995. The effects of opioid and $\square_2$ adrenergic blockage on non-steroidal anti-inflammatory drug analgesia in sheep. J. Vet. Pharmacol. Therap. 18:161–166.

Chambers, J. P., K. J Stafford and D. J. Mellor. 2002. Analgesics: what use are they in farm animals?

Proc NZ Soc Anim. Prod. 62: 359-362.
Chandrasekharan, N. V., H. Dai, K. L. T. Roos, N. K. Evanson, J. Tomsik, T. S. Elton, and D. L. Simmons. 2002. COX-3, a cyclooxygenase-1 variant inhibited by acetaminophen and other analgesic/antipyretic drugs: cloning, structure, and expression. Proc. Natl. Acad. Sci. USA 99: 13926–13931. Available on line: http://www.pnas.org/cgi/doi/10.1073/pnas.162468699. Accessed: 10 Jul. 2004.
Chapman, C. R., K. L. Casey, R. Dubner, K. M. Foley, R. H. Gracely, and A. E. Reading. 1985. Pain measurement: an overview. Pain 22:1–31.
Chase, C. C., Jr., R. E. Larsen, R. D. Randel, A. C. Hammond, and E. L. Adams. 1995. Plasma cortisol and white blood cell responses in different breeds of bulls: A comparison of two methods of castration. J. Anim. Sci. 73:975–980.
Cheng, Z, Q. McKeller and A. Nolan. 1998.Pharmacokinetic studies of flunixin meglumine and phenylbutazone in plasma, exudate and transudate in sheep. *J. Vet. Pharmacol. Ther.* 21:315-321.
Cicerone. 2002. The Cicerone Project: Newsletter No. 19, April 2002. http://www.cicerone.org.au/archives/newsletter_19.pdf accessed 23 March 2006.
Conn P. M., C. A. McArdle, W. V. Andrews, and W. R. Huckle. 1987. The molecular basis of gonadotropin-releasing hormone (GnRH) action in the pituitary gonadotrope. Biol. Reprod. 36:17-35.
Conn P. M., W. R. Huckle, W. V. Andrews, and C. A. McArdle. 1988. The molecular mechanism of action of gonadotropin-releasing hormone (GnRH) in the pituitary. Rec. Prog. Horm. Res. 43:29-61.
Cook, R. B., J. D. Popp, J. P. Kastelic, S. Robbins, and R. Harland. 2000. The effects of active immunization against GnRH on testicular development, feedlot performance, and carcass characteristics of beef bulls. J. Anim. Sci. 78:2778–2783.
Cottrell, D. F., and V. Molony. 1995. Afferent activity in the superior spermatic nerve of lambs – the effects of application of rubber castration rings. Vet. Res. Commun. 19:503–515.
Cox, J. E. 1987. Surgery of the Reproductive Tract in Large Animals. 3rd ed. Liverpool University Press, Liverpool, UK.
Cox, T. 1978. Stress. Macmillan Education, London, UK.
Craig, A. D. 2003. A new view of pain as a homeostatic emotion. Trends Neurosci. 26:303-307.
Cronin, G. M., F. R. Dunshea, K. L. Butler, I. McCauley, J. L. Barnett, and P. H. Hemsworth. 2003. The effects of immuno- and surgical-castration on the behaviour and consequently growth of group-housed, male finisher pigs. Appl. Anim. Behav. Sci. 81:111–126.
Cross, J.R., B.D. Schanbacher, and J.D. Crouse. 1984. Sex, age and breed related changes in bovine testosterone, and intramuscular collagen. Meat Sci. 10 187-
Crowe, M. A., W. J. Enright, D. J. Prendiville, C. A.Morrison, and J.F. Roche. 1994a. Active immunization against prostaglandin $F_{2\alpha}$: effect of conjugate dose and booster interval on antibody titers and estrous behavior in postpubertal beef heifers. J. Anim. Sci. 72: 1778-1785.
Crowe, M. A., W. J. Enright, and J. F. Roche. 1994b. Prostaglandin $F_{2\alpha}$ immunization of prepubertal beef heifers: effects of conjugate dose and timing of immunization relative to puberty on the onset of puberty and subsequent ovarian function. J. Reprod. Immunol. 27: 227-240.
Crowe, M. A., W. J. Enright, P. Swift, and J. F. Roche. 1995a. Growth and estrous behavior of heifers actively immunized against prostaglandin $F_{2\alpha}$. J. Anim. Sci. 73: 345-352.
Crowe, M. A., W. J. Enright, and J. F. Roche. 1995b. Immunisation of heifers against prostaglandin $F_{2\alpha}$. Livest. Prod. Sci. 42: 213-221.
Crowe, M. A., W. J. Enright, and J. F. Roche. 1995c. Effects of single or primary plus booster prostaglandin $F_{2\alpha}$ immunization regimens on immune, ovarian and growth responses of heifers. J. Anim. Sci. 73: 2406-2417.

Curran S., J. P. Crowley, and P. McGloughlin. 1965. The effect of spaying and hormone implantation on the growth and carcass quality of beef heifers. Ir. J. Agric. Res. 4:93-100.
Dahl, V., and J. C. Ræder. 2000. Non-opioid postoperative analgesia. Acta Anaesthesiol. Scand. 44:1191–1203.
Dart, C. M. 1999. Advantages and disadvantages of using alpha-2 agonists in veterinary practice. Aust. Vet. J. 77:720–722.
DEFRA 2003. Code of recommendations for the welfare of livestock – Cattle. Defra Publications, Admail 6000 London, SW1A 2XX.
De Rossi, R., G. V. Bucker, and J. V. Varela. 2003. Perineal analgesic actions of epidural clonidine in cattle. Vet. Anaesth. Analg. 30:63–70.
Désiré, L., A. Boissy, and I. Veissier. 2002. Emotions in farm animals: a new approach to animal welfare in applied ethology. Behav. Process. 60:165–180.
Devey, J. J., and D. T. Crowe. 1997. The physiological response to trauma. Compend. Contin. Educ. Pract. Vet. 19:962–975.
Dinniss, A. S., D. J. Mellor, K. J. Stafford, R. A. Bruce, and R. N. Ward. 1997a. Acute cortisol responses of lambs to castration using a rubber ring and/or a castration clamp with or without local anaesthetic. N. Z. Vet. J. 45:114–121.
Dinniss A. S., K. J. Stafford, D. J. Mellor, R. A. Bruce, and R. N. Ward. 1997b. Acute cortisol responses of lambs castrated and docked using rubber rings with or without a castration clamp. Aust. Vet. J. 75: 494-496.
Dinusson W. E., F. N. Andrews, and W. M. Beeson. 1950. The effects of stilbestrol, testosterone, thyroid alteration and spaying on the growth and fattening of beef heifers. J. Anim. Sci. 9:321-330.
Dobromylskyj, P., P. A. Flecknell, B. D. Lascelles, P. J. Pascoe, P. Taylor, and A. Waterman-Pearson. 2000. Management of postoperative and other acute pain. Pages 81–145 in Pain Management in Animals. P. Flecknell and A. Waterman-Pearson, ed. Harcourt Publishers Ltd., London, UK.
D'Occhio M. J., G. Fordyce, B. M. O'Leary, T. E. Trigg, and M. J. Lindsey. 1992. Suppression of fertility in female cattle under range conditions with an anti-GnRH vaccine. Proc. 12th Internat. Cong. Anim. Reprod. 3:1207-1209.
Dray, A. 1995. Inflammatory mediators of pain. Br. J. Anaesth. 75:169–176.
Drost M, Savio, JD, Barros CM, Badinda L and Thatcher WW. Ovariectomy by colpotomy in cows. J. Amer. Vet. Med. Assoc. 1992; 200: 337-339.
Dubner, R., and K. Ren. 2000. Assessing transient and persistent pain in animals. Pages 359–369 in Textbook of Pain. P. D. Wall and R. Melzack, ed. 4th ed. Harcourt Publishing Ltd., London, UK.
Duncan, I. J. H., and V. Molony, 1986. Preface. In: Proceedings of a workshop held in Roslin, Scotland, 25–26 Oct. 1984. I. J. H. Duncan, and V. Molony, ed. Commission of the European Communities, Luxembourg, Belgium.
Eager, R. A., J. Price, E. Welsh, and N. K. Waran. 2003. Preliminary investigations of behavioural and physiological responses to castration in horses. Page 12 in Proceedings of the British Society of Animal Science Annual Meeting, York, UK.
Earley, B., and M. A. Crowe. 2002. 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. 80:1044–1052.
Egdahl, R. 1959. Pituitary–adrenal response following trauma to the isolated leg. Surgery. 46:9–21.
Eicher, S. D., and J. W. Dailey. 2002. Indicators of acute pain and fly avoidance behaviors in Holstein calves following tail-docking. J. Dairy Sci. 85:2850–2858.
Ewer, T.K. 1942. Lamb castration and docking. N. Z. J. Agric.65:337-339.
Faulkner, D. B., T. Eurell, W. J. Tranquilli, R. S. Ott, M. W. Ohl, G. F. Cmarik, and G. Zinn. 1992.

Performance and health of weanling bulls after butorphanol and xylazine administration at castration. J. Anim. Sci. 70:2970–2974.
Faulkner, P., and D. M. Weary. 2000. Reducing pain after dehorning in dairy calves. J. Dairy Sci. 83:2037–2041.
Feinstein, M. 2003. Acoustic markers of stress in sheep. Page 59 in Proceedings of the 29th Irish Grassland and Animal Production Association, Tullamore, Co. Offaly, Ireland.
Fell, L. R., and D. A. Shutt. 1989. Behavioural and hormonal responses to acute surgical stress in sheep. Appl. Anim. Behav. Sci. 22:283–294.
Fenton, B. K., J. Elliot, and R. C. Cambell. 1958. The effects of different castration methods on the growth and well-being of calves. Vet. Rec. 70:101–102.
Field, R.A., G.E. Nelms, and C.O. Schoonover. 1966. Effects of age marbling and sex on palatability of beef. J. Anim. Sci., 25:360-366.
Field, R. A. 1971. Effect of castration on meat quality and quantity. J. Anim. Sci. 32:849–858.
Fields, H. L., and A. I. Basbaum. 2000. Central nervous system mechanisms of pain modulation. Pages 309–329 in Textbook of Pain. P. D. Wall and R. Melzack, ed. 4th ed. Harcourt Publishing Ltd., London, UK.
Filmer, J.F. 1938. Lamb tailing: a comparison of results obtained with the searing iron and knife. Aust. Vet. J. 14: 189-191.
Finnerty, M., W. J. Enright, C. A. Morrison, and J. F. Roche. 1994. Immunization of bull calves with a GnRH analogue-human serum albumin conjugate: effect of conjugate dose, type of adjuvant and booster interval on immune, endocrine, testicular and growth responses. J. Reprod. Fertil. 101:333–343.
Finnerty, M., W. J. Enright, D. J. Prendiville, L. J. Spicer, and J. F. Roche. 1996. The effect of different levels of gonadotropin-releasing hormone antibody titres on plasma hormone concentrations, sexual and aggressive behaviour, testes size and performance of bulls. Anim. Sci. 63:51–63.
Fisher, A. D., M. A. Crowe, E. M. O'Nuallain, M. L. Monaghan, J. A. Larkin, P. O'Kiely, and W. J. Enright. 1997a. Effects of cortisol on *in vitro* interferon-γ production, acute phase proteins, growth, and feed intake in a calf castration model. J. Anim. Sci. 75:1041–1047.
Fisher, A. D., M. A. Crowe, E. M. O'Nuallain, M. L. Monaghan, D. J. Prendiville, P. O'Kiely, and W. J. Enright. 1997b. Effects of suppressing cortisol following castration of bull calves on adrenocorticotropic hormone, *in vitro* interferon-γ production, leukocytes, acute phase proteins, growth, and feed intake. J. Anim. Sci. 75:1899–1908.
Fisher, A. D., M. A. Crowe, M. E. Alonso de la Varga, and W.J. Enright. 1996. Effect of castration method and the provision of local anaesthesia on plasma cortisol, scrotal circumference, growth and feed intake of bull calves. J. Anim. Sci. 74:2336–2343.
Fisher, A. D., T. W. Knight, G. P. Cosgrove, A. F. Death, C. B. Anderson, D. M. Duganzich, and L. R. Mathews. 2001. Effects of surgical or banding castration on stress responses and behaviour of bulls. Aust. Vet. J. 79:279–284.
Flecknell, P. 2000. Animal pain – an introduction. Pages 1–7 in Pain Management in Animals. P. Flecknell and A. Waterman-Pearson, ed. Harcourt Publishers Ltd., London, UK.
Fordyce, G., P. B. Hodge, N. J. Beaman, A. R. Laing, C. Campero, and R. K. Shepherd. 1989. An evaluation of calf castration by intra-testicular injection of a lactic acid solution. Aust. Vet. J. 66:272–276.
Garner, F.H. and H.G. Sanders. 1936. The effects of different methods of castration and docking on the growth of lambs. J. Agric. Sci. 26: 296-300.
George, L. W. 2003. Pain control in food animals. In: Recent Advances in Anesthetic Management of Large Domestic Animals (Doc. No. A0615.1103). E. P. Steffey, ed. International veterinary Information Service, Ithaca, New York, US. Available:

http://www.ivis.org/advances/Steffey_Anesthesia/george/chapter_frm.asp?LA=1. Accessed 9 Feb. 2004.
Glencross R. G. 1984. A note on the concentrations of plasma oestradiol-17 and progesterone around the time of puberty in heifers. Anim. Prod. 39:137-140.
Graf, B., and M. Senn. 1999. Behavioural and physiological responses of calves to dehorning by heat cauterization with or without local anaesthesia. Appl. Anim. Behav. Sci. 62: 153-171.
Graham, M. J., J. E. Kent and V. Molony. 1997. Effects of four analgesic treatments on the behavioural and cortisol responses of 3-week-old lambs to tail docking. The Vet. J. 153: 87-97.
Grant, C. 2004. Behavioural responses of lambs to common painful husbandry procedures. Applied Animal Behaviour Science 87: 255-273.
Grant, C., R.N. Upton. 2001. The anti-nociceptive efficacy of low dose intramuscular xylazine in lambs. Res. Vet. Sci. 70: 47-50
Grant, C., R.N. Upton, and T. R. Kuchel. 1996. Efficacy of intra-muscular analgesics for acute pain in sheep. Aust. Vet. J. 73: 129-132
Grandin, T. 1997. Assessment of stress during handling and transport. J. Anim. Sci. 75:249–257.
Gregory, K. E., and J. J. Ford. 1983. Effects of late castration, zeranol and breed group on growth, feed efficiency and carcass characteristics of late maturing bovine males. J. Anim. Sci. 56:771–780.
Grisel, J. E., M. Fleshner, L. R. Watkins, and S. F. Maier. 1993. Opioid and nonopioid interactions in two forms of stress-induced analgesia. Pharmacol. Biochem. Behav. 45:161–172.
Grondahl-Nielsen, C., H. B. Simonsen, J. Damkjer Lund, and M. Hesselholt. 1999. Behavioural, endocrine and cardiac responses in young calves undergoing dehorning without and with use of sedation and analgesia. Vet. J. 158: 14-20.
Grubb, T. L., T. W. Reibold, R. O. Crisman, and L. D. Lamb. 2002. Comparison of lidocaine, xylazine, and xylazine- lidocaine for caudal epidural analgesia. Vet. Anaesth. Analg. 29:64–68.
Habermehl N.L. 1993. Heifer ovariectomy using the Willis spay instrument: technique, morbidity and mortality. Can. Vet. J. 34: 664-667.
Hamernik D. L., J. R. Males, C. T. Gaskins, and J. J. Reeves. 1985. Feedlot performance of hysterectomized and ovariectomized heifers. J. Anim. Sci. 60:358-362.
Hardy, R., and S. Meadowcroft. 1986. The performance and behaviour of bulls kept indoors. Pages 18–25 in Indoor Beef Production. Farming Press Ltd., Ipswich, Suffolk, UK.
Harvey-Clark, C.J., K. Gilespie and K.W. Riggs. 2000. Transdermal fentanyl compared with parenteral buprenorphine in post-surgical pain in swine: a case study. Lab. Anim. 34: 386-398.
Hay, M., A. Vulin, S. Génin, P. Sales, and A. Prunier. 2003. Assessment of pain induced by castration in piglets: behavioral and physiological responses over the subsequent 5 days. Appl. Anim. Behav. Sci. 82:201–218.
Hayes, R. L., G. J. Bennet, P. G. Newlon, and D. J. Mayer. 1978. Behavioral and physiological studies of non-narcotic analgesia in the rat elicited by certain environmental stimuli. Brain. Res. 155:69–90.
Herrero, J. F. and P. M. Headley. 1996. Reversal by naloxone of the spinal antinociceptive actions of a systemically-administered NSAID. Br. J. Pharmacol. 118:968–972.
Herskin M. S., R. Muller, L. Schrader, and J. Ladewig. 2003. A laser-based method to measure thermal nociception in dairy cows: Short-term repeatability and effects of power output and skin condition. J Anim Sci. 81:945-954.
Herskin, M. S., 2004. Responses of dairy cattle toward acute stress and novelty – behaviour, physiology and nociception. Ph.D. Thesis. Department of Animal Science and Health, The Royal Veterinary and Agricultural University, Copenhagen, Denmark.
Higgins, A. J., P. Lees, and A. D. Sedgwick. 1987. Development of equine models of inflammation.

Vet Rec. 120:517–522.
Hill, G. M., W. E. Neville, Jr., K. L. Richardson, P. R. Utley, and R. L. Stewart. 1985. Castration method and progesterone-estradiol implant effects on growth rate of suckling calves. J. Dairy Sci. 68:3059–3061.
Hoke, J.F., F. Cunningham, M.K. James. K.T. Muir, and W.E. Hoffman. 1997. Comparative pharmacokinetics and pharmacodynamics of remifentanil, its principle metabolite (GR90291) and alfentanil in dogs. J. Pharmacol. Exp. Ther. 281: 226-232.
Holton, L. L., E. M. Scott, A. M. Nolan, J. Reid, E. M. Welsh, and D. Flaherty. 1998. Comparison of three methods used for assessment of pain in dogs. J. Am. Vet. Med. Assoc. 212:61–66.
Holton, L., J. Reid, E. M. Scott, P. Pawson, and A. Nolan. 2001. Development of a behaviour-based scale to measure acute pain in dogs. Vet. Rec. 525–531.
Hosie B. D., J. Carruthers, and B. W. Sheppard. 1993. Lamb castration: some practical considerations. Proc. Sheep Vet. Soc., 1992 16:93-95.
Hosie, B. D., J. Carruthers, and B. W. Sheppard. 1996. Bloodless castration of lambs: results of a questionnaire. Br. Vet. J. 152:47–55.
Horstman L. A., C. J. Callahan, R. L. Morter, and H. E. Amstutz. 1982. Ovariectomy as a means of abortion and control of estrus in feedlot heifers. Theriogenology 17:273-292.
Hoskinson R. M., R.D.G. Rigby, P. E. Mattner, V. L. Huynh, M. D'Occhio, A. Neish, T. E. Trigg, B. A. Moss, M. J. Lindsey, G. D. Coleman and C. L. Schwartzkoff. 1990. Vaxtrate: An anti-reproductive vaccine for cattle. Aust. J. Biotechnol. 4:166-170.
Huang, J. H., J. G. Thalhammer, S. A. Raymond, and G. R. Strichartz. 1997. Susceptibility to lidocaine of impulses in different somatosensory afferent fibres of rat sciatic nerve. J. Pharmacol. Exp. Ther. 292:802–811.
Huxsoll, C. C., E. O. Price, and T. E. Adams. 1998. Testis function, carcass traits, and aggressive behavior of beef bulls actively immunized against gonadotropin-releasing hormone. J. Anim. Sci. 76:1760–1766.
IASP. 2003. IASP Pain Terminology. The International Association for the Study of Pain. Seattle, USA. Available: http://www.iasp-pain.org/terms-p.html. Accessed 29 Dec. 2003.
Jago, J. G., J. J. Bass, and L. R. Mathews. 1997. Evaluation of a vaccine to control bull behaviour. Proc. N. Z. Soc. Anim. Prod. 57:91–95.
Jennings, P. B. 1984. Testicular surgery. Page 1062 in The Practice of Large Animal Surgery. Vol. 2. W. B. Saunders, Philadelphia, Pennsylvania, US.
Jones, R. S. 1997. Anaesthesia in cattle: Regional and local analgesia. Ir. Vet. J. 50:734–740.
Jongman, E. C., J. P. Morris, J. L. Barnett, and P. H. Hemsworth. 2000. EEG changes in 4-week-old lambs in response to castration, tail docking and mulesing Aust. Vet. J. 78:339–343
Jubb, T.F., G. Fordyce, M.J. Bolam, D.J. Hadden, N.J. Cooper, T.R. Whyte, L.A. Fitzpatrick, F. Hill and M.J. D'Occhio. 2003. Trial introduction of the Willis dropped ovary technique for spaying cattle in northern Australia. Aust. Vet. J. 81: 66-70.
Keane, M. G. 1999. Effects of time of complete or split castration on performance of beef cattle. Ir. J. Agric. Food Res. 38:41–51.
Keane, M. G., and M. J. Drennan. 1998. Time for castration in beef cattle. Drystock Farmer 15:12. Available: http://www.icsaireland.com/dsf151.htm. Accessed 12 April 2004.
Kehlet, H. 1991. Neurohumoral response to surgery and pain in man. Page 35–40 in Proceedings of the 6th World Congress on Pain. M. R. Bond, J. E. Charlton, and C. J. Woolf, ed. Elsevier, Amsterdam, The Netherlands.
Kehlet, H. 1994. Postoperative pain relief – what is the issue? Br. J. Anaesth. 72:375–378.
Kelly, D. D. 1982. The role of endorphins in stress-induced analgesia. In: Verebey, K., ed. Opioids in Mental Illness: Theories, Clinical Observations, and Treatment Possibilities. Ann. N. Y. Acad. Sci. 398:260–326.

Kelly, D. D., ed. 1986. Stress-induced analgesia. Ann. N. Y. Acad. Sci. 467:1–449.
Kenny, F. J., and P. V. Tarrant. 1984. Influence of preslaughter behaviour on meat quality. Pages 189–192 in Proceedings of the International Congress on Applied EtholoIgy in Farm Animals, Kiel.
Kent, J. E., and V. Molony. 2003. Guidelines for the recognition and assessment of animal pain. Online presentation from the Animal Welfare Research Group, Royal (Dick) School of Veterinary Studies, University of Edinburgh, Summerhall, Edinburgh, Scotland. Available: http://www.vet.ed.ac.uk/animalpain/. Accessed 12 Dec. 2003.
Kent, J. E., and J. Goodall. 1991. Assessment of an immunoturbidimetric method for measuring equine serum haptoglobin concentrations. Equine Vet. J. 23:59–66.
Kent, J. E., M. V. Thrusfield, I. S. Robertson, and V. Molony. 1996. Castration of calves: a study of methods used by farmers in the United Kingdom. Vet. Rec. 138:384–387.
Kent, J. E., R.E. Jackson, V. Molony, and B. D. Hosie. 2000. Effects of acute pain reduction methods on the chronic inflammatory lesions and behaviour of lambs castrated and tail docked with rubber rings at less than two days of age. Vet. J. 160:33-41
Kent, J. E., M. V. Thrusfield, V. Molony, B. D. Hosie, and B. W. Sheppard. 2004. Randomised, controlled field trial of two new techniques for the castration and tail docking of lambs less than two days of age. Vet. Rec. 154:193–200.
Kent, J. E., V. Molony, and I. S. Robertson. 1993. Changes in plasma cortisol concentration in lambs of three ages after three methods of castration and tail docking. Res. Vet. Sci. 55:246–251.
Kent, J. E., V. Molony, and I. S. Robertson. 1995. Comparison of the Burdizzo and rubber ring methods for castrating and tail docking lambs. Vet. Rec. 136:192–196.
Kent, J. E., V. Molony, and M. J. Graham. 1998. Comparison of method for the reduction of acute pain produced by rubber ring castration or tail docking of week-old lambs. Vet. J. 155:39–51.
Kent, J. E., V. Molony, and M. J. Graham. 2001. The effect of different bloodless castrators and different tail docking methods on the responses of lambs to the combined burdizzo rubber ring method of castration. The Vet. J. 162: 250-254.
Khan, Z.P., C.N. Ferguson, and R.M. Jones. 1999. Alpha-2 and imidazoline receptor agonists. Their pharmacology and therapeutic role. Anaesthesia 54: 146-165.
King, B. D., R. D. H. Cohen, C. L. Guenther, and E. D. Janzen. 1991. The effect of age and method of castration on plasma cortisol in beef calves. Can. J. Anim. Sci. 71:257–263.
Kitchell, R. L., and R. D. Johnson. 1985. Assessment of pain in animals. Pages 113–140 in Animal Stress. G. P. Moberg, ed. Am. Physiol. Soc., Bethesda, Maryland, US.
Knight, T. W., G. P. Cosgrove, M. G. Lambert, and A. F. Death. 1999a. Effects of method and age at castration on growth rate and meat quality of bulls. N. Z. J. Agric. Res. 42:255–268.
Knight, T. W., G. P. Cosgrove, A. F. Death, and C. B. Anderson. 1999b. Effect of interval from castration of bulls to slaughter on carcass characteristics and meat quality. N. Z. J. Agric. Res. 42:269–277.
Knight, T. W., G. P. Cosgrove, A. F. Death, and C. B. Anderson. 2000. Effect of age of pre- and post-pubertal castration of bulls on growth rates and carcass quality. N. Z. J. Agric. Res. 43:585–588.
Koolhaas, J. M., S. M. Korte, S. F. De Boer, B. J. Van Der Vegt, C. G. Van Reenen, H. Hopster, I. C. De Jong, M. A. W. Ruis, and H. J. Blokhuis. 1999. Coping styles in animals: current status in behavior and stress-physiology. Neurosci. Biobehav. Rev. 23:925–935.
Kyles, A.E., M. Papich, and E.M. Hardie. 1996. Disposition of transdermally administered fentanyl in dogs. Amer. J. Vet. Res. 57: 715-719.
Lay, D. C., T. H. Friend, R. D. Randel, C. L. Bowers, K. K. Grissom, and O. C. Jenskins. 1992. Behavioural and physiological effects of freeze or hot-iron branding on crossbred cattle. J. Anim. Sci. 70:330–336.

Le Bars, D., A. H. Dickenson, and J. C. Besson. 1979. Diffuse noxious inhibitory controls (DNIC). I. Effects on dorsal horn convergent neurons in the rat. Pain 10:283–304.

Le Bars, D., M. Gozariu, and S. W. Cadden, 2001. Animal models of nociception. Pharmacol. Rev. 53:597–652.

Lee, I., N. Yamagishi, K. Oboshi, and H. Yamada. 2003. Effect of epidural fat on xylazine-induced dorsolumbar epidural analgesia in cattle. Vet. J. 165:330–332.

Lees, P., P. Delatour, A. P. Foster, R. Root, and D. Baggot. 1996. Evaluation of carprofen in calves using a tissue cage model of inflammation. Br. Vet. J. 152:199–211.

Lents, C. A., F. J. White, L. M. Floyd, R. P. Wettemann, and D. L. Gay. 2001. Method and timing of castration influences performance of bull calves. Animal Science Research Report: Beef and Dairy Cattle, Swine, Poultry, Sheep, Horses and Animal Products, August 2001 (Publication: P986). Oklahoma Agricultural Experiment Station, Oklahoma State University. Available: http://www.ansi.okstate.edu/research/2001rr. Accessed: 25 Jul. 2003.

Lessard, M., A. A. Taylor, L. Braithwaite, and D. M. Weary. 2002. Humoral and cellular immune responses of piglets after castration at different ages. Can. J. Anim. Sci. 82:519–526.

Lester, S. J., D. J. Mellor, R. N. Ward, and R.J. Holmes 1991. Cortisol responses of young lambs to castration and tailing using different methods. N. Z. Vet. J. 39: 134-138.

Lester, S. J., D. J. Mellor, R.J. Holmes, R. N. Ward, and K. J. Stafford. 1996. Behavioural and cortisol responses of lambs to castration and tailing using different methods. N. Z. Vet. J. 44: 45-54.

Levine, J. D., and D. B. Reichling. 2000. Peripheral neural mechanisms of inflammatory pain. Pages 59–84 in Textbook of Pain. P. D. Wall and R. Melzack, ed. 4th ed. Harcourt Publishing Ltd., London, UK.

Loeffler, K. 1986. Assessing pain by studying posture, activity and function. Pages 49–55 in Assessing Pain in Farm Animals. Proceedings of a workshop held in Roslin, Scotland, 25–26 Oct. 1984. I. J. H. Duncan, and V. Molony, ed. Commission of the European Communities, Luxembourg, Belgium.

Loeser, J. D. and R. Melzack. 1999. Pain: an overview. Lancet 353:1607–1609.

Lumb, B. M. 2004. Hypothalamic and midbrain circuitry that distinguishes between escapable and inescapable pain. News Physiol. Sci. 19:22–26.

Macaulay, A. S. 1989. Physiological and behavioral responses of bull calves to different methods of castration. Ph.D. Thesis, Texas A&M Univ., College Station, US.

Macaulay, A. S., and T. H. Friend. 1987. Use of hormonal responses, open-field tests, and blood cell counts of beef calves to determine relative stressfulness of different methods of castration. J. Anim. Sci. 65(Suppl. 1):436. (Abstr. 577).

MAF. 2003. Research Results: 2002/03 Research Final Report Summaries. Pages 7–10 in Ministry of Agriculture and Forestry (MAF) Policy Information Paper 03/50, Wellington, New Zealand. Available: http://www.maf.govt.nz/publications. Accessed 27 Feb. 2004.

Marshall, B. L. 1977. Bruising in cattle presented for slaughter. N. Z. Vet. J. 25: 83-86.

Martin, P. and P. Bateson. 1986. Measuring behaviour. Cambridge Univ. Press, London, UK.

Matejec, R., R. Ruwoldt, R. H. Bodeker, G. Hempelmann, and H. Teschemacher. 2003. Release of beta-endorphin immunoreactive material under perioperative conditions into blood or cerebrospinal fluid: significance for postoperative pain? Anesth. Analg. 96:481–486.

McCormack, K. 1994a. Non-steroidal anti-inflammatory drugs and spinal nociceptive processing. Pain 59:9–43.

McCormack, K. 1994b. The spinal actions of non-steroidal anti-inflammatory drugs and the dissociation between their anti-inflammatory and analgesic effects. Drugs 47(Suppl. 5):28–45.

McGlone, J. J., R. I. Nicholson, J. M. Hellman, and D. N. Herzog. 1993. The development of pain in young pigs associated with castration and attempts to prevent castration-induced behavioral changes. J. Anim. Sci. 71:1441–1446.

McMahon, S. B. 1997. Are there fundamental differences in the peripheral mechanisms of visceral and somatic pain? Behav. Brain Sci. 20:381–391.
McMahon, S. B., N. Dmitrieva, and M. Koltzenburg. 1995. Visceral pain. Br. J. Anaesth. 75:132–144.
McMeekan, C. M., D. J. Mellor, K. J. Stafford, R. A. Bruce, R. N Ward, and N. G. Gregory. 1997. Effect of shallow and deep scoop dehorning on plasma cortisol concentrations in calves. N. Z. Vet. J. 45: 72-74.
McMeekan, C. M., D. J. Mellor, K. J. Stafford, R. A. Bruce, R. N Ward, and N. G. Gregory. 1998a Effects of local anaesthesia of 4 to 8 hours' duration on the acute cortisol response to scoop dehorning in calves. Res Vet. Sci. 64: 147-150.
McMeekan, C. M., K. J. Stafford, D. J. Mellor, R. A. Bruce, R. N Ward, and N. G. Gregory. 1998b Effects of regional analgesia and/or a non-steroidal anti-inflammatory analgesic on the acute cortisol response to dehorning in calves. Res Vet. Sci. 64: 147-150.
McMeekan, C. M., K. J. Stafford, D. J. Mellor, R. A. Bruce, R. N. Ward, and N. G. Gregory. 1999. Effects of a local anaesthetic and a non-steroidal anti-inflammatory analgesic on the behavioural responses of calves to dehorning. N. Z. Vet. J. 47:92–96.
Mears, G. J., and F. A. Brown. 1997. Cortisol and -endorphin responses to physical and psychological stressors in lambs. Can. J. Anim. Sci. 77:689–694.
Mellema, S. C., M. G. Doherr, B. Wechsler, S. Thueer, and A. Steiner. 2006. Influence of local anaesthesia on pain and distress induced by two bloodless castration methods in young lambs. Vet. J., in press.
Mellor, D. J., V. Molony, and I. S. Robertson. 1991. Effects of castration on behaviour and plasma cortisol concentrations in young lambs, kids and calves. Res. Vet. Sci. 51:149–154.
Mellor, D. J., and L. Murray. 1989a. Effects of tail docking and castration on behaviour and plasma cortisol concentrations in young lambs. Res vet. Sci. 46: 387-391.
Mellor, D. J., and L. Murray. 1989b. Changes in the cortisol responses of lambs to tail docking, castration and ACTH injection during the first seven days after birth. Res. Vet. Sci.: 46: 392-395.
Mellor, D. J., C. J. Cook, and K. J. Stafford. 2000. Quantifying some responses to pain as a stressor. Pages 171-198 in The Biology of Animal Stress: Basic Principles and Implications for Animal Welfare. G. P. Moberg and J. A. Mench, ed. CABI Publishing, Oxon, UK.
Mellor, D. J., K. J. Stafford, S. E. Todd, T. E. Lowe, N. G. Gregory, R. A. Bruce, and R. N. Ward. 2002. A comparison of catecholamine and cortisol responses of young lambs and calves to painful husbandry procedures. Aust. Vet. J. 80:228–233.
Mellor, D., and K. Stafford. 1999. Assessing and minimising the distress caused by painful husbandry procedures in ruminants. In Pract. 436–446.
Mellor, D.J., and K.J. Stafford. 2004. Physiological and behavioural assessment of pain in ruminants: Principals and caveats. ATLA 32 (Supplement 1): 267-271.
Melzack, R. 1975. The McGill pain questionnaire: major properties and scoring methods. Pain 1:277–299.
Menefee, L. A. and Katz, M. P. 2003. The PainEDU.org Manual: A Clinical Companion. 2nd ed. Inflexxion, Inc., Newton, Massachusetts, US. Available: http://www.painedu.org/manual/manual.pdf. Accessed 19 Feb. 2004.
Merrell, W.J., L. Gordon, A.J. Wood, S. Shay, E.K. Jackson, and M. Wood. 1990. The effect of halothane on morphine disposition of the liver and kidney to morphine glucuronidation in the dog. Anesthesiology 72: 308-314.
Millan, M. J. 1999. The induction of pain: an integrative review. Prog. Neurobiol. 57:1–164.
Milligan, B. N., T. Duffield, and K. Lissemore. 2004. The utility of ketoprofen for alleviating pain following dehorning in young dairy calves. Can. Vet. J. 45: 140-143.
Moberg, G. P. 1985. Biological response to stress: key to assessment of animal well-being. Pages

27–49 in Animal Stress. G. P. Moberg, ed. Am. Physiol. Soc., Bethesda, Maryland, US.
Moberg, G. P. 1996. Suffering from stress: An approach for evaluating the welfare of an animal. Act. Agric. Scand. Sect. A., Animal Sci. Suppl. 27:46–49.
Moberg, G. P. 2000. Biological response to stress: implications for animal welfare. Pages 1–21 in The Biology of Animal Stress: Basic Principles and Implications for Animal Welfare. G. P. Moberg, and J. A. Mench, ed. CABI Publishing, Wallingford, Oxon, UK.
Mohammed, A., and M.S. Liman. 1998. Xylazine (Chanazine) as an epidural anaesthetic agent in sheep. Sm. Rum. Res. 27: 85-87.
Molony, V. 1986. Assessment of pain by direct measurement of cerebro-cortical activity. Pages 79–85 in Assessing Pain in Farm Animals. Proceedings of a workshop held in Roslin, Scotland, 25–26 Oct. 1984. I. J. H. Duncan, and V. Molony, ed. Commission of the European Communities, Luxembourg, Belgium.
Molony, V. 1997. Comments on Anand and Craig (Pain 67:3–6). Pain 70:293.
Molony, V., and J. E. Kent. 1993. Behavioural responses of lambs of three ages in the first three hours after three methods of castration and tail docking. Res. Vet. Sci. 55: 236-245.
Molony, V., and J. E. Kent. 1997. Assessment of acute pain in farm animals using behavioral and physiological measurements. J. Anim. Sci. 75:266–272.
Molony, V., J. E. Kent, and I. S. Robertson. 1993. Behavioural responses of lambs of three ages in the first three hours after three methods of castration and tail docking. Res. Vet. Sci. 55:236–245.
Molony, V., J. E. Kent, and I. S. Robertson. 1995. Assessment of acute and chronic pain after different methods of castration of calves. Appl. Anim. Behav. Sci. 46:33–48.
Molony, V., J. E. Kent, B. D. Hosie, and M. J. Graham. 1997. Reduction in pain suffered by lambs at castration. Vet. J. 153:205–213.
Molony, V., J. E. Kent, and I. J. McKendrick. 2002. Validation of a method for assessment of an acute pain in lambs. Appl. Anim. Behav. Sci. 76:215–238.
Morgan, J. B., T. L. Wheeler, M. Koohmaraie, J. D. Crouse, and J. W. Savell. 1993. Effect of castration on myofibrillar protein turnover, endogenous proteinase activities, and muscle growth in bovine skeletal muscle. J. Anim. Sci. 71:408–414.
Morisse, J. P., J. P. Cotte, and D. Huonnic. 1995. Effect of dehorning on behaviour and plasma cortisol responses in young calves. Appl. Anim. Behav. Sci. 43: 239-247.
Morrow-Tesch, J., J. W. Dailey, and H. Jiang. 1998. A video data base system for studying animal behavior. J. Anim. Sci. 1998. 76:2605–2608.
Morton, D. B. and P. H. M. Griffiths. 1985. Guidelines on the recognition of pain, distress and discomfort in experimental animals and a hypothesis of assessment. Vet. Rec. 116:431–436.
Muldoon, R. (n.d.). The Farmvet Cattle Manual. 2nd ed. Jude Publications Ltd., Dublin 2, Ireland.
Mullen, P. A. 1964. Some observations on the effects of the method and time of castration of calves for barley beef production. Br. Vet. J. 120:518–523.
Murata H. 1997. Effects of burdizzo castration on peripheral blood lymphocyte parameters in calves. Vet. J. 153:229–231.
Murrell, J. C., C. B. Johnson, K. L. White, P. M. Taylor, Z. L. Haberham, and A. E. Waterman-Pearson. 2003. Changes in the EEG during castration in horses and ponies anaesthetized with halothane. Vet. Anaesth. Analg. 30:138–146.
NAHMS. 1998. Part III: Reference of 1997 Beef Cow-Calf Production Management and Disease Control. National Animal Health Monitoring System (NAHMS), USA. Available: http://www.aphis.usda.gov/vs/ceah/cahm/Beef_Cow-Calf/bf97des3.pdf. Accessed 30 Jan. 2004.
New Zealand National Animal Welfare Advisory Committee, 2005. Animal Welfare (Painful Husbandry Procedures) Code of Welfare no. 7. Issued under the Animal Welfare Act, 1999.

ISBN 0-478 29800 5. Accessible at: http://www.biosecurity.govt.nz/animal-welfare/codes/painful-husbandry/index.htm
Nolan, A., A. Livingston and A. Waterman. 1987. Antinociceptive actions of intravenous alpha 2-adrenoceptor agonists in sheep. J. Vet. Pharmacol. Ther. 10: 202-209.
Nolan, A. M. 2000. Pharmacology of analgesic drugs. Pages 21–52 in Pain Management in Animals. P. Flecknell and A. Waterman-Pearson, ed. Harcourt Publishers Ltd., London, UK.
Oireachtas, 1965. Protection of Animals (Amendment) Act 1965. The Irish Statute Book online database. Available http://193.178.1.79/1965_10.html. Accessed 15 Mar. 2001.
Ong, R. M., J. P. Morris, J. K. O'Dwyer. J. L. Barnett, P. H. Hemsworth, and I. J. Clarke. 1997. Behavioural and EEG changes in sheep in response to painful acute electrical stimuli. Aust. Vet. J. 75:189–193.
Otto, K. A., and C. E. Short. 1998. Pharmaceutical control of pain in large animals. Appl. Anim. Behav. Sci. 59:157–169.
Otto, K.A., K.H.S. Steiner, F. Zailskas, and B. Wippermann. 2000. Comparison of the postoperative analgesic effects of buprenorphine and pitramide following experimental orthopaedic surgery in sheep. J. Exp. Anim. Sci. 41: 133-143.
Owens, M.E. 1984. Pain in infancy: conceptual and methodological issues. Pain 20: 213-230.
Pang, W. Y., B. Earley, T. Sweeney and M. A Crowe. 2006. Effect of carprofen administration during banding or burdizzo castration of bulls on plasma cortisol, in vitro interferon-γ production, acute phase proteins, feed intake, and growth. J. Anim. Sci. 84: 351-359.
Parrassin, P. R., V. Thénard, R. Dumont, M. Grosse, J. M. Trommenschlager, and M. Roux. 1999. Effet d'une castration tardive sur la production de bœufs Holstein et Montbéliards (Article in French). INRA Prod. Anim. 12:207–216.
Pascoe, P.J., W.D. Black, J.M. Claxton and R.E. Sansom. 1991. The pharmacokinetics and locomotor activity of alfentanil in the horse. J. Vet. Pharmacol. Ther. 14: 317-325.
Peters K. E., E. G. Bergfeld, A. S. Cupp, F. N. Kojima, V. Mariscal, T. Sanchez, M. E. Wehrman, H. E. Grotjan, D. Hamernik and J. E. Kinder. 1993. Pulsatile secretion of LH is necessary for development of fully functional corpora lutea (CL) but is not required to maintain CL function in heifers. J. Anim. Sci. 71 (Supplement 1):216.
Petrie, N. J., D. J. Mellor, K. Stafford, RA Bruce and R. N. Ward. 1996. Cortisol responses of calves to two methods of disbudding used with and without local anaesthetic. N. Z. Vet J. 44: 9-14.
Pollard, J.C., V. Roos, and R.P. Littlejohn. 2001. Effects of an oral dose of acetyl salicylate at tail docking on the behaviour of lambs aged three to six weks. Appl. Anim. Behav. Sci. 71: 29-42.
Prendiville, D. J., W. J. Enright, M. A. Crowe, M. Finnerty, N. Hynes, and J.F. Roche. 1995a. Immunization of heifers against GnRH: antibody titers, ovarian function, body growth and carcass characteristics. J. Anim. Sci. 73: 2382-2389.
Prendiville, D. J., W. J. Enright, M. A. Crowe, L. Vaughan, and J. F. Roche. 1995b. Immunization of prepubertal beef heifers against GnRH: immune, estrus, ovarian and growth responses. Journal of Anim. Sci. 73: 3030-3037.
Prendiville, D. J., W. J. Enright, M. A. Crowe, M. Finnerty, and J. F. Roche. 1996. Normal or induced secretory patterns of luteinising hormone and follicle-stimulating hormone in anoestrous gonadotrophin-releasing hormone-immunized and cyclic control heifers. Anim. Reprod. Sci. 45: 177-190.
Presser, H.A. 1983. Grazier's knowledge of, and use of methods of blowfly strike prevention and treatment. Proceedings of the Second National Symposium – Sheep Blowfly and Flystrike in Sheep, University of New South Wales.
Price, J., A. M. Nolan. 2001. Analgesia of newborn lambs before castration and tail docking with rubber rings. Vet. Rec. 149: 321-324.
Price, E. O., T. E. Adams, C. C. Huxsoll, and R. E. Borgwardt. 2003a. Aggressive behaviour is

reduced in bulls actively immunized against gonadotropin-releasing hormone. J. Anim. Sci. 81:411–415.

Price, J., N. Clarke, E. M. Welsh, and N. Waran. 2003b. Preliminary evaluation of subjective scoring systems for assessment of postoperative pain in horses. Vet. Anaesth. Analg. 30:97. (Abstr.)

Price, J., S. Catriona, E. M. Welsh, and N. K. Waran. 2003c. Preliminary evaluation of a behaviour-based system for assessment of post-operative pain in horses following arthroscopic surgery. Vet. Anaesth. Analg. 30:124–137.

Price, M. A., and T. Tennessen. 1981. Preslaughter management and dark-cutting in the carcass of young bulls. Can. J. Anim. Sci. 61:205–208.

Primary Industries Standing Committee, 1991. Model code of practice for the welfare of animals: The Sheep. Primary Industries Report Series 29. CSIRO Publishing, ISBN 0 643 05117 1.

Primary Industries Standing Committee. 2004. Model Code of Practice for the Welfare of Animals: Cattle, Second Edition. Primary Industries Standing Committee Report 85. Publishers: CSIRO Publishing, ISBN 0 643 09116 5.

Pritchett, L. C, C. Ulibarri, M. C. Roberts, R. K. Schneider, and D. C. Sellon. 2003. Identification of potential physiological and behavioral indicators of postoperative pain in horses after exploratory celiotomy for colic. Appl. Anim. Behav. Sci. 80:31–43.

Purchas, R.W. 1995. Effect of sex and castration on growth and composition. In *Growth regulation in farm animals: advances in meat research* Volumne 7 pp 203-254. Eds: AM Pearson and TR Dutson, Elsevier Applied Science, New York.

Raja, S. N., R. A. Meyer, M. Ringkamp, and J. N. Campbell. 2000. Peripheral neural mechanisms of nociception. Pages 11–57 in Textbook of Pain. P. D. Wall and R. Melzack, ed. 4th ed. Harcourt Publishing Ltd., London, UK.

Ray D. E., W. H. Hale and J. A. Marchello. 1969. Influence of season, sex and hormonal growth stimulants on feedlot performance of beef cattle. J. Anim. Sci. 29: 490-495.

Reibold, T. 2003. Anesthetic management of cattle. In: Recent Advances in Anesthetic Management of Large Domestic Animals (Doc. No. A0603.0201). E. P. Steffey, ed. International veterinary Information Service, Ithaca, New York, US. Available: http://www.ivis.org/advances/Steffey_Anesthesia. Accessed 9 Feb. 2004.

Rieger D., S. Roberge, D. H. Coy, and N. C. Rawlings 1989. Effects of an LHRH antagonist on gonadotrophin and oestradiol secretion, follicular development, oestrus and ovulation in heifers. J. Reprod. Fertil. 86:157-164.

Robertson, I. S. 1966. Castration in farm animals: its advantages and disadvantages. Vet. Rec. 78:130–135.

Robertson, I. S., J. C. Wilson, and H. M. Fraser. 1979. Immunological castration in male cattle. Vet Rec. 15:105:556–557.

Robertson, I. S., J. E. Kent, and V. Molony. 1994. Effect of different methods of castration on behaviour and plasma cortisol in calves of three ages. Res. Vet. Sci. 56:8–17.

Robinson T. J. 1977. Reproduction in cattle. In: Reproduction in Domestic Animals 3rd edition. H. H. Cole and P. T. Cupps (Eds), New York Academic Press, New York pp 433-441.

Roche J. F. and J. P. Crowley. 1973. The long-term suppression of heat in cattle with implants of melengestrol acetate. Anim. Prod. 16: 245-250.

Rubinstein, M., J. S. Mogil, M. Japón, E. C. Chan, R. G. Allen, and M. J. Low. 1996. Absence of opioid stress-induced analgesia in mice lacking □-endorphin by site-directed mutagenesis. Proc. Natl. Acad. Sci. USA 93:3995–4000.

Rutherford, K. M. D. 2002. Assessing pain in animals. Anim. Welfare 11:31–53.

Sanford, J. 1992. Guidelines for the detection and assessment of pain and distress in experimental animals: initiatives and experience in the United Kingdom. Pages 515–524 in Animal Pain. C. E. Short and A. Van Poznak, ed. Churchill Livingstone, Edinburgh, Scotland.

Sanford, J., R. Ewbank, V. Molony, W. D. Tavernor, and O. Uvarov. 1986. Guidelines for the recognition and assessment of pain in animals. Vet. Rec. 118:334–338.

Sawyer, D.C., R.H. Rech, RA Durham, T Adams, MA Richter and EL Striler. 1991. Dose response to butorphanol administered subcutaneously to increase visceral nociceptive threshold in dogs. Am. J. Vet. Res. 52: 1826-1830.

SCAHAW. 2001. The welfare of cattle kept for beef production. Publication of the European Commission, Health and Consumer Protection Directorate-General by the Scientific Committee on Animal Health and Animal Welfare (SCAHAW) SANCO.C.2/AH/R22/2000. Adopted 25 April 2001. Available: http://europa.eu.int/comm/food/fs/sc/scah/out54_en.pdf. Accessed 20 Dec. 2003.

Scherk-Nixon, M. 1996. A study of the use of a transdermal fentanyl patch in cats. J. Amer. Anim. Hos. Assoc. 32: 19-24.

Schreiner, D. A., and P. L. Ruegg. 2002. Responses to tail docking in calves and heifers. J. Dairy Sci. 85:3287–3296.

Schwartzkopf-Genswein, K. S., J. M. Stookey, and R. Welford. 1997. Behavior of cattle during hot-iron and freeze branding and the effects on subsequent handling ease. J. Anim. Sci. 75:2064–2072.

Scott, P. R., N. D. Sargison, W. D. Strachan, and C. D. Penny. 1996. Assessment of intrathecal lignocaine analgesia for open castration of rams. Br. Vet. J. 152: 481-483.

Seideman, S. C., H. R. Cross, R. R. Oltjen and B. D. Schanbacher. 1982. Utilization of intact male for red meat production: a Review. J. Anim. Sci. 55:826–840.

Servière, J. 2001. What is pain? How we can measure pain? 1st plenary meeting of Working Group 1 on Measuring Animal Welfare, COST action 846 (http://www.cost846.unina.it/). Clermont-Ferrand, France, 26–28th April, 2001.

Seykora, T. 2000. Practical techniques for dairy farmers. 3rd ed. University of Minnesota, St. Paul, Minnesota, US. Available: http://www.ansci.umn.edu/faculty/Seykora.htm. Accessed 15 Jan. 2004.

Shafford, H. L., B. D. X. Lascelles, and P. W. Hellyer. 2001. Preemptive analgesia: managing pain before it begins. Vet. Med. 96:478–491.

Shutt, D. A., L. R. Fell, R. Connell, A. K. Bell, C. A. Wallace, and A. I. Smith. 1987. Stress-induced changes in plasma concentrations of immunoreactive □-endorphin and cortisol in response to routine surgical procedures in lambs. Aust. J. Biol. Sci. 40:97–103.

Shutt, D. A., L. R. Fell, R. Connell, and A. K. Bell. 1988. Stress responses in lambs docked and castrated surgically or by the application of rubber rings. Aust. Vet. J. 65:5–7.

Skarda, R. T. 1986. Techniques of local analgesia in ruminants and swine. Vet. Clin. North Am. Food Anim. Pract. 2:621-663.

St. Jean, G. 1995. Male reproductive surgery. Vet. Clin. North Am. Food Anim. Pract. 1:55–93.

Stafford, K. J., D. J. Mellor, and C. M. McMeekan. 2000. A survey of the methods used by farmers to castrate calves in New Zealand. N. Z. Vet. J. 48:16–19.

Stafford, K., D. Mellor, and P. Wilson. 2001. The use of behaviour to compare the pain caused by different husbandry procedures in livestock. Page 11 in Proceedings of the 28th Annual Conference of the Australasian Society for the Study of Animal Behaviours. The University of Queensland, Australia.

Stafford, K., D. Mellor, S. Todd, R. Bruce, and R. Ward. 2002. Effects of local anaesthesia or local anaesthesia plus a non-steroidal anti-inflammatory drug on the acute cortisol response of calves to five different methods of castration. Res. Vet. Sci. 73:61–70.

Stafford, K.J., D.J. Mellor, S.E. Todd, R.N. Ward and C.M. McMeekan. 2003. The effect of different combinations of lignocaine, ketoprofen, xylazine and tolazoline on the acute cortisol response to dehorning in calves. N. Z. Vet. J. 51:219-226.

Steen, R. W. J. 1995. The effect of plane of nutrition and slaughter weight on growth and food efficiency in bulls, steers and heifers of three breed crosses. Livest. Prod. Sci. 42:1–11.

Steiner, A., R. Bettschart, and U. Schatzmann. 2002. Kastration von männlichen Lämmern und Kälbern: Erläuterungen und Kommentare zu Art. 65 TSchV. (Article in German). Schweiz. Arch. Tierheilkd.144:107–113.

Steiner, B., A. Kamm, and R. Bettschart-Wolfensberger. 2003. Influences of carprofen and the experience of the surgeon on post-castration pain in lambs. Vet. Anaesth. Analg. 30:91–92. (Abstr.)

Steven, B.J., C.C. Johnston, and L. Horton. 1994. Factors that influence the behavioral pain responses of premature infants. Pain 59: 101-109.

Stookey, J. M. 1996. Painful procedures and misconceptions. Paper presented at Animal Care '96: Modern Agriculture organized by the Manitoba Farm Animal Council, November 28, 1996, in Winnipeg, Manitoba. Available: http://www.usask.ca/ wcvm/herdmed/applied-ethology/articles/manitoba.html. Accessed: 12 Oct. 2003.

Stumpf T. T., M. W. Wolfe M. S. Roberson G. Caddy G, R. J. Kittok, B. D. Schanbacher, H. E. Grotzan, and J. E. Kinder. 1992. Bovine luteinizing hormone (LH) isoforms and amounts of messenger ribonucleic acid for alpha- and LH beta-subunits in pituitaries of cows immunized against LH-releasing hormone. Biol. Reprod. 47: 776-781.

Sutherland, M. A., D. J. Mellor, K. J. Stafford, N. G. Gregory, R. A. Bruce, R. N. Ward, and S. E. Todd. 1999. Acute cortisol responses of lambs to ring castration and docking after the injection of lignocaine into the scrotal neck or testes at the time of ring application. Aust. Vet. J. 77: 738-741.

Sutherland, M. A., K. J. Stafford, D. J. Mellor, N. G. Gregory, R. A. Bruce, and R. N. Ward, S. E. 2000. Acute cortisol responses and wound healing in lambs after ring castration plus docking with or without application of a castration clamp to the scrotum. Aust. Vet. J. 78: 402-405.

Sutherland, M. A., D. J. Mellor, K. J. Stafford, N. G. Gregory, R. A. Bruce, and R. N. Ward. 2002a. Effect of local anaesthetic combined with wound cauterisation on the cortisol response to dehorning in calves. Aust. Vet. J. 80: 165-167.

Sutherland, M. A., D. J. Mellor, K. J. Stafford, N. G. Gregory, R. A. Bruce, and R. N. Ward. 2002b. Cortisol responses to dehorning of calves given a 5-h local anaesthetic regimen plus phenylbutazone, ketoprofen, or adrenocorticotropic hormone prior to dehorning. Res. Vet. Sci..73: 115-123.

Sylvester, S. P., K. J. Stafford, D. J. Mellor, R. A. Bruce, and R. N. Ward. 1998a. Acute cortisol responses of calves to four methods of dehorning by amputation. Aust. Vet. J. 76: 123-126.

Sylvester, S. P., D. J. Mellor, K. J. Stafford, R. A. Bruce, and R. N. Ward, 1998b. Acute cortisol responses of calves to scoop dehorning using local anaesthesia and / or cautery of the wound. Aust. Vet. J. 76: 118-122.

Taylor, A. A., and D. M. Weary. 2000. Vocal responses of piglets to castration: identifying procedural sources of pain. Appl. Anim. Behav. Sci. 70:17–26.

Taylor, A. A., D. M. Weary, M. Lessard, and L. Braithwaite. 2001. Behavioural responses of piglets to castration: the effect of piglet age. Appl. Anim. Behav. Sci. 73:35–43.

Tennessen, T., M. A. Price, and R. T. Berg. 1985. The social interactions of young bulls and steers after re-grouping. Appl. Anim. Behav. Sci. 14:37–47.

Termann, G. W., E. R. Penner, and J. C. Liebeskind. 1986. Stimulation-produced and stress-induced analgesia: cross-tolerance between opioid forms. Brain Res. 372:167–171.

Thornton, P. D., and A. E. Waterman-Pearson. 1999. Quantification of the pain and distress responses to castration in young lambs. Res. Vet. Sci. 66:107–118.

Thornton, P. D., and A. E. Waterman-Pearson. 2002. Behavioural responses to castration in lambs. Anim. Welfare 11:203–212.

Thuer, S., S. Mellema, M.G. Doherr, B. Wechsler, K. Nuss and A. Steiner.2006. Effect of local anaesthesia on short- and long-term pain induced by two bloodless castration methods in calves. Vet. J., in press.
Ting, S.T.L., B. Earley, J.M.L. Hughes, and M. A. Crowe. 2003a. 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. 81: 1281-1293.
Ting, S.T.L., B. Earley, and M. A. Crowe. 2003b. Effect of repeated ketoprofen administration during surgical castration of bulls on cortisol, immunological function, feed intake, growth and behavior. J. Anim. Sci. 81: 1253-1264.
Ting, S.T.L., B. Earley, and M. A. Crowe. 2004. Effect of cortisol infusion patterns and castration on metabolic and immunological indicies of stress response in cattle. Dom. Anim. Endocrinol. 26: 329-349.
Ting, S.T.L., B. Earley, I. Vessier, S. Gupta, and M. A. Crowe. 2005. Effect of age of Holstein-Friesian calves on plasma cortisol, acute-phase proteins, immunological function, scrotal measurements and growth in response to burdizzo castration. Anim. Sci. 80: 377-386.
Toates, F. 1995. Stress: Conceptual and Biological Aspects. John Wiley and Sons Ltd., Chichester, West Sussex, UK.
Tricklebank, M. D., and G. Curzon, ed. 1984. Stress-Induced Analgesia. John Wiley and Sons, New York, US.
Twycross, R. G. 2000. Opioids. Pages 1187–1214 in Textbook of Pain. P. D. Wall and R. Melzack, ed. 4th ed. Harcourt Publishing Ltd., London, UK.
Vane, J. R., and R. M. Botting. 1998. Anti-inflammatory drugs and their mechanisms of action. Inflamm. Res. 47(Suppl. 2):S78–S87.
Veissier I., J. Rushen, D. Colwell, and A. M. de Passillé. 2000. A laser-based method for measuring thermal nociception of cattle. Appl. Anim. Behav. Sci. 66:289–304.
Vickers, K. J., L. Niel, L. M. Kiehlbauch, and D. M. Weary. 2005. Calf response to caustic paste and hot-iron dehorning using sedation with and without local anesthesia. J. Dairy Sci. 88: 1454-1459.
Vowles, B. 1976. Bruising of carcasses cost us millions. J. Agric. (Victoria) 74: 388-392.
Wall, P. D. 1988. The prevention of postoperative pain. Pain 33:289–290.
Walters, E. T. 1994. Injury-related behaviour and neuronal plasticity: an evolutionary perspective on sensitization, hyperalgesia, and analgesia. Int. Rev. Neurobiol. 36:325–427.
Warner, T. D., and J. A. Mitchell. 2002. Cyclooxygenase-3 (COX-3): Filling in the gaps toward a COX continuum? Proc. Natl. Acad. Sci. USA 99:13371–13373. Available on line: http://www.pnas.org/cgi/doi/10.1073/pnas.222543099. Accessed: 10 Jul. 2004.
Warnick, V. D., C. W. Arave, and C. H. Mickelsen. 1977. Effects of group, individual, and isolated rearing of calves on weight gain and behavior. J. Dairy Sci. 60:947–953.
Waterman A.E., A.M. Nolan, and A. Livingston. 1987. Influence of idazoxan on the respiratory blood gas changes induced by alpha 2-adrenoceptor agonist drugs in concious sheep. Vet. Rec. 121:105-107
Waterman A.E., A. Livingston, and A. Amin. 1990. Analgesia and respiratory effects of frntantl in sheep. Journal of the Association of Veterinary Anaesthetists of Great Britain and Ireland 17: 20-23.
Watts, J. M., and J. M. Stookey. 1999. Effects of restraint and branding on rates and acoustic parameters of vocalization in beef cattle. Appl. Anim. Behav. Sci. 62:125–135.
Watts, J. M., and J. M. Stookey. 2000. Vocal behaviour in cattle: the animal's commentary on its biological processes and welfare. Appl. Anim. Behav. Sci. 67:15–33.
Weary, D. M., L. A. Braithwaite, and D. Fraser. 1998. Vocal response to pain in piglets. Appl. Anim.

Behav. Sci. 56:161–172.
Weaver, A. D. 1986. Bovine surgery and lameness. Blackwell Scientific Publications, Oxford, UK.
Weissman, C. 1990. The metabolic response to stress: an overview and update. Anesthesiology 73:308–327.
Welsh, E. M., and A. M. Nolan. 1995a. Effect of flunixin meglumine on the thresholds to mechanical stimulation in healthy and lame sheep. Res. Vet. Sci. 58:61–66.
Welsh, E. M., and A. M. Nolan. 1995b. The effect of abdominal surgery on thresholds to thermal and mechanical stimulation in sheep. Pain 60:159–166.
Welsh, E. M., G. Gettinby, A. M. Nolan. 1993. Comparison of a visual analogue scale and a numerical rating scale for assessment of lameness using sheep as a model. J. Am. Vet. Res. 54:976–983.
White, R. G., J. A. DeShazer, C. J. Tressler, G. M. Borches, S. Davey, A. Waninge, A. M. Parkhurst, M. J. Milanuk, and E. T. Clemens. 1995. Vocalization and physiological response of pigs during castration with or without a local anesthetic. J. Anim. Sci. 73:381–386.
Wilder-Smith, O. H. G., E. Tassonyi, C. Senly, Ph. Otten, and L. Arendt-Nielsen. 1996. Surgical pain is followed not only by spinal sensitization but also by supraspinal antinociception. Br. J. Anaesth. 76:816–821.
Wiltbank J. N., and L. E. Casida. 1956. Alteration of ovarian activity by hysterectomy. J. Anim. Sci. 15: 134-140.
Wood, G. N., V. Molony, S. M. Fleetwood-Walker, J. C. Hodgson, and D. J. Mellor. 1991. Effects of local anaesthesia and intravenous naloxone on the changes in behaviour and plasma concentrations of cortisol produced by castration and tail docking with tight rubber rings in young lambs. Res. Vet. Sci. 51:193-199.
Woolf, C. J. 1989. Recent advances in the pathophysiology of acute pain. Br. J. Anaesth. 63:139–146.
Woolf, C. J. 1995. Somatic pain–pathogenesis and prevention. Br. J. Anaesth. 75:169–176.
Woolf, C. J., and M. S. Chong. 1993. Pre-emptive analgesia: treating postoperative pain by preventing the establishment of central sensitization. Anesth. Analg. 77:362–379.
Woolf, C. J., and P. D. Wall. 1986. Morphine-sensitive and morphine-insensitive actions of C-fibre input on the rat spinal cord. Neurosci. Lett. 64:221–225.
Woolf, C. J., and S. W. N. Thompson. 1991. The induction and maintenance of central sensitisation in dependent on N-methyl-D-aspartic acid receptor activation: implications for the treatment of post-injury hypersensitivity states. Pain 44:293–299.
Worrell, M. A., D. C. Clanton, and C. R. Calkins. 1987. Effect of weight at castration on steer performance in the feedlot. J. Anim. Sci. 64:343–347.
Yamada, K., and T. Nabeshima. 1995. Stress-induced behavioral responses and multiple opioid systems in the brain. Behav. Brain Res. 67:133–145.
Youngquist, R.S., H.A. Garverick, and D.H. Keisler. 1995. Use of umbilical cord clamps for ovariectomy in cows. J. Am. Vet. Med. Assoc. 207:474-475.
Zimbelman R. G., and L. W. Smith. 1966. Control of ovulation in cattle with melengestrol acetate. I effects of dose and route of administration. J. Reprod. Fertil. 11: 185-191.
Zimmer, A., A. M. Zimmer, J. Baffi, T. Usdin, K. Reynolds, M. König, M. Palkovits, and E. Mezey. 1998. Hypoalgesia in mice with a targeted deletion of the tachykinin 1 gene. Proc. Natl. Acad. Sci. USA 95:2630–2635.
Zimmermann, M. 1986. Behavioural investigations of pain in animals. Pages 16–27 in Assessing Pain in Farm Animals. Proceedings of a workshop held in Roslin, Scotland, 25–26 Oct. 1984. I. J. H. Duncan, and V. Molony, ed. Commission of the European Communities, Luxembourg, Belgium.
Zinn, S. A., L.T Chapin, W. J. Enright, and H.A. Tucker. 1989. Growth, carcass composition, and

serum hormone responses to photoperiod amd ovariectomy in heifers. Anim. Prod. 49:365-373.
ZoBell, D. R., L. A. Goonewardene, and K. Ziegler. 1993. Evaluation of the bloodless castration procedure for feedlot bulls. Can. J. Anim. Sci. 73:967–970.
Zweiacher, E. R., R. M. Durham, B. D. Boren, and C. T. Gaskins. 1979. Effects of method and time of castration of feeder calves. J. Anim. Sci. 49:5–9.