Castration of male livestock and the potential of immunocastration to improve animal welfare and production traits: Invited Review

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Abstract
Growing consumer awareness about animal welfare has led to the assessment of the impact of common farming practices, such as physical castration, on animal well-being under production conditions. Physical castration is used in livestock industries to prevent indiscriminate breeding, control aggression, and improve meat and carcass quality. In terms of animal welfare, physical castration causes pain, decreased growth performance, infection, and mortality. An alternative approach to castration is thus warranted that will ensure optimal growth without compromising the castrated animal’s wellbeing. Immunocastration has proved to be an effective method of suppressing the development and functioning of the reproductive system in various domesticated and wildlife species. The effect of immunocastration on production performance is well-documented for both swine and cattle. Although ram lambs used for meat production are often physically castrated, information regarding the potential application of immunocastration in sheep is limited. However, immunocastration may potentially improve the welfare, performance, and meat quality of ram lambs used in commercial meat production systems. The purpose of this review is to compare the application and the effects of immunocastration on male livestock to highlight and motivate the need for further research into its use on ram lambs.

Keywords: Carcass traits, GnRH, meat quality, sheep

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Introduction
Consumer awareness about the welfare of production animals has increased recently, with the physical castration of livestock receiving considerable attention. Recently, the Global Meat News’ State of the Industry Survey Report (2015) stated that, “eighty-three percent of meat industry professionals strongly agreed that the global meat industry must put more emphasis on animal welfare and impose tougher regulations”. This point of view was resonated in the European Union’s decision to voluntarily ban the physical castration of piglets without anaesthesia from 2018 (Font-i-Furnols et al., 2012). Males used for lamb and beef production are often castrated without pain mitigation to promote fattening and assist with management. Additionally, it is expected that the banning of physical castration may soon be enforced in the mutton and beef industries.

Although intact males have a faster growth rate and superior feed efficiency than castrates (Field, 1971; Pauly et al., 2009; Sales, 2014), various management and welfare issues exist regarding the raising of intact males (Cronin et al., 2003; Price et al., 2003). Heavy or more physiologically developed intact male carcasses are also penalized at the abattoir due to various meat quality issues. These issues include boar taint in heavy boars and the tendency for older bulls to develop dark, firm and dry meat. Thus, boars over 100 kg (approximately 22 weeks old) and bulls or rams with one or more permanent incisors are marked “MD” and receive a lower price per kg (SAMIC, 2006). There is thus a need to formulate alternative management practices that will ensure efficient growth of male animals that will result in optimum carcass and meat quality, without having to compromise animal welfare.

Immunocastration, also known as immunocastration, has shown promise in this regard, and to date has been successfully applied in the international and local pork industry (Needham et al., 2016). Immunocastration, resulting from the administration of a vaccine designed to block the action of gonadotropin-releasing hormone (GnRH) from the hypothalamus, ultimately disrupts the normal functioning of the testes, resulting in a suppression of spermatogenesis and testosterone production. Various immunocastration vaccines have been formulated and tested in sheep (Parthasarathy et al., 2002; Ülker et
al., 2002; Oatley et al., 2005; Karakuş et al., 2013); however, to date, no formal commercialized product is available for use in sheep.

For the purpose of this review, the production of both intact and castrated meat-producing livestock species will be discussed, along with the associated concerns of farming intact or castrated males. The technique of immunocastration will be explained, and its application in various livestock and wildlife species highlighted. Due to the variation in effects seen with small-scale vaccines manufactured for research purposes, research using commercially available products such as Bopriva® (cattle) and Improvac® (pigs) will receive particular emphasis. The review will focus on the influence of immunocastration on meat production, indicating how immunocastration can potentially assist in addressing the welfare issues raised with physical castration, while highlighting the potential beneficial influence on production parameters, carcass traits, and meat quality in lambs.

Production and management of male livestock

The production of intact males poses various handling, management, and carcass and meat quality issues (Seideman et al., 1982; Cronin et al., 2003; Price et al., 2003). Handling intact male animals can be dangerous to both the handler and the animal, and thus castration at an early age is usually preferred. Post-pubertal bulls are especially difficult to manage from a human safety aspect due to their size, and can cause damage to pasture and infrastructure (Seideman et al., 1982; Aasen, 2000). Management issues include having to either maintain intact males in isolation or at low stocking densities to either prevent or minimise the incidence and associated effects of aggressive and sexual behaviour (Aasen, 2000). In addition to this, males are often kept isolated from females to prevent indiscriminate breeding, as with extensive cattle production (Winter, 1996). The need to isolate intact males can complicate management further if a breeding enterprise is being maintained in conjunction with slaughter animal production where indiscriminate breeding can occur, should cull males indvertibly enter the breeding female herd.

Intact male livestock may be the preferred choice compared to castrates and females, due to their superior growth, leaniness of carcass, and feed efficiency (Gispert et al., 2010; Sales, 2014). These production traits can largely be ascribed to the effect of male androgens, such as testosterone, that promote lean muscle growth (Snochowski et al., 1981). The impact of testosterone on fat deposition can either be viewed as a positive or negative, depending on the market demands. For example, currently in the South African pork market, lean carcasses are favoured and thus intact males are preferred, while the risk of boar taint is often not considered. In the production of lamb and beef, emphasis is on the finishing of livestock with a certain degree of fatness, with an economic value generally placed on carcasses with a medium fat covering. Currently, beef and sheep carcasses in the A2 and A3 grading categories, according to SAMIC (2006), fetch the highest price per kg in the South African red meat market (RPO, 2017). Sheep and cattle carcasses from lean intact males generally score lower on fat covering when slaughtered at the same age as castrated male or female animals. Intact male animals are thus maintained longer in the finishing phase to deposit more fat, which ultimately negates the benefit of their superior feed efficiency. Therefore, a balance needs to be achieved where the most economical carcass is produced. Furthermore, the value of intact male carcasses can be decreased due to bruising and lesions from aggressive and sexual behaviour, which is a problem seen particularly in feedlot systems (Seideman et al., 1982).

Motivation for castration

Castration is not limited to use in livestock species, but also finds application in companion animals, horses maintained for recreational purposes, and, more recently, wildlife (De Nys et al., 2010). The typical purpose of castration is to ease handling and management by controlling sexual and aggressive behaviour. Another important management use of castration is the prevention of unwanted pregnancies; whether it be in mixed herds intended for slaughter, the accidental breeding of stud animals by those males not intended for breeding purpose, or population control (Ladd et al., 1994). The control of indiscriminate breeding becomes particularly important in the livestock industry when prolonged finishing of slaughter animals is required, such as in extensive systems, where male animals may reach puberty prior to slaughter (Amatayakul-Chantler et al., 2013). This is typically experienced when free-range animals are the end product.

The use of castration as a tool to improve meat quality is important in livestock species such as pigs, sheep, and cattle. Castrating male livestock decreases the anabolic potential of the animal and results in the increased deposition of fat. As mentioned, this can be beneficial in the sheep and cattle industries. However, the degree of fatness of a carcass not only influences the value of the carcass, but also the meat quality of the carcass, as fatness influences juiciness, which in turn is related to the tenderness of the meat. A meta-analysis of literature using bloodless castration techniques summarized that castrated rams had decreased weight gain, feed efficiency, and leanness; however, tenderness was improved (Sales, 2014).
Not only do male steroid hormones contribute to behavioural issues, it can contribute to unwanted flavours and aromas. An example of this is an objectionable sensory quality of pork from intact male pigs, known as boar taint (Patterson, 1968). The testes of boars produce a pheromone known as androstenone, which is stored within the salivary glands and released during pre-copulatory activities (Bonneau et al., 1982). However, androstenone is also lipophilic and is thus deposited within the adipose tissue. An unpleasant smell and taste of urine or sweat is described by those sensitive to androstenone when the pork of an entire male pig is cooked and androstenone is present in the tissue, which results in consumer acceptability issues (Font-i-Furnols, 2008). The meat from intact male goats is also perceived to have an unpleasant aroma and flavour termed “buck odour” and castration has shown to improve the palatability of the resultant meat (Zamiri et al., 2012), which indicates the possible involvement of male steroid hormones produced by the testes.

**Concerns with castration**

Various methods can be used to physically castrate livestock. The testicles can be excised surgically from the scrotum or by placing a rubber ring/band around the neck of the scrotum, with the latter method resulting in ischaemia and sloughing of the testicles and scrotum due to necrosis (Winter, 1996). Alternatively, a portion of the spermatic chord, blood vessels, nerves, and scrotal tissue can be destroyed using the closed crushing/ Burdizzo technique, which also leads to testicle atrophy due to ischaemia; however, with this method the testicles remain intact. Surgical castration is generally favoured in swine; however, depending on the country’s legislation, it may or may not stipulate the use of pain mitigation. Generally, band castration, as well as Burdizzo castration, tends to be favoured in rams and bulls; however, surgical castration is also used. Again, the use of pain mitigation may or may not be mandatory in these practices (Melches et al., 2007). Local anaesthesia can be used to reduce the pain experienced with castration; however, this does have cost implications and not all legislation requires it to be used during castration.

To quantify the pain response to castration, factors such as cortisol levels, behaviour, and posture are often taken into consideration, with both the short and long-term responses investigated to fully describe the effects of castration on the welfare of male animals. Rams surgically castrated under sedation with local anaesthesia indicated more immediate and frequent pain responses, resulting in a decreased feed intake and weight loss when compared to rams castrated by using the band and Burdizzo castration methods where local anaesthesia was also used (Melches et al., 2007). Although Burdizzo castration resulted in a more pronounced immediate pain response when compared to band castration, wound healing occurred faster and with fewer complications after Burdizzo castration. Surgical and band castration resulted in a compromised recovering ability of the animals, with purulent secretion, infection, and abscesses the most common problems occurring. Although band castration showed less immediate pain responses, the castrated rams exhibited an increased level, and prolonged period, of pain due to an extended healing period of $12.3 \pm 11.5$ days, with the sloughing of the testes occurring at $35 \pm 6.9$ days. Rams surgically castrated took on average $4.9 \pm 4.3$ days to heal, and the Burdizzo-castrated rams on average $1.3 \pm 1.0$ days. Even though all treatments received pain relief, pain was however still experienced by the rams, and it can be assumed that the animals’ wellbeing was not improved (Melches et al., 2007).

According to Baird and Wolfe (1998), ram lambs are typically castrated shortly after birth since animal handling is easier and fewer post-operative complications are experienced. However, it may be more favourable to castrate rams at a later age, typically found with slower growing rams who did not reach slaughter weight prior to puberty, or rams culled from breeding stock after selection based on performance testing.

Currently, legislation in certain countries dictates as to when certain castration techniques can be applied; however, some regulations do not adequately describe when veterinary intervention and pain mitigation is required. According to welfare codes under Mutilations Regulations (Permitted procedures, England) (2007), ram lambs in the United Kingdom must be castrated using rubber rings before seven days of age, but before 12 weeks of age using other techniques, with pain mitigation required after three months of age. Canadian regulations also stipulate that rams be castrated after colostrum intake, but before seven days of age with pain mitigation being required on rams older than three months of age (NFACC, 2013). The Australian Model Code of Practice (2006) for sheep states that rams need to be castrated within 12 weeks after birth and that anaesthesia must be used if castration needs to be done after six months of age. Similarly, New Zealand requires castration to be done as early as possible but pain mitigation is only required for rams older than six months of age (NAWAC, 2010). However, no formal or readily available guidelines exist for the physical castration of rams in South Africa.

Other factors that should be considered with physical castration, is the risk of morbidity and mortalities, as well as various labour-related issues. Firstly, persons performing the technique need to skilled to do so,
using appropriate hygienic methods and well-maintained tools. Furthermore, if local anaesthesia is used, this frequently requires the administration by a registered veterinarian, which has additional time and cost implications. One also needs to consider the stress of herding, handling, and restraining the animals to perform these techniques at an appropriate age using appropriate facilities. Post-castration inspections need to be performed regularly, which requires skilled labour, increased handling and time. The importance of technique choice, pain mitigation use, recovery, and monitoring of castrated lambs is highlighted by Melches et al. (2007). Therefore, physical castration can be a time-consuming process where skilled labour is required and the welfare of the animals can be compromised.

Physical castration of livestock may also increase the input costs per animal as well as the loss in yield per animal due to poorer feed efficiency and growth rates (Sales, 2014). Direct costs include the cost of the castration procedure itself, pain mitigation (should it be chosen or required to be used), the prevention of infection and the treatment of complications. Further financial losses are incurred when the animal experiences morbidity, decreasing growth performance in response to both pain and lack of anabolic hormones, and when mortalities arise resulting from infection or complications. Complications and the associated financial implications regarding physical castration can be prevented using immunocastration. Amatayakul-Chantler et al. (2013) reported that adverse issues were experienced in 8 % of surgically castrated bulls raised on pasture, while those bulls immunocastrated experienced no complications related to the castration procedure. It is for these aforementioned reasons that alternatives to physical castration be investigated, while still controlling the problems associated with intact male production and preventing the welfare issues associated with both intact male and castrate production.

**Immunocastration and its application**

Active immunization against gonadotropin-releasing hormone (GnRH) has shown potential in replacing physical castration and has been successfully implemented as part of management programs. D’Occhio (1993) reviewed the reproductive consequences of fertility control using immunological suppression of various reproductive hormones. Furthermore, Thompson (2000) reviewed the technical aspects of the immunocastration in various livestock species which may be consulted for further information on the development of commercial vaccines. The principle of immunocastration centres on the “blocking” of the action of the gonadotropin-releasing hormone. Gonadotropin-releasing hormone, also known as Luteinizing hormone-releasing hormone (LHRH), is transported by the hypophysial portal systems to the anterior pituitary. The short exposure time of the GnRH to the blood system during transport from the hypothalamus to the pituitary gland is the only opportunity for exposure of GnRH to circulating antibodies. If antibodies specific to GnRH are exposed to GnRH during this stage, GnRH will bind to GnRH antibodies specific antibodies that essentially “neutralizes” the hormone, either by preventing diffusion through the capillaries or by occupying the binding site on GnRH which prevents it binding to the anterior pituitary.

The GnRH itself is too small to be immunogenic, and various techniques have been used to fool the animal’s system into recognizing GnRH as foreign. Such techniques typically involve conjugating GnRH to a large, non-self or foreign protein using various sites and methods of conjugation. Numerous techniques have shown success in producing sufficient GnRH-antibody titers; however, the application of such vaccines have been limited regarding commercial use. The type of adjuvant used, and the number of immunizations required to elicit a response, are two constraining factors that hampers the use of immunovaccines. The variation in the composition and design of vaccines manufactured on small scale for research purposes, as well as variation in the response experienced with different types of adjuvants complicates and limits the extrapolation and comparison from available results. Commercial vaccines have been designed to minimise adverse reactions to the adjuvant in the relative species as well as to minimise frequency of vaccinations. However, other factors also influence the results seen from immunocastration, such as the interval between vaccinations, the timing of the second vaccination relative to slaughter, the age of the animal, the duration of the study, as well as the nutritional strategy applied. These factors thus need to be considered when comparing results. Commercially available vaccines include Bopriva® (Zoetis™) for cattle and Improvac® (Zoetis™) for swine. Previously, Vaxstrate (Arthur Webster Pty Ltd, Castle Hill, N.S.W.) was available for use in heifers but has been discontinued.

Immunocastration may be used commercially to improve the on-farm welfare of male livestock species by circumventing many of the concerns with physical castration methods. A major benefit of immunocastration is preventing the pain associated with the castration procedures and the risk of wound infection. Thus, the incidences of morbidity and mortalities due to wound healing complications on-farm may be reduced. Immunocastration still requires the animal to be handled; however, producers are not constrained to the short timeframe in which physical castration is recommended to be performed after birth. Producers can wait until later in the growth of the animal to handle them, potentially integrating the vaccination schedule with other routine vaccinations or dosing. The early handling and separation of lambs
from their mothers for castration and tail docking procedures may be rendered unnecessary, decreasing the stress of such an exercise on both lambs and ewes. Due to the decreased risk of infection and removing the risk of wound healing complications, this may actually decrease the need to further handle the animals to treat them for such infections. The administration procedure of the immunocastration vaccine is simple in comparison to physical castration methods and does not require the presence of a veterinarian.

With regards to improving the animal welfare of intact male livestock on-farm, using immunocastration will provide the same welfare benefits as physical castration in terms of fertility and behavioural control. Control of aggressive behaviour decreases fighting-related injuries as well as carcass bruising in male animals. The prevention of pregnancies in a mixed-gender herd is also essential in maintaining the welfare of those female animals intended for slaughter. It has also been suggested that immunocastration may have a positive effect on the immune system by improving splenic immune markers and immune cytokines (Han et al., 2016). Thus, the animal’s immune status and well-being may actually benefit from immunocastration. However, further investigation into these benefits on a commercial scale is yet to be quantified. An economic comparison looking into the indirect benefits of improved animal welfare from immunocastration on production parameters needs to be considered.

Swine

Immunocastration with Improvac® has been used in swine to prevent boar taint while improving growth and carcass performance in comparison to physical castrates. The vaccination schedule for Improvac® has been designed to minimise the impact on fat deposition and feed efficiency while allowing sufficient clearance time for compounds associated with boar taint (Claus et al., 2007). Following the recommended vaccination schedule, the primary vaccination appears to have no significant effect on the testosterone production in swine; with antibodies against GnRH increasing within three to five days after the booster vaccination and peaking four to six days after the booster vaccination (Claus et al., 2007). Subsequently, luteinizing hormone (LH) and testosterone levels decline almost simultaneously within four to eight days and five to ten days, respectively, after the booster injection, and remain stable for approximately 44 days after the booster (Claus et al., 2007). It has been demonstrated that immunocastrated swine are unique with regards to their hormone profile such as oestradiol, growth hormone (GH) and insulin-like growth factor 1 (IGF-1). Although immunocastrated pigs have low levels of oestradiol compared to surgical castrates, their GH levels are high and comparable to that of intact boars (Brunius et al., 2011; Bauer et al., 2009). As a result, IGF-1 levels in immunocastrates are intermediate to those of intact and surgically castrated males (Brunius et al., 2011). The IGF-1 levels in immunocastrates were shown to gradually decrease five days after the booster and stabilising within six to ten days (Claus et al., 2007). Thus immunocastrates could have a higher anabolic lean growth potential than surgical castrates even though testosterone production is compromised, provided their nutritional needs are met. This potential change in anabolic growth potential and nutritional requirements was investigated by increasing dietary lysine in the diets of immunocastrates, showing that their cutting yields improved and backfat thickness decreased in comparison to surgical castrates (Boler et al., 2011). Responses to varying dietary protein content also differed between immunocastrates and intact males with regards to backfat deposition, also indicating a possible difference in anabolic growth potential and nutritional requirements between immunocastrates and intact boars (Needham & Hoffman, 2015a). However, the addition of ractopamine hydrochloride at 10 mg/kg to the diet of immunocastrates can improve the lean meat yield and carcass traits (Needham & Hoffman, 2015b).

In group-housing based trials, immunocastrated swine performed better than intact males, most likely due to their decreased activity including aggressive and sexual behaviour (Dunshea et al., 2001). These immunocastrates were also leaner and had a more improved feed efficiency than surgical castrates in the trial, even though feed intake has been shown to increase in immunocastrated pigs compared to intact boars. This increase in feed intake could be a combination of increased feeding activity due to decreased aggressive and sexual behaviour as well as the absence of the appetitive suppression effect of androgens. Although dietary protein level did not influence feed intake per se in individually housed immunocastrates, immunocastrates experienced improved feed efficiency when dietary protein content was increased (Needham et al., 2016a). The extent to which the increase in feed intake seen in immunocastrates influences fat deposition largely depends on the period between the booster and slaughter, as the increase in feed intake is seen approximately two weeks after the booster vaccination regardless of its timing (Lealifano et al., 2011). Likewise, the effects of immunocastration on carcass traits and yields depend on the vaccination schedule used and the age of the pigs when it was applied; which also appears to be the case in other livestock species.
Cattle

In bulls, immunocastration, with Bopriva® has been successful in decreasing testosterone levels to those comparable to physical castrates within 14 days after the booster (Amatayakul-Chantler et al., 2013) and thereby controlling aggressive and sexual behaviour (Huxsell et al., 1998) as well as decreasing overall activity (Janett et al., 2012). The use of Bopriva® in cattle has shown consistent immune responses in individuals, which is not always shown to be experienced with small-scale vaccines manufactured for research purposes (Thompson, 2000).

Steers are preferred in beef enterprises for it is easier to manage their behaviour, have an improved fat deposition and thus carcass grading, as well as meat quality. However, as with other livestock species, the castrated steers grow slower and are less feed efficient, when compared to intact males. The fattening period of cattle is much longer relative to that of, for example, sheep or pigs and thus the possibility of the animals reaching puberty prior to slaughter becomes more of a concern, particularly when cattle are finished on pasture. Such an example of this is the large beef production industry in Brazil, Namibia, and Botswana that finish cattle on pasture until they are 30 to 36 months of age. In Brazil, the industry tends to practise late castration at 18 to 24 months of age to take advantages of male steroid hormones and the associated growth and feed efficiency as much as possible. Bulls in extensive systems can be destructive with regards to infrastructure as well as pasture and thus need to be managed carefully. For instance, bulls cannot be grazed near cows as the risk of them breaking through fences to get to the females is high and can cause indiscriminate breeding. Not only is this a welfare issue in slaughter cows, it also presents a huge threat to heifers not ready to be mated. A further issue associated with castration in extensive production units in tropical areas such as Brazil include the risk of infection of the healing wound by the screw worm fly, Cochliomyia hominivorax, should preventative and therapeutic treatment fail, which also requires extra input costs (Muniz et al., 1995).

When compared to physically castrated steers, the effects of immunocastration on growth performance, carcass traits and meat quality are generally favourable. Immunocastrated bulls vaccinated twice (20 and 25 months of age) with Bopriva® and raised on pasture have been shown to have greater average daily gains (ADGs), hot carcass weights and dressing percentages in comparison to late physical castrates (25 months) (Amatayakul-Chantler et al., 2013). This improvement in growth performance seen in immunocastrated bulls could be attributed to having a longer exposure time to the male steroid hormones before testosterone levels reach those similar to the physical castrates after the booster vaccination, as well as the absence of pain and the associated growth setbacks of physical castration. Furthermore, the immunocastrated cattle showed no negative effects on carcass or meat quality traits with regards to subcutaneous fat thickness, rib eye area, meat colour, fat colour, cooking loss and tenderness (Amatayakul-Chantler et al., 2013).

When used in a feedlot system, immunocastration has been shown to improve carcass traits and beef colour attributes in comparison to surgical castrated and intact bulls, respectively (Miguel et al., 2014). Meat from immunocastrated cattle showed greater redness and lower darkness than intact bulls, which could indicate a possible advantage with regards to retailing. Late castration in feedlot systems is also preferred in late maturing animal breeds, as they tend to take longer to reach the desired carcass weight and fatness. When immunocastration is applied after puberty, carcass traits change from those of intact bulls to long-term castrated bulls (D’Occhio et al., 2001). Thus, the flexibility with regards to when immunocastration is applied can allow the manipulation of carcass traits in bulls of varying maturity types. Positive results have been experienced with regards to applying immunocastration to Bos indicus and Bos indicus crossbred cattle in both extensive and feedlot systems (Amatayakul-Chantler et al., 2012; Amatayakul-Chantler et al., 2013; Miguel et al., 2014). Immunocastrated bulls appear to have greater development in the hindquarter than steers and bulls, indicated by an increase in the leg perimeter of the hindquarter (Miguel et al., 2014) and thus a higher proportion of economically important cuts. No differences have been reported for carcass length, length of the leg and depth of the chest between these sexes (Ribeiro et al., 2004, Freitas et al., 2008; Miguel et al., 2014).

Another approach feedlots use to improve the growth performance of steers and late maturing animals is the insertion of growth implants. Growth implants are routinely used in many feedlot systems; however, their use is limited by bans such as the European Economic Community’s decision to prevent hormone-treated meat products from being sold in European nations from January 1989 (FAS, 2015). Immunocastration (Bopriva®) has been successfully applied along with the use of anabolic implants (Component E-S; Elanco™ and Synovex Choice; Zoetis™) in a trial consisting of 1600 animals and 400 bulls per treatment (Amatayakul-Chantler et al., 2012). Although the anabolic potential of the immunocastrates was compromised due to the deficiency in testosterone, immunocastrates with growth implants had greater final body weights than bulls with and without growth implants, as well as immunocastrates without implants. The immunocastrates with growth implants also had heavier hot carcass weights in comparison to bulls and
immunocastrates without growth implants. Despite the negative effect on tenderness associated with growth implants, meat tenderness was improved in all immunocastrate treatments in comparison to intact bulls. Thus, Amatayakul-Chantler et al. (2012) concluded that the use of Bopriva® could improve growth performance in combination with implants and meat quality with or without implants.

As mentioned, the effect of immunocastration on growth performance and fat deposition depends on the vaccination interval used and the time between the castration effect and slaughter. This is indicated by the variation in results found in cattle; with no differences in fat thickness seen between steers, bulls and immunocastrates in Nellore and crossbred cattle in feedlot (Miguel et al., 2014), Nellore cattle on pasture (Ribeiro et al., 2004) and Bos taurus animals in feedlot (Adams et al., 1993; Adams et al., 1996; Huxsoll et al., 1998). No differences were found in fat thickness between composite bulls and immunocastrates (Cook et al., 2000), as well as between Bos taurus immunocastrates and steers (Aïssat et al., 2002) and Bos indicus immunocastrates and steers (Amatayakul-Chantler et al., 2013). It is thus important that the timing of vaccination with regards to slaughter is considered in terms of the desired fat deposition, which has a large influence on profitability of a carcass. Not only is fat deposition important for the grading of beef carcasses, it also has important implications with regards to the eating experience of red meat. Intramuscular fat influences the juiciness and thus tenderness of meat, which is one of the most important sensory qualities of red meat (Mancini & Hunt, 2005).

However, meat colour is one of the first quality attributes a consumer considers when buying meat and thus the impact of immunocastration on meat colour needs to be considered. Immunocastrated cattle have greater L*, a* and b* CIE colour values than bulls, indicating that they have lighter, redder and more yellow meat (Miguel et al., 2014). However, no differences in CIE colour values were observed by Amatayakul-Chantler et al. (2012) and Amatayakul-Chantler et al. (2013) and thus this warrants further investigation. Similarly, the effects of immunocastration on tenderness, measured by instrumental shear force, varies with those indicating it has no effect (Cook et al., 2000; Ribeiro et al., 2004; Amatayakul-Chantler et al. 2013; Miguel et al., 2014) versus Amatayakul-Chantler et al. (2012) who reported that immunocastrates had more tender meat than bulls. However, it is important to note that numerous factors such as the ante-mortem stress, the killing process, post-mortem interventions, and even the method used to cook the samples prior to evaluation for tenderness can influence the shear force values and thus these too require further investigation.

Another important factor influencing meat quality is the muscle pH post mortem. Muscle pH24 was higher in bulls than steers and immunocastrates (Miguel et al., 2014) possibly due to ante-mortem stress, as bulls are argued to be more susceptible to stress as a result of their temperament (Field, 1991). This can be supported by the differences seen in activity levels between bulls and immunocastrates (Janett et al., 2012). This increase in pH seen in bulls could explain the lower L* colour values in comparison to immunocastrates. Although pH was influenced, no effects were seen on cooking loss values between immunocastrates, bulls and steers (Miguel et al., 2014, Ribeiro et al., 2004; Amatayakul-Chantler et al., 2013).

Immunocastration has been applied in heifers and cows to prevent unwanted pregnancies and oestrus through suppressing the oestrus cycle (Bell et al., 1997). This suppression of oestrus in immunocastrated females also prevents mounting behaviours and their associated injuries, thus improving their welfare. Immunocastration in females decreases the serum progesterone levels, thus decreasing ovarian and uterine weights as well as weight gain (Adams & Adams, 1990). However, this decrease in weight gain could be improved with the use of anabolic growth implants such as Synovex-H (Adams & Adams, 1990). Therefore, immunocastration also has the potential to be an easily applied tool to improve the welfare of heifers and cows used for beef production.

Small ruminants

Immunocastration has been investigated in both sheep and goats; however, no commercial vaccine currently exists for either of these species. However, immunocastration of rams can potentially be used in circumstances where late castration is preferred such as stud breeding programs, where ram lambs are not castrated shortly after birth, but selection of breeding rams occurs after monitoring body weight and wool quality, as in the case of wool or dual-purpose breeds. Immunocastration can thus also potentially be used on cull rams to potentially improve carcass and meat quality.

Vaccines used for immunocastration have either been prepared by the researchers themselves or off-label use of commercial products has been practiced. Such an example is the use of Vaxstrate in goat bucks to control behaviour (Godfrey et al., 1996). Vaxstrate was a conjugated ovalbumin GnRH immunocastration vaccine designed for use in cattle; however, it was discontinued in 1995 due to the fact that heifers treated with it continued to cycle (Hoskinson et al., 1990). Immunocastration of bucks with Vaxtrate successfully decreased scrotal circumference and testes remained small for more than a year following the first vaccination and thus indicating a long-term effect. Odour scores associated with seasonal reproductive
behaviour and agonistic behaviour were also decreased (Godfrey et al., 1996). Recombinant ovalbumin-GnRH vaccines were used successfully in bucks, decreasing testosterone production, testicular and accessory gland development as well as decreasing seminiferous tubule diameter and basal membrane thickness (Ulker et al., 2009).

Recombinant ovalbumin-GnRH vaccines have also been used in Karakas ram lambs (17 weeks old), successfully interrupting testicular growth with no effects seen on body weight compared to intact rams (Ulker et al., 2002). Immunocastrates had greater chest widths than intact rams but not significantly different from physical castrates with no further differences seen in the various carcass measurements, including dressing percentage and carcass weights, between sexes. Furthermore, no differences were found in wholesale cut weights or in dissected muscle and bone weights between sexes, although, immunocastration and physical castration increased subcutaneous and intramuscular fat weights (Ulker et al., 2002). In conclusion to the study by Ulker et al. (2002), immunocastrates were shown to be intermediate to physical castrates and intact rams in many of the carcass traits studied.

Similar results were found when rams were immunocastrated at 10 weeks of age and entering a feedlot at 27 weeks of age for 70 days, using the same vaccination technique as Ulker et al. (2002) but including a second booster vaccination (3 injections in total) (Ulker et al., 2003). In comparison to intact males, live weights, weight gain, loin eye muscle area, backfat thickness, carcass weights, dressing percentage, offal items, and wholesale cut weights were not affected by immunocastration. Further research into the effects of immunocastration using recombinant fusion proteins on testicular development by Ulker et al. (2005) indicated that all rams immunised at 10 weeks of age produced ejaculates which contained no mature spermatozoa and the testes seminiferous tubule diameter was decreased along with thickening and hyalinization of the basal membrane.

Another method for manufacturing an immunocastration vaccine is the use of GnRH-keyhole limpet hemocyanin (KHL) conjugate emulsified with Freund’s Complete Adjuvant (FCA). This vaccination technique was used to vaccinate Western Whiteface rams at 32.6 ± 1 kg, causing decreased testosterone and testisile weights at slaughter with a resultant decrease in mounting frequencies and ejaculations in the growing period (Kiyma et al., 2000). Two adjuvants were also compared for vaccination, indicating that FCA achieved the greatest GnRH antibody titres at slaughter and greatest decrease in sexual behaviours. In contrast to Ulker et al. (2003), immunocastration decreased feed efficiency and rate of gain in comparison to intact rams but did not differ from physical castrates. However, the feeding period required for the immunocastrates to reach a slaughter weight of 58 kg was intermediate to the other two sexes, while yielding more desirable yield grades with less fat and marbling than physical castrates. These results indicated a possible difference in nutrient partitioning for growth and fat deposition between immunocastrates and physical castrates (Kiyma et al., 2000). Immunocastration increased dressing percentages in comparison to intact rams, which could be due to the smaller testes weight in comparison to intact males as well as a decrease in kidney and pelvic fat in comparison to physical castrates (Kiyma et al., 2000).

Passive immunocastration has been performed by vaccinating sheep with KHL, drawing blood samples and isolating the GnRH-KHL antibodies (Parthasarathy et al., 2002). These antibodies where then injected into the rams which formed part of the experiment. Although this was successful in decreasing testosterone, repeated vaccinations were required to elicit a more persistent decrease in testosterone and sexual behaviour. However, for ease of management and cost, it is favourable to have a minimum number of vaccinations required to elicit a desirable immune response along with a flexible vaccination schedule.

Only two studies have investigated the extra-label use of Improvac® to vaccinate ram lambs (Janett et al., 2003; Needham et al., 2016b). Administering two separate doses of 2 mL each, three weeks apart suppressed testosterone secretion and decreased testicular growth for at least three months after the booster vaccination without significant effects on growth in comparison to intact rams (Janett et al., 2003). Improvac® shows promise in the application of immunocastration in rams to commercial systems; however, the directions of use have been developed for swine and thus warrant further investigation in sheep in order to establish the optimal use. This includes establishing whether the vaccination schedule is flexible with regards to the time period between vaccinations, the timing of the second vaccination with regards to slaughter in order to maintain growth performance, while potentially improving carcass traits and meat quality.

Needham et al. (2016b) investigated three injection intervals, namely two, three or four weeks between first and second vaccination (2 mL each) on ram lambs maintained extensively on kikuyu pasture. All treatment animals were slaughtered at the same age, four weeks after the second vaccination. No differences were observed for overall ADG between treatments. However, all vaccination intervals successfully decreased scrotal circumferences within one week after the secondary vaccination. Although no differences were reported for slaughter weight, hot carcass weight, backfat thickness, and linear carcass...
measurements, differences were found in terms of the percentage contribution of the gastrointestinal tract to total carcass weight. Thus, the effect on gut fill and feed intake also warrants further investigation.

**Non-livestock species**

Immunocastration has been used in non-livestock species for various reasons, e.g. in dogs and cats as a method of fertility control (Ladd *et al*., 1994). Immunocastration has been used to study antler growth in red deer stags (Lincoln *et al*., 1982), showing a varying response to vaccination when antler growth and hardening were considered. The stag with the greatest GnRH antibody titre did not show antler hardening, thus remaining “in velvet” for longer than six months, while the other three stags shed their antler prematurely, consequently growing new antlers. All stags had a reduced testis size and interrupted normal sexual behaviour. Immunocastration has also been used to study the role of melatonin in the seasonal reproductive cycle of stags, as the responses to melatonin are dependent on the presence of GnRH (Lincoln *et al*., 1984). Immunocastration was used in both stallions and mares (Garza *et al*., 1988) to suppress reproduction, with the first successful report of its use in stallions (Schanbacher & Pratt, 1985). Immunocastration also showed promise to control aggressive behaviour in wild and captive African elephants by successfully decreasing androgen production (De Nys *et al*., 2010). Research into immunocastration of primates indicated that an increased GnRH-antibody titre and decreased testosterone production were associated with a reduced prostate weight (Giri *et al*., 1991). However, the application of immunocastration in humans has reached beyond fertility control and has been investigated to control prostate and breast cancers, these being dependent on the secretion of gonadal steroid hormones.

**Conclusion**

The management practice of immunocastration, applied in several species, has proven to be effective in controlling reproductive behaviour and aggression, with varying influences on growth performance and carcass traits. Immunocastration presents an opportunity to circumvent many of the welfare concerns associated with physical castration. When the sheep industry is compared to the cattle and pork industry, it is evident that extensive research is required to develop protocols for the potential of immunocastration to improve growth and carcass characteristics of sheep, without impacting negatively on animal welfare in production systems. It is also important to assess the potential of the technique from the perspective of the producer, abattoirs, and ultimately the consumer to motivate its use as a welfare-friendly castration technique to improve the sustainability of sheep production systems on all levels of the industry.

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**Authors’ Contributions**

TN formulated and executed this review article as part of her PhD research thesis. HL and LCH were responsible for the supervision, editing and development of the article.

**Conflicts of Interest Declaration**

There are no conflicts of interest.

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