

Local Anesthesia for Husbandry Procedures and Experimental Purposes in Farm Animals

Maria Laura Marongiu
*Department of Scienze Zootecniche,
University of Sassari,
Italy*

1. Introduction

Surgical husbandry practices carried out on farm animals in many management systems are: castration, docking, disbudding, dehorning, spaying, ear notching, ear tagging, branding-hot, branding-freeze, mulesing, teeth grinding, teeth clipping, tusk grinding, nose ringing, tail nicking, beak trimming. The management of farm animals is based on the ability to control them and many aspects of their environments.

The standards of husbandry and welfare during animal production are becoming important factors influencing consumer perceptions in many markets. Welfare attention on surgical husbandry practices for farm animals focuses on the fact that many of the procedures involve innervated tissues.

One of the approaches available for addressing welfare concerns surrounding these procedures is performing them without pain by the use of local anesthesia.

Food-animal practitioners commonly perform local-anesthetic techniques due to the dangers associated with general anaesthesia. Local anesthetic techniques usually are simple, cheap and have relatively few side effects.

The problems involved in anaesthetizing farm animals for husbandry procedures are usually less complicated than those encountered when local anesthetics have to be used in these animals for experimental purposes where it is important that anesthesia should have little or no influence on the result of the experiment.

Blood serial sampling is required for many applied reproduction and nutrition trials with farm animals. The experimental design of these researches very often includes repeated samplings of large volumes of blood for metabolites and hormones analysis. In addition, the harvested blood can be used for analysis of biochemical, toxicological or immunological parameters, for examination or culture of micro-organisms, for production of antibodies.

The use of topically applied local anesthetics is very useful in removing sensation from the vessel puncture.

There are several features of local anesthesia which render it particularly helpful in veterinary practice. Local anesthetics provide a reversible regional loss of sensation, reduce

pain, thereby facilitating surgical procedures. Many surgical procedures can be carried out satisfactorily using different local anesthetics.

Whether or not sedation is necessary as an adjunct will depend on the species, temperament and health of the farm animal, and on the magnitude of the procedure.

Many operations, including some husbandry procedures and practices for experimental purposes, are performed on standing animals. Local anesthesia, enabling protracted operations in standing animals, eliminates the dangers associated with forcible casting and restraint, and prolonged recumbency.

The techniques are not difficult to learn and do not involve the use of expensive or complicated equipment.

2. Local anesthetics

In 1860, cocaine, the oldest anesthetic, was extracted from the leaves of the *Erythroxylon coca* bush. In 1884, Sigmund Freud and Karl Koller were the first to use it as an anesthetic agent during ophthalmologic procedures.

Procaine, a synthetic alternative to cocaine, was not developed until 1904. Procaine is an ester of para-aminobenzoic acid (PABA). As procaine is metabolized, PABA, a known allergen, is released as a metabolic product. The potential for severe allergic reactions limits the use of procaine and other ester-type anesthetic agents.

Tetracaine, another ester-type anesthetic, was introduced in 1930. Tetracaine is more potent than procaine, and it causes similar allergic reactions.

In 1943, an alternative class of anesthetics was discovered when Lofgren developed lidocaine. This agent is an amide derivative of diethylaminoacetic acid, not PABA; therefore, it has the benefit of a low allergic potential.

Since then, multiple amide-type anesthetics have been introduced into clinical use. Slight chemical alterations to the compounds have imparted beneficial characteristics, including increased duration and potency, to each. These compounds offer the surgeon more choices, and anesthetics can be appropriately matched to different procedures.

The lidocaine is the most widely used general-purpose local anesthetic in veterinary use. It possesses reasonably rapid onset of action, with good spreading properties. It may cause some local irritation and swelling. It is available in a variety of concentrations or injection; with and without epinephrine; and in the form of solutions, creams, jellies, sprays etc.

Duration of action is variable (depending on uptake) but will be around one hour without epinephrine, and two hours with epinephrine.

The bupivacaine has a prolonged duration of action: up to eight hours when combined with epinephrine. It is therefore used whenever long action is required.

The mepivacaine causes very little swelling and edema in the area of injection, possibly as it lacks vasodilatory action. Onset of action is faster and reliability of block greater than with prilocaine.

The prilocaine has slower onset of action, and spreads less well compared to lidocaine. The unique ability of prilocaine to cause dose-dependent methemoglobinemia limits its clinical usefulness.

Other local anesthetics are:

The proparacaine is used to anesthetize the cornea of the eye. When dropped on the cornea it has a rapid onset of action (within 1 minute) and lasts for about 15-30 minutes. It is nonirritant, and does not affect the size of the pupil.

The amethocaine is well absorbed by surfaces and is used on mucous membranes.

The procaine, an older drug with slow onset of action and poor spreading powers has been superseded by the more modern drugs.

The cocaine is the only one to cause vasoconstriction. It is now not used as a local anesthetic because of its potential for abuse.

Newer long acting local anesthetics with less cardiotoxicity, e.g. ropivacaine or levobupivacaine, are now available for man, but are currently very expensive for veterinary use.

3. Physiology of nerve conduction

Reviewing the physiology of nerve conduction is important before any discussion of local anesthetics. Nerves transmit sensation as a result of the propagation of electrical impulses; this propagation is accomplished by alternating the ion gradient across the nerve cell wall, or axolemma.

In the normal resting state, the nerve has a negative membrane potential of -70 mV. This resting potential is determined by the concentration gradients of 2 major ions, Na^+ and K^+ , and the relative membrane permeability to these ions (also known as leak currents).

The concentration gradients are maintained by the sodium/potassium ATP pump (in an energy-dependent process) that transports sodium ions out of the cell and potassium ions into the cell. This active transport creates a concentration gradient that favors the extracellular diffusion of potassium ions.

In addition, because the nerve membrane is permeable to potassium ions and impermeable to sodium ions, 95% of the ionic leak in excitable cells is caused by K^+ ions in the form of an outward flux, accounting for the negative resting potential. The recently identified 2-pore domain potassium (K2P) channels are believed to be responsible for leak K^+ currents.

When a nerve is stimulated, depolarization of the nerve occurs, and impulse propagation progresses. Initially, sodium ions gradually enter the cell through the nerve cell membrane. The entry of sodium ions causes the transmembrane electric potential to increase from the resting potential. Once the potential reaches a threshold level of approximately -55 mV, a rapid influx of sodium ions ensues. Sodium channels in the membrane become activated, and sodium ion permeability increases; the nerve membrane is depolarized to a level of $+35$ mV or more.

Once membrane depolarization is complete, the membrane becomes impermeable to sodium ions again, and the conductance of potassium ions into the cell increases. The process restores the excess of intracellular potassium and extracellular sodium and reinstates the negative resting membrane potential.

Alterations in the nerve cell membrane potential are termed the action potential. Leak currents are present through all the phases of the action potential, including setting of the resting membrane potential and repolarization.

4. Mechanism of action of local anesthetics

Local anesthetics inhibit depolarization of the nerve membrane by interfering with both Na^+ and K^+ currents. The action potential is not propagated because the threshold level is never attained.

Although the exact mechanism by which local anesthetics retard the influx of sodium ions into the cell is unknown, two theories have been proposed.

The membrane expansion theory postulates that the local anesthetic is absorbed into the cell membrane, expanding the membrane and leading to narrowing of the sodium channels. This hypothesis has largely given way to the specific receptor theory.

This theory proposes that the local anesthetic diffuses across the cell membrane and binds to a specific receptor at the opening of the voltage-gated sodium channel. The local anesthetic affinity to the voltage-gated Na^+ channel increases markedly with the excitation rate of the neuron. This binding leads to alterations in the structure or function of the channel and inhibits sodium ion movement.

Blockade of leak K^+ currents by local anesthetics is now also believed to contribute to conduction block by reducing the ability of the channels to set the membrane potential.

On the basis of their diameter, nerve fibers are categorized into 3 types. Type A fibers are the largest and are responsible for conducting pressure and motor sensations. Type B fibers are myelinated and moderate in size. Type C fibers, which transmit pain and temperature sensations, are small and unmyelinated. As a result, anesthetics block type C fibers more easily than they do type A fibers.

All local anesthetics have a similar chemical structure, which consists of three components: an aromatic portion, an intermediate chain, and an amine group. The aromatic portion, usually composed of a benzene ring, is lipophilic, whereas the amine portion of the anesthetic is responsible for its hydrophilic properties.

The degree of lipid solubility of each anesthetic is an important property because its lipid solubility enables its diffusion through the highly lipophilic nerve membrane. The extent of an anesthetic's lipophilicity is directly related to its potency.

Local anesthetics are weak bases that require the addition of hydrochloride salt to be water soluble and therefore injectable. Salt equilibrates between an ionized form and a nonionized form in aqueous solution.

Equilibration is crucial because, although the ionized form is injectable, the nonionized base has the lipophilic properties responsible for its diffusion into the nerve cell membrane. The duration of action of an anesthetic or the period during which it remains effective is determined by its protein-binding activity, because the anesthetic receptors along the nerve cell membrane are proteins.

The intermediate chain, which connects the aromatic and amine portions, is composed of either an ester or an amide linkage. This intermediate chain can be used in classifying local anesthetics.

5. Nerve block for husbandry procedures in farm animals

Lidocaine is the most common local anaesthetic drug in worldwide veterinary use. It is used to alleviate the acute pain experienced by animals during and for 1-2 hours after a number of painful procedures, including some husbandry practices in farm animals (Mellor & Stafford, 2000; Stafford & Mellor, 2005a, b).

It is a short-acting local anaesthetic that is usually cleared from the site of injection quickly enough for its effects to last for about 60–120 minutes.

Lidocaine block of the corneal nerve prior to dehorning of calves virtually eliminates the plasma cortisol response indicative of pain for about 2 hours (Stafford and Mellor, 2005a).

There are other local anaesthetics such as bupivacaine and mepivacaine, with different characteristics, that may be useful in husbandry procedures. For instance, bupivacaine blockade of the corneal nerve of calves virtually eliminates the cortisol response to dehorning for about 4 hours (Stafford & Mellor, 2005a). However, most such local anaesthetics are not licensed for livestock in many countries.

Epidural nerve block is produced by injecting local anaesthetic into the epidural space of the spinal cord (Flecknell & Waterman-Pearson, 2000).

Effective epidural analgesia can also be achieved by injecting alpha-2 agonists such as xylazine epidurally and this is used when castrating adult cattle because it has the added advantage of being accompanied by sedation.

A lidocaine-xylazine mixture produces effective epidural analgesia in cattle castrated using a castration clamp (Burdizzo®) and extends the duration of analgesia.

6. Systemic and toxic effects of local anesthetics

Accidental intravenous injection of local anesthetics is the most common cause of adverse reaction associated with local anesthetic administration. In severe cases it can cause cardiac arrest.

When the plasma concentration of local anesthetics is excessive, sufficient cardiac sodium channels become blocked so that conduction and automaticity become adversely depressed. For example, excessive plasma concentration of lidocaine may slow conduction of cardiac impulses through the heart, manifesting as increased PR interval and widened QRS complex on the ECG.

Effects of local anesthetics on calcium and potassium ion channels and local anesthetic induced inhibition of cyclic adenosine monophosphate (cAMP) production may also contribute to cardiac toxicity.

Bupivacaine is more cardiotoxic than lidocaine. It is always important to draw back on syringe to check to be not in vein before injecting local anesthetics.

General overdose depends on blood levels, therefore is influenced by total dose and speed of uptake from the tissues.

As a very rough guide, the toxic dose of lidocaine would be 8 mg/kg and 4 mg/kg of bupivacaine.

In very small animals such as small mammals (goat kids) and birds this amount can be easily exceeded using solutions of standard concentration, so it must be diluted carefully and used with caution.

Signs of overdose are initial sedation, followed with increasing dosage by twitching, convulsions, coma and death.

Reports implicate prilocaine, benzocaine, lidocaine and procaine as causative agents to produce methemoglobinemia in some animals.

7. Methods of producing local anesthesia

Common methods of producing local anesthesia are:

- Surface (topical) anesthesia
- Intrasynovial anesthesia
- Infiltration anesthesia
- Spinal anesthesia
- Intravenous regional local anesthesia
- Regional anesthesia.

7.1 Surface (topical) anesthesia

This refers to the use of local anesthetics in solution sprays as well as in various creams and ointments; drops into the eye; sprays or brush in laryngeal area, infuses into the nostrils, urethra, or rectum.

7.2 Intrasynovial anesthesia

Used in joints, bursa, and tendon sheaths. Useful for both diagnosis of lameness, and for general pain relief. The local anesthetic chosen must cause minimal irritation, and great care in sterility is necessary as infection in these sites occurs easily.

7.3 Infiltration anesthesia

By this method the nerve endings are affected at the actual site of operation. Most minor surgery can be done this way, excluding surgery on teats in cattle or small animals digits.

Problems occur through infection (never inject local analgesic through infected tissues), irritation, distortion of the wound, swelling and some delay in post-operative healing.

A variation of infiltration anesthesia designed to minimize these effects is field anesthesia. Here, walls of anesthesia are made by infiltrating the tissues around (rather than at) the surgical site.

Advantages include absence of distortion of the anatomical features in the line of incision; muscle relaxation and no interference to healing. An example of a field anesthesia technique which is widely used in cattle is the Inverted L or 7 block for anesthesia of the abdominal fossa.

Ring blocks whereby the tissue all around a distal organ is infiltrated with local anesthetic, is another form of field anesthesia: examples of where this is used is on the teats of cattle (epinephrine must not be used here, as vasoconstriction could lead to ischemic necrosis and sloughing of tissue) or around the limb of cattle.

7.4 Spinal anesthesia

Spinal anesthesia is the injection of local anesthetic around the spinal cord. When local anesthetics such as lidocaine or bupivacaine are used, all the segmental nerves (sensory and motor) which pass through the anesthetic are paralyzed, although when opioids are used only sensory block occurs.

Spinal anesthesia is divided into two types: epidural and true spinal.

Epidural (or extradural) anesthesia refers to depositing of local anesthetics into the extradural space. The needle enters the spinal canal, but does not penetrate the meninges. The anesthetic is therefore limited to the canal outside the dura mater.

True spinal anesthesia refers to the subarachnoid access in which the needle penetrates the dura mater, and the analgesic is injected into the cerebrospinal fluid.

7.4.1 Epidural anesthesia in cattle

For caudal and epidural anesthesia the injection site used is between coccygeal C1 and C2. For a 500 kg bovine 5-10 ml 2% lidocaine will give caudal anesthesia without causing hind limb ataxia or paralysis.

Onset of paralysis of the tail should occur in 1-2 minutes. The block will last 1-2 hours. Larger doses will produce increasingly anterior effects.

By the time 100-150 ml 2% lidocaine is injected, the block will be sufficiently anterior to allow surgery of the hindlimbs, mammary tissue, flanks and abdominal wall. However, the bovine will be recumbent. Injection of local anesthetics can be carried out at the lumbosacral junction in order to produce an anterior block with less anesthetic.

There is a danger of accidental subarachnoid injection. Segmental epidural anesthesia, where the anesthetic is injected into the epidural space at the region required can be used for analgesia of any 'segment' with less overall side effects. It is more difficult to perform; penetration of the meninges is likely, but in skilled hands it is a very useful technique.

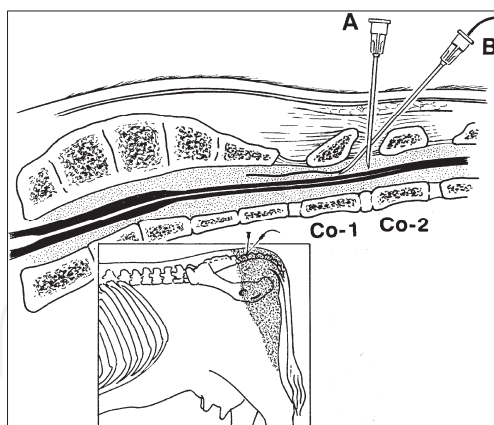


Fig. 1. For caudal and epidural anesthesia in cattle the injection site used is between coxyls Co-1 and Co-2 (Modified from Thurmon *et al*, 1996)

7.4.2 Epidural anesthesia in the sheep and goat

In both sheep and goats, anterior epidural anesthesia, induced by injection at the lumbosacral junction is easily performed and provides excellent analgesia and muscle relaxation for abdominal surgery.

Recumbency may occur but is not a problem in these small animals. As in cattle, there is a risk of subarachnoid injection.

7.4.3 Epidural anesthesia in the horse

Hind limb ataxia is a serious problem, so only caudal epidural techniques are used. These are useful for various obstetrical manipulations and surgery on the rectum, vagina and tail.

The technique is less reliable than in cattle. Site of injection is usually sacrococcygeal junction but can be between C1 and C2. For a 500 kg horse, a mixture of 50 mg of xylazine and 6 ml of 2% mepivacaine (may be repeated for another dose) may prove very effective.

7.5 Intravenous regional local anesthesia

In this technique, a limb vein is catheterized. The limb is then exsanguinated (Esmarch's bandage), and a tourniquet placed around the limb, at a pressure adequate to prevent arterial circulation (> 150 mmHg).

Local anesthetic (preferably without epinephrine) is then injected into the vein. After a period of 15 minutes the area distal to the tourniquet is anesthetized until the tourniquet is removed.

Potential problems are: a) Difficulty in finding the vein once the limb is exsanguinated (this is why it is best to have a catheter in place first). c) Cardiac arrhythmias or even arrest (this is due to an inadequate tourniquet). d) Failure to take effect. (common reasons are

inadequate tourniquet, inadequate time, and lack of exsanguination). e) Collapse when tourniquet is removed (this is because of anoxic waste products re-entering circulation); it is preferable if the animal is recumbent at this time.

7.6 Regional anesthesia

This term is used where specific nerves to the area concerned are blocked. Examples include specific nerve blocks to the limbs; paravertebral blocks; cornual block (for dehorning) and many others.

7.6.1 Paravertebral anesthesia

Paravertebral anesthesia refers to the perineural injection of local anesthesia about the spinal nerves as they emerge from the vertebral canal through the intervertebral foraminae.

The technique may theoretically be carried out in any species, and at any level of the spinal cord but in practice, its main use is to provide anesthesia of the lumbar region in ruminants.

Its advantage is that it provides analgesia and muscle relaxation of the whole area covered by the segmental nerves blocked.

Several different methods of achieving paravertebral anesthesia have been described.

All methods approaching from the dorsal surface are equally effective.

The method described whereby the needle is inserted ventral to the transverse processes of the spine has the disadvantage that the dorsal branches of the segmental nerves are not blocked, thus some skin sensitivity remains.

Paravertebral anesthesia is easy to carry out, and almost always effective, except in the very large beef breeds where it may be very difficult to locate the necessary landmarks.

7.6.2 Proximal paravertebral block (Farquharson, Hall or Cambridge Technique)

Indicated for standing laparotomy surgery such as C-section, rumenotomy, cecotomy, correction of gastrointestinal displacement, intestinal obstruction and volvulus.

The dorsal aspect of the transverse processes of the last thoracic (T-13) and first and second lumbar (L-1 and L-2) vertebrae is the site for needle placement.

The dorsal and ventral nerve roots of the last thoracic (T-13) and 1st and 2nd lumbar spinal nerves emerging from the intervertebral foramina are desensitized. 10-20 ml of 2% lidocaine is injected to each site and onset of analgesia occurs usually within 10 minutes after injection

Increased skin temperature due to vasodilation (paralysis of cutaneous vasomotor nerves) indicates effective block. Duration of analgesia is approximately 90 minutes.

7.6.3 Distal paravertebral block (Magda, Cakala, or Cornell technique)

Indication is the same as the proximal paravertebral block.

The dorsal and ventral rami of the spinal nerves T13, L1 and L2 are desensitized at the distal ends of L-1, L-2 and L-4. A 7.5-cm, 18-gauge needle is inserted ventral to the tips of the

respective transverse processes in cows where approximately 10-20 ml of a 2% lidocaine solution are injected in a fan-shaped infiltration pattern.

The needle is completely withdrawn and reinserted dorsal to the transverse process, where the cutaneous branch of the dorsal rami is injected with about 5 ml of the analgesic.

The procedure is repeated for the second and fourth lumbar transverse processes.

10-20 ml 2% lidocaine is used per site and onset and duration of analgesia are similar to the proximal technique.

7.6.4 Local nerve blocks of the head

Cornual nerve block - The cornual nerve block in cattle is indicated for dehorning and treating horn injury. Ophthalmic division of the fifth cranial nerve is desensitized by the injection of the anesthetic (3-5 ml of 2% lidocaine) on the upper third of the temporal ridge, about 2.5 cm below the base of the horn. The nerve is relatively superficial, about 0.7-1 cm deep.

Onset of analgesia occurs 10-15 minutes following injection and duration of analgesia is approximately one hour.

In adult cattle with well-developed horns, a ring block around the base of the horn may be necessary.

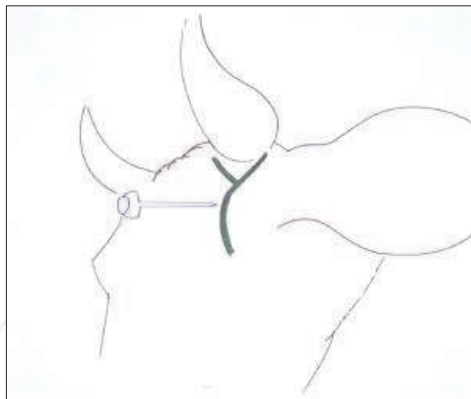


Fig. 2. Needle placement site for cornual nerve block in cattle

The cornual nerve block in goats is indicated for dehorning, not as easy as in the cow as there are two branches of the nerve (lacrymal and infratrochlear branches).

It must not be used in kids, as tend to use a total overdose of local anesthetics in these very small animals.

Auriculopalpebral block in cattle and horses - Auriculopalpebral nerve supplies motor fiber to the orbicularis oculi muscle. It runs from the base of the ear along the facial crest, past and ventral of the eye, giving off its branches on the way.



Fig. 3. Needle placement sites for cornual nerve block in the goat (Modified from Thurmon *et al*, 1996)

The needle is inserted in front of the base of the ear at the end of the zygomatic arch and is introduced until its point lies at the dorsal border of the arch. 10-15 ml of 2% lidocaine are injected.

Onset of analgesia occurs 10-15 minutes and duration of analgesia is approximately one hour. This block does not produce analgesia of the eye or the lids. In conjunction with topical analgesia (2% lidocaine), it is useful for the removal of foreign bodies from the cornea and conjunctival sac. Also used, but less frequently, in other species.

This block has no sensory effects but paralyzes the muscles of the eyelid. It is used to keep the eye open, for example, as an adjunct in ophthalmic surgery.

This is one of the most commonly used techniques to block the motor function of the upper eye lid for ophthalmic surgery, preventing eyelid closure during examination of the eyeball.

Retrobulbar nerve block in cattle - Widely used in practice to enucleate the eye. May also be used in many other species.

Peterson's eye block in cattle - Requires more skill and specific anatomic knowledge than retrobulbar nerve block, but involves less risk in damaging surrounding anatomic structure around the eye globe, and less volume requirement reducing potential for systemic toxicity and expense.

The point of injection is the notch formed by the supraorbital process cranially, the zygomatic arch ventrally, and the coronoid process of the mandible caudally.

An one inch, 14 gauge needle is inserted through a desensitized skin as far anterior and ventral as possible in the notch.

A 4-5 inch, 18 gauge straight or slightly curved needle is inserted at the point of injection mentioned above in a horizontal and slightly posterior direction until it hits the coronoid process of the mandible.

The needle must be gently manipulate anteriorly until its point passes medially around the coronoid process, then advanced to the pterygopalatine fossa rostral to the solid bony plate that is in close proximity of the orbitorotundum foramen. Following aspiration, 7–15 ml of local anesthetics are injected.

Oculomotor, trochlear, abducens, and three branches of the trigeminal nerve (ophthalmic, maxillary, and mandible) are desensitized in 10–15 minutes following injection.

7.6.5 Brachial plexus block

Brachial plexus block is suitable for inducing analgesia for the surgery on the front limb, any area below distal part of humerus.

The technique should be performed in a well-sedated or anesthetized animal.

This block can be used in small ruminants, calves, and foals.

Brachial plexus block is relatively simple and safe to perform and produces selective anesthesia and relaxation of the limb and analgesia to the forelimb.

This technique places a local anesthetic in close proximity to brachial plexus nerves that include the radial, ulnar, median, musculocutaneous and axillary nerves.

The brachial plexus nerves derived from C-6, C-7, C-8 and T-1 spinal nerves roots.

Gradual sensation and loss of motor function occurs within 10-30 minutes depending on the type of drugs used. Anesthesia lasts for approximately 2-6 hours, and total recovery requires approximately 6-9 hours.

A 20-22 gauge spinal needle is inserted medial to the shoulder joint and directed parallel to the vertebral column toward the costochondral junction.

In large size animal, if no blood is aspirated into the syringe as the needle is withdrawn, approximately 10-15 ml of 2% lidocaine or 0.5 % bupivacaine at 3 mg/kg with dilution up to 20-30 ml is slowly injected.

Local anesthetics are injected to brachial plexus which would diffuse into the area to effect.

8. Local anesthesia for husbandry procedures in farm animals

Some of the husbandry objectives are met by practices that are painful for the animals concerned. The behavioural and physiological responses, and by inference the pain, caused by particular husbandry procedures may be reduced by choosing methods that cause less pain, by carrying out the procedures in young rather than older animals and by using pain-relieving drugs, such as local anesthetics.

For each species several such practices may be carried for different reasons: to minimize the risk of injury to animals and people (e.g. dehorning); to reduce aggressive behaviour and make male animals easier to handle (e.g. castrating oxen); to prevent carcass damage such as bruising (e.g. dehorning); to enhance carcass quality (e.g. castration); to prevent damage to the environment (e.g. nose ringing in pigs); to aid in identification (e.g. ear marking or notching, branding);

Cattle can be subjected to the following painful husbandry procedures: disbudding, dehorning, castration, branding and ear notching or tagging. In addition, some heifers may be spayed, and dairy cattle may have their tails docked.

Disbudding is used to mean the prevention of horn growth before it has become advanced, and dehorning means the amputation of horns at any stage after their growth has progressed beyond the early budding stage. Disbudding of calves at a very young age is recommended.

Cautery disbudding is preferable, but extreme escape behaviour of the calf shows that application of the hot iron is painful. This behaviour, and the often less obvious response that occurs with surgical disbudding, can both be eliminated using local anaesthetic blockade of the corneal nerve or a ring block around the base of each horn bud.

Removal of horns from mature cattle without anaesthetics is very painful. Dehorning mature animals may be more painful than most other procedures.

The behavioural response to the pain caused by the act of amputating the horn can be eliminated using local anaesthetic blockade of the corneal nerve or by a ring block around the horn base.

Effective corneal nerve blockade using local anaesthetic eliminates the initial peak of the plasma cortisol response and cortisol concentrations remain at pre-treatment levels for about 2 hours. Thereafter the concentrations increase for about 6 hours before returning to pre-treatment levels (McMeekan *et al.*, 1998a).

This is interpreted to indicate that effective corneal nerve blockade eliminates pain for about 2 hours, after which some pain is experienced. This delayed pain is probably dull and not as acutely sore as the initial pain of horn amputation. To eliminate the acute cortisol response for at least 12 hours the dehorned animal needs to be given a systemic analgesic along with the local anaesthetic; a combination of an NSAID (non-steroidal anti-inflammatory drug) with a local anaesthetic is effective in this regard (McMeekan *et al.*, 1998b; Stafford *et al.*, 2003; Milligan *et al.*, 2004; Stewart *et al.*, 2009).

When local anaesthetic is given before dehorning, cautery of the wound to control haemorrhage also reduces the plasma cortisol response, and by inference the pain experienced by cattle, for at least 24 hours (Sutherland *et al.*, 2002).

Castration is a standard husbandry practice in most cattle production systems and it is painful. The cortisol response to clamp castration is less than the response to rubber-ring or surgical castration, which suggests that the clamp is less painful (Stafford *et al.*, 2002).

Local anaesthesia placed in the distal scrotum and testicles eliminates or reduces the pain-related behaviours seen at castration by these methods. It eliminates the plasma cortisol response to castration by rubber ring or band. This is because the tight ring or band stops blood and lymph perfusion of the testicles and scrotum so that the local anaesthetic remains in those tissues beyond the time required for anoxic death of the pain receptors and associated nerves.

Heifers are spayed to prevent mis-mating and to prevent mating of cull cows in extensive farming systems. The ovaries are removed either through the vagina in larger cows and

heifers following epidural anaesthesia or in smaller heifers through an incision in the flank. A flank incision is certainly painful and warrants local anaesthesia.



Fig. 4. Cautery disbudding in the calf

Tail docking young calves by rubber ring or cautery is not especially painful, and local anaesthetic either given as a tail ring block or an epidural can be used to alleviate the pain.

Ear tagging and is a common way of identifying individual animals. Ear tags or ear notches are used also to indicate the ownership of cattle. Little work has been done on reducing the pain caused by these procedures, and as it is not easy to anaesthetize the ears using local anaesthetic, systemic analgesia would be preferable.

Branding by hot iron or freeze branding are common means of identifying cattle both for ownership and for recognizing individual animals. Little work has been done on reducing the pain caused by these procedures.

As multiple injections of local anaesthetic in the area to be branded are impractical, systemic analgesia would probably reduce but not eliminate the pain experienced following branding.

The most common painful husbandry procedures used in sheep are castration, tail docking and ear tagging or notching. These procedures are generally carried out on lambs.

Local anaesthetic injected into the scrotum and testicles eliminates the plasma cortisol response and by inference the acute pain caused by rubbering castration (Dinniss *et al.*, 1997). Kent *et al.* (1998) found that lidocaine injected into the neck of the scrotum was more effective than injection into the testicles, but Dinniss *et al.* (1997) showed that intratesticular injections were just as effective but practically much easier to execute than scrotal neck injections.

Local anaesthetics have less impact on responses to surgical or clamp castration, and with these techniques a systemic analgesic such as an NSAID is required together with local anaesthesia to eliminate the pain caused by castration.

Squirting local anaesthetic into the scrotal neck and on to the spermatic cords before they are severed towards the inguinal area may reduce the pain experienced by lambs following surgical castration where the spermatic cords are drawn out and broken by traction.

Tail docking is carried out on woolly sheep. Local anaesthesia may be injected as a ring block around the tail (subcutaneously), but this is difficult and time consuming. The use of local anaesthetics greatly reduced behavioural indicators of pain (Kent *et al.*, 1998).

Ear tagging or ear notching in sheep are similar to those carried out in cattle.

Disbudding is carried out on young goats before the horn bud becomes too large. Local anaesthetic is often used when disbudding goats.

Castration and ear tagging or ear notching and the use of analgesia are conducted in goats in a manner similar to those used in cattle and sheep.

The management of pigs ranges from intensive indoor to extensive outdoor approaches. Piglets are subject to a number of painful procedures including castration, teeth clipping, tail docking and, if they are going to live outdoors, rings may be inserted into their noses.



Fig. 5. Piglet castration

Traditionally, pigs have been castrated surgically. Local anaesthetics prevented pain-related behaviours in 2-week-old piglets, but not in 7-week-old piglets (McGlone & Heilman, 1988).

Gaseous anaesthesia technology suited to pig farms is being developed and it may soon become normal to give piglets a general anaesthetic and then to castrate them, clip teeth and dock tails at one time.

Local anaesthesia and sedation could be used to reduce the pain caused by ring placement.

Horse castration is carried out in many countries under general anaesthesia, or standing under sedation and with local anaesthesia (Ohme & Prier, 1974).

Beak trimming is the most important amputation carried out on chickens and turkeys. Beak trimming is acutely painful and food intake levels decrease following it (Glatz, 1987).

Behavioural and physiological evidence suggests that pain and beak sensitivity persists for weeks or months after trimming (Craig and Swanson, 1994). A local analgesic (bupivacaine and diethyl sulfoxide) administered to the cut beak of 6-week-old chicks after trimming prevents at least some of the acute pain and the reduction in feed intake usually seen in the first 24 hours after trimming.

9. Using farm animals for experimental purposes

In many countries, laboratory animals (mainly rodents) but also farm animals (mainly horses, cattle, sheep and goats) are used in research, testing and teaching.

Experiments conducted on farm animals may cause pain which ought to be eliminated or reduced to minimum for ethical and scientific reasons.

The suffering associated with surgical procedures may be prevented with the use of local anaesthetics. Most of them, if injected or inhaled, have an effect on physiological functions of animal body which may distort the results of an experiment, but this is also true for the pain which triggers stress reaction. The experiments may be performed without anaesthesia only in exceptional cases, when it is necessary from the scientific point of view.

Reliable results of experiments on farm animals are largely dependent on the standardisation of the factors affecting physiological reactions of these animals and on the broad idea of their wellbeing. The main factors influencing the quality of experiments conducted on farm animals include: their biological status (sex, age, body mass); health condition; nutrition; maintenance conditions; animal headquarters (ventilation, temperature, humidity, lighting, noise); exposure to stressogenic stimuli; proper care; the choice of appropriate experimental techniques. Meeting these requirements allows to obtain repeatable, reliable results of experiments and to create proper living conditions.

Experiments conducted on animals often require blood sampling. It is important to safeguard the welfare of farm animals from which blood is harvested for research purposes. Contemporary animal welfare requirements are more stringent than they have been in the past, and it is appropriate that there should be guidelines to protect the welfare of animals used in blood harvesting operations.

For the research purposes, blood harvesting usually implicates the removal of a relatively large volume of blood over a short period of time, i.e. more than would usually be required or routine diagnostic tests.

It is in the interests of good science as well as the welfare of the animals used that stress on the animals is kept to a minimum. If the process of harvesting is stressful for the animal because of handling, pain or discomfort, physiological changes occur which may compromise the quality of the scientific result obtained.

10. Topical anesthetics

Although local areas of anaesthesia can be produced by subcutaneous injection of local anaesthetics, the process of injection may itself cause pain. A number of attempts have been made to obtain suitable formulations for effective topical application to the skin.

Local anaesthetic creams are generally ineffective when applied to intact animal skin because they are poorly absorbed. This has limited their use to topical anaesthesia of mucous membranes. To diffuse through nerve membranes the local anaesthetic must be in the form of the unchanged base, but formulations in which the lipid soluble free base dissolves easily achieve poor penetration of unbroken skin.

This problem has been overcome with a eutectic combination of lidocaine and prilocaine. When mixed together at room temperature crystals of these drugs form an oily liquid. No additional solvent is necessary, so droplets of an oil in water emulsion of lidocaine and prilocaine each have a concentration of 80% of active drug compared with the 20% of conventional formulations. The total concentration of local anaesthetic remains low at 5%.

Lidocaine-prilocaine cream produces effective topical dermal anaesthesia. The advantages of avoiding painful needle punctures are self-evident. Not only is animal discomfort reduced but also the procedure is easier to carry out.

11. Local anesthesia for vessel puncture

Pain associated with vessel puncture has long been accepted as an unavoidable consequence of blood collection and intravenous drug administration. The degree of pain associated with the procedure is believed to be minimal, provided that a fine gauge needle is used and that the animal is expertly restrained and the operator skilled in the technique.

In many instances, however, it is necessary to use larger gauge needles and this may produce a detectable reaction from the animal. Such responses are also noted more frequently when over-the-needle type cannulae are inserted to provide long-term vascular access.

When vessel puncture is undertaken by relatively inexperienced staff, repeated attempts may be necessary before the procedure is carried out successfully. Under these circumstances, the animal may experience greater pain or discomfort than when the technique is undertaken by a skilled operator.

There has been considerable debate as to the nature of pain in animals, since it is unclear what form animal experiences may take. It has been suggested that one constructive approach is to accept that animals are capable of sensory experiences which, given the opportunity, they avoid and which modify their biochemistry, physiology, and behaviour in a species-specific way. Many of the stimuli that produce these reactions in animals would produce the sensation described as pain in man, and hence nociceptive reactions in animals such as withdrawal of the limb, vocalizations and aggressive behaviour may be interpreted as one type of response to pain.

In human anaesthetic practice, it has been demonstrated that pain caused by the intravessel insertion of needles and cannulae can be alleviated by the topical application of local anaesthetic cream. The feasibility of using a similar technique in animals has been shown.

A commercially available local anaesthetic cream (EMLA®) can be used for application prior to vessel puncture in farm animals. EMLA cream consists of a eutectic mixture of lignocaine base (25 mg/ml) and prilocaine base (25 mg/ml), together with an emulsifier, a viscosity increasing agent and water and with the pH of the cream adjusted to pH 9.4 with sodium hydroxide.

12. Blood sampling in farm animals

The farm animals used for blood collection should be more than 6 months old and preferably fully grown adults. They must be in good body condition and in good health.

Horses should be at least 3 years old and at least 400 kg body weight. Horses with a body condition score of 3 or less must not be bled.

Sheep and goats should be at least 12 months old. Sheep should weigh at least 40 kg. Goats vary greatly in size according to breed, so a minimum weight cannot be given for the species, but they should be in good body condition.

Cattle should be at least 18 months old and should weigh at least 250 kg if 18 to 24 months of age and at least 300 kg if older.

If growing animals are used their diet must be nutritious, supplemented with iron, and fed at appropriate above-maintenance levels to allow for replacement of blood as well as steady growth.

The animals to be bled must be accustomed to handling so that they are relaxed and calm throughout the harvesting procedure. Excitement and fear can cause splenic contraction which results in altered blood parameters.

The design of the bleeding facilities and methods of restraint must be such that the procedure can be carried out efficiently with the minimum of stress to the animals.

Cattle and horses must be standing when bled.

It is preferable to bleed sheep and goats in the standing position, but where large numbers of sheep and goats are bled, it may be acceptable to strap them in lateral recumbency.

The harvesting procedure should begin as soon as the animal is restrained, and animals should be kept under close supervision during the bleeding process to guard against inhalation of ruminal contents or the development of ruminal bloat. After release they should be allowed to return to their paddock at their own pace.

The skin over the sampling site may be clipped or shaved to facilitate placement of the needle and the site may be cleaned with disinfectant such as alcohol. It is important that time be taken to locate the vessel accurately and that it be distended by gentle pressure before the needle is inserted.

A needle with as large a bore size as possible should be used to ensure efficient blood withdrawal without collapsing the vessel, without causing haematoma formation and without causing blood pressure to drop too rapidly.

Immediately after removal of blood, all animals must have unrestricted access to water.

As concerning the volume and frequency of bleeding for adult animals, not more than 15% of the estimated circulating blood volume should be removed in any 4-week period, i.e. 0.9% liveweight in cattle and sheep and 1.1% liveweight in goats and horses.

Circulating blood volume (litres) can be estimated from body weight (kg) using a conversion factor of 0.06 for cattle and sheep, 0.07 for goats and 0.075 for horses. As a guide,

1% of body weight is the weight of 16 to 17% of the circulating blood volume in sheep and cattle; about 13% in horses and about 14% in goats.

If more than 15% of blood volume is removed, consideration should be given to fluid replacement using lactated Ringer's solution with 5% dextrose.

For young animals, the volumes removed should be relatively less. For animals 6 months old, not more than 10% circulating blood volume should be removed, with incremental increases to the maximums above when fully grown (more than 12 months old for sheep and goats, 18 months old for cattle and 3 years old for horses).

If too much blood is drawn too quickly or too frequently without replacement, animals may develop hyperpnoea (deep and rapid breathing) and may go into a state of hypovolaemic shock. In the longer term the removal of too much blood causes anaemia, muscle weakness, increased susceptibility to cold, reduced exercise tolerance and ill-thrift, particularly if management and nutrition are suboptimal.

If 15% to 20% of the blood volume is removed, cardiac output and blood pressure will be reduced. Removal of 30% to 40% can induce shock.

Inexpert bleeding techniques can result in bruising around the vein, haematoma formation and/or inflammation at the site.

12.1 Bleeding technique in cattle

Blood can be collected from the jugular vein in cattle of all ages or from the tail (coccygeal) vein of older cattle.

A variety of collection devices may be used: vacutainers, bleeding tubes, syringe and needle. Restraint should ensure quick, easy and safe collection of the sample causing minimal distress.

This may involve use of a bail, race, or crush for tail bleeding. For jugular bleeding the animal may require minimal restraint (e.g. halter) or may need to be restrained in a crush with head bail and the employment of a halter or nose grips. Use of nose grips should be avoided wherever possible.

Operators should use gloves and disinfect them between animals to prevent the transmission of blood-borne diseases. Equipment such as vacutainer holders should also be cleaned between animals.

Jugular bleeding - The animal must be restrained with the head elevated and the jugular groove exposed. The jugular vein is raised by pressure at the base of the jugular groove. The needle is passed through the skin and into the vein by a firm thrust directed at an angle of 20° to the skin surface and the blood sample is withdrawn.

Tail bleeding - Restraint should prevent the animal from moving away during the procedure. The tail must be raised vertically with one hand until it is horizontal with the ground.

Approximately 150 mm from the base of the tail, the groove lying in the ventral midline of the tail is located. Midway along the body of a coccygeal vertebra, the needle must be inserted perpendicularly to the surface of the skin to a depth of a few millimetres and the

blood sample is withdrawn. Pressure must be applied to the venipuncture site after withdrawal of the needle until the bleeding stops.



Fig. 6. Tail bleeding in cattle

13. Conclusion

Most of the husbandry procedures used today were developed many years ago. They were usually selected to be carried out quickly, easily, cheaply and with inexpensive equipment, and to be generally safe for the animals and people involved.

At the time of their development, little significance was attributed to any associated animal pain. Since the mid-1990s, many advances have been made in the field of animal pain research but much remains to be done.

It is necessary a full analysis of matters that should be considered when deciding whether or not, and how, to undertake particular painful husbandry procedures.

Public attention on the welfare consequences of surgical husbandry procedures used on farm animals is increasing. This suggest that alternative approaches must be considered.

The best way to reduce the pain and distress caused by horn injuries or horn removal would be to select for polled cattle. At present the common dairy breeds, Friesian and Jersey, are horned. It may be possible for such breeds to be bred polled if an effort were made to do so and this would completely remove the necessity for disbudding or dehorning.

A possible alternative to castration in cattle could be the use of immunocastration. The vaccines used for this are now available, and it is a matter of seeing whether this practice is acceptable to producers and consumers.

Also spaying heifers could be avoided by rendering the cows infertile: this is now possible immunologically.

Tail docking of dairy cows is prohibited in some countries and in many natural and organic programmes. It is a procedure that should be phased out, because there is no scientific justification for it.

Microchips to identify cattle are becoming a feasible option to replace branding for identification and their placement will be less painful than branding. However, they are not really suited to everyday identification and it will take some time before hand-held identity chip readers become a widely used tool on cattle farms.

Another alternative for animal identification is DNA testing. The cost of DNA testing is steadily falling and it may become economically feasible in the future.

Immunocastration vaccines for lambs are likely to become available in the near future and they could be used to eliminate the pain caused by castration if their use is acceptable throughout the production and consumption chain and provided that they are cheap enough.

It is possible to breed sheep with reduced wool in the perineal area and for shorter and less woolly tails. This would reduce the necessity of docking to reduce flystrike, but shearing would still be impeded by the presence of the tail.

Identity microchips may reduce the need for ear marking and tagging in the future, but they are economically and practically difficult to use on large commercial sheep farms at present.

The Australian wool industry aims to phase out mulesing by 2010. This will be facilitated by breeding Merino sheep with fewer wrinkles in the perineal area and the use of anti-fly vaccination or long-lasting insecticides.

Immunocastration is a possible alternative to surgical castration in pigs and may become more a widely accepted practice.

A combination of using specific genetic lines of laying hens that have a low tendency to feather peck, and the use of particular environmental features, might reduce cannibalism to the degree that beak trimming is not necessary.

Although it is generally seen as preferable for the future not have to perform surgery to achieve husbandry outcomes, there are several reasons why the use of local anesthesia should not be discounted.

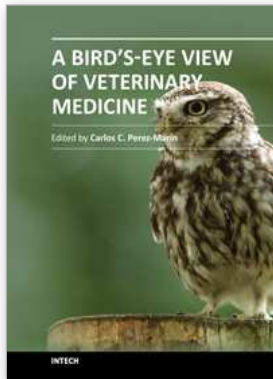
Firstly, genetic improvement takes time. Even for a trait such as polledness in cattle, where only a few genes control the polled condition, there would be a significant time lag following the identification of the gene(s) and development of a test before homozygous breeding animals were disseminated throughout the cattle population. There is also likely to be some time delay before the development and implementation of some of the non surgical approaches currently under investigation.

Removal of blood is one of the most common procedures performed on animals for experimental purposes. The choice of a technique appropriate for the purpose and the species, by a trained staff, and the use of local anesthesia are essential for ensuring that any pain, distress or discomfort is kept to a minimum.

Minimisation of such adverse effects is important for scientific as well as ethical and legal reasons, since they can cause biological changes which may affect the blood sample, and hence the validity of the research results and the number of animals used to achieve the scientific objective.

14. References

- Dinniss, A.S., Mellor, D.J., Stafford, K.J., Bruce, R.A. & Ward, R.N. (1997). Acute cortisol responses to lambs to castration using rubber ring and/or a castration clamp with or without local anaesthetic. *New Zealand Veterinary Journal*, Vol.45, pp. 114-121
- Flecknell, P. & Waterman-Pearson, A. (2000). *Pain Management in Animals*, W.B. Saunders, London, UK
- Glatz, P. (1987). Effects of beak trimming and restraint on heart rate, food intake, body weight and egg production in hens. *British Poultry Science*, Vol.28, No.4, pp. 601-611
- Hall, L.W. & Clarke, K.W. (1991). *Veterinary Anaesthesia*, Baillière Tindall, London, UK
- Kent, J.E., Molony, V. & Graham, M.J. (1998). Comparison of methods for the reduction of acute pain produced by rubber ring castration of week-old lambs. *Veterinary Journal*, Vol.155, pp. 39-51
- McGlone, J.J. & Heilman, J.M. (1988). Local and general anesthetic effects on the behaviour and performance of two and seven week old castrated and uncastrated piglets. *Journal of Animal Science*, Vol.66, pp. 3049-3058
- McMeekan, C.M., Mellor, D.J., Stafford, K.J., Bruce, R.A., Ward, R.N. & Gregory, N.G. (1998a). Effects of local anaesthesia of 4 or 8 hours duration on the acute cortisol response to scoop dehorning in calves. *Australian Veterinary Journal*, Vol.76, pp. 281-285
- McMeekan, C.M., Stafford, K.J., Mellor, D.J., Bruce, R.A., Ward, R.N. & Gregory, N.G. (1998). Effect of regional analgesia and/or a non-steroidal antiinflammatory analgesic on the acute cortisol response to dehorning in calves. *Research in Veterinary Science*, Vol.64, pp. 147-150
- Mellor, D.J. & Stafford, K.J. (2000) Acute castration and/or tailing distress and its alleviation in lambs. *New Zealand Veterinary Journal*, Vol.48, pp. 33-43
- Milligan, B.N., Duffield, T. & Lissemore, K. (2004). The utility of ketoprofen for alleviating pain following dehorning of young dairy calves. *Canadian Journal of Veterinary Research*, Vol.45, pp. 140-143
- Ohme, F.W. & Prier, J.E. (1974). *Large Animal Surgery*, Williams and Wilkins, Baltimore, Maryland
- Stafford, K.J., Mellor, D.J., Todd, S.E., Bruce, R.A. & Ward, R.N. (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. *Research in Veterinary Sciences*, Vol.73, pp. 61-70
- Stafford, K.J., Mellor, D.J., Todd, S.E., Ward, R.N. & McMeekan, C.M. (2003). Effects of different combinations of lignocaine, ketoprofen, xylazine and tolazoline on the acute cortisol response to dehorning in calves. *New Zealand Veterinary Journal*, Vol.51, pp. 219-226
- Stafford, K.J. & Mellor, D.J. (2005a). Dehorning and disbudding distress and its alleviation in calves. *Veterinary Journal*, Vol.169, pp. 337-349
- Stafford, K.J. & Mellor, D.J. (2005b). The welfare significance of the castration of cattle: a review. *New Zealand Veterinary Journal*, Vol. 53, pp. 271-278
- Stewart, M., Stookey, J.M., Stafford, K.J., Tucker, C.B., Rogers, A.R., Dowling, S.K., Verkerk, G.A., Schaefer, A.L. & Webster, J.R. (2009). Effects of local anaesthetic and a nonsteroidal anti-inflammatory drug on pain responses of dairy calves to hot-iron dehorning. *Journal of Dairy Science*, Vol.92, pp. 1512-1519
- Sutherland, M.A., Bryer, P.J., Krebs, N. & McGlone, J.J. (2008). Tail docking of pigs: acute physiological and behavioural responses. *Animal*, Vol.2, pp. 292-297
- Thurmon, J.C., Tranquilli W.J. & Benson, G.J. (1996). *Veterinary Anesthesia*, Williams & Wilkins, Baltimore, USA



A Bird's-Eye View of Veterinary Medicine

Edited by Dr. Carlos C. Perez-Marin

ISBN 978-953-51-0031-7

Hard cover, 626 pages

Publisher InTech

Published online 22, February, 2012

Published in print edition February, 2012

Veterinary medicine is advancing at a very rapid pace, particularly given the breadth of the discipline. This book examines new developments covering a wide range of issues from health and welfare in livestock, pets, and wild animals to public health supervision and biomedical research. As well as containing reviews offering fresh insight into specific issues, this book includes a selection of scientific articles which help to chart the advance of this science. The book is divided into several sections. The opening chapters cover the veterinary profession and veterinary science in general, while later chapters look at specific aspects of applied veterinary medicine in pets and in livestock. Finally, research papers are grouped by specialisms with a view to exploring progress in areas such as organ transplantation, therapeutic use of natural substances, and the use of new diagnostic techniques for disease control. This book was produced during World Veterinary Year 2011, which marked the 250th anniversary of the veterinary profession. It provides a fittingly concise and enjoyable overview of the whole science of veterinary medicine.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Maria Laura Marongiu (2012). Local Anesthesia for Husbandry Procedures and Experimental Purposes in Farm Animals, *A Bird's-Eye View of Veterinary Medicine*, Dr. Carlos C. Perez-Marin (Ed.), ISBN: 978-953-51-0031-7, InTech, Available from: <http://www.intechopen.com/books/a-bird-s-eye-view-of-veterinary-medicine/local-anesthesia-for-husbandry-procedures-and-experimental-purposes-in-farm-animals>

INTECH

open science | open minds

InTech Europe

University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China

Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821