Current concerns, considerations and consequences of velvet antler harvest in New Zealand

V Walsh, P Wilson, P Chambers, S Forsyth and N Caulkett

Abstract

Velvet antler is currently harvested in New Zealand by chemical or physical restraint and local anaesthesia Our expanding export market to North America, and the strict regulations that food products, and drugs used in food producing animals are under, by the Food and Drug Administration (FDA) of the USA, knowledge of these regulations and the consequences of finding drug residues in harvested velvet is now clearly a requirement Awareness of carcinogenic metabolites from the breakdown of the commonly used chemical restraint and local anaesthetic agents has lead a search for alternate protocols for velvet antler removal as a prerequisite for continued export of velvet product to North America The FDA is currently concerned about xylazine now that its metabolite, 2,6-xylidine has been shown to be carcinogenic in rats Similarity in the chemical structure and metabolism of lignocaine has also put this local anaesthetic "in the limelight" as far as it's possible regulatory status, and the potential for finding similar residues of the same carcinogenic metabolites as xylazine

This presentation outlines FDA regulations relating to the use of drugs in food producing animals and the tolerance of drugs with carcinogenic potential It will also review the chemical immobilising agents that are currently available, and give an overview of potentially useful chemical alternative restraint agents, with a comparison of these drugs and the potential for their use in a non-veterinarian supervised situation Being aware of the breakdown of the commonly used sedative xylazine, to the carcinogenic metabolite, 2,6-xylidine will aid in highlighting the need to reduce its use within this industry and search for alternative methods for velvet antler harvest in this country. Comparison of the amide and ester linked local anaesthetic agents is also included to emphasis the differences in the mechanism of metabolism between the different classes of agents and the potential for use of ester linked local anaesthetic to reduce the likelihood of drug and metabolite deposition into harvested velvet

Introduction

Velveting of deer is the removal of a highly innervated and vascular living tissue from a live animal Any person that removes velvet antler has a legal responsibility according to the Animal Welfare Act (1999) to provide general or local anaesthesia of sufficient power to prevent that animal feeling pain Many other countries have similar legal requirements [16] Methods for local analgesia and chemical restraint must be safe for the animal, and not product unwanted or harmful residues for the consumer. The Deer Industry's velvet antler marketing strategy is directed towards the potentially lucrative North American nutraceutical or functional food market The USA market is heavily regulated in terms of food safety and purity. Thus, chemicals used during the removal of velvet antlers are under scrutiny Veterinarians and deer farmers need to be aware of the basis of these concerns, and the industry must assure our markets that our products are safe and pure, and comply with regulations This paper reviews regulatory issues, and examines potential alternatives to animal remedies currently used during velvet antler removal, which may provide greater assurance of compliance with regulations in the marketplace

Current velvet removal techniques

Velvet is removed in New Zealand by either chemical restraint with a sedative and local anaesthesia, or physical restraint local anaesthesia The main sedatives used for chemical restraint during velvet removal include, xylazine or xylazine combinations, with opiods fentanyl or carfentanil, or with ketamine. Local anaesthesia is achieved by lignocaine hydrochloride, or less commonly by bupivacaine or mepivacaine, by ring block around the antler pedicle, or specific nerve block

Export market requirements

The export markets for velvet antler have traditionally been Asian countries, which are lowly regulated markets. Introduction of our velvet antler into North America has heightened the legal aspects of exporting a "food product" to a highly regulated market The USA has one of the most thorough pesticide and animal drug regulatory systems in the world, with rigorous approval, monitoring and enforcement processes The main agencies playing a role in regulation are the Food and Drug Administration (FDA) and the Food Safety Inspection Service (FSIS) [13] The end products of velvet antler have also recently changed from additive type products to nutraceutical products such as athletic performance enhancers Until recently, velvet antler has been loosely classified as a "food additive" and residue issues associated with it have only been a technicality, as the FDA hasn't recognised it as a food However, the use in food supplements has moved velvet antler into the food product category, and therefore under the scrutiny of these international regulatory bodies

Regulatory issues

The USA Food and Drug Administration (FDA) is the primary federal agency responsible for the regulation of food and drug products intended for use in humans and animals in the USA The Centre for Food Safety and Applied Nutrition regulates the majority of human foods The Centre for Veterinary Medicines (CVM) ensures the human food safety of animals drug products that enter the human food supply as residues in milk, meat and eggs produced from treated animals. While the CVM is responsible for performing the safety assessments for animal drug residues, the United States Department of Agriculture (USDA) Food Safety Inspection Service (FSIS) is primarily responsible for testing meat for microbiological contamination and animal drug residues [11] The FDA must approve all drugs that are used, either partly, or wholly in food-producing animals in the United States. In 1988 a food market survey by the FDA found that 67% of consumers polled considered that drug residues were a serious health hazard, 28% considered residues somewhat of a hazard and 5% were unsure. Whether this was based on a question of absolutely any residue present or a specific residue at a specific level is uncertain but whatever the question, consumer perception about a health issue whether correctly interpreted or not will have a serious impact on regulatory policy. Currently the presence of a drug residue renders that product adulterated and constitutes a violation of the Federal Food Drug and Cosmetic Act [9]

When prescribing or using a drug in a food producing animal, a veterinarian that agent must bear two major responsibilities, firstly for the welfare of that animal and secondly, to guarantee public safety Most agents used in food producing animals have the potential to become deposited into tissue that is then turned into food products Issues associated with this deposition relate to the capability of residues of a drug, or its metabolite, having some pharmacological activity in the consumer. As far as some groups of drugs are concerned, e g the penicillin antibiotics, the concerns include the ability of the agent to cause potentially fatal allergic reactions in humans as well as to exacerbate or accelerate the production of antibiotic resistance With other agents e g diethylstilbestrol (DES) its use in food producing animals has become illegal due to the link between in utero levels of DES and a rare vaginal cancer in women [16]

Drug residues

A drug residue is defined as any compound present in the edible tissue of a treated animal that results from the use of the drug This includes the drug itself, its metabolites and any substance formed in or on food as a result of use of that drug Originally animal drugs were approved based on a "no residue" or "zero tolerance" policy While the "no residue" concept was acceptable to consumers and politicians, the zero tolerance actually represents the sensitivity of the analytical methods used to monitor drug residues, not a true zero value As analytical methods improved, the zero tolerance level continually needed to be lowered To correct this problem the agency adopted a negligible tolerance policy, which was generally assigned as 0 1 ppm (0 1 mg/kg) in all edible tissues However, this was not related to the potential hazard of the compound. The CVM then adopted its current risk assessment procedure, whereby the tolerance is based on toxicological, residue and metabolism data.

The current model is: the risk from animal residue equals the hazard of the drug product times the exposure to the drug residues [11]

Generally, violative residues and reactions in humans from the use of anaesthetic agents in food producing animals has not been a major concern, this is because of the pharmacokinetic properties and clinical usage of these agents Anaesthetic agents are generally only used in the short term as single bolus injections and therefore accumulation in tissue unlikely [14] Most agents have a short half-life, and animals are usually not slaughtered in the immediate period after administration Xylazine however, has been quantitatively identified as a residue in velvet antler At 25 to 72 minutes after administration of xylazine, between 70 – 220 nanograms of xylazine has been identified per gram of velvet antler harvested. This is equivalent to 0 07 – 0 22 mg/kg [7] To the authors knowledge no work has been done to identify any metabolites of xylazine in this product However based on the negligible tolerance policy the level assigned is 0 1 mg/kg in edible tissues. Therefore the levels of xylazine in most cases may be in breach of this Because of the unique situation of velvet antler removal, the food product is in fact generated in the period where blood and tissue levels of these agents are likely to be rising to a maximum point Because of the striking vascularity of velvet antler, drug deposition is probable unless a tourniquet is applied at a point prior to sedation, which of course is an impossible situation Even if a tourniquet were to be applied prior to sedation this may not guarantee xylazine leakage past the tourniquet [10] Fenton (2000) stated "The only difference between consuming velvet antler and meat or milk from animals treated with drugs is the total volume of product consumed, and thus the amount of drug exposure would be considerably less This still doesn't make it right "[8]

Regulation of carcinogens

The Delaney Clause of the Food Drug and Cosmetics Act prohibits the use of carcinogenic compounds in food producing animals According to FDA regulations a sponsored compound considered to be a suspect carcinogen must undergo testing to assess whether it is carcinogenic and if so the quantitative aspects of its carcinogenic response [3] There is, however, an exception to this clause the DES proviso, which states that no residue of that carcinogenic compound will be found in food producing animals under conditions of use reasonably certain to be followed in practice The carcinogenic potential of a compound is evaluated based on structure, results of genetic toxicity tests, and toxicological studies [11] 2.6-xyladine is a by-product of metabolism of both lignocaine and xylazine and was found to be carcinogenic in male and female rats. This determination was based on observed significant increases in the incidence of adenomas and carcinomas of the nasal cavity and an increases incidence of subcutaneous fibromas and fibrosarcomas in male and female rats [3]

Extra-label drug use

Extralabel use of a drug occurs when it is used in a species in which it is either/or not approved, at a dose not stated or for a purpose it is not intended for The passage of the Animal Medicinal Drug Use Clarification Act (AMDUCA) in the USA in 1996 has allowed veterinarians to use drugs including human preparation in an extralabel manner, provided there is data to support the human food safety of such use A similar process, relying on the approved NZ Veterinary Association code of practice, will occur in NZ when the ACVM Act is fully implemented in 2001

Withholding period

The withdrawal or withholding period of a drug is a term that represents the interval that is required after dosing for tissue concentrations of a drug or its metabolites to deplete to less than a specified concentration that is deemed safe for human consumption The withdrawal time is closely related to the half-life of the agent and in general, with knowledge of the half-life of a drug, a withdrawal time can be estimated or extrapolated The half life is the time taken for the concentration of the drug to be depleted by 50%. In ten half lives there will only be 0 1% of the original concentration of that drug left Using a time period of ten half lives is a rule of thumb for estimation of a potential withdrawal period. However, this estimation does not take into account active accumulation of a drug in a specific tissue, concentrations of active and inactive metabolites that may still be present in those tissues or the difference between toxic and non-toxic agents It is recommended that a safety margin also be

included into this withdrawal time estimation depending on the carcinogenic and toxigenic potential of the agent in question.

For drugs that are used extra-label, for instance human drugs used in animals, there is an United States based information/electronic database system available to veterinarians to aid in avoiding residue deposition in animal tissue The Food Animal Residue Avoidance Database (FARAD) is a computerised database system developed by the FDA to allow veterinarians access to pharmacokinetic data and international labels of various drugs that are used in food producing animals in an off license manor FARAD was developed to provide information to prevent residue deposition in food products. Residue and pharmacokinetic information is also used by FARAD personnel to help develop withdrawal recommendations for some extra-label drug uses to aid in the mitigation of other problem residues [6]

Sedative agents of use or potential use for chemical restraint

Sedatives are often used for restraint of stags for velvet antler removal. The properties of an ideal chemical restraint agent are easy to administer (can be given by the intramuscular or subcutaneous route), rapid onset of action and latent period (time from drug administration to peak effect), effective predictable sedation, rapid, uneventful recovery, predictable duration of effect, reversible, small volume; non irritant to tissues, inexpensive, no residue deposition; and above all, safe in the target species and for the person administering the agent There are no agents available currently that cover all of these aspects A few groups of sedatives provide most of the properties but may have other properties that are of a disadvantage

The sedative agents that are currently used by veterinarians, or are of potential use for the purpose of velvet antler removal include, the alpha two-agonist agent xylazine, the opioid agents, the phenothiazine agent acetylpromazine, butyrophenone compounds, the phencyclidine / dissociative anaesthetic agents and the benzodiazepines.

Alpha-2 agonist agents

Xylazine is the most commonly used sedative agent for velvet removal in New Zealand It provides, predictable potent sedation with short onset of action, good analgesia and has a reversal agent Its main disadvantages include cardiopulmonary depression, lack of registration for use in food producing animals in the United States and the recent identification of a carcinogenic by product of metabolism. Several unsuccessful attempts have been made by manufacturers of xylazine to obtain approval for the use of xylazine in food producing animals in the USA.[3] Its registration in food producing animals in the USA is unlikely to occur, due to FDA regulations regarding carcinogenic drugs. While xylazine itself has not been tested for carcinogenicity, it has been tested for mutagenicity and has been found to be weakly mutagenic [17] 2,6-xylidine was found to be carcinogenic in rats, based on observed significant increases in the incidence of cancer [3] In 1996 the World Health Organisation FAO/WHO expert committee considered the issue of residues of xylazine and other veterinary drugs and were unable to establish an acceptable daily intake (ADI) for xylazine because a metabolite 2,6-xylidine, is genotoxic and carcinogenic The committee was unable to establish a maximum residue limit (MRL) because there is a lack of information about the metabolism and residue depletion in edible tissue

Detomidine and medetomidine are the other alpha-2 adrenergic agents available in New Zealand They are registered for use in horses, cattle, dogs and cats These drugs may offer an advantage over xylazine but no information about metabolism of these agents is available. There is still the likelihood that they will become deposited in velvet tissue prior to removal Similarities in structure to xylazine, suggest similar metabolism and metabolic products may also be produced.

Opioids

The opioids are a group of drugs that provide some advantages over many of the other sedative agents available including profound and predictable sedation and analgesic properties The legal requirements that need to be followed when administering opioid agents to animals preclude use in a general farming situation, since they are classified as Prescription Animal Remedy Class III agents because of their potential to produce addiction, and danger to people. As such they can only be administered by a veterinary surgeon The opioids produce profound respiratory depression in humans, leading to respiratory arrest through inhibiting the actions of carbon dioxide on the respiratory centre in the medulla The newer, more potent opioids etorphine and carfentanil are more potent than morphine (carfentanil has a potency 10,000 times that of morphine). They are also easily absorbed through skin and mucous membranes and therefore care must be taken when handling these agents Because of the regulatory status and the potential for adverse drug reactions in humans consuming velvet containing even small amounts of these agents, residues are unlikely to be well tolerated and they are not a feasible alternative for routine use in velvet harvesting Currently, combinations of fentanyl/azaperone/xylazine and carfentanil/xylazine are registered in NZ for use in deer

Phenothiazines

Drugs within the phenothiazine class are classified as antipsychotic or neuroleptic agents All drugs in this class have a wide range of central and peripheral effects, but the degree of activity varies from one compound to another. They have the ability to produce dose dependant sedation but do not have intrinsic analgesic properties and thus are very seldom used alone They are more commonly combined with an opioid or alpha-2 adrenergic agent in a combination known as neuroleptanalgesia. Mild vasodilation is produced by blockade of alpha-adrenergic receptors In most patients this is well tolerated but can cause severe hypotension in sick or debilitated animals. They are potent antiemetic agents and have a spasmolytic activity on the gastrointestinal tract of ruminants that can lead to relaxation of the cardiac sphincter and consequential regurgitation and potentially aspiration of ruminal contents

Acetylpromazine is the most commonly available phenothiazine and is used extensively in most species, with a similar dose rate across species Plasma pharmacokinetic data for horses and metabolism in food animals has been reported although few residue data is available in the published literature [5] In general, the onset of action after intramuscular injection is at least fifteen to twenty minutes and the duration of action is up to twelve hours Acetylpromazine is not registered for use in food producing animals in the United States. Because of prolonged duration of action, FARAD have recommended a meat withdrawal period of at least seven days. Acepromazine is approved in Canada and Australia for meat producing animals

Butyrophenones

In humans the butyrophenones are a group of agents that produce sedation similar to the phenothiazine but can be associated with some unpleasant side effects including hallucinations, agitation and aggression Like the phenothiazines, butyrophenones have minimal effects on the cardiovascular system with mild hypotension produced by alpha-adrenergic blockade They are also potent antiemetic agents The most commonly used butyrophenone is azaperone, which is marketed as Stresnil® and registered for the use in pigs If combined with an opioid agent, azaperone gives more predictable sedative effects and the dose can be reduced by one tenth The combination of xylkazine/azaperone/fentanyl ("Fentazin") is licenced for use in deer in NZ Droperidol is another butyrophenone that is marketed in combination with the opioid fentanyl in Innovar Vet®. Haloperidol has been used in fallow deer, producing excellent calming effects but its use in larger species of antelope has been unpredictable All of these three agents have very prolonged durations of action up to eight hours and with no reversal agent, deer would remain sedated and potentially vulnerable for this period. The major metabolite of azaperone, azaperol also has pharmacological activity and has been found to be weakly mutagenic, and thus potentially carcinogenic

Phencyclidines

The phencyclidine anaesthetic agents are amongst the most widely used agents in most species in veterinary medicine, and include ketamine and tiletamine They produce predictable dose-dependant sedation through to general anaesthesia and can be administered by most routes, including absorption through mucous membranes Unlike many general anaesthetic and sedatives, these agents tend to have a positive effect on the cardiovascular system, causing an overall increase in blood pressure The main disadvantages are, large and muscle rigidity produced if used alone. Muscular rigidity is overcome by combination with a benzodiazepine such as diazepam or zolazepam. Unfortunately the absorption of diazepam from subcutaneous or intramuscular sites is unpredictable due to the chemical properties of the vehicle it is dissolved in The other alternative to the benzodiazepines is xylazine, which also produces dose dependant sedation as well as muscle relaxation. The mixture "Xylaket" is licenced for use in deer in NZ

The main advantage of tiletamine over ketamine is that it comes in a premixed powder formulation (Zoletil®) in combination with zolazepam (a benzodiazepine). It can be made up to a concentrated solution by adding a smaller amount of distilled water, reducing the overall volume of drug to be administered The zolazepam is also water-soluble and so the absorption from subcutaneous or intramuscular sites is more predictable than diazepam This drug is however, still expensive and this may preclude its use in deer Ketamine is approved for use in non-food animals. There is no published residue data for edible tissues However, there is extensive pharmacokinetic data for serum and plasma in calves, sheep and swine [5]

Benzodiazepines

The benzodiazepines are a group of agents used extensively in human anaesthesia because of their extremely predictable, profound sleep producing effects In most animal species the sedative effects are not as potent and there is marked individual variability They are used most commonly in combination with other agents for muscle relaxation or for drug synergism. The most commonly used benzodiazepine is diazepam, which is available in tablet and injectable formulations, there is species variability in the absorption of diazepam orally and the effects seen in deer species have ranged from sedation through to manic behaviours The injectable form of diazepam has an unpredictable absorption pattern when given by the subcutaneous or intramuscular routes and so it is recommended it be given by the intravascular route only.

Table 1: Comparison of the pharmacological effects of various sedative agents.

Drug	Class	Sedation	Analgesia	Reversible	Duration	Side effects	Mutagenic / Carcinogenic
Xylazine	Alpha-2	✔✔✔	✔✔✔	✔	Short	Cardiopulmonary	✔ (Muta) ✔✔✔ (Car)
Fentanyl	Opioid	✔✔✔	✔✔✔	✔	Short	Cardiopulmonary	✗
Etorphine	Opioid	✔✔✔	✔✔✔	✔	Short	Cardiopulmonary	✗
Carfentanil	Opioid	✔✔✔	✔✔✔	✔	Short	Cardiopulmonary	✗
Acepromazine	Phenothiazine	✔✔	✗	✗	Long	Mild hypotension	✗
Azaperone	Butyrophenone	+/-	✗	✗	Long	Mild hypotension	✔ (Mut)
Dropendol	Butyrophenone	+/-	✗	✗	Long	Mild hypotension	✗
Halopendol	Butyrophenone	+/-	✗	✗	Long	Mild hypotension	✗
Ketamine	Phencyclidine	✔✔✔	✔✔	+/-	Moderate	Muscular rigidity	✗
Tiletamine	Phencyclidine	✔✔✔	✔✔	+/-	Moderate	Muscular rigidity	✗
Diazepam	Benzodiazepine	+/-	✗	✔	Moderate	None	✗

Local anaesthetic agents

Local anaesthetics include a large group of agents that reversibly block propagation of the action potential along the nerve axon resulting in dose dependant analgesia and muscle paralysis They are unique in that they are active at the site of application and indeed, systemic absorption not only decreases the relative potency of the agents, it also results in a shorter duration of action and increases the potential for systemic toxicity Most local anaesthetic agents need to be injected to produce their effects, as the skin provides a barrier to absorption. There are several agents that are available in a topical form but these require a relatively long period of time under an occlusive bandage for adequate absorption and usually only anaesthetise the tissue a few millimetres below the site of absorption.

Pharmacokinetics

The pharmacokinetic properties determine the potency, onset of action and duration of action

Lipid solubility determines potency

High lipid solubility would be expected to promote drug entry into membranes by increasing the rate of diffusion By promoting interaction with hydrophobic components of the receptors, high lipid solubility will increase potency and duration of effect [4,18]

Ionisation pKa determines onset of action

Drugs exist in ionised and non-ionised forms The non-ionised form is primarily responsible for the action of that drug as it is more lipid soluble and thus able to penetrate neural tissue better The pKa of a chemical compound may be defined as the pH at which its ionised and unionised forms are in equal concentrations. The onset of anaesthesia is directly related to the rate of diffusion through the nerve sheath, which in turn is correlated with the amount of drug present in the base form.[4,18] The percentage of a specific local anaesthetic drug, which is present in the base form when injected into a tissue whose pH is 7 4, is inversely proportional to the pKa of that agent. For example lignocaine has a pKa of 7 74, and is 65% ionised and 35% non-ionised at a tissue pH, while Chloroprocaine with a pKa of 8 7is 95% ionised and 5% non-ionised, at a tissue pH of 7 4 [4] Ionisation is relevant to the solubility and activity of local anaesthetic agents Because the ionised forms are more water soluble than free bases the drugs are dispensed as their hydrochloride salts in acidic solutions which helps to stabilise the esters which are readily hydrolysed in alkaline conditions The pH of plain solution of ester may be as low as 2 8 compared to 4 4 - 6 4 for the amide agents. Decreasing the ionisation of an agent by alkalinisation will effectively raise the initial concentration gradient of diftusible drug, thereby increasing the rate of drug transfer and decreasing the latent period of the nerve block.[18]

Protein binding determines duration of action

The protein binding characteristics of local anaesthetic agents primarily influences the duration of action Agents such as procaine are poorly bound to proteins and possess a short duration of action Protein accounts for about 10% of the nerve membrane Therefore agents which penetrate the axolemma and attach more firmly to the membrane protein will tend to possess a prolonged duration of anaesthetic activity [4]

Amide linked local anaesthetic agents

Local anaesthetics can be categorised into two groups, based on their molecular structure. Groups are metabolised in-vivo by different mechanisms and have different potentials for allergic reactions

The amide-linked local anaesthetics are the group of agents most commonly used in both human and veterinary medicine and include lignocaine, bupivacaine and mepivacaine They are metabolised by the liver and in most species the major metabolite of this group is the carcinogenic by-product 2,6-xylidine [2;12] (Note that this is the same metabolite as xylazine) Lignocaine is the agent most widely used and its metabolism has been extensively studied in humans with 2,6-xylidine being the major urinary metabolite [15] The current withholding period for lignocaine use in cattle in the United

Kingdom is 28 days,[19] but the Veterinary Medicines Doctorate has recently advised against its use in food producing animals.[1] In the USA, FARAD has advised a withholding period of 24 hours in all food-producing animals, while in Canada the meat-withholding period in cattle is seven days [19]

Ester linked local anaesthetic agents

This group includes tetracaine, procaine and chloroprocaine The ester-linked agents are currently almost never used in veterinary medicine In contrast to the amide linked anaesthetic agents these agents are primarily metabolised by plasma, red blood cell and liver esterases to para-aminobenzoic acid (PABA) Half-lives of these agents in plasma of normal human adults are usually only minutes for chloroprocaine and procaine and a little longer for tetracaine [18] The advantage of these agents for velvet antler removal would be that they are metabolised very rapidly and thus if a toxic reaction occurs it should be relatively short lived They may even be metabolised by plasma and red cell esterases after the point of velvet removal

The hydrolysis products of procaine and chloroprocaine have been measured in humans and are thought to be inactive The end products are thought not to be carcinogenic although the aminobenzoic acids may contribute to rare allergic reactions seen in humans.[18] These agents tend to have a slow onset of action relative to the amide-linked agents Manipulation of the pKa of the drug however, may speed the onset of action and onset of latent period in the immediate pre-operative stage and work is currently being carried out to assess this method.

Conclusions

Both of the currently used techniques for removal of velvet antler meet the legal requirements for the humane removal of velvet antler. However, they do not meet the requirements of our major potential marketplace for use of these agents in food producing animals in respect of deposition of residues of both sedative and local anaesthetic agents, and deposition of potentially carcinogenic compounds.

The high regulatory requirements of our newer export markets prompt consideration of different methods than the currenly used xylazine, lignocaine or physical restraint and lignocaine methods The carcinogenic potential of both of these agents and the nature of removal of a highly vascular food product during an anaesthetic period is a concern However, all agents are likely to become deposited in velvet antler to some degree and therefore residues are a certainty, particularly when a parenterally administered agent is used.

The use of local anaesthetic agents with the aid of physical restraint in a hydraulic crush is currently used on many farms However, an alternative local anaesthetic to lignocaine must be found because of the carcinogenic by-products of metabolism of this agent. There is a suggestion that application of a tourniquet prior to injection of anaesthetic may mean that local anaesthetic may not be deposited into velvet antler. However, in humans, even after applying a tourniquet with application pressures up to 300mmHg above systolic blood pressure leakage of local anaesthetic agent has still been noted [10] This aspect needs investigation for velvet antler removal

A further option is the use of the other readily available amide linked local anaesthetic agents mepivacaine and bupivacaine However, because metabolism of these agents is similar to lignocaine, they are likely to be broken down to very similar carcinogenic by-products. The other major group of local anaesthetics, the ester-linked agents, are broken down rapidly by plasma esterase activity and therefore the likely hood of finding residues is less They do not appear to be metabolised to 2,6 xylidine offering a major advantage over the amide linked local anaesthetic agents. The slow onset of action of these agents and their allergic potential are currently theoretical limitations for use, but manipulation of the physiochemical properties of this group may increase their potential use in the near future

References

1 Anderson R Use of Lidocaine in Foods Animals The Veterinary Record 2000,82

2 Boyes R N , A Review of the Metabolism of Amide Local Anaesthetics Agents British Journal of Anaesthesia 1975, 47 225

3 Chamberlain P L , Brynes S D , The regulatory status of xylazine for use in food-producing animals in the United States J Vet Pharmacol Ther 1998, 21 322-329

4 Covino B G , Pharmacology of Local Anaesthetic Agents In Nunn UB, ed General Anaesthesia Butterworths, 1989 1036-1048

5 Craigmill, A L , Rangel-Lugo, M , Damian, P , Riviere, J Extralabel use of Tranquilizers and General Anaesthetics J Am Vet Med Assoc 1997 211 302-304

6 Damian, P , Craigmill, A , Riviere, J , Breaking New Ground J Am Vet Med Assoc 1997 210 633-634

7 Dickson, S J , Stone, H M , Queree, E A , Xylazine (Rompun) Levels in Deer Antler Velvet New Zealand Journal of Agricultural Research 1983, 26 93-94

8 Fenton R Drug residues in velvet 2000

9 Guest, G B , Paige, J C , The magnitude of the tissue residue problem with regard to consumer needs J Am Vet Med Assoc 1991, 198 805-808

10 Hoffmann, A C , van Gressel, E , Ryser, J E , Forster, A , Quantitative evaluation of tourniquet leak during i v regional anaesthesia of the upper and lower limbs in human volunteers British Journal of Anaesthesia 1995, 75 269-273

11 Miller M A , Quality control and safety of animal products Canadian Journal of Animal Science 1999, 79 533-538

12 Nelson, S D Garland, W A Breck, G D Trager, W F , Quantification of lidocaine and several metabolites utilizing chemical-ionization mass spectrometry and stable isotope labeling Journal of Pharmaceutical Sciences 1977, 66 1180-1189

13 Norcross, M A , Brown, J L , Food safety and inspection service initiatives for tissue residue reduction in meat and poultry J Am Vet Med Assoc 1991 198 819-824

14 Papich M G , Drug residue considerations for anesthetic and adjunctive drugs in food producing animals Veterinary Clinics of North America 1996, 12 693-706

15 Parker, R J , Colins, J M , Strong J M , Identification of 2,6-Xylidine as a Major Lidocaine Metabolite in Human Liver Slices Drug Metabolism and Disposition 1996, 24 1167-1173

16 Payne, M A Baynes, R E Sundoll, S E Craigmill, A C Webb, A I Riviere, J E , Drugs prohibited from extralabel use in food animals 2000

17 Preiss A M , Investigation with the Salmonella/microsome test, psychopharmaceuticals used in meat production Mutagenic Research 1982, 104 333-337

18 Tucker, G T , Mather, L E , Properties, absorption and disposition of local anesthetic agents In Cousins, ed Neural Blockade in clinical anesthesia and management of pain J B Lippincott Company, Philadelphia 47 - 120

19 Wright RG Medicines and withdrawal times for farmed deer Proceedings of the International Wildlife Ranching Symposium, Toronto Nov 1999 2001 In Press

20 Wilson P R , Mellor D J , Stafford K J , Haigh J C Velvet antler removal International welfare, ethical and legal issues In Antler Science and Product Technology Proceedings of the Antler Science and Product Technology Society, Banff, Canada, April 2000 Eds Sim J and Sunwoo J In Press