

Introduction

Sheep (Ovis aries) have been domesticated for over 10,000 years and figure prominently in the story of civilisation and human survival, as evidenced by numerous biblical references, religious practices and symbols and cultural rituals that involve this species, not to mention their importance to agriculture over several millennia. Sheep are widespread across the world, having adapted to many different climatic conditions and econiches (Ryder, 1983). During the past 40 years, sheep have also been the subject of considerable research from the viewpoint of physiological function and animal production, are now regarded as one of the most studied non-human, non-rodent species.

Many different breeds of sheep have evolved and intensive breeding for particular purposes has resulted in many strains. The size of different breeds of sheep varies, with typical body weights of ewes ranging from 30 kg for Welsh Mountain sheep, 45 kg for Merinos, 55 kg for Clun Forest breed, 65 kg for Cheviots, 75 kg for Dorset Horns and 90 kg for Lincolns (Hecker, 1983). It is worthwhile understanding some of the background of the various breeds of sheep and the specialisations which they may possess. For example, the ancestors of the Merino, famous throughout Australia as a producer of fine wool, derive from Spain and North Africa and are highly adapted to a hot arid environment. As such, they have kidneys capable of concentrating urine and therefore conserving water to a much greater degree than strains that evolved in colder climates of Northern Europe (McFarlane, 1968). Another well-known feature of the Merino is the copious folds of skin around its neck.

Sheep have been used as experimental subjects in such diverse fields of study as endocrinology and reproductive physiology, cardiovascular physiology, fluid and electrolyte homeostasis, immunology, neurophysiology and neuroanatomy, thermoregulation, haematology, nutrition and gastroingestive behaviour, intestinal physiology. In regard to the last, ruminants with being specialised fourchambered stomachs, sheep have been studied extensively in their own right, with much knowledge accruing in regard to ruminant nutrition and animal production. The study of the sheep fetus has also been extensive, and much of our knowledge of fetal physiology derives from these studies. Another aspect of the sheep is the availability of post-mortem sheep tissues from abattoirs. This has enabled the collection (in vast numbers) of organs such as the pituitary from the sheep, enabling the discovery and characterisation of a number of new hormones eg. the various hypothalamic releasing hormones which control the secretion of a range of pituitary hormones.

Advantages of using sheep for experimentation

There are several reasons why sheep make excellent experimental subjects for physiological studies. Their body weight and size approximates to that of a human, and they adapt rapidly and extremely well to a laboratory situation. In general they have a placid nature positively handlers and relate to and experimenters, possibly a result of their adaptation to domestication which has occurred over many generations. After an introduction of a sheep to the laboratory pen or metabolism crate, and one to two weeks of regular daily handling, patting and food rewards, together with the company of other sheep, there results a confident, unstressed, healthy animal, with a strong bond often developing between sheep and experimenters. This enables experiments investigating physiological function in conscious, unstressed animals to be performed successfully. The size of the sheep enables ease of introduction of catheters or cannulas (using either local or general anaesthesia) into various blood vessels, bladder, rumen, salivary duct or cerebral ventricles for the purpose of obtaining samples of blood or other body fluids for chemical analysis. Their size also enables sufficient blood to be withdrawn for chemical and hormonal analysis with minimal effects on cardiovascular function, which is not always possible in small rodents. Sheep recover robustly from anaesthesia and experimental surgery and provided appropriate care is taken are not usually troubled by post-operative or post-experimentation infection (Hecker, 1974). Great care is necessary in preserving asepsis when the brain or fetus are involved in order to avoid life-threatening infections.

Compared to rodents, sheep are long-lived and in this country are relatively inexpensive for their size. With the provision of adequate food and water, well-maintained and well-cleaned facilities, and sympathetic handlers and experimenters, sheep can thrive in a laboratory and thoughtful, well executed experiments can yield a wealth of physiological information relevant to human and animal physiology and medicine.

Nutrition

Apart from being adequate in amount and composition to meet requirements for protein and energy, feed for sheep must also satisfy a set of interrelated behavioural and physiological Ruminants have cyclical activities factors. which are geared to demands for water and food and rest periods necessary for the processes of rumination and digestion. Sheep apply an impressive array of behavioural adaptations to their herbivorous mode of life. For example, their exploration of feed and their learned and innate preferences and selectivities are being investigated only now but should be borne in mind in the laboratory environment.

Sheep possess a complex digestive system to deal with their mixed diet of digestible plant components and relatively indigestible cellulose. Feed takes 25-35 hours to pass through the gut and is exposed to microbial fermentation in the rumen during this time, which provides microorganisms and the products of cellulose breakdown for digestion. Sieving processes are involved, with large particles being regurgitated for re-mastication by the process of rumination (or 'chewing the cud') and smaller particles of less than one to two mm passing into the stomach. Sheep ruminate for six to seven hours per day and this readily observable activity is a guide to health and well-being. Side benefits of ruminal fermentation include accessory food factors such as water-soluble vitamins and protein elaborated by microbes from simple nitrogen compounds.

Feeding standards for sheep have been published in the UK, the USA and Australia. The Australian treatise (Corbett, 1990) has a comprehensive experimental and theoretical framework. Requirements of digestible organic matter, energy, crude protein and bypass protein, fibres, minerals and vitamins given in these standards are average values. Under practical conditions, however, individual responses of sheep must be accounted for and animals have to be fed according to effect.

Two simple and well accredited rations for laboratory sheep are a 50% mixture of lucerne and wheaten chaff, and a pelleted ration composed of lucerne chaff (50%), wheat grain (10%), bran (18%), pollard (20%), and crude salt (2%) (to control urinary calculi by increasing fluid intake). Although lucerne chaff is valuable for its high concentration of calcium as well as protein, its quality can vary considerably and is a factor to consider if performance is unexpectedly low. In most other rations, calcium demands have to be met by the addition of ground limestone. Nutritional deficiencies have not been observed with the two rations described above. A guide to the weekly feed requirements for maintenance of different classes of sheep is given in Table 1.

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Class of sheep	Hay	Oats	Wheat
	Kg	kg	kg
Weaners	4.0	2.6	2.2
Adult dry sheep	5.4	3.5	3.0
Ewes in late pregnance	y 7.4	4.9	4.1
Lactating ewes	14.0	11.0	9.5

The maintenance requirement for a 35 kg wether is 5.2 megajoules per day. This is provided by a weekly intake of 2.8 kg of maize, 3.0 kg of either wheat, barley or sorghum or 3.6 kg of oats, which indicates the relative energy of these grains. At a practical level, the addition to these grains of 15% by weight of lupins gives an impressive lift in feed value because of its high content of non-degradable or bypass protein. Factors such as adequate trough space to prevent competition and storage conditions to protect feed against contamination are important components of good feeding practice. Work on the effect of olfaction on feed selection in the USA has shown that only 5% of feed contaminated by faecal odours of coyote, fox or cougar was eaten compared with 95% of similar pellets without contamination.

Investigators working with housed sheep must also be aware of the critical need these animals will have for physical fibre (rumen 'scratch' factor). The demand for rumination / salivation behaviour is important and failure to provide physical fibre (ie roughage > 5cm) results in behavioural dysfunctions (wool biting, stereotypic bar chewing etc), some of which can result in pathology (wool 'balls') and serious stress to sheep that become the target of biting.

Some merino sheep can survive for up to 10 days without water and can lose one-third of their liveweight in the process. Requirements range from 2.4 litres per day for growing sheep of 30 kg body weight to 12 litres per day for 60 kg ewes in early lactation. Water requirements for sheep in the laboratory are met by *ad libitum* access to clean water. The same imperatives apply whether troughs or self-drinkers are used. Water must be clean, free flowing and algae-free throughout the animal house.

Faecal contamination and faecal odours may inhibit drinking and predispose to urinary calculi. Water supply throughout a sheep house must be able to cope with peak demand on a hot day.

Housing

Being highly social animals, sheep must always be transported and housed in groups or at least in pairs so that they are always able to see another sheep. Without this 'social contact' sheep will quickly become agitated and distressed. If absolutely necessary, sheep may be kept in front of a full length mirror for short periods to prevent the stress of isolation becoming a problem, but it must be emphasized that this is only a short term (hours maximum) solution.

Sheep breeds vary widely in their capacity to adapt to heat and cold. Like all mammals, sheep are forced to increase heat production to maintain temperature core body as environmental temperature drops. The critical temperature at which this occurs varies from 0°C for adult sheep in full fleece to 20-25°C for newly shorn animals to 30-36°C for new born lambs. Shorn adult merinos can bring peak metabolism into play to withstand ambient temperatures of -60°C. At the other extreme, merinos are farmed for wool production under dry conditions with peak daily ambient temperatures of 49°C. Coping mechanisms are stretched to withstand these extremes and give no guidance to the conditions required in sheep houses.

Sheep can be housed simply but require full protection against wind, rain, extremes of temperature and humidity. Timber, even though rough-cut bush timber can be used for construction and is probably superior to metal. However, it may not be acceptable for housing off-farm where presentation is important. Fittings must not provide injurious hazards when sheep are being moved. The commonly available metal floors are unsuitable for long term housing of sheep because sheep become footsore on them and show hesitancy in moving and lying down. Traditional slatted hardwood floors as used in shearing sheds are satisfactory and superior to concrete. Wooden floors may be considered more difficult to maintain in some situations where cleanliness of surfaces is paramount, so slatted hard plastic floors may be a suitable alternative. The plastic does have the disadvantage of becoming slippery when wet, however drop - through slats for urine and faeces can eliminate the need for regular washing down and provided the sheep ar not scouring, the floor remains dry. One consideration is to have slats run opposite to, and not parallel with, the direction in which sheep move in lanes. If sheep gain the impression of height, they baulk.

Space allowance should be determined from basic principles. Areas of 1.2 square metres per sheep are suggested as a guide. However, literal application of space allowances is an undesirable scenario for developing considerate animal care because it diverts attention from the animals themselves. Unless there are specific experimental requirements, sheep ought to be able to move around in an individual pen and be able to lie in an orientation they choose. Groups of more than 12 in a pen may lead to erratic results in experiments. Groups of eight may be acceptable. Experiments in which groups of 50-60 sheep are held in single large pens are probably invalid because of the behavioural tensions which occur.

In spite of possessing a fleece, sheep have limits to their heat and cold tolerance. Roof extractor fans are important for the summer heat. Sheep should not be housed in contact with corrugated iron walls that face the summer sun. Even sheep which are fully fleeced will die if exposed to cold wet winds. Thought must be given to sleet and gales blowing up though slatted floors.

Management

Virtually all sheep in Australia have fleeces rather than hair and must be shorn each year. If housed sheep are dipped immediately after shearing to control lice, mortalities of 10-15% from septicaemia can be expected and the surviving sheep will have hepatic, splenic and pulmonary abscesses.

Overgrown hoofs occur when sheep are housed. Trimming should cause no bleeding and conform to the anatomy of the foot so that sheep can stand and walk normally. Feet bleed when the living tissue involved in the hoof growth tissue is cut and healing of this damaged tissue will distort the foot. Competent trimming and inspection of feet cannot take place unless the sheep is held in a cradle.

Diseases

Sheep may be affected by many different diseases of an infectious, parasitic, nutritional or neoplastic nature. It is beyond the scope of this article to examine these. Disease is not a major concern in well-housed sheep which have been vaccinated against the common clostridial diseases and are free of footrot and lice at the outset. However, sheep in sheep houses can become fly-blown. Infection with *Strongyloides papillosus* can occur where animals are held on concrete which is hosed down and there is a reservoir of this nematode parasite in the cohabiting population of rats. Posthitis can be a problem and requires early intervention where it occurs. Urolithiasis occurs relatively frequently in some animal houses and should prompt a complete review and overhaul of the watering system to ensure that sheep have access to abundant clean, cool water.

Dietetic disorders can occur in housed sheep and are most commonly associated with high grain diets, which entail the risk of lactic acidosis, particularly if sheep unused to grain are allowed to engorge. Some animals appear to be incapable of adapting to pelleted rations with high grain content. Copper toxicity has been reported in housed sheep and can be controlled by access to soil to provide molybdenum. For further information see Brightling (1988) and Blood and Radostits (1989).

Zoonoses

A few diseases can be transmitted to people who are in contact with sheep tissue or in the environment of sheep. These include Q-fever (a respiratory disease which may have lifethreatening consequences) and scabby mouth, a mild skin eruption. The dog tape worm *Echinococcus granulosus* can infect various organs of the sheep. The cysts in sheep are harmless to humans, but sheep offal should not be fed to dogs. For further information on zoonoses of sheep and other species see Stevenson and Hughes (1988).

Anaesthesia and some general experimental Techniques

Sheep respond well to and recover quickly from general anaesthesia. General anaesthesia can be induced by an injection of sodium thiopentone (19 mg/kg body weight), into the jugular vein and after intubation of the trachea, anaesthesia can be maintained at the correct depth for several hours by inhalation of a gas mixture of isoflurane with air/oxygen. Prior to general anaesthesia, animals should be deprived of water and food for 24 hours to limit regurgitation. The most convenient blood vessel for making an intravenous injection or for obtaining blood samples is the jugular vein. It is important to make sure that this region of the neck has been well shorn. Skin should be cleaned and sterilised before needles are inserted into the vein. An iodine - alcohol solution is satisfactory for this purpose and as a surgical skin preparation. Indwelling venous cannulas can also be conveniently inserted into the jugular vein through a needle. Local anaesthesia around the point of insertion should be utilised when larger gauge needles are introduced into a vein. Indwelling cannulas should be removed as soon as possible after use to minimise thrombus formation. Urine may be continually collected from a retention catheter inserted into the bladder. By using a speculum to expose the urethral opening, bladder catheterisation is a simple procedure in ewes, but catheters should not be left in the bladder for more than 2-3 days as discomfort will ensue. Saliva from the parotid duct may be continually sampled from a polvethelene cannula inserted into the parotid duct and brought to the surface through the cheek (Abraham et al., 1976).

A number of surgical procedures have been adopted successfully in sheep to prepare them for experiments some weeks later. These preparations allow access to blood vessels or specific organs in the conscious, undisturbed animal during experiments. For example, the carotid artery (s) can be enclosed in loops of skin in the neck (Denton, 1957), allowing access to arterial blood for sampling or for easy measurement of arterial blood pressure. The copious skin folds of the neck of the Merino make this breed or its cross-breeds ideally suited for this purpose. This also applies to autotransplantation of glands such as the adrenal gland (Goding and Wright, 1964) or ovary

(Goding et al., 1967) into the neck for ease of This technique has been utilised access. successfully for studying adrenal and reproductive physiology of sheep. Stereotaxic frames (Radford, 1967) and atlases (Richard, 1967; Welento et al., 1969; McKenzie and Smith, 1973) have also been described for use in neurophysiological studies in sheep, and cerebrospinal fluid samples can be obtained or intracerebroventricular infusions made through guide tubes permanently implanted into the lateral or third cerebral ventricles or cisterna magna (Mouw et al., 1974). Rumen fistulae can be prepared to gain access to the rumen (Hecker, 1974).

Euthanasia can be performed by intravenous injection of sodium pentobarbitone (at least 100 mg/kg).

Problems & complications associated with general anaesthesia in sheep:

Difficult intubation Regurgitation & aspiration of rumen content Bloat/rumen distension Hypoxaemia Hypoventilation Hypotension/poor perfusion Hypothermia

The following protocols are aimed at minimising complications and problems.

1. <u>Pre-anaesthetic preparation</u>

- In sheep food should be withheld for 24 hours and water for 8-12 hours depending on environmental temperatures and animals' state of health.
- Ideally body weight should be obtained as sheep can vary in weight fro 35-65 kg depending on breed, sex, and health status. A physical examination including assessment of temperature, cardiac function, pulmonary ventilation, and hydration status including assessment mucous membrane colour and pulse quality should be performed. If

indicated blood samples collected from the jugular vein should be analysed to assist in determining health status or to provide preoperative base values.

2. Pre-anaesthetic sedation & induction

Sedation: Diazepam 0.2-0.3 mg/kg IV Induction: a. Diazepam 0.2-0.3 mg/kg IV followed by Ketamine 2-5 mg/kg IV b. Alfaxan CD 1-2 mg/kg IV

- Note: Following sedation a 16 gauge 3 ¹/₄ or 5 ¹/₄ inch percutaneous jugular catheter should be placed and secured to allow for administration of induction agents. supplemental parenteral anaesthetics and analgesics, and IV fluids. When using Ketamine for induction diazepam may have to be readministered following before catheterisation and ketamine administration. Sheep should be placed in recumbency and the head sternal supported in elevated position before administering induction agents.
- Other peripheral veins can be catheterised but in our experience the jugular vein is most suitable for catheter placement and for catheter maintenance.
- A variety of premedication/induction protocol for general anaesthesia in sheep have been described, but we use the above protocol most commonly and find it provides good and safe condition for intubation without undue cardiopulmonary depression of the patient.

3. <u>Endotracheal intubation</u>

In the dorsally or sternally recumbent sheep a tie (soft rope or similar) is placed around each the upper and lower jaw to facilitate opening the mouth and holding the head and neck elevated and extended. Using a laryngoscope the larynx is visualised and approximately 2 ml of lignocaine 20% is dripped on to the larynx using a syringe with 5 ¹/₄ inch catheter without stylet (alternatively local anesthetic spray can be used). The endotracheal tube (ET) is inserted, secured and the cuff inflated. At this point the head can be lowered and the sheep positioned for surgery.

Note: ET sizes for adult sheep may vary from 7.5 – 9.0 mm internal diameter. ETs need to have a cuff and cuffs need to be checked for leaks beforehand. A guide or stylet can be used to facilitate intubation. A guide can either be placed in the lumen of the ET for reinforcement or introduced into the trachea and the ET subsequently fed over it. In the latter procedure the guide has to be at least twice the length of the ET. Once the sheep is positioned for surgery the cuff should pressure be checked bv compressing the rebreathing bag and only leave enough air/pressure in the cuff to provide an airtight seal.

4. <u>Maintenance of anaesthesia</u>

Any of the commonly used inhalation anaesthetics in veterinary practice including isoflurane, and sevoflurane are suitable for maintenance of anaesthesia. The anaesthetic agent of choice is isoflurane. Halothane is rapidly losing acceptance as an anaesthetic agent due to its occupational health and safety risks to operating personnel. It also limited availability has and causes arrhythmias. The use of sevoflurane is limited by its high cost of purchase compared to either halothane or isoflurane. In humans, the rate of induction and recovery from sevoflurane anaesthesia exceeds that with Parenteral protocols including isoflurane alfaxolone, propofol, and propofol with ketamine administered in increments when needed or given as a constant infusion have been used. We found parenteral maintenance not to have significant advantages if used instead of inhalation maintenance (I.e. parenteral maintenance may be of advantage in special circumstances) and unless the duration of anaesthesia is short (< 30 min) can be much more costly compared to

halothane and isoflurane maintenance. It was our experience that when using parenteral maintenance anaesthesia of patient monitoring had to be intense as individual patients have different anaesthetic dose requirements which if not adjusted has the potential for disaster. Also parenteral anaesthesia does not eliminate the necessity of endotracheal intubation as sheep regurgitate regardless of the maintenance agent. In halation anaesthesia has the advantage of the sheep breathing an oxygen rich gas mixture, which minimises the common intraoperative complication of hypoxaemia in this species. In our experience we found recovery in sheep from both inhalation and parenteral anaesthesia to be comparable i.e. good. Parenteral anaesthesia can however carry the risk of prolonged recovery.

MAC in Sheep:

Halothane	0.7 - 0.9
Isoflurane	1.0 - 1.5
Sevoflurane	3.3

- Typical vaporiser setting for maintenance with halothane and isoflurane is 1-2.5%. In general there is a tendency when anaesthetising sheep to run the vaporiser setting too high.
- For administration of inhalation anaesthesia standard human rebreathing circle type breathing systems with a soda lime container of 1-2 litres and a 2-3 litre rebreathing bag can be used.

5. <u>Supportive care and monitoring</u>

Supportive care includes:

Proper positioning and padding: padding of 3-5 cm thick foam mattress or similar, neck area should be elevated by placing rolled up towel under neck/shoulder to allow for drainage of saliva & rumen content

- *Temperature maintenance*: despite the fleece sheep become hypothermic during anaesthesia and measures similar to those commonly used in small animal anaesthesia should be used i.e. heat lamps, insulating blankets, heat pads. Hypothermia decreases metabolism resulting in decreased anaesthetic requirement
- *Fluid therapy*: Polyionic fluids containing an alkalinizing agent are ideal (Hartmann,s, Plasmalyte 148) and are generally administered at a rate of 10 ml/kg/hr.

Monitoring:

Depth of anaesthesia:

- Physical signs: Possibly the best method for determining depth of anaesthesia is a combination of corneal reflex (opening the eve with two fingers and lightly touching the cornea), plus the shape of the pupil (constricted pupils are more rectangular while dilated pupils are oval shaped; the shape of the pupil (where clearly visible) is a good indicator of anaesthetic depth. The most definitive indicator of anaesthetic depth spontaneous movement or chewing is motions upon painful stimulation, which indicate inadequate anaesthetic depth. Active regurgitation evident as peristaltic movements of oesophagus in the neck at times accompanied by swallowing movements is another reliable sign of light level of anaesthesia. Passive regurgitation characterised by a continuous flow of rumen fluid may indicate deep anaesthesia.
- During light anaesthesia the eyes may be positioned dorso-laterally and muscle tone in the eye lid and palpebral reflex present. A centrally positioned eye with dilated pupil, relaxed eyelid and absent palpebral reflex may indicate deep anaesthesia.
- Note: Determination of anaesthetic depth in sheep using physical signs is relatively difficult and if uncertain about the level of anaesthesia should be reduced until signs of light anaesthesia are evident at which

time the anaesthetic level can be increased if required.

Cardiopulmonary parameters: During inhalation anaesthesia both blood pressure and pulmonary ventilation will decrease with increasing anaesthetic depth. Mean arterial blood pressure should be above 60 mmHg in order to maintain adequate tissue perfusion. As a general rule if blood pressure in a major artery is not palpable the mean blood pressure may be less than 60. Pulmonary ventilation, the product of tidal volume and rate respiratory is decreased during inhalation anaesthesia, mostly due to reduced tidal volume. Normal respiratory rate and tidal volume in awake sheep is around 40 breaths/min and 7 - 10 ml/kg respectively and remain similar during inhalation anaesthesia. Shallow breathing as gauged by movements of rebreathing bag can indicate deep anaesthesia. Ideally capnography and or arterial blood gas analysis should be performed to assess ventilation objectively, particularly during prolonged anaesthesia.

Blood pressure/tissue perfusion

Blood pressure: The auricular artery on the abaural surface of the ear, the saphenous artery, and the digital artery can be palpated for pulse pressure. Manual palpation of pressure is only a subjective blood assessment of blood pressure and more advanced techniques should be used for anaesthetics of longer duration. The Doppler technique with the probe placed on the ventral surface of the distal carpus and the cuff proximal to that around the carpus provides a means of assessment of systolic pressure. As a rough guideline if systolic pressure is less than 80 mmHg hypotension is severe enough to result in inadequate tissue perfusion. Systolic, diastolic and mean arterial blood pressure can be measured from a percutaneous catheter placed in the auricular artery and connected to an electronic pressure gauge which will. Catheterisation of the auricular artery is

easily achieved and can even be done in awake sheep. Mean pressure in anaesthetised sheep should be above 60 mmHg.

Tissue perfusion: Mucous membrane colour is used as an indicator of tissue perfusion, although the method is subjective. Pulse oximetry as a non invasive method of detecting blood flow and haemoglobin saturation with oxygen. The clothe pin like probe can be placed on the tongue and the pulse oximeter displays a continuous pulse signal and haemoglobin saturation value (S_pO_2) . As a general rule efforts should be made to maintain S_pO_2 above 90%. Due to profuse salivation in anaesthetised sheep the tongue may be slippery and the pulse oximeter probe may not stay in place. Placing one or two layers of a gauze swab between the tongue and probe may overcome this problem.

Capnography

Capnography is a non-invasive method of measuring CO_2 in the air exhaled by the patient and provides a continuous is measure of pulmonary ventilation. The end expiratory CO₂ is an estimate of arterial PCO₂. In anaesthetised sheep the difference between arterial and alveolar CO₂ can be up to 10 mmHg and therefore capnography should ideally be used in conjunction with arterial blood gas analysis i.e. at least one arterial blood sample should be analysed in order to determine the accuracy of capnography in a particular patient. In awake sheep normal arterial PCO₂ is around 35 mmHg and during anaesthesia inhalation can increase considerably. PCO₂ values above 80 mmHg will lead to cerebral oedema and patients remain unconscious long after termination of anaesthesia. Effort should be made to maintain PCO₂ below 55 mmHg, and when using capnography efforts should be made to avoid any increase from values obtained in the early phase of anaesthesia.

6. Recovery from anaesthesia

- As soon as possible sheep should be repositioned in sternal recumbency or near sternal recumbency to allow for rumen gas to escape. The ET with the cuff inflated should be left in place until the sheep are swallowing spontaneously and can be seen to make chewing motions. The ET is then removed with the cuff inflated. Ensure that patient can breathe i.e. move air. Keep patient positioned in sternal recumbency and support if necessary.
- Efforts should be directed towards warming the animal using insulting materials like blankets or external heat sources such as heat lamps for example.

Pain management and analgesia

- Pain and painful stimulation causes physical discomfort and stress which result in altered homeostasis including cardiopulmonary, endocrine, metabolic and thermoregulatory abnormalities and behavioural changes.
- Assessment of pain in sheep and ruminants generally is difficult. Painful animals may exhibit physical signs including tachypnea, tachycardia, elevated blood pressure and body temperature. Interpretation of behaviour as an indicator of pain is difficult and sheep being herd animals and animals of prey generally do not display overt signs of pain. Behaviour indicating pain may include abnormal gait or stance, vacant stare, teeth grinding, exaggerated avoidance behaviour. guarding of repetitive motor activity, painful limb. reluctance stand. to inappetence, and separation from flock and lagging behind.
- Ideally an analgesia protocol should be designed considering the type and duration of painful procedure and aiming at critical evaluation of the effectiveness of the protocol.

- Ideally analgesia should be administered preemptively
- Analgesic drugs used in sheep include opioids, α₂ -adrenergic agonists, NSAIDs, and local anaesthetics.
- The effectiveness of opioids for analgesia in sheep is controversial. Most information on opioid analgesia in sheep is based on experimental data and should be applied to clinical conditions with care. In general opioids in sheep are less useful for treatment of pain compared to dogs and cats. μ-agonists such as morphine and fentanyl are poorly effective in sheep when administered epidurally or spinally.
- α_2 adrenergic agonists produce analgesia and sedation in sheep both when administered systemically and epidurally. Sedation generally outlasts analgesia. α_2 adrenergic agonists can cause pulmonary/cardiopulmonary changes and hypoxaemia. In sheep analgesia is more likely to be achieved with α_2 - adrenergic agonists than with opioids.
- NSAIDs provide analgesia through their antiinflammatory effects peripherally but in sheep seem to also have centrally mediated analgesic properties. Compared to opioids and α_2 - adrenergic agonists NSAIDs are longer acting. NSAIDs may be useful for treatment of orthopaedic and visceral pain. NSAIDs can induce gastro intestinal ulcerations. Due to the longer duration of action and absence of sedative and behaviour modifying effects NSAIDs are particularly suitable for preemptive administration.

The following may be useful when planning analgesic therapy:

Parenteral analgesia

 Fentanyl at a dose of 0.01 mg/kg IV provided analgesia of rapid onset but short duration (< 1hr) for painful mechanical and thermal stimuli. Fentanyl may precipitate abnormal behaviour. Transdermal fentanyl i.e. fentanyl patches (100 µg/60 kg) might be an option for prolonged, possibly up to 3 days, analgesia.

- Buprenorphine at a dose of 0.005-0.01 mg/kg IV, IM, SC can produce primarily cutaneous analgesia (thermal stimulus) for 3-4 hr duration. It can be readministered at 4-6 hr intervals by IM, SC route. Onset of action is slow and abnormal behaviour such as agitation is possible.
- Butorphanol doses range from 0.1-0.5 mg/kg IV, SC which decrease the responsiveness to thermal stimuli at lower doses and at higher doses produces sedation and decreased responsiveness to pinch stimuli at various sites and to nasopharyngeal stimulation. It is questionable wether butorphanol provides visceral analgesia. Butorphanol can cause ataxia and altered behaviour including agitation and vocalisation.
- **Xylazine** at a dose of 0.05 mg/kg IV can produce good analgesia for mechanical and thermal painful stimuli for approximately 45-60 min. Xylazine causes sedation and recumbency.
- **Detomidine**, 0.05 mg/kg IM has been used in sheep and found to be of longer analgesic duration than xylazine and less associated with hypoxaemia.
- Medetomidine 0.005 mg/kg produces analgesia and sedation for approximately 1 hr. Side effects are likely similar to other α₂
 - adrenergic agonisits.
- Flunixin (2.2 mg/kg IV) is an effective analgesic in sheep although less potent than α₂ adrenergic agonisits. Duration of action is approximately 3-6 hrs and readministration of 2.3 mg/kg Q 12 hrs or 1.1 mg/kg Q 8 hrs has been recommended.
- **Phenybutasone** IV or PO at a dose range of 2-6 mg/kg can be used in sheep and presumably similar to cattle readministered once daily.
- **Carprofen** has been studied in sheep and 4.0 mg/kg administered IV found to provide a therapeutic plasma levels for at least 72 hrs.
- **Pethidine** (2.0 mg/kg i.m.) is an effective opioid analgesic in sheep likely to

experience strong post-operative pain that will offer 24 hours relief. Pethidine causes sedation and recumbency.

• Meloxicam (0.5 mg/kg s.c., i.v. every 24 hours for maxmum of 3 days) is an effective NSAID based analgesic that works by relieving inflammation and the associated pain.

Local and regional anaesthesia/analgesia

- Using local anaesthetics as an adjunct to general anaesthesia can greatly improve the quality of anaesthesia and early postoperative recovery without altering mentation.
- Lignocaine and bupivacaine are the most commonly used local anaesthetics in veterinary practice. Lignocaine has a rapid onset of action (minutes) and short duration of action (60-90 min) while bupivacaine has a slow onset of action (15-20 min) and longer duration of action (4-6 hrs). The toxic dose of lignocaine if given IV is 3-7 mg/kg and 1-2 mg/kg for bupivacaine. Volumes for local infiltration should not exceed the toxic volume in order to minimise possible complications of Local toxicity. and regional anaesthesia/analgesia in combination with sedation can be useful for procedures including castration and dehorning and disbudding.
- Local anaesthetics can be used for analgesia in the forelimb, (brachial plexus nerve block), intraarticular analgesia, analgesia of lateral thoracotomy (intercostal nerve block), analgesia for midline sternotomy (intrapleural block 1.5 mg/kg bupivacaine)

Epidural and spinal anaesthesia/analgesia

Epidural analgesia is achieved by depositing a local anaesthetic or analgesic into the spinal canal outside the meninges. Spinal or intrathecal analgesia refers to the injection of analgesic drugs into the subarachnoid space, which is smaller than the epidural space. In sheep the technique of spinal anaesthesia is most commonly practiced. The spinal needle is placed into the spinal canal at the lumbosacral junction, which results in penetration of the meninges, evident by CSF appearing in the needle. Injection of local anaesthetics will result in loss of sensory and motor function in the pelvic area including the hind limbs.

In sheep analgesics suitable for spinal analgesia include the local anaesthetics and α_2 - adrenergic agonisits. **Xylazine** (20) mg/ml) at a dose of 0.05 mg/kg (± 2 mg in 1ml saline) or **detomidine** at a dose of 0.01 mg/kg (± 0.5 mg in 1 ml saline) can be injected into the CSF (subarachnoid space). Intrathecal xylazine has a fast onset of action (±20 min), longer duration of analgesia (± 100 min) and produced higher noticeptive threshold compared to detomidine (onset \pm 50 min, duration \pm 60 min). Sedation can occur with spinally administered α_2 - adrenergic agonisits. Doses i.e. volume of lignocaine (2%) and **bupivacaine** (0.5%) for subarachnoid lumbosacral anaesthesia is 0.1-0.15 ml/kg.

Table 2. Useful physiological data on sheep. Some data have been adapted with modifications from Hecker (1983) and Scoggins *et al.*, (1984)

Heart rate	50-80 beats/min
Maximum heart rate	260-280 beats/min
Mean arterial pressure	70 mm Hg
Cardiac output	115-133 ml/kg/min
Stroke volume	74 ml/beat
Extracellular fluid volume	246 ml/kg
Plasma volume	37 ml/kg
Blood volume	49 ml/kg
Interstitial fluid volume	190 ml/kg
Packed cell volume	20-45%
Haemoglobin	9-15 g/100 ml
Whole blood clotting time	7-13 min
Rectal temperature	38-39.5°C
Respiratory rate	15-40 breaths/min
Maximum respiratory rate	350 breaths / min
Respiratory dead space	100 ml
Tidal volume	4-9 ml/kg
Glomerular filtration rate	1.2 ml/kg
Effective renal plasma flow	7.6 ml/kg

Table 3. Concentrations of some ions and molecules in plasma, cerebrospinal fluid (CSF), parotid saliva and bile of sheep. Some measurements were adapted with modifications from Hecker (1983) and Scoggins *et al.*, (1984).

	Plasma	CSF	Parotid saliva	Bile
Sodium mM	142-148	150	30-185	150
Potassium mM	4.0-5.0	2.8	4-100	4.2
Calcium mM	2.4	1.2	0.2	-
Magnesium mM	0.9	0.9	-	-
Chloride mM	105-110	131	9-16	118
Bicarbonate mM	27	24	103-125	-
Phosphate mM	1.5	0.4	25-64	-
Osmolality mosm/L	290	290	284	-
Glucose mM	3	3		
рН	7.42	7.45	8	_

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