APPROACHES TO POSTOPERATIVE PAIN MANAGEMENT FOR EQUINES

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David Bardell highlights various methodologies that can be applied to the treatment of pain, from systemic to local and regional analgesia

TWO difficulties of post-operative pain management can be recognition that the animal is in pain and quantifying the degree of discomfort.

Assessment of pain in nonverbal species is difficult, very subjective and usually relies on a consideration of physiological parameters, behaviour assessment and a degree of anthropomorphising.

Different assessors have been shown to attribute very different levels of pain to certain conditions, including routine surgery such as castration.

Horses, as a species, tend not to be overtly demonstrative of pain unless it is moderate to severe, and they show considerable variation in the way they respond.

Consideration for post-operative pain management should begin prior to any surgery. A thorough, planned approach to patient analgesia will facilitate the surgical process by maximising the quality of the anaesthetic period and make postoperative pain management easier. Pre-emptive administration of analgesic drugs will optimise the achieved effect. Knowledge of the drug action site and the receptor types involved will allow the use of drugs with synergistic or additive actions, thus maximising analgesia – the multi-modal analgesia approach.

Consideration of the stages in the nociceptive pathway will facilitate a balanced approach to analgesia. These stages are as follows:

• transduction is the conversion of mechanical, chemical or thermal insult into an electrical signal occurring at the receptors;

• transmission is the conduction of that signal to the central nervous system;

• modulation is how the incoming signal is processed and relayed within the central nervous system; and

• perception involves higher centres. An animal must be conscious to perceive nociceptive input as pain.

Post-operative pain may have both visceral and somatic components, depending on the procedure.

Visceral pain tends to be poorly localised, ill-defined and, in humans, is described as dull or aching in nature. This is often due to diffuse inflammation, ischaemia or tension on the mesentery.

Somatic pain is localised, originates from musculoskeletal tissue and skin, and is often described by human patients, as sharp or throbbing. This is the type of pain created by surgical incision.

Acute pain is the normal physiological response to a noxious stimulus. It is designed to be protective, being linked to the withdrawal reflex, thus preventing further damage and triggering behavioural changes intended to maximise healing.

However, the nervous system is dynamic and adaptable, and severe or prolonged noxious input can lead to upregulation and alteration of the way information from the peripheral tissues is interpreted, leading to the development of a chronic pain state. This is deleterious to the animal and serves no useful purpose. Acute pain is generally easier to recognise, assess and manage; chronic pain can be very difficult and frustrating to treat.

A good analgesic plan will consist of systemically administered drugs, in combination with local or regional analgesic techniques if possible. The drugs chosen should, ideally, be licensed for analgesia in horses by the prescribed route. However, licensed drugs administered by an unlicensed route or unlicensed drugs may, on occasion, be indicated and appropriate.

Systemic analgesia

Any degree of surgical intervention will create an inflammatory response. Tissue trauma causes the release of many intracellular compounds and arachidonic acid from the cell membranes. This upregulates cyclo-oxygenase enzyme expression and initiates a complex cascade of events that

ultimately results in the production of prostaglandins and the classic signs of inflammation–heat, pain and swelling.

Prostaglandins act to sensitise and recruit peripheral nociceptors in the locality of the damaged tissue by lowering the threshold stimulus required to initiate an impulse in the Aä and C neurones associated with pain signalling, a process known as peripheral sensitisation. This increases the amount of nociceptive input to the central nervous system, resulting in an over-exaggerated response to a normally painful stimulus (hyperalgesia).

NSAIDs act by inhibiting the cyclo-oxygenase enzymes, interrupting the arachidonic acid cascade and limiting this upregulation of input to the central nervous system (CNS).

The mode of action is primarily at the transduction phase in the periphery, although there is now evidence that they also limit COX-2 mediated PGE2 expression in central neurones. By preventing these fibres from becoming more sensitive, they also affect signal modulation. Following elective surgery in healthy horses, there is every indication for the use of these drugs. Preparations licensed for use in horses in the UK include: phenylbutazone; flunixin meglumine; carprofen; meloxicam; vedaprofen; suxibuzone; ketoprofen; and metamizole. Of these, it is worth noting that vedaprofen is the only NSAID with a specific license for pre-operative administration, and metamizole is only available in combination with butylscopolamine. These are the most widely used analgesic drugs, available in both injectable and oral forms, making postoperative administration flexible and convenient.

Opioid use in horses often seems to be controversial, with excitement reactions often quoted as a potential side effect. This largely stems from early experimental work using high doses in pain-free horses. When employed in painful animals at clinically relevant doses, this effect is rarely seen. Indeed, a degree of sedation may be evident and be useful in postoperative management.

There are only two opioids licensed for use in horses, which are butorphanol for intravenous (IV) use and pethidine by the intramuscular (IM) route. Pethidine is a Schedule 2 drug and subject to restrictions on storage, record-keeping and disposal, while orphanol is not subject to such restrictions. Opioid receptors are present in the central nervous system and peripheral tissues. Upregulation in the periphery occurs following inflammation and trauma. Different receptor subtypes mediate different “qualities” of analgesia – due, in part, to their differing distributions. Analgesia is mediated by both mu (µ) and kappa (?) receptors. It is generally considered that µ-receptormediated analgesia is more profound, but visceral pain is more responsive to ê opioid receptor agonists. Butorphanol (ì receptor antagonist and ? receptor agonist) and pethidine (µ receptor agonist) are both short acting in horses – generally reported as approximately 30 to 90 minutes for butorphanol and one hour for pethidine.

A constant rate infusion protocol for butorphanol has been described for extended analgesia following colic surgery. When infused at 13µg/kg-1/ hr-1 for 24 hours post-surgery, it resulted in

improved comfort, reduced weight loss, shorter hospitalisation time and less expense when compared to horses that did not receive this treatment. These horses showed a transient decrease in faecal output, but less overall adverse effects than following a single IV bolus of butorphanol.

Although they are not licensed, the use of both morphine and methadone is growing in popularity. Their duration of effect (four to six hours) makes them attractive options and both are pure ì agonists. Dose ranges of 0.1mg/kg-1 to 0.25mg/kg-1 IV or IM have been reported as safe. Repeated administration should be undertaken with care, due to the potential to develop gastrointestinal tract impactions, but it is worth remembering that pain and distress will also have a negative effect on propulsive gut motility.

Alpha-2 agonist compounds all have profound analgesic properties, and three are licensed for use in horses: xylazine, detomidine and romifidine. The relative degree of analgesia provided by these three agents is controversial. Romifidine has tended to be regarded as the least analgesic, although this view has now been called into question. Receptors are found in similar locations in the central nervous system to the opioid receptors, and activation triggers a similar G-protein-coupled mechanism. This makes them synergistic with the opioids. All agents are capable of producing profound sedation, which may limit their use as systemic agents for post-operative pain management in some cases.

Local anaesthetic agents are traditionally associated with local or regional anaesthesia, but lidocaine can be administered intravenously. Originally considered to be a prokinetic drug, the evidence for this is debatable. However, it does appear to have anti-inflammatory properties and limits reperfusion injury to ischaemic tissues. It has useful analgesic properties when administered systemically (50µg/ kg-1/min-1 to 100µg/kg-1/min-1 IV), although the mode of action is not fully understood.

Ketamine used at sub-anaesthetic doses shows profound analgesic properties, and is useful in acute surgical pain management and chronic pain states due to its blocking action at N-methyl-D-aspartate (NMDA) receptors in the central nervous system. There is also evidence that it has activity at several other receptor types, including opioid receptors. Experimentally, ketamine has been demonstrated to be safe when administered as a bolus at up to 0.5mg/kg-1 IM or as an intravenous infusion up to 0.8mg/kg-1/hr-1 for 12 hours.

The use of novel agents, such as tramadol and gabapentin, has been described in experimental situations or individual case reports. Some of these treatments may become more widely adopted as more is learned about optimal doses and dosing intervals.

Local and regional analgesia

Epidural anaesthesia is a very useful technique for pain management in horses.

The technique is relatively straightforward, well tolerated and can be performed at the first intercoccygeal space or the lumbosacral junction. Nothing is specifically licensed for administration by the epidural route in the horse, but the use of several analgesic classes are well documented. Preservative-free preparations should be used.

Of the opioids, evidence suggests that butorphanol is ineffective by this route. Pethidine has been used experimentally and found to have some effect at ameliorating responses to mechanical nociceptive stimulation. Morphine and methadone have proven to be a clinically useful at doses of 0.12mg/kg-1 to 0.2mg/kg-1. Morphine has a delayed onset time (four to six hours) but an extended duration, variably quoted as between 12 and 24 hours. Methadone has a more rapid onset (approximately 15 minutes), but a shorter duration (approximately five hours). Combining the two in a single injection gives an extremely useful cocktail, with rapid onset and extended duration. Sterile saline can be used to dilute the drug to the required total volume, which will vary depending on the size of the horse and the region to be treated. Applications include perineal, lumbosacral, hindlimb and thoracic pain. For analgesia following hindlimb surgery, 10ml to 12ml would be appropriate in a 500kg horse. Xylazine (0.17mg/kg-1) and detomidine (40µg/kg-1 to 60µg/kg-1) either alone or in combination with other agents are useful, with a rapid onset and good analgesic properties. There can be significant systemic uptake from the epidural space, resulting in a sedated animal. Detomidinemorphine combinations have been shown to improve postoperative hindlimb lameness scores under both experimental and clinical conditions.

Epidural catheters can be placed for longer-term pain management, avoiding repeated needle puncture. These can be a challenge to maintain but are certainly worth considering in appropriate cases. Commercial kits contain all the necessary elements and are easy to use.

Local anaesthetic nerve blocks may be applicable for analgesia in some cases. Lidocaine and mepivacaine both have a fairly short duration of action (two to three hours), which limits their practicality. Bupivacaine is widely used in human medicine and in small animal veterinary medicine due to its extended duration of effect (six to eight hours).

An alternative is to use a diffusion catheter, implanted into the surgical site at the end of the procedure, allowing continuous or intermittent instillation of a local anaesthetic solution without the need for repeated needle puncture.

Catheters with various diffusion lengths are available commercially, or home-made versions can be fashioned from canine urinary catheters. Local anaesthetics can be used epidurally, but this is restricted to anaesthetising the tail and perineal region. It is important not to administer too large a volume, as this may spread too far cranially, leading to ataxia and recumbency.

Adjunctive measures

Although post-operative analgesia revolves around medical management of the inflammatory

process – ensuring that the body's response is appropriate and longer-term deleterious sequelae do not develop – there are other important aspects to pain management.

Hygiene and support of the surgical site is very important. Wound infection will amplify the inflammatory response, delay healing and increase the chance of chronic pain. Movement at a surgical site will delay healing and contribute to discomfort from tension in adjacent tissues. Immobility of an unstable area or wound by bandaging will encourage rapid healing.

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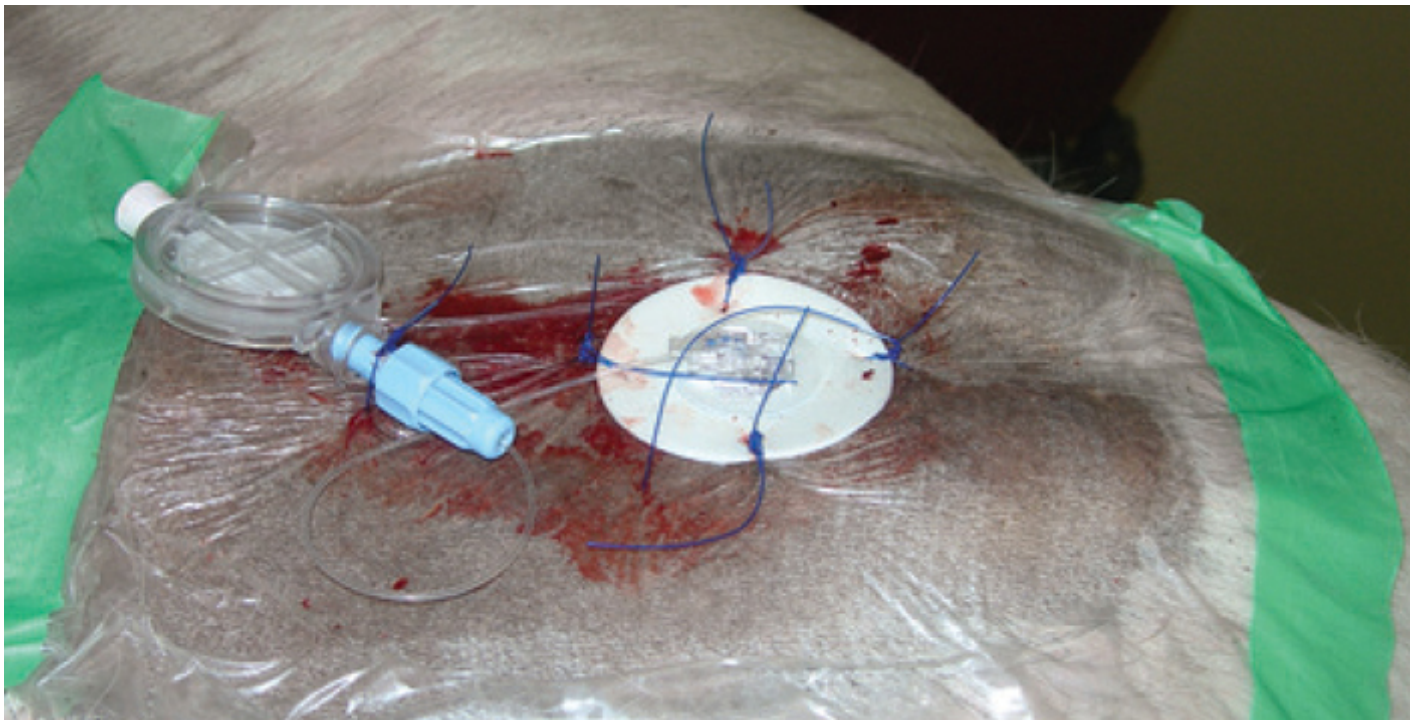
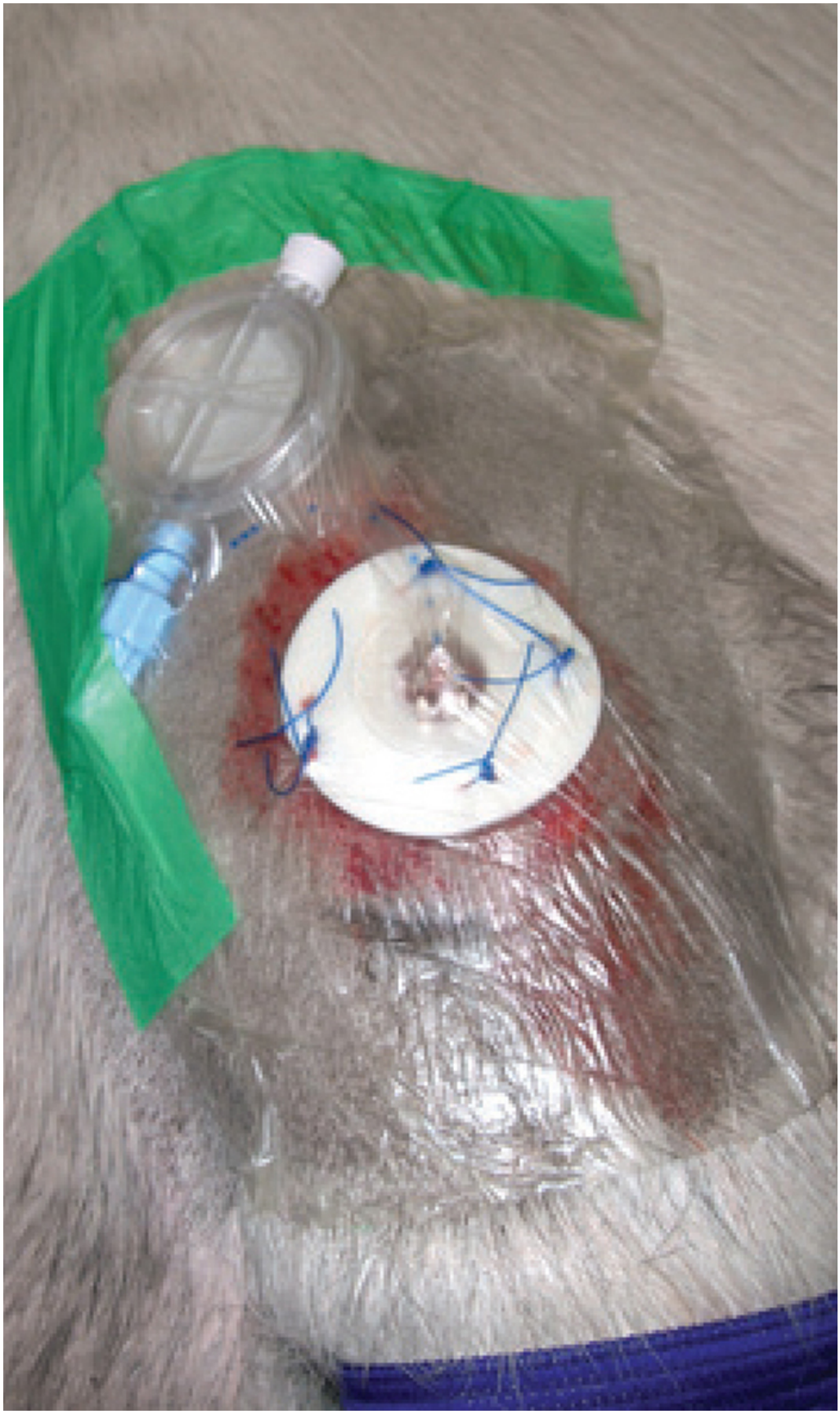


Above and right: epidural catheters can be placed at the intercoccygeal or lumbosacral spaces. The lumbosacral position is slightly more technically demanding, but tends to result in a more secure placement, being less prone to being damaged by the horse. Here, both positions are illustrated in the same animal, with a lumbosacral catheter being placed after the original intercoccygeal catheter became dislodged.



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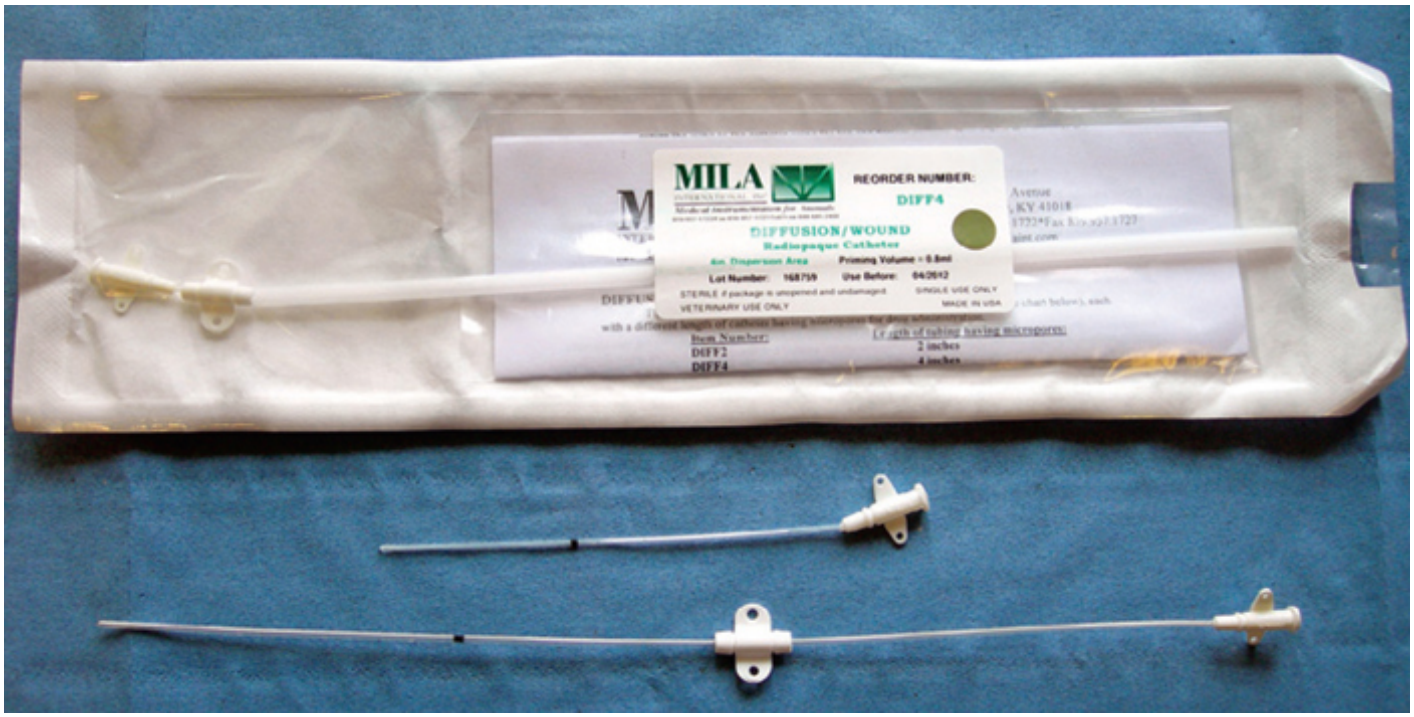
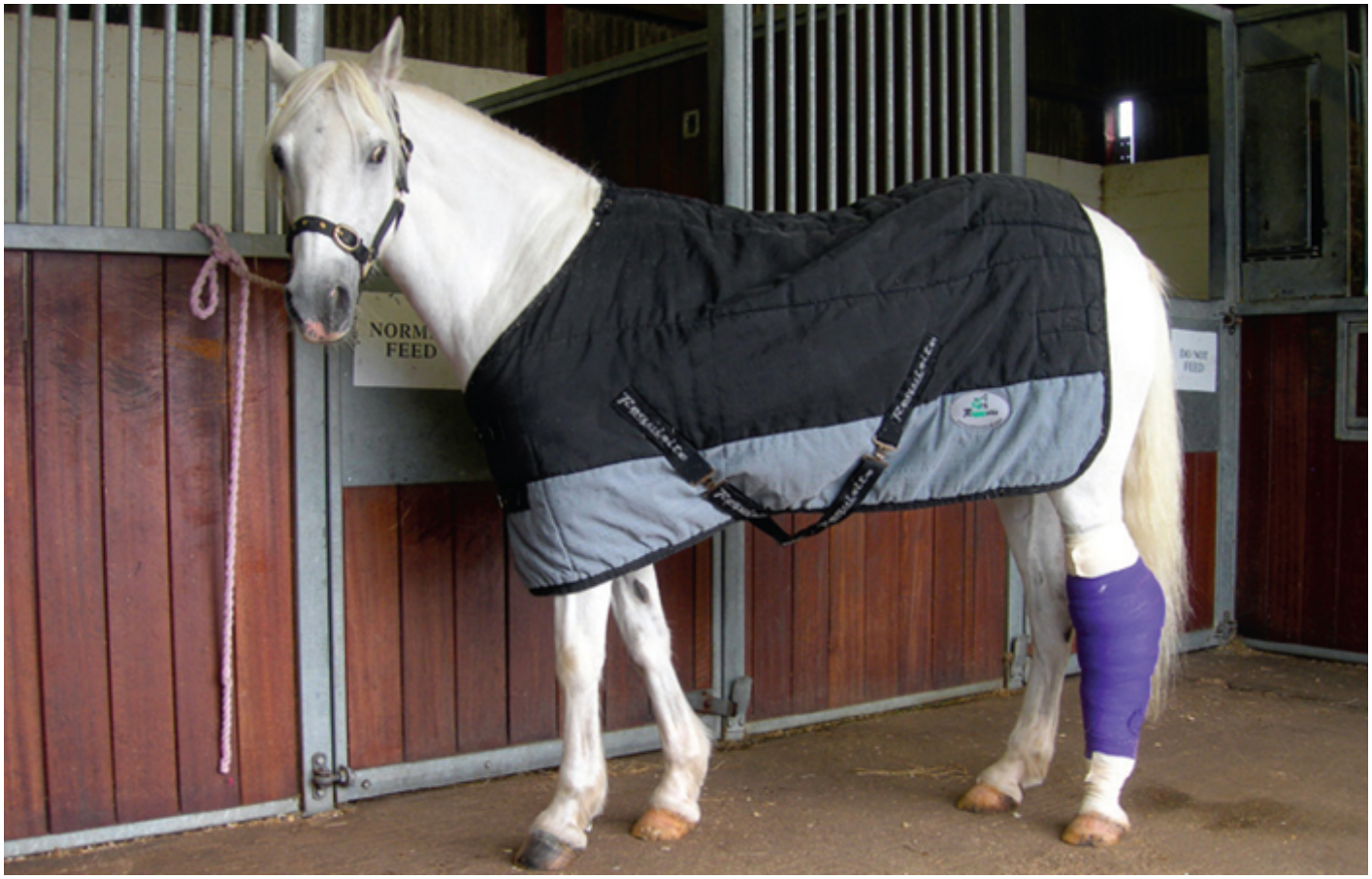


Above: Examples of commercial wound-diffusion catheters, which can provide analgesia

directly at the site of a surgical wound.

Commercial kits contain everything needed for placing an epidural catheter, making this procedure very convenient.



Good, firm support bandaging can go a long way to improving comfort postoperatively.

Care should be taken to ensure bandages are not tight, or slip and produce localised areas of pressure.