According to the International Association for the Study of Pain, pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Language is used to describe sensations and emotions, but it is not a prerequisite for feeling these; i.e. lack of ability to verbally communicate in no alters the perception of pain in human neonates, non-verbal adults and animals. For these reasons, IASP added to its definition of pain a caveat; inability to communicate in no way negates the possibility that an individual is experiencing pain and is in need of appropriate pain-relieving treatment. Animal pain has been defined by Maloney et al as “an aversive, sensory experience representing awareness by the animal of danger or threat to the integrity of its tissues; it changes the animal’s physiology and behavior to reduce or avoid the damage, to reduce the likelihood of its recurrence and to promote recovery; non-functional pain occurs when the intensity or duration of the experience is not appropriate for the damage sustained and when physiological and behavioral responses are unsuccessful in alleviating it.”

Pain is typically described by one of three classifications; the relation to its primary function or inciting event (physiologic or pathologic), site of origin (somatic, visceral or neuropathic) or duration (acute or chronic). Physiologic pain or first pain is mediated by high-threshold myelinated A delta fibers. Its major function is to warn of potential tissue damage if the behavior or action is continued. Physiologic pain is generally transient, arises from a short stimulus inducing little or no tissue damage and results in a well-localized, rapid, sharp, pricking sensation. Pathologic pain or second pain is mediated primarily by higher threshold, thinly myelinated A delta or non-myelinated C nerve fibers. Extended tissue discomfort and abnormal sensitivity result from intense or prolonged stimuli which cause tissue damage. Pathologic pain is the pain that veterinarians must effectively diagnose and treat in our patients.

Somatic pain, also referred to as fast pain, is caused by the activation of pain receptors in either the body surface or musculoskeletal tissues (e.g. skin, bone, joint, connective tissue and muscle). Cutaneous derived superficial somatic pain tends to be sharp, well-localized and persistent allowing for instant and precise recognition of superficial tissue trauma. Deep somatic pain originates from bones, joints and muscles, is generally perceived as dull or aching/burning and less well-localized than superficial somatic pain. It is generally longer lasting than somatic pain. Visceral pain or slow pain is caused by the activation of pain receptors in the thoracic, abdominal or pelvic organs from infiltration, inflammation, compression, distension or stretching. Visceral pain is vague and not well localized and is usually perceived as pressure-like, deep squeezing, dull or diffuse. Parasympathetic and sympathetic pathways transmit the nociceptive impulses. Wounds such as clamping, cautery, cutting, needle puncture are painful to somatic structures but may not be felt at all in the visceral organs or may be perceived as a dull discomfort rather than sharp insult. Neuropathic pain is caused by injury or malfunction to the spinal cord and/or peripheral nerves. Neuropathic pain is typically a burning, tingling, shooting, stinging, or "pins
and needles" sensation, is diffuse and occurs at the level or below the level of injury.

These different types of pain respond differently to pain medications and thus pain origin may have some therapeutic implications. Visceral pain is generally more responsive to kappa opioid agonists such as butorphanol than it is to traditional mu agonists such as morphine. Neuropathic pain is poorly sensitive to opioid medications in human patients. Visceral pain may also modulate sympathetic and parasympathetic activity to alter reflexes and motor activity in the gastrointestinal system so treatment may have a direct effect on organ function.

Acute pain is provoked by a specific disease or injury, serves a useful biologic purpose, is associated with skeletal muscle spasm and sympathetic nervous system activation, and is self-limited. It is of short duration and occurs secondary to surgery or trauma. Acute pain prompts recognition of an injury and protection of the injury to expedite recovery. Chronic pain, in contrast, may be considered a disease state. It is pain that outlasts the normal time of healing, if associated with a disease or injury or is associated with progressive diseases such as chronic osteoarthritis. Chronic pain serves no biologic purpose, has no recognizable end-point and can have profound negative effects on various physiologic functions and the sense of well-being. The therapy of acute pain is aimed at treating the underlying cause and interrupting the nociceptive signals. The therapy of chronic pain must rely on a multidisciplinary approach and should involve more than one therapeutic modality.

Nociception is "the neural processes of encoding and processing noxious stimuli." It is the afferent activity produced in the peripheral and central nervous system by stimuli that have the potential to damage tissue. This activity is initiated by nociceptors, (also called pain receptors), that can detect mechanical, thermal or chemical changes above a set threshold. Once stimulated, a nociceptor transmits a signal along the spinal cord, to the brain. Nociception includes the processes of transduction, transmission, modulation and perception and triggers a variety of autonomic responses and may also result in the experience of pain.

Each step in the process provides opportunities for possible pharmacologic intervention to diminish pain perception and the adverse physiologic responses that occur secondary to pain. Multimodal analgesia, administering analgesic drugs that act to diminish pain at multiple steps in the process, is an effective way to improve analgesic therapy without the increased risk of adverse effects seen with increasing doses of a single therapeutic agent.

Being able to treat pain effectively requires that we can recognize it and that we can in some way measure or quantify it. It is accepted that people who work with horses recognize when they are painful and most veterinarians believe that horses experience pain. In fact, the literature has many general descriptions of pain behaviors but these tend to be nonspecific and usually related to severe pain. Often these general behaviors do not specify the location and type of pain and do not correlate with its severity. Many horses may be experiencing varying degrees of pain that we do not recognize because of more subtle changes in behavior. As equine veterinarians we often forced to choose between ideal pain control and compelling reasons for avoiding analgesics such as fear of causing further injury by removing the protective function, cost and side effects.

Assessing pain in horses is not as simple as observing overt signs of pain or taking a heart rate.
Price and colleagues demonstrated that subtle behavior changes are more sensitive than heart rate. Several pain assessment scales have been developed for horses including simple descriptive, numerical and visual analog scales. Each seems to be useful in the model it was developed in but none have achieved widespread acceptance in routine clinical practice or pain research.

Pain leads to alterations in cortisol, insulin, glucagon and other stress hormones lead to a catabolic state characterized by hyperglycemia, lipolysis, and protein catabolism and resultant weight loss and impaired wound healing. Humoral and cellular immunity are inhibited during the surgical stress response because of sympathetic stimulation, increased cortisol release and endogenous opioid activity. This leads to increased incidence of postoperative infections and enhanced risk for tumor metastasis in humans.

Beneficial effects of decreasing the post-surgical stress response through provision of adequate post-operative analgesia have been extensively documented in human patients have been shown to include improved wound healing, fewer cardiopulmonary complications (heart attack, thromboembolism), decreased risk of gastrointestinal ileus, decreased hypercoagulability, fewer post-operative infections, less weight loss, and shortened time to discharge from the hospital. The ultimate effect of analgesic protocols on outcome remains controversial however, regardless of evidence of improvement in individual pathophysiologic parameters. Despite the controversy, in a 2005 review of the consequences of inadequate postoperative pain relief and chronic persistent postoperative pain in human patients, Joshi and Oggunnaide stated “it is now well accepted that inadequately treated pain and associated stress response have significant physiologic and psychologic consequences, which may lead to organ dysfunction and increase postoperative mortality and morbidity.”

Whether these associations can be made in equine patients is up for debate as well. But in 2004, Sellon et al found that horses treated with a butorphanol continuous rate infusion for the first 24 hours after colic surgery lost less weight and were discharged from the hospital sooner than horses receiving saline control. The study included 31 horses in a randomized, placebo-controlled double blind investigation of horses undergoing exploratory celiotomy for abdominal pain. All horses received flunixin meglumine at standard doses before and after surgery. Horses receiving butorphanol infusions had more normal posture and social behaviors than control horses. Horses in pain were described as displaying decreased locomotion, standing quietly in the back of the stall with head and neck lowered and ears immobile and exhibiting minimal responses to human intervention. The conclusion that these horses were in significant pain was further supported by observations that butorphanol-treated horses had lower plasma cortisol concentrations than did control horses.

Traditional equine analgesia therapy has consisted of a limited number of drugs relative to human and small animal patients. The primary analgesics used in equine practice include NSAIDs (primarily phenylbutazone and flunixin), alpha-2 agonists (xylazine and detomidine) and an opioid (butorphanol). Over the last 10 years, other drugs have been used successfully in place of or in combination with traditional equine analgesics as well as the use of some traditional equine drugs in non-traditional indications or routes of administration to achieve more complete equine pain management.
Nonsteroidal anti-inflammatory drugs (NSAIDs) have been the mainstay of treatment for pain and inflammation in horses for many decades. Phenylbutazone (2-4 mg/kg q 12-24 hrs) and flunixin meglumine (0.25-1.0 mg/kg q 6-24 hrs) have been used successfully for many years as anti-inflammatory agents in the treatment of acute and chronic musculoskeletal and gastrointestinal pain in the horse. Other drugs in this category include ketoprofen (1-2 mg/kg q 12-24 hrs) and carprofen (0.7 mg/kg q 24 hrs). Whilst all are considered under the broad heading of NSAIDs, they are chemically distinct and have different efficacy and toxicity profiles. Toxicity generally relates to the gastrointestinal, renal or hepatic system and is most likely with inappropriate (e.g., overdose) use. However, idiopathic right dorsal colitis can be seen with short-term label dosing. Clinically, neonatal patients appear to be more susceptible to these undesired effects. A unique non-systemic option for NSAID administration (Surpass – 1% diclofenac sodium) is now also available and may provide local relief of pain and inflammation (for osteoarthritis) without systemic side effects. An improvement in lameness, pain, mobility and owner impression of these was noted in 30-74% of horses at a dose of approximately 75 mg (or a 5 inch ribbon of the topical cream) applied twice daily; interestingly horses receiving the placebo showed an improvement ranging from 23 – 50% in these same parameters.

NSAIDs have been associated with gastric ulceration, ulceration of the right dorsal colon, and renal papillary necrosis. The cause of these adverse effects relates to the mechanism of action of the drugs themselves. NSAIDs work by inhibiting the enzyme cyclooxygenase (COX), which is responsible for the production of inflammatory mediators known as prostaglandins. There are two different isoforms of the COX enzyme, known as COX-1 and COX-2. A third isoform (COX-3) has been found in other species, but its relevance in the horse is unknown. In general, COX-1 is involved in normal day-to-day ‘housekeeping’ activities in the body, while COX-2 is expressed to a greater degree in inflammation. The rationale behind newer NSAIDs, known as COX-2 specific inhibitors, is that blocking COX-2 will block the harmful effects of inflammation, but reduce the risk of adverse effects by allowing the COX-1 enzyme to continue to perform its normal functions.

Multiple COX-2 specific inhibitors are available for use in humans and small animal species. In veterinary medicine, drugs such as etodolac, meloxicam, deracoxib and firocoxib are considered to be COX-2 specific. Recently, firocoxib, a COX-2 specific NSAID has been licensed for use in horses. The label indication is for the treatment of osteoarthritis in horses. The doses are 0.1 mg/kg (oral paste) and 0.09 mg/kg (IV injection). Recently a study by Cox et al (2012 ACVIM poster) evaluated a loading dose that showed a single 3X dose followed by daily label doses achieved near steady state plasma levels compared to steady state label doses reached by day seven. Toxicity studies show that firocoxib causes fewer lesions in the gastrointestinal tract compared to phenylbutazone when administered at the recommended doses. At elevated doses including up to 12.5 times the label dose, some toxicities were seen but no reported deaths.

Opioids are often used in the control of perioperative pain in other species but have been less widely used in horses because of concerns regarding possible adverse effects. The combination of an opioid drug with a NSAID provides synergistic analgesia and represents a relatively straightforward approach to multimodal analgesia. Butorphanol has been the most widely used of the opioid drugs in equine medicine. It is predominantly a kappa agonist and therefore has
fewer and less severe adverse effects as compared to morphine and other mu agonists. Butorphanol is not sedative in adult horses when used on its own. It is approved for use IV but is often administered IM for analgesic effects. Absorption of butorphanol after IM administration is very rapid (half-life of absorption of 6 min) but systemic availability after IM injection is surprisingly low (37%) in adult horses. Terminal half-life after IM administration is 0.57 hrs. To maintain targeted plasma butorphanol concentrations above 10 ng/mL, administration of 0.08 mg/kg IM every 3 hours may be necessary. High intravenous doses of butorphanol administered (0.5 mg/kg) are associated with excitatory behavior, increased locomotion and inhibition of gastrointestinal activity.

These effects are less frequently observed with lower doses or when the drug is administered IM or by continuous rate infusion (CRI). When used as a CRI, butorphanol may decrease gastrointestinal motility and fecal production should be monitored appropriately. If a decrease in fecal production is observed, administration of mineral oil via nasogastric tube and/or decreasing infusion rates is recommended. Butorphanol CRI should rarely be continued for more than 12-24 hours. For post-operative colics, it is administered as a CRI at 13 μg/kg/hr. If a CRI is not practical, similar effects can be achieved by adding 10-20 mg of butorphanol to a 5 L bag of LRS and administering at a rate of 1-2 L/hr. The rate can be adjusted if the horse begins to show adverse effects. Epidural butorphanol may potentiate lidocaine-induced analgesia but is unlikely to provide significant analgesia when used as the sole agent. Unlike adult horses, neonatal foals receiving butorphanol by IV or IM injection appear profoundly sedated. This may represent differences in opioid receptor distribution or differences in P glycoprotein distribution within the central nervous system of neonates as compared to adults.

Other opioids that have been used as analgesic medications in horses include fentanyl, morphine and methadone. Transdermal fentanyl patches have been used in horses of all ages without significant reported adverse effects. However, recent experimental data demonstrates that absorption of drug is erratic at best, peak drug concentrations are often below the predicted therapeutic range, and even when administered intravenously, fentanyl may not be an effective analgesic agent for horses (Sellon personal communication). Therefore, use of fentanyl patches in adult and neonatal horses cannot be recommended at this time. Morphine may be used intravenously as an analgesic agent in combination with alpha 2 agonists. When used intravenously as a sole analgesic agent, it may result in profound excitation. Anecdotally, IM morphine use is not associated with CNS excitation and this may represent an underappreciated analgesic option. Morphine may be administered epidurally on its own or in combination with detomidine to provide effective analgesia of the caudal half of the body. Epidural morphine administered at 0.05 to 0.1 mg/kg produces segmental analgesia; dorsal nerve brances of the lumbosacral plexus appear to be preferentially affected. Morphine is typically used at doses of 0.1 to 0.2 mg/kg diluted to 10-20 ml with 0.9% saline (total volume of 0.04 ml/kg body weight). Analgesic effects are seen within 2030 minutes and may last 8-24 hours without adverse effects on motor function. Some surgeons have anecdotally reported efficacy of intra-articular morphine for control of pain associated with arthroscopy or arthrotomy. Oral opioids are rarely used in horses; however, there are anecdotal reports that oral tramadol and methadone may be efficacious.
Tramadol is fairly unique among opioids since it is well absorbed orally in most species. Oral absorption in horses unfortunately is lower than in other species. However, with higher doses, an analgesic effect may be achieved. Currently, 10 mg/kg orally, twice daily is the recommended dose. Higher doses may be more effective, but carry an increased risk of side effects.

Buprenorphine is a partial opioid agonist that separates itself from other opioid drugs because of its longer duration of action. It has the potential to be used as a twice daily treatment for pain management in horses. It may also be given sublingually, as an alternative to injection in horses that will not tolerate needles. Unfortunately, adverse effects such as CNS excitement and decreased gastrointestinal motility may be seen in some horses receiving the drug.

Ketamine (KET) possesses analgesic and anti-inflammatory activity at sub-anesthetic doses, suggesting a benefit of long-term KET treatment in horses suffering from pain, inflammatory tissue injury and/or endotoxemia. It is a noncompetitive antagonist at N-methyl-D-aspartate receptors in the spinal cord. It also has effects on opioid, monoaminergic, and muscarinic receptors, as well as voltage-sensitive Ca2+ channels. It can be used in nerve blocks, as well as epidurally. Subanesthetic amounts of ketamine have been used to provide analgesia in small animals and human patients. Additionally, administration of a subanesthetic dose of ketamine had immunomodulating effects in dogs with experimentally induced endotoxemia (namely, blunting of plasma TNF-alpha activity). Following oral or IM administration in people, serum concentrations of ketamine as low as 0.04 and 0.150 μg/mL, respectively, have been associated with analgesia.

Constant rate infusions of ketamine have also been studied in horses. Doses of 0.8 mg/kg/hr IV were shown to be safe, but not effective based on the pain model described, even though concentrations were in a range considered to be therapeutic in humans (Mean 0.137 μg/mL). A more recent study suggested a CRI of 1.5 mg/kg/hr, with higher doses producing an increase in heart rate and respiratory rate.

Gabapentin is used in human and small animal medicine for the treatment of neuropathic pain. Recent work has shown that gabapentin binds to the α2δ subunits of voltage dependent calcium channel complexes. These α2δ subunits have been found in numerous tissues in humans and rats, including the brain, and affinity for this binding site has been correlated to the anti-hyperalgesic potency of gabapentin versus other similar drugs. Once bound to the subunit, gabapentin acts in an inhibitory manner, resulting in a decrease in calcium influx in presynaptic nerve terminals and inhibition of the release of excitatory amino acids. Gabapentin has successfully been used for the treatment of post-operative neuropathy in a horse at a dose of 2.5 mg/kg PO q8-12h.

Suggested Reading

Multiple authors. In Depth: Pain Management, AAEP Focus on the Foot Symposium Proceedings, Columbus, OH, 2009; 199-226.


