Physiology of Pain and Pain Assessment in Small Animals

What is pain? This manuscript will address the fundamental physiology of the development of pain as it is crucial to understanding how to intercept, treat and block pain. Pain is an unpleasant sensory experience that arises from tissue or nerve damage. Locally, damage to nerve endings creates an intense chemical signal that is carried to the CNS, processed by the spinal cord and brain, and perceived as pain.

The four basic steps in the pain signal cascade involve the alteration of chemical signals into electrical signals by nerve endings (transduction), the movement of the pain signal in an afferent (towards the CNS) direction, transmission, the uptake and processing of the pain signal in the dorsal horn of the spinal cord (modulation) and the ultimate interpretation of the pain signal at the level of consciousness by the brain (perception).

Transduction: Specialized nerves called nociceptors terminate in tissues and the nerve endings are constantly bombarded with stimuli. Chemical, thermal, pressure stimuli are sensed by these nerve endings and transduced into an action potential that flows in an afferent direction. There are three types of nerve fibers involved in the transmission of this stimulus: A and C fibers, with A fibers having three sub-types: Aα, Aβ, and Aδ. The fibers involved directly with pain are the Aδ and C fibers. These fibers have the ability to respond to low intensity or high intensity stimuli of a chemical, thermal, or mechanical nature.

Aδ fibers are responsible for the “pricking” or pointed sensation of pain (also called “first pain”). These fibers discharge at a faster rate to the CNS than the C fibers and so the CNS retrieves a higher volume of signals owing to a finer interpretation of them. Most C fibers are high threshold and are responsible for slower-onset “second” pain signals providing a dull, throbbing, burning or aching sensation after the insult. Additionally, both types of nerve fibers contain silent or sleeping nerve endings that can be recruited during extensive tissue damage.

Transmission: The peripheral nervous system is responsible for the transmission and conduction of signals afferently and efferently (to and from the CNS). Afferent fibers are sensory whereas efferent fibers are motor neurons. Afferent fibers terminate in the dorsal root of the spinal cord and efferent fibers begin at the ventral root. Dermatomes are expanses of body surface innervated by specific peripheral nerves originating in the dorsal root. The signal is transmitted to the dorsal root by somewhat myelinated Aδ and unmyelinated C fibers.

Modulation: Signals approaching and then entering the spinal cord are modulated (amplified or deamplified) by the spinal cord. The spinal cord contains both grey matter and white matter, the former of which makes up the dorsal and ventral horns and the intermediate zone. The nociceptors enter the spinal cord through the dorsal nerve root and terminate. They relay signals through a synapse to the neurons in the dorsal root grey matter. A variety of neurotransmitters mitigate this process including; Substance P, glutamate and aspartate (excitatory NT’s), GABA (inhibitory), nitric oxide (NO), ATP, serotonin and norepinephrine. These neurotransmitters act on AMPA, KAI, and NMDA receptors which are excitatory, OR on GABA and other inhibitory receptors. Most peripheral signals result in glutamate binding to excitatory receptors such as AMPA, KAI, or NK receptors. NMDA receptors begin to be stimulated with prolonged inputs from Aδ and C fibers. Stimulation of GABA receptors provides inhibitory input to the spinal cord. Actual modulation of the signal in the spinal cord is achieved by a flux of excitatory and inhibitory neurotransmitters working at excitatory or inhibitory receptors. The combinations either enhance excitatory signals, inhibit excitatory signals, enhance inhibitory signals, or inhibit inhibitory signals. Additionally, gate control theory may explain some of this phenomenon as well. Gate control theory explains why we tend to rub areas that hurt, or even press into painful areas and describe a pain relief or euphoric sensation. The theory states that thick fibers (touch, pressure) tend to send signals that inhibit excitatory cells in the spinal cord and thin fibers (pain fibers) tend to excite excitatory neurotransmission and cause pain. This also explains the use of TENS in analgesic

treatment- as the TENS unit stimulates non-nociceptive fibers bombarding the nervous system with the thick fiber inputs and thus relieving pain.

Perception: Pain signals must be collected, processed and interpreted and this happens at multiple locations in the brain. The reticular activating system (RAS) receives inputs and coordinates motor activity in response to painful stimuli (reflex, etc). The thalamus sends signals to the limbic system which responds in multiple ways including conditioned fear and anxiety, memory, emotion, among others. Periaqueductal grey matter (PAG) is responsible for facilitative or inhibitory signal processing at the level of the brain.

Several types of pain exist; from somewhat normal functioning of the CNS to deranged and modified responses to noxious stimuli. Physiologic pain is considered a normal pain signal sent to the CNS and is processed relatively normally. A sharp prick or poke would result in a response typical of any creature defending itself and would not last indefinitely but would be finite. Pathological pain involves a deranged diseased response to a stimulus and includes terminology such as:

Allodynia: Painful response with non-noxious stimulus

Hyperalgesia: Exaggerated response to noxious stimuli

Hyperpathia: Prolonged response to noxious stimuli

Physiologic consequences of pain can tax the body and involve multiple organ systems including the cardiovascular, pulmonary, gastrointestinal, renal, endocrine, nervous and immune systems. Effects of pain on these body systems are shown in the table below.

Body System	Physiologic response to pain
Cardiovascular	Tachycardia, Hypertension, Vasoconstriction
Pulmonary	Hypoxia, Hypercarbia, Atelectasis
GI	Nausea, Vomiting, Ileus
Renal	Oliguria, Urine retention
Endocrine	Increased adrenergic (fight or flight) activity, increased metabolism
Nervous	Anxiety, fear, sedation, fatigue
Immune	Immunosuppression

As pathologic pain is the majority of the pain we will treat the discussion will focus mainly on this. Several mechanisms exist that contribute to a prolonged exaggerated response to a painful stimulus. These include: peripheral and central sensitization, and “windup” phenomenon. To explain these we must look at what happens locally at the site of tissue injury. At the area of tissue damage many inflammatory mediators are released to facilitate blood flow, WBC mobilization, and perform other signaling duties. All of these chemicals create an “inflammatory soup” and terminal endings of nociceptors lie in that soup. Peripheral nociceptors become increasingly sensitive to signals- altering the amount and amplitude of signals sent to the CNS.

Primary hyperalgesia occurs as the nerves are damaged and are exposed to the inflammatory soup, and this damage and heightened sensitivity to signals can spread to surrounding tissues, termed secondary hyperalgesia. These heightened responses occur as a result of the inflammatory (also called sensitizing) soup and this produces neuroplastic changes in nociceptors changing some of the high-threshold fibers into low-threshold fibers and activates silent and sleeping nerve endings/nociceptors.

Central sensitization occurs with changes in the excitability and response to stimuli in the spinal cord. This contributes to secondary hyperalgesia and painful sensations outside the territory of the original tissue damage. Normally, slightly noxious stimuli are transmitted to the dorsal horn of the spinal cord by Aδ and C fibers and mediated by glutamate (excitatory) acting on AMPA and KAI receptors. This signaling is modulated additionally by GABA and glycine (inhibitory) released to dampen the signal. Pathologic pain signals or chronic signals activate additional excitatory neurotransmitters such as

Substance P and activate NMDA and NK receptors. As these signals propagate they "windup" producing prolonged responses to painful stimuli and secondary hyperalgesia. These changes can also recruit non-noxious nerve fibers (Aβ) fibers to now contribute to and carry nociceptive signals.

Visceral pain seems to be mediated by Aδ and C fibers traveling along sympathetic and parasympathetic networks to organs. Viscera do not seem to have nerve endings with nociceptive specificity. This means that much input from trauma/damage/disease in organs is not sent to the CNS for processing. Clamping or cutting directly into viscera produce little response but diffuse processes (peritonitis) produce severe pain.

Many behaviors can indicate pain in dogs and cats and to some extent the response to pain is individualistic. In general, patients that have an abnormal body posture, abnormal gait, abnormal movement and/or vocalizing can be considered to be in pain.

Common Manifestations of Pain

Abnormal Posture	Hunched Praying position Sitting or lying in abnormal position
Abnormal Gait	Stiff gait Partial or no weight bearing on limb Lame Reluctance to move
Abnormal movement	Thrashing Restlessness Circling
Vocalizing (intermittent, constant or when touched)	Screaming Whining Crying Purring (cats)
Behavior	Aggressive Submissive Obtunded
Facial expressions	Dogs: Glazed, dull, fixed glare Cats: Squinted eyes, dull, unkempt,

Adapted from Gaynor & Muir Handbook of Veterinary Pain Management

In order to be more objective about pain assessment and pain level, pain scoring has become a popular and important tool in the management of these patients. Although all the items above are proven behaviors and clinical signs of pain they are still highly open to interpretation and thus subjective. Pain scales help objectify the level of pain in our non-verbal patients. They also help focus the clinical importance of assessing and managing pain and also help identify pain in patients where it might be overlooked such as cats or stoic dogs. Initially, pre-emptive pain scoring can help categorize procedures or disease into mild, moderate or severe pain. Minor pain is associated with (but not limited) minor surgical procedures (abscess), dental prophylaxis, ear cleanings and placing of sutures. Moderate procedures include anal sac surgery, mass removals, cystotomy, ovariohysterectomy, castration and severe laceration repair. Severe pain includes ear canal ablation, thoracotomy, fracture repair, limb amputation and exploratory laparotomy.

Many pain scales exist but the author prefers the Colorado State University Canine and Feline Acute Pain Scales. It relies on a 0-4 rating (0 being no pain and 4 being severe pain). The scale includes

psychological, behavioral, and pictoral descriptions of animals in varying levels of pain. It additionally has a category for response to palpation- to objectively measure a continued response to palpation of an affected body part. To properly use this scale the staff member should start with a quiet observation of the patient in its cage while not disturbing or rousing it. After the observation period the patient is handled and the affected area palpated to assess the response. The scale provides little room for disagreement as it contains very objective language and artist renderings of varying levels of pain. However, it lacks solid validation. The links to the free access of these scales are found below:

CSU Canine Acute Pain Scale:
CSU Feline Acute Pain Scale: