**Review of the Pain Pathway**

According to the IASP (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.” The IASP further states that “The

inability to communicate verbally does not negate the possibility that an individual is

experiencing pain and is in need of appropriate pain-relieving treatment.”1

Nociception

is the detection of a noxious stimulus (that in humans results in “pain”). Nociceptors are

free (naked) nerve endings that encode mechanical, chemical, thermal energy into

electrical impulses.

Fibers of primary sensory neurons

**Aβ fibers**: large myelinated low threshold fibers that transduce pressure and innocuous

sensations.

**Aδ fibers**: small myelinated, high threshold fibers that transduce sharp well localized

pain.

**C fibers**: small unmyelinated (slow), high threshold fibers that transmit slow, burning,

diffuse pain.

Aδ and C fibers have a variable distribution and density.

Somatic nociceptors are both deep and superficial in the skin, subcutaneous tissues,

muscles, tendons, joint capsules, periosteum, subchondral bone, and fascia.

Visceral nociceptors are located in the peritoneum, pleura, internal organs, blood

vessels. They are mostly silent nociceptors (c-fiber) and respond to distention, spasm,

ischemia, and inflammation. Interestingly, visceral nociceptors (vs somatic nociceptors)

are not always activated in life threatening disease not always painful (i.e. perforation).

**Classic pain pathway is divided into 4 parts.**

1**. Transduction**: stimuli from periphery to neural pathway

1st order neurons are naked nerve endings in periphery with cell bodies in dorsal horn

ganglia. They encode mechanical, chemical, thermal or electrical stimulus that is

“transduced” to afferent action potentials on Aδ or C fibers. The action potentials are

propagated by Na+

channels. 1st order neurons synapse with neurons in dorsal horn

(2nd order neurons).

2. **Transmission**: rostral movement of action potentials within pain pathway

Transmission of action potential occurs via ascending spinal tracts within the spinal

cord. The spinothalamic tract (STT) is most prominent nociceptive pathway although

many alternative routes are present. The transmission of 2nd order neurons terminates

in the thalamus.

3. **Modulation**: inhibition or enhancement of signal

Inhibition of nociceptive signal can occur peripherally via local effects at the nociceptor:

local anesthetics, opioids, and NSAIDs can act those peripheral sites. More centrally

inhibition can occur at the dorsal horn of the spinal cord; opioids, serotonin, α-2

agonists, and NMDA-antagonists can decrease pain transmission. Enhancement of

nociceptive signal can occur peripherally due to primary hyperalgesia from allogens (pain producing substances) from the tissues (e.g. histamine). Central enhancement

can occur due to secondary hyperalgesia and windup.

4. **Perception**: conscious perception of noxious stimuli is generally considered pain.

3rd order neurons transmit information from the thalamus to higher (cortical) brain

centers. If a patient is anesthetized with a general anesthetic and a toe is clamped,

the entire pain pathway is activated up to the cerebral cortex (which is asleep). Without

the conscious perception the patient does not “feel” pain. However, if the general

anesthetic removed (turned off); the brain is now awake while the entire pain pathway is

activated.

**TYPES OF PAIN**

1)**Acute pain** facilitates tissue repair. The pain response is proportional to the injury and

generally responds well to most analgesics such as opioids and NSAIDs.

2)**Chronic pain** is long lasting (in humans it is longer than 3-6 month duration) and often is

not proportional to the stimulus. The neuroendocrine response attenuated and there is

poor response to conventional analgesics.

3)**Neuropathic Pain** is produced as a result of nerve damage (compression, transection,

inflammation, chemical, radiation, surgery, tumor). There is an altered sensory

processing of stimuli or ectopic activity (discharge) from axons, neuroma, or cell bodies.

Pain is often described as burning or shooting.

4)**Referred Pain** is usually associated with visceral pain.