NMDC221 Session 14: Nervous System Disease Part I
Recommended Reading

Topic Summary

Nervous System Disease: Part I
- Overview of the principles and considerations for the nutritional management of the nervous system

Pain
- Nutritional management & consideration of drug-nutrient interactions
Nervous System

- Made up of the brain, spinal cord (central nervous system) and nerves (peripheral nervous system).
- The nerves take information to the periphery (efferent) or to the CNS (afferent).
- Nerves are under direct voluntary control (somatic nervous system) or involuntary control (autonomic nervous system).
- Autonomic nervous system is further broken down into sympathetic NS (fight or flight) & parasympathetic NS.
- Neurotransmitters are the chemical messengers that actuate action potentials in nerves and adjust muscular or organ functions. (Bullock et.al. 2007)
## Nervous System

<table>
<thead>
<tr>
<th>Neurotransmitter</th>
<th>Main Precursors</th>
<th>Usage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serotonin</td>
<td>L-Tryptophan, 5-hydroxytryptophan, vitamin B6, magnesium, zinc, vitamin C, tetrahydrobiopterin (BH4) &amp; folate</td>
<td>Sleep, Mood, Brain Activity, Appetite. Deficiency of B3 shunt tryptophan away from serotonin production (kynurenicine pathway)</td>
</tr>
<tr>
<td>Endogenous Opioids</td>
<td>Tryptophan, vitamin B3, B6, magnesium, zinc.</td>
<td>Analgesia &amp; euphoria. Serotonin stimulates the release of opioids. Dl-phenylalanine can increase opioids by inhibiting enkephalinase (opioid breakdown)</td>
</tr>
<tr>
<td>Taurine</td>
<td>Taurine. Methionine &amp; cysteine manufacture</td>
<td>Inhibitory amino acid NT in the brain. Sleep, memory, concentration. Taurine increases histamine &amp; ACh in the brain</td>
</tr>
</tbody>
</table>

(Osiecki, Meeke & Smith, 2005, p. 25; Osiecki, 2006; Bryant & Knights, 2011)
# Nervous System

<table>
<thead>
<tr>
<th>Neurotransmitter</th>
<th>Main Precursors</th>
<th>Usage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glutamate</td>
<td>Glutamine</td>
<td>Main stimulatory NT in brain &amp; SC. Stimulates over 70% of excitatory synapses in the brain. Memory, concentration, learning, alertness &amp; attention span.</td>
</tr>
<tr>
<td>GABA</td>
<td>Glutamine, vitamin B6</td>
<td>Inhibitory NT. Sleep, Anxiety, Addictions</td>
</tr>
<tr>
<td>Acetylcholine</td>
<td>Choline, vitamin B1, B5, acetyl-l-carnitine, magnesium</td>
<td>Controls PSNS. Link between nerves, muscles and organs. Memory, Cognitive Function, learning, ANS &amp; fine motor control. Vit C facilitates release of Ach from synapses</td>
</tr>
</tbody>
</table>

(Osiecki, Meeke & Smith, 2005, p. 25)
## Nervous System

<table>
<thead>
<tr>
<th>Neurotransmitter</th>
<th>Main Precursors</th>
<th>Usage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dopamine</strong></td>
<td>Phenylalanine &amp; Tyrosine. Vitamin B6, Magnesium, Zinc</td>
<td>Cognitive Arousal, Emotional Status, Mood, Fine Motor Function. Motivation</td>
</tr>
<tr>
<td><strong>Adrenaline</strong></td>
<td>Phenylalanine &amp; Tyrosine</td>
<td>Arousal, Stress</td>
</tr>
<tr>
<td><strong>Noradrenaline</strong></td>
<td>Phenylalanine &amp; Tyrosine. SAMe, vitamin B3, BH4 &amp; folate</td>
<td>Stimulatory NT that co-ordinates hormone release from the thymus. Cognitive Arousal, Emotional Status, Mood, Fine Motor Function</td>
</tr>
</tbody>
</table>

*(Osiecki, Meeke & Smith, 2005, p. 25)*
# Nervous System

<table>
<thead>
<tr>
<th>NT</th>
<th>Main Precursors</th>
<th>Usage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycine</td>
<td>Glycine</td>
<td>Inhibitory amino acid NT. Aids in sleep, pain, production of endorphins</td>
</tr>
<tr>
<td>Histamine</td>
<td>Histidine, Vitamin B6</td>
<td>Improves resistance to stress &amp; anxiety (increases alpha brainwaves). Generates wakefulness.</td>
</tr>
<tr>
<td>Aspartic acid</td>
<td>Aspartic acid</td>
<td>Excitatory amino acid NT in the SC. Made from glutamic acid</td>
</tr>
<tr>
<td>Adenosine</td>
<td>All cells of the body</td>
<td>Inhibitory NT involved in sleep. Neuroprotective agent and is essential for energy production. Inhibits the release of glutamic acid &amp; aspartic acid.</td>
</tr>
</tbody>
</table>

(Osiecki, Meeke & Smith, 2005, p. 25)
By Amie Steel (Adapted from Bhagavan, 2002 & ExPASy, 2007)
Phenylalanine → Tyrosine → L-dopa → Dopamine → Noradrenalin → Adrenalin → Vanillic Acid

Key enzymes and co-factors:
- Phenylalanine monoxygenase
- Tyrosine monoxygenase
- Aromatic amino acid decarboxylase
- Dopamine β-hydroxylase
- Methyltransferase
- Monoamine oxidase

Co-factors and cofactors:
- Tetrahydrobiopterin (BH₄), Folate, vitamin C, Fe
- Fe, B₆, BH₄, B₃
- B₆, Mg
- Cu, Vitamin C
- SAMe (B₁₂, folate, methionine)
- B₂

Related compounds:
- Melanin
- Thyroid hormones
- Tetrahydrobiopterin (BH₄)
- Folate, vitamin C, Fe, B₆, B₃, Cu, Vitamin C
- SAMe (B₁₂, folate, methionine)
- B₂

By Amie Steel (Adapted from Gropper et.al. 2005)
Stress
Stress

- Defined as any disturbance that may be caused by:
  - Heat or cold
  - Chemical toxin
  - Micro-organisms
  - Physical trauma
  - Strong emotional reaction

- Such disturbances can trigger the stress response.
  (Pizzorno & Murray, 2000)
Stress

- The *General adaption syndrome* is composed of three phases:
  - Alarm
  - Resistance
  - Exhaustion

- These phases are largely controlled and regulated by the adrenal glands.

(Pizzorno & Murray, 2000)
# Stress

<table>
<thead>
<tr>
<th>Alarm</th>
<th>Resistance</th>
<th>Exhaustion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased secretion of glucocorticoids</td>
<td>Glucocorticoid secretion returns to normal</td>
<td>Increased glucocorticoid secretion but eventually marked decreased secretion</td>
</tr>
<tr>
<td>Increased activity of sympathetic nervous system</td>
<td>Sympathetic activity returns to normal</td>
<td>Stress triad (hypertrophied adrenals, thymus &amp; lymph nodes, ulcers in stomach &amp; duodenum)</td>
</tr>
<tr>
<td>Increased noradrenaline secretion by adrenal medulla</td>
<td>Noradrenaline secretion returns to normal</td>
<td></td>
</tr>
<tr>
<td>Fight-or-flight syndrome of changes</td>
<td>Fight-or-flight syndrome disappears</td>
<td></td>
</tr>
<tr>
<td>Low resistance to stressors</td>
<td>High resistance (adaptation) to stressor</td>
<td>Loss of resistance to stressor; may lead to death</td>
</tr>
</tbody>
</table>

(Thibodeau & Patton, 2007)
Stress

Alarm Reaction

- ‘Fight or flight response’
- Triggered by reactions in the brain which ultimately cause the pituitary gland to release adrenocorticotropic hormone (ACTH). ACTH causes the adrenals to secrete adrenaline and other stress-related hormones.
- The aim of the alarm reaction is to counteract danger by mobilizing the body’s resources for immediate physical activity.

(Pizzorno & Murray, 2000)
Stress

Resistance Reaction

- Continues the response of ‘fighting a stressor’ long after the short lived effects of the alarm phase. Cortisol and other corticosteroids are responsible for the resistance reaction (convert protein to energy and promote the retention of sodium, to keep blood pressure elevated).

- The resistance reaction provides the changes required for meeting emotional crisis, performing strenuous tasks and fighting infection.

- Prolonged resistance reaction or continued stress increases the risk of diseases, such as diabetes, hypertension and cancer.

(Pizzorno & Murray, 2000)
Stress

Exhaustion
- May be partial or total collapse of a body function or specific organ.
- Two of the major causes of exhaustion are loss of potassium ions and depletion of adrenal glucocorticoid hormones like cortisone.
- The loss of potassium results in cellular dysfunction and possible cell death.
- Adrenal glucocorticoid store depletion decreases glucose control, resulting in hypoglycemia.
- Prolonged stress places a tremendous load on many organ systems, especially the heart, blood vessels, adrenals and immune system.

(Pizzorno & Murray, 2000)
Stress

Tryptophan & Cortisol

- Tryptophan depletion leads to a decrease in morning cortisol in obsessive compulsive patients and insomniacs
- This may be related to lower production of serotonin in tryptophan depleted patients
- Evening cortisol was not affected

(Vielhaber et al, 2005)
Stress

Nutritional Treatment
Lifestyle management is the cornerstone of treatment for stress
- Elimination of stimulant or mind altering food/drink, refined carbohydrates and sugars
- Increase protein & complex carbohydrates
- Regular meals and snacks
- Improve potassium to sodium ratio
- Identify and eliminate food intolerances
- Stress management techniques

(Pizzorno & Murray 2000)
### Stress

<table>
<thead>
<tr>
<th>Supplement</th>
<th>Range</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin C</td>
<td>500-5,000mg</td>
<td>Major nutrient required by the adrenal gland. Co-factor for the production of neurotransmitters</td>
</tr>
<tr>
<td>Vitamin B5</td>
<td>200-500mg</td>
<td>Adrenal function. Synthesis of steroid hormones</td>
</tr>
<tr>
<td>Vitamin B6</td>
<td>50-150mg</td>
<td>Adrenal function. Synthesis of steroid hormones</td>
</tr>
<tr>
<td>Zinc</td>
<td>10-100mg</td>
<td>Rate limiting co-factor in neurotransmitter synthesis</td>
</tr>
<tr>
<td>Magnesium</td>
<td>300-1000mg</td>
<td>Rate limiting co-factor in neurotransmitter synthesis. Co-factor in energy production. Neuromuscular transmission</td>
</tr>
</tbody>
</table>
Nutritional and Holistic approaches to Pain Management
Pain

Prevalence

- Australian adults with chronic pain were 17.1% of males and 20.0% of females. Prevalence increased with age.
- Most of these reported that the pain interfered with their daily lives
- Pain is highly subjective and has both sensory and emotional aspects
- The sensation of pain involves peripheral and central nerve pathways
- The psychological component or emotional response will be influenced by other factors such as anxiety levels, age, sex, culture, previous pain experiences

(Blyth et al, 2001; Bryant & Knights, 2011)
<table>
<thead>
<tr>
<th>LOWERS pain threshold = more perceived pain</th>
<th>RAISES pain threshold = less perceived pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anger</td>
<td>Diversion</td>
</tr>
<tr>
<td>Anxiety, fear, fright</td>
<td>Anti-anxiety agents</td>
</tr>
<tr>
<td>Tiredness &amp; sleeplessness</td>
<td>Sleep, rest</td>
</tr>
<tr>
<td>Depression</td>
<td>Anti-depressant agents</td>
</tr>
<tr>
<td>Isolation</td>
<td>Empathy</td>
</tr>
<tr>
<td>Pain</td>
<td>Anesthetics, analgesics</td>
</tr>
</tbody>
</table>

(Bryant & Knights, 2011)
Pain

Acute Pain
  o Severe discomfort, generally sharp, localised, may radiate, sudden onset
  o Associated with anxiety, restlessness, ↑heart rate, ↑blood pressure, sweating, pallor
  o Pain anticipated to last typically < 1 month

Chronic Pain
  o Persistent of recurring pain ( > 3 months)
  o Dull aching, diffuse (poorly localized)
  o Person may be depressed, withdrawn, expressionless, exhausted

(Bryant & Knights, 2011)
Pain

Pain Management

- Treat the cause where possible
- Try to keep the patient pain-free (combination of orthodox and complementary). Faster recovery if pain is relieved, rather than having to “suffer” until the next dose
- Dose at regular specified intervals, especially for chronic pain
- Avoid the chronic pain stress cycle. Antidepressants or nutrients that support inhibitory neurotransmitters may be beneficial in some patients and may assist with better sleep patterns
- Prevent adverse opioid drug side effects

(Bryant & Knights, 2011)
Pain

- Nociceptors convert mechanical, thermal or chemical stimulations that injure or threaten body’s tissues into nerve impulses that generate sensation of pain via Peripheral Nervous System (PNS) to spinal cord
- Spinal cord releases substance P which activates neurons which transmit further nerve impulses of pain to the brain
- Norepinephrine & serotonin are both released & reduce release of substance P
- Serotonin stimulates release of opioids which reduce sensation of pain & reduce release of substance P

(Bryant & Knights, 2011)
# Pain Categories

<table>
<thead>
<tr>
<th>Nociceptive</th>
<th>Neuropathic</th>
<th>Pain matrix dysfunction</th>
<th>Pain syndromes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanical LBP</td>
<td>Nerve entrapment and compression Avulsion dorsal roots</td>
<td>Fibromyalgia</td>
<td>Complex regional pain syndrome</td>
</tr>
<tr>
<td>Cancer</td>
<td>Phantom limb pain Central pain: Multiple sclerosis Spinal cord injury Stroke</td>
<td>Chronic whiplash-associated disorder Headache: Migraine Episodic tension-type</td>
<td>Chronic LBP syndrome</td>
</tr>
<tr>
<td>Arthritis</td>
<td>Small fiber neuropathy: Diabetic neuropathy Guillain-Barré Post-herpetic pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burns</td>
<td></td>
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</tbody>
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Pain

Nociceptive Pain

- Neural activity is normal and appropriate – this is the transmission of information regarding tissue damage or threat of damage
- Arises from stimulation of deep or superficial nociceptors
- Throbbing, burning, stinging, dull ache. Deep, diffuse, nagging. May be referred
- E.g. mechanical lower back pain, cancer pain, arthritis pain burns.
- Somatic pain responds best to NSAIDs, visceral pain responds best to opioid analgesics

(Bryant & Knights, 2011)
Pain

Nociceptive Pain

- Somatic nociceptive pain arises from bone, joint, muscle, skin, or connective tissue.
- Direct trauma to tissues is the typical cause of this type of pain.
- Visceral pain arises from visceral organs like the gastrointestinal tract or pancreas.
- Visceral nociceptive pain may arise from the organ or capsule or from obstruction of a hollow viscus causing intermittent, poorly localized pain.

(Goci et al, 2013)
Nociceptive Pain

Role of cytokines in sensitisation of nociceptors during inflammation and the underlying mechanisms leading to hyperalgesia.

Two key pathways involved:

- Cox 2
- B2-adrenoceptors (bradykinin)
- Also histamine & serotonin,

Glucocorticoids inhibit the synthesis of cytokines and activation of Cox-2.

Image: Wall and Melzack, 2013
Peripheral Sensitisation

• Sensitization of peripheral nociceptors as a mechanism underlying the increased sensitivity to subsequent stimulation that takes place following tissue injury.

• Chemical mediators released into the tissues because of tissue injury promote sensitization of peripheral nociceptors.

• One of the most fundamental influences on nociceptor sensitivity is the pH of the surrounding tissue.

• Combinations of inflammatory mediators, plus chemical mediators with altered tissue pH, appear to be more effective in inducing sensitization than individual chemical mediators.

Image: Maciewicz and Wittink, 1997
Pain

Neuropathic Pain
- Pathologic neural activity – pain is a disease rather than a symptom. Caused by neurochemical, gene expression or arises from a primary lesion, alteration or dysfunction (injury) of PNS or CNS.
- Burning, shooting and/or tingling pain.
- Includes pains such as post-herpetic neuralgia, limb amputation, diabetic neuropathy
- Does not always respond well to opioid analgesics
- Other forms of drugs may be needed as adjunctive therapies such as anticonvulsants, local anaesthetics or tricyclic antidepressants

(Bryant & Knights, 2011)
Pain

Pain Matrix Dysfunction

- Dysregulation of pain excitatory and inhibitory mechanisms in CNS
- Diffuse deep pain, hyperalgesia, allodynia
- E.g. fibromyalgia, episodic tension-type headache, migraine

(Bryant & Knights, 2011)
Pain

Non Pharmacological Analgesia
- RICE
- Massage, physical therapy
- Counter irritants
- TENS
- Acupuncture
- Psychotherapy
- Surgery
- Support groups
- CAM

(Kumar & Clark, 2009)
Pain

Gate Control Theory

- The dorsal horn of the spinal cord (‘gate’) allows pain sensations to be sent to the thalamus and the cortex of the brain.
- An ‘open gate’ shows increased sensitivity to pain.
- A ‘closed gate’ has diminished nerve reception of pain.
- TENS, ice applications and rubbing have been found to inhibit pain transmission.
- Endogenous opioids (enkephalins, endorphins and dynorphins) can modify a pain sensation.

(Bryant & Knights, 2007)
B. GATE CLOSED – PAIN STIMULUS BLOCKED

1. Painful stimulus

2. Interneuron activated by:
   - Efferent impulses from the brain
   - Afferent impulses from touch stimulus

3. Interneuron releases Enkephalin

4. Opiate receptors blocked by Enkephalin

5. Substance P not released

6. Gate closed transmission blocked on afferent tract

Other sites for endorphin and enkephalin release

Afferent touch a-beta thick fibers

Afferent pain fiber

Nociceceptor

Substance P neurotransmitter

Enkephalin
Central Sensitivity Syndromes

- A concept based on many common abnormalities shared by chronic pain conditions this is a “top-down” pathophysiological model of stress-related disorders
- Alterations in the central stress circuits in susceptible individuals play a primary role in the pathogenesis of symptoms
- Two main disturbances include alterations in serotonergic system and dysregulation of the HPA-axis.
- Abnormalities in the level of other neurotransmitters have also been suggested such as noradrenaline, dopamine, endocannabinoid deficiency, and the increase of substance P (SP) in the spinal fluid
Pain

○ Once the CNS hyper-reactivity becomes expressed, any or all the effector arms (e.g., increased visceral nociception, neurogenic inflammation, neuroendocrine disturbances and autonomic dysfunction) can be involved. (Larauche, Mulak and Tache, 2012)

• Psychogenic and immune stress can induce HPA activating (neuroendocrine) and neurotransmitter changes in the brain and increase brain sensitisation to subsequent stress = increased stress vulnerability

• Increased stress can impact on pain perception as well as reducing regulatory mechanisms that reduce pain via suppressing inflammation (Silverman and Sternberg, 2012)
Pain / Inflammation / HPA axis

- High IL6 and TNFa = exaggerated activation of HPS axis
- The pro-inflammatory cytokines stimulate glucocorticoid (GC) release by acting on all 3 levels of HPA axis
- Cortisol reduces regulation of inflammatory response
- HPA axis disturbance at any level can lead to hypocortisolism or impairments in local factors affecting GC availability and function including at the site of glucocorticoid receptors (GCR).
- GCR can cause GC resistance by preventing cells and tissue from responding adequately

(Silverman and Sternberg, 2012)
Pain / Inflammation / HPA axis

• Cortisol availability at the cellular level is influenced by various local factors and leads ultimately to reduced expression or binding affinity.
• Even when the concentration of GC is normal or high, impaired counter regulatory control of immune responses can still occur at a cellular level.
• Causes of Glucocorticoid Resistance:
  – Polymorphism or mutation
  – Chronic inflammation +++
  – Exposure to infectious agents
  – Chronic stress
  – Chronic exposure to exogenous GC

(Silverman and Sternberg, 2012)
<table>
<thead>
<tr>
<th>Supplement</th>
<th>Dosage</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chondroitin Glucosamine Green lipped mussel extract</td>
<td>1200mg 1500mg 500-3000mg</td>
<td>Arthritic pain. Reduces tumor necrosis factor-α (TNFα), nitrous oxide (NO) and prostaglandin E2 (PGE2) production to give analgesic action</td>
</tr>
<tr>
<td>SAMe</td>
<td>200-800mg</td>
<td>Arthritis. Analgesic (conversion of SAMe to spermidine &amp; spermine is analgesic &amp; anti-inflammatory)</td>
</tr>
<tr>
<td>Fish oil</td>
<td>1,000-6,000mg</td>
<td>Ω-3 encourage anti-inflammatory metabolite production in cell membranes and reduce the expression of cell adhesion molecules. Anti-inflammatory action</td>
</tr>
<tr>
<td>d-Phenylalanine</td>
<td>150-600mg</td>
<td>Inhibits enkephalinase to stop the breakdown of endogenous opioids</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>300-4000mg</td>
<td>Essential amino acid in serotonin production – serotonin stimulates the release of endogenous opioids</td>
</tr>
</tbody>
</table>

(Edmonds et.al. 1997; Bottiglieri, 2002; Osiecki, 2006; Braun & Cohen, 2010)
<table>
<thead>
<tr>
<th>Supplement</th>
<th>Dose</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin E</td>
<td>100-1000iu</td>
<td>Anti-inflammatory action, neuroprotective</td>
</tr>
<tr>
<td>N-acetyl Cysteine</td>
<td>100-1,500mg</td>
<td>Increases glutathione levels. Management of post-endodontic (root canal) pain due to reduction of IL-6, TNFα and IL-17</td>
</tr>
<tr>
<td>Vitamin B6</td>
<td>100mg</td>
<td>Neuroprotective, Orofacial pain, hyperalgesia</td>
</tr>
<tr>
<td>Acetyl L-Carnitine</td>
<td>3000mg</td>
<td>Symptomatic pain relief and improves nerve conduction and regeneration, mitochondrial preservation</td>
</tr>
<tr>
<td>Lipoic Acid</td>
<td>600mg</td>
<td>ALA &amp; LA encourage the production of anti-inflammatory eicosanoids in cell membranes. Reduces AGE formation in diabetic peripheral neuropathy</td>
</tr>
<tr>
<td>Lactobacillus rhamnosus GG</td>
<td>10-40 billion CFU</td>
<td>Abdominal Pain (Functional), NSAID use (erosive gastritis)</td>
</tr>
<tr>
<td><strong>Pain:</strong></td>
<td></td>
<td></td>
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<tr>
<td>---</td>
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</tr>
<tr>
<td>Garlic</td>
<td>900mg</td>
<td>Anti-inflammatory. Inhibits COX-2, NO &amp; NF-kappa activation</td>
</tr>
<tr>
<td>Ginger</td>
<td>1-2gms</td>
<td>Anti-inflammatory. Inhibits NO, COX-1 &amp; COX-2, LOX, TXA2, PGE2 synthesis</td>
</tr>
<tr>
<td>Turmeric</td>
<td>2g daily dose extract</td>
<td>Anti-nociceptive effect by acting on the dorsal root ganglia, acts via opioid receptors and attenuates the effect of the release of NO. Anti-inflammatory.</td>
</tr>
<tr>
<td>Quercetin</td>
<td>600-3000mg</td>
<td>Neuroprotective via modulation of inflammatory mediators</td>
</tr>
</tbody>
</table>
| Capsaicin | 0.025% - 0.075% capsaicin gel | pain-sensitive nerves, neuropathic pain syndromes Shingles, diabetic neuropathy, joint pain – osteoarthritis  
(Braun & Cohen, 2010; Goci E, et al, 2013) |
## Pain

<table>
<thead>
<tr>
<th>Drug</th>
<th>Action</th>
<th>Side Effects</th>
<th>Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioids:</strong></td>
<td>Opioid receptor inhibitor (reduce substance P from dorsal horn neurons)</td>
<td>CNS: Suppress respiratory centre &amp; the cough reflex, sedation, dysphoria, miosis (constriction of pupil), nausea, vomiting, hypotension, bradycardia, prolonging labour. Tolerance, dependence &amp; addiction PNS – constipation, sphincter muscle spasm, spinal reflex suppression, Histamine release can cause bronchoconstriction &amp; formication.</td>
<td><strong>L-tyrosine:</strong> Can increase analgesia. Additive effect.  <strong>Fibre:</strong> May prevent gastric upset and constipation. Concurrent use of water, fibre, and water rich foods may be beneficial.  <strong>Alcohol:</strong> Impaired alertness, constipation, impaired judgment</td>
</tr>
<tr>
<td>Opium,</td>
<td>Euphoric action inhibits pain perception.</td>
<td></td>
<td></td>
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<tr>
<td>Morphine,</td>
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<td></td>
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<tr>
<td>Codeine,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxycodone,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pethidine,</td>
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<td></td>
<td></td>
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<tr>
<td>Tramadol</td>
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(Bullock et.al. 2007; Braun & Cohen, 2010; Bryant & Knights, 2011)
## Pain

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<tbody>
<tr>
<td>Non-Opioid Analgesics:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paracetamol</td>
<td>Inhibits prostaglandin production within the CNS, with some COX inhibition (no anti-inflammatory benefits) giving it analgesic and antipyretic properties.</td>
<td>Skin rash &amp; nausea Overdose (10-15gms or 20-30 tablets) will cause severe liver damage due to depletion of glutathione, and possibly lead to death. Not effective for lower back pain.</td>
<td>Alcohol: greater potential to cause liver damage when taken together</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Vitamin C: prolong the amount of time paracetamol stays in the body</td>
</tr>
<tr>
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<td></td>
<td>Beta-Carotene: reduces toxic effects</td>
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<td></td>
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<td></td>
<td>Quercetin, Taurine and thioproline, Oleanolic acid, OPCs (Grape seed), N-acetyl cysteine, methionine and SAMe: reduce liver damage from toxicity by stimulating glutathione production</td>
</tr>
</tbody>
</table>

(Bullock et.al. 2007; Braun & Cohen, 2010; Bryant & Knights, 2011)
## Pain

<table>
<thead>
<tr>
<th>Drug</th>
<th>Action</th>
<th>Side Effects</th>
<th>Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Steroidal Anti-inflammatory Drugs</td>
<td>Anti-inflammatory via inhibition of prostaglandins through the reduced release of cyclo-oxygenase enzymes (aspirin, ibuprofen). Used for Acute coryza, influenza, sinusitis, tonsillitis</td>
<td>Dyspepsia, nausea, vomiting, diarrhoea/constipation, gastritis due to inhibition of mucous productive prostaglandins.</td>
<td>Nutrients with COX inhibitory effect (Vitamin E &amp; fish oil etc..): additive pain relief</td>
</tr>
<tr>
<td>(NSAID’s): ibuprofen, aspirin, diclofenac, indomethacin, piroxicam</td>
<td></td>
<td></td>
<td>Garlic, Ginger, Grapeseed, Turmeric: increased blood thinning when used with aspirin.</td>
</tr>
<tr>
<td></td>
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<td>Vitamin C: reduced absorption with aspirin.</td>
</tr>
</tbody>
</table>

(Kumar Clark, 2005; Bullock et.al, 2007; Bryant & Knights, 2011)
## Pain

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<thead>
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<tbody>
<tr>
<td>COX-2 selective NSAIDs: Celecoxib</td>
<td>COX-2 is formed in inflammatory conditions. Don’t inhibit COX-1 so have no GIT side effects or alter platelet aggregation. Useful for patients that can’t use non-specific NSAIDs.</td>
<td>Increased risk of cardiovascular &amp; thrombotic adverse effects. Renal damage due to inhibition of vasodilator prostaglandins resulting in heart failure and hypertension in some patients.</td>
<td>Nutrients with COX inhibitory effect (Vitamin E &amp; fish oil etc..): additive pain relief</td>
</tr>
</tbody>
</table>

(Bullock et.al, 2007; Bryant & Knights, 2011)
Pain

Adjuvant Analgesics

Depending on the cause and type of pain, adjuvant therapies may be indicated. These include:

- Tricyclic antidepressants (neuropathic pain)
- Corticosteroids (pain associated with inflammation, and space occupying lesions)
- Psychotropic drugs
- Bisphosphonates (osteoporotic drugs)
- Clonidine (antihypertensive)
- Capsaicin
- Ketamine
- Gabapentin (anti-seizure medication and also used for neuralgia.

(Bryant & Knights, 2011)
References


References


References

Thibodeau, GA & Patton, KT (2007), Anatomy and physiology. 6th ed. Mosby, St. Louis


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