Introduction To Analgesics And Pain:

Analgesics:

Analgesics can be defined as "Drugs that relieve pain by acting at some points in pain signaling mechanisms."
Analgesics treat psychological and emotional factors as well.
For veterinary Medicines a similar terminology is used i.e Anti-nociceptive.

Now What is Pain?

Pain:

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. It is also considered as a complex body response to noxious (Harmful, Injurious) stimuli followed by emotional response to it.
Pain is a subjective experience hard to define exactly, even though we all know what we mean by it.
Painful conditions that are directly not linked to tissue injury are called neuropathic pains. They are very common and are the major cause of disability and distress. The amount of pain that a particular stimulus produces depends on many other factors than the stimulus itself. With many pathological conditions tissue injury is the immediate cause of the pain. However in some cases the pain may be a false perception i.e a psychological one.

Classification Of Analgesics Drugs:

Pain killer Drugs can be classified into the following Major classes;

- **Centrally acting Analgesics**: Also called opioid analgesics (named from opium), opiates or Narcotic Analgesics. morphine is their prototype Drug.
- **Peripherally acting Analgesics**: They are also called Non-narcotic analgesics. NSAIDS are included in this category. However Paracetamol is An NSAID grouped under Analgesics.

These two major classes have further Extended subdivisions which will be discussed in this post.

Centrally acting opioid Analgesics:

Morphine its derivatives and its analogues are classified together under the term opioid or opioids. However there is a minor difference between these two terminologies. "opioids" refers to any opium like substance whether endogenous or synthetic which is able to produce morphine like effects and are antagonized by naloxone. on the other hand opiates term has been restricted to refer only to synthetic morphine like substances/drugs. opiates are chemically non-peptidergic in structure.

opoid analgesics are classified into the following classes.

- Naturally occurring opium alkaloids
• Partially synthetic derivatives of Morphine
• Synthetic Morphine Like drugs

**Naturally occurring opium alkaloids:**

The following list of drugs is included in naturally occurring opioids Analgesics.

- Morphine
- Codeine
- Thebaine
- Papaverine
- Nascapine

All these Drugs are obtained from **papaver somniferum** in crude form.

**Partially synthetic derivatives of morphine:**

This class includes the following Drugs;

- Heroin (diacetyl morphine)
- Codeine - Also used as cough suppressant.
- Ethyl morphine - cough suppressant property.
- Dihydrocodeine
- Hydrocodone
- Oxycodone
- Hydromorphone
- Oxymorphone
- Metopon
- Etorphine

**Synthetic Morphine like drugs:**

These analgesics are further classified into following subclasses

- **Phenyl pinedine series** - includes pethidine, fentanyl, sofentanyl and alfetanyl.
- **Methadone series** - Methadone and doxproprophoxyphein are included in this class of Methadone series.
- **Benzomorphan series** - Pentazocine, cyclazocine and loperamide are included in this class. Pentazocine is a partial agonist and should not be used with a full agonist i.e morphine. Loperamide is opioid however it has no analgesic effect because it cannot cross blood brain barrier. Loperamide is only used as antidiarrhoeal.

**Peripherally acting analgesics:**
Non-narcotic analgesics act peripherally. Commonly they are called NSAIDS (non-steroidal anti-inflammatory drugs), however NSAIDS and peripherally acting analgesics are different class of drugs. To be more specific NSAIDS and paracetamol are subclasses of peripherally acting analgesics (because majority of analgesics have anti-inflammatory properties as well. With exception of paracetamol which is peripherally acting analgesics having weak anti-inflammatory activity). They do not cause narcosis and dependencies so they are non-narcotic. The clinical uses of these drugs are as analgesics, antipyretics and as anti-inflammatory.

Mechanism of action of non-opioid analgesics:

The primary mechanism of action of non-opioid analgesics is based upon cox enzymes (cyclooxegenases). Cox enzymes are also called prostaglandins synthetazes.

There are three types of cox enzymes.

- **Cox-1 enzyme** – this is basic constitutive enzyme expressed in most tissues when needed in case of injury for pain signaling and hemostasis. Majority of analgesics side effects is due to cox-1 inhibition. When cox is blocked, more and more arachidonic acid will be available for other pathways like leukotrienes formation. That’s why aspirin should not be given to asthmatic patients.

- **Cox-2 enzyme** – its main function is cytoprotection it produce prostaglandins that produce mucous to protect epithelia. This enzyme is produced in inflammatory tissue, it is activated in cytokines such as tumour necrosis factor. Cox 2 release is as an inflammatory response and Nsaids action is mainly due to inhibition of this enzyme.

- **Cox-3 enzyme** – this enzyme is found in brain. (paracetamol act on this enzyme because of its dominant effect as anti-inflammatory in absence of peroxidases in brain tissues and because paracetamol is lipophilic).

Classification of non-opioid analgesics:

Analgesics are classified on two criteria;

1. Based upon cox enzyme selectivity.
2. Based upon the chemistry.

Classification based upon cox selectivity:

On basis of cox selectivity NSAIDS are classified into the following classes;

- **Relatively selective for cox-1 enzyme**: these will cause more side effects. Drugs included in this class are aspirin, endomethacine, piroxicin, sulindac, tolmetin.

- **Less selective for cox-1 enzyme**: ibufropin and paracetamol are in this class. Paracetamol is thought to have more cox-3 inhibition.
• **Equipotent on both enzymes:** naproxen, furbiprofin and diclofenac are equipotent on both cox 1 and 2 in terms of selectivity.

• **More selective for cox 2 enzyme:** these drugs are with least side effects and least ulcerative properties. Drugs included in this class are celecoxib, ruficoxib (withdrawn from market due to toxicities) and nimsulide.

**Classification based upon chemistry:**

On basis of chemistry nsaids are classified into following drugs classes.

• Salicylates
• Propionic acid derivatives – naproxen, ibufropin.
• Phenyl alkanoic acid derivatives – flurbiprofen.
• Indole derivatives.
• Pyrazolone derivatives.
• Phenyl acetic acid derivatives – Diclofenac.