Pain

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Definition

- Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage.

Classification

Pain classified

- Acute pain < 12 weeks
- Chronic pain > 12 weeks

- Surgical pain
- Non-surgical pain

- Nociceptive: caused by stimulation of nociceptors
- Neuropathic: caused by nerve damage

Types of pain

Nociceptive pain (most common)

Somatic:

Sharp

Hot, Stinging

Localized to injury site

Visceral:

Dull, Cramping, Colicky

Poorly localized

Might be referred

Neuropathic pain

History of peripheral/central nerve damage

Poorly localized
Spontaneous and paroxysmal
Phantom phenomena
Responds to neuropathic analgesia and poorly to opioids.

Transmission of pain

- Pain is sensed first by peripheral receptors
- Then it’s transmitted by various nerves to the central nervous system through (pathways).
- Perception and reflexes are initiated in the CNS (brain and spinal cord).

Nociceptive pain receptors

- **Nociceptors**: is a free, unmyelinated nerve ending capable of transmitting pain.
- They respond to:
- **K +**
- **Histamine**
- **Bradykinin**
- **Leukotrienes and prostaglandins** **Serotonin**

Types of nociceptive pain

- **Superficial or cutaneous pain**, due to skin damage and characterized by sharp, well localized pain.

- **Deep pain**, a dull aching and poorly localized pain arising from structures such as muscles, tendons and ligaments.

- **Visceral pain**, a dull, diffuse and poorly localized pain arising from the viscera; for example, spasm or overdistension of a hollow viscus.

Pain pathways

1- first order:

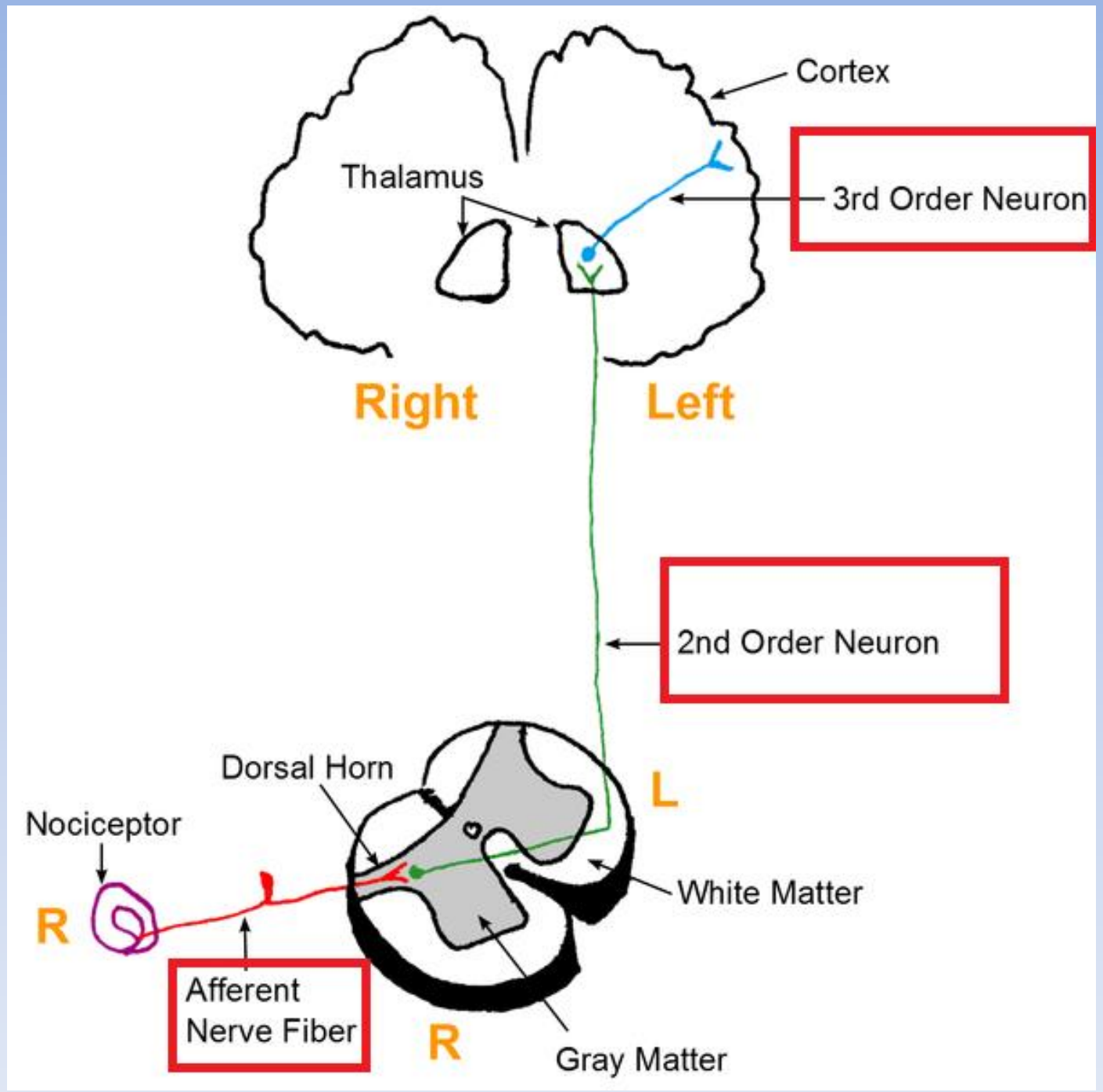
- From receptor to dorsal horn of spinal cord
- Via C or Aδ nerve fibers

2- second order:

- From dorsal horn to the thalamus, in the spinothalamic tract

3- third order:

- from thalamus to somatosensory cortex


Cortex
Thalamus
3rd Order Neuron
Right
Left
2nd Order Neuron
Dorsal Horn
L
Nociceptor
White Matter
R
Afferent
Nerve Fiber
R
Gray Matter

Neuropathic pain

- Might be caused by direct trauma to nerve
- And may be caused by systemic diseases
- Most common cause is Diabetes Milletus

Acute pain

- Pain caused by noxious stimulation from injury, a disease process, and usually lasts less than 3-6 weeks.
- Nociceptive pain serves to detect, localize, and limit tissue damage.

Types of Acute pain

I- Somatic pain:

- A- **Superficial somatic pain** from skin, subcutaneous tissues.
- well localized and described as a sharp, pricking, throbbing, or burning sensation.
- B- **Deep somatic pain** from muscles, tendons, joints, or bones.
- Pain usually has a dull, aching quality and is less well localized.

Types of Acute pain

II- Visceral pain:

- Caused by a disease process or abnormal function involving an internal organ or its covering (e.g., parietal pleura, pericardium, or peritoneum).
- Usually dull aching and poorly localized
- Might be localized or referred.

Chronic pain

- Defined as pain that persists beyond the usual course of an acute disease or after a reasonable time for healing to occur (1–6 months).
- May be nociceptive, neuropathic, or mixed.
- When the sympathetic system plays a major role, it is termed *sympathetically maintained pain*.

Systemic response to pain

Acute pain:

- Can affect nearly every organ function and may adversely affect perioperative morbidity and mortality
- **Cardiovascular:** Hypertension, tachycardia, enhanced myocardial irritability, may precipitate myocardial ischemia.
- **Respiratory:** Increase total body O2 consumption and CO2 production.
- **Gastrointestinal and urinary:** ileus and urinary retention.
- **Endocrine:** Increases catabolic hormones (catecholamines, cortisol, and glucagon) and decreases anabolic hormones.

Systemic response to pain

Chronic Pain

- Neuroendocrine stress response observed **only** in patients with severe recurring pain.
- Sleep and affective disturbances, particularly depression, are often prominent.

Evaluation of the Pain

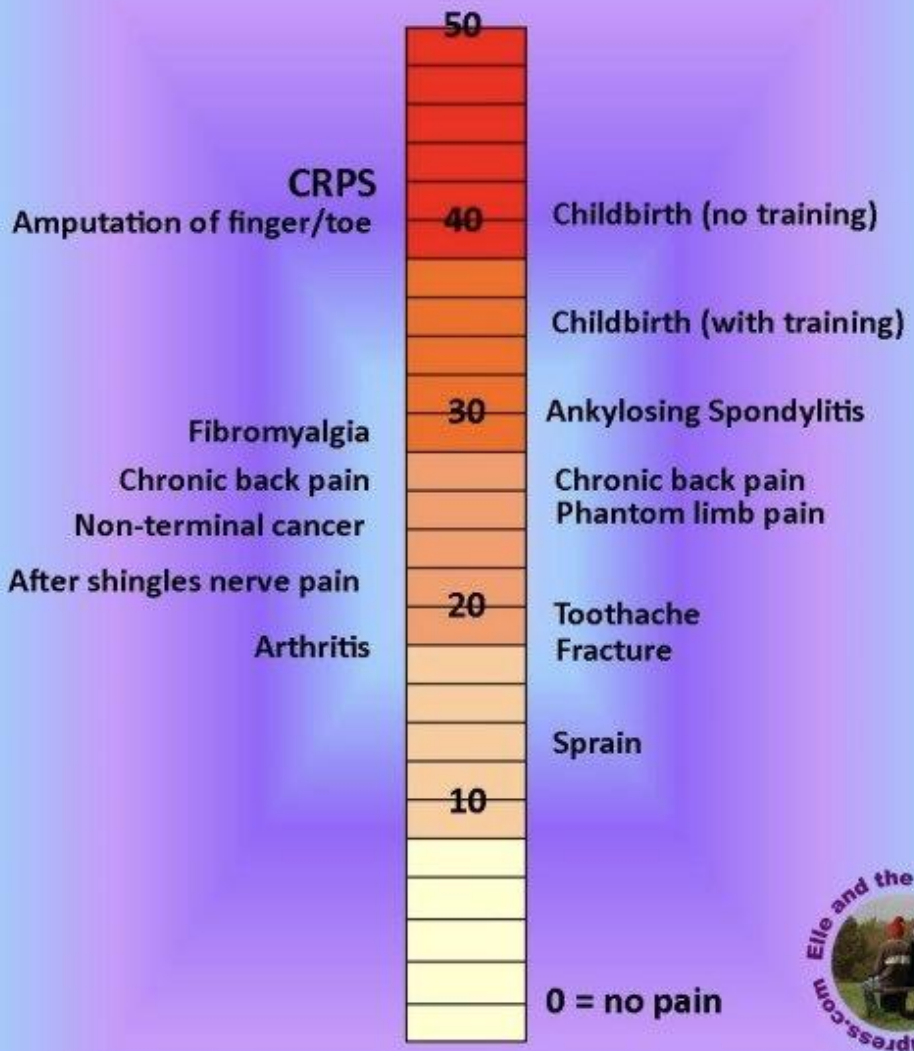
- **Pain Measurement**
- The numerical rating scale, Wong-Baker FACES rating scale, visual analog scale (VAS), and McGill Pain Questionnaire (MPQ) are most commonly used.

Measurement of Pain

- 1- visual analogue scale:
  the patient puts a mark on a 10cm scale that represents pain severity.
- 2- verbal rating scale:
  the patient describes the pain; mild, moderate or severe.
- 3- numeric rating scale:
  the patient rates the pain from 10.

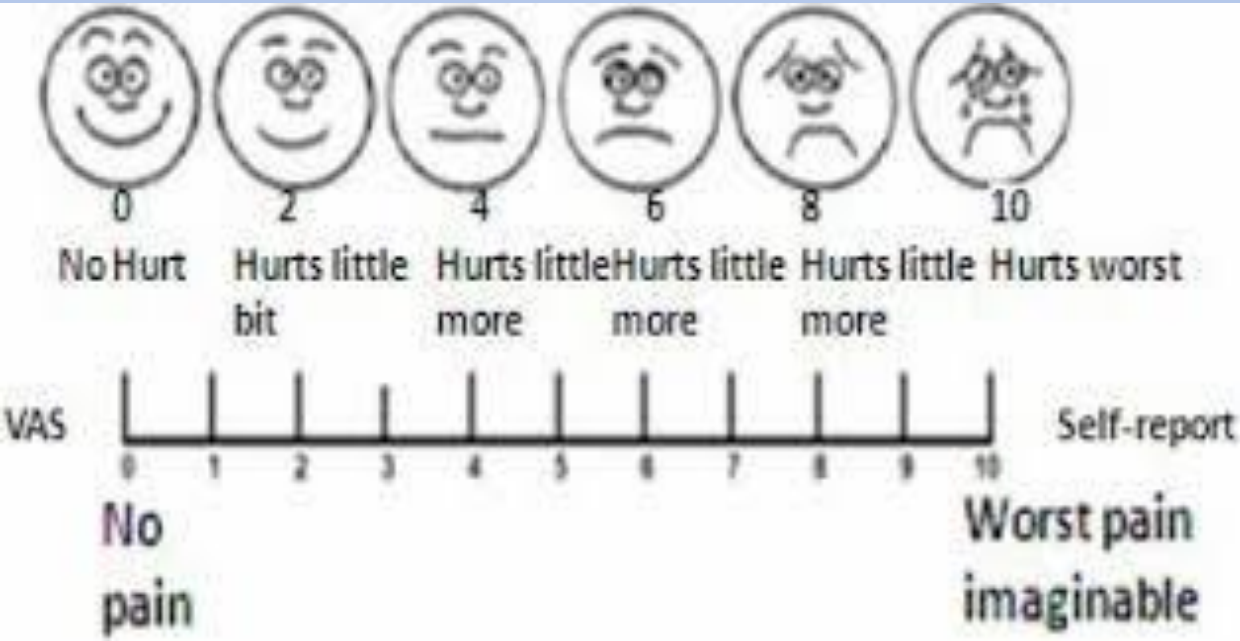
The McGill Pain Index

elleandtheautognome.wordpress.com



Rigorously tested scientific pain scale.
Overall score is determined by compiling various numerical and cross-referenced descriptive words, allowing direct comparison

Visual analogue scale



Psychological Evaluation

Most commonly used tests are:

- Minnesota Multiphasic Personality Inventory (MMPI)
- Beck Depression Inventory.

Other tools

- Mainly used for chronic pain
- **Electromyography and Nerve Conduction Studies**
- Distinguish between neurogenic and myogenic disorders.
- Useful for confirming the diagnosis of entrapment syndromes, radicular syndromes, neural trauma, and polyneuropathies,

Treatment of Pain

1- pharmacological treatment:

- Might be oral or injectable or as patches.
- NSAIDs, Paracetamol, Opioids, Neuroleptics, antispasmodics, corticosteroids.
- Good for acute and chronic pain


FENTANYL
50 mcg/hr

NHS Highland

Adult Oral Analgesic Step Ladder (Acute Pain)

Raigmore Hospital

Paracetamol
1g 4 times a day regularly
reduce dose to 15mg/kg if <50kg

If no contraindications
Add NSAID

Ibuprofen 400 mg 3 times a day
OR
Naproxen 500mg twice a day if required

PLUS

Paracetamol

Add Opioid

Tramadol MR 100mg twice a day and 50mg, 6 hourly PRN (Max. PRN 200mg in 24hours)

PLUS

NSAID

PLUS

Paracetamol

Opioid

STOP tramadol
START Oramorph 10 or 20 mg 1 hourly as required OR oxycodone 5 or 10mg 2 hourly

PLUS

NSAID

PLUS

Paracetamol

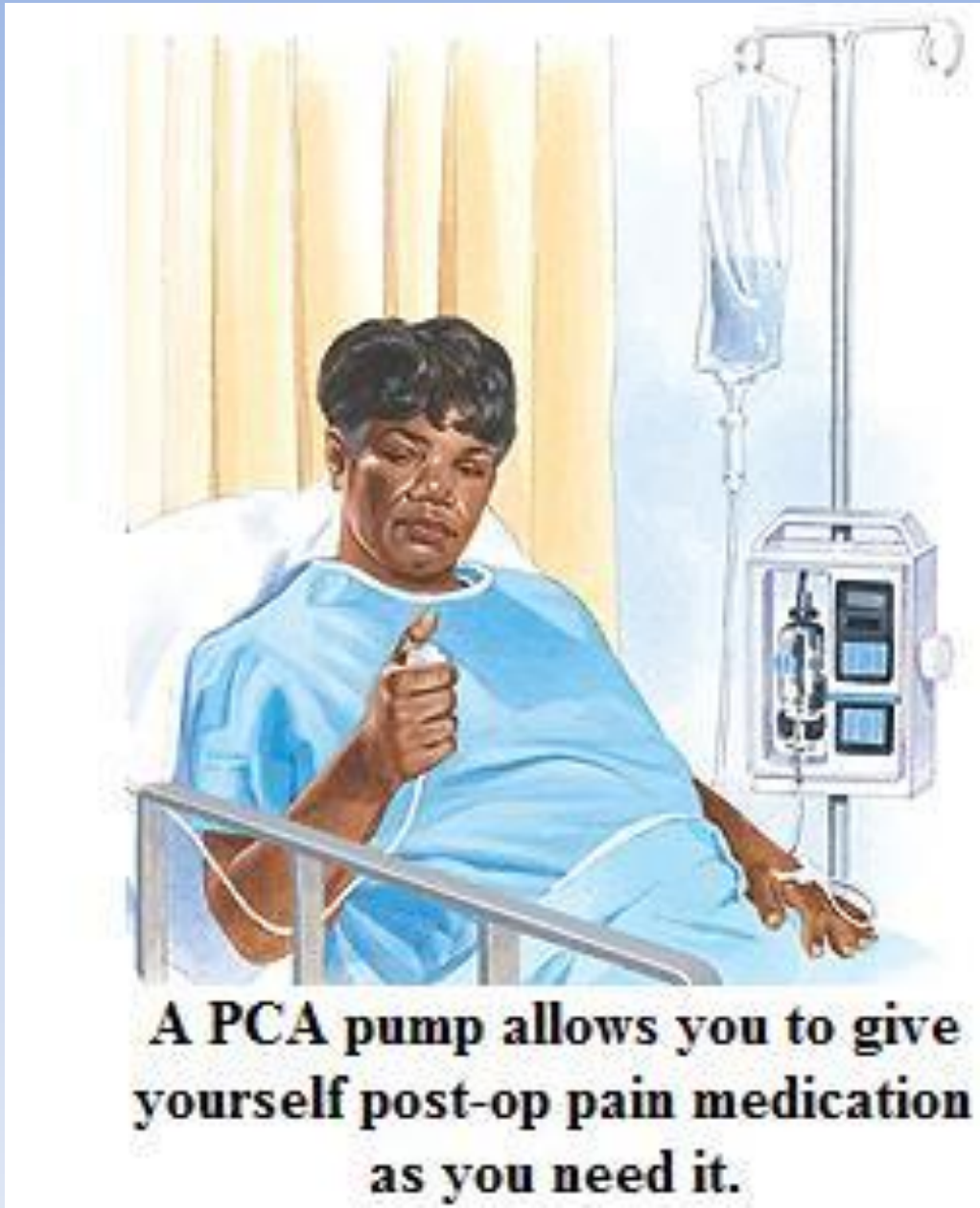
Mild Pain — Increasing Pain — Severe Pain

- IV paracetamol should be used when the patient is not reliably absorbing fluids.
- For patients at risk of respiratory despression, consider tramadol in preference to morphine.
- Patients with severe pain require parenteral opioids. Use PCA or the subcutaneous algorithm.

Responsibility:	Acute Pain Team
Last update :	Oct 2018
Review date :	Oct 2020

Medical Illustration.November 2018-00247

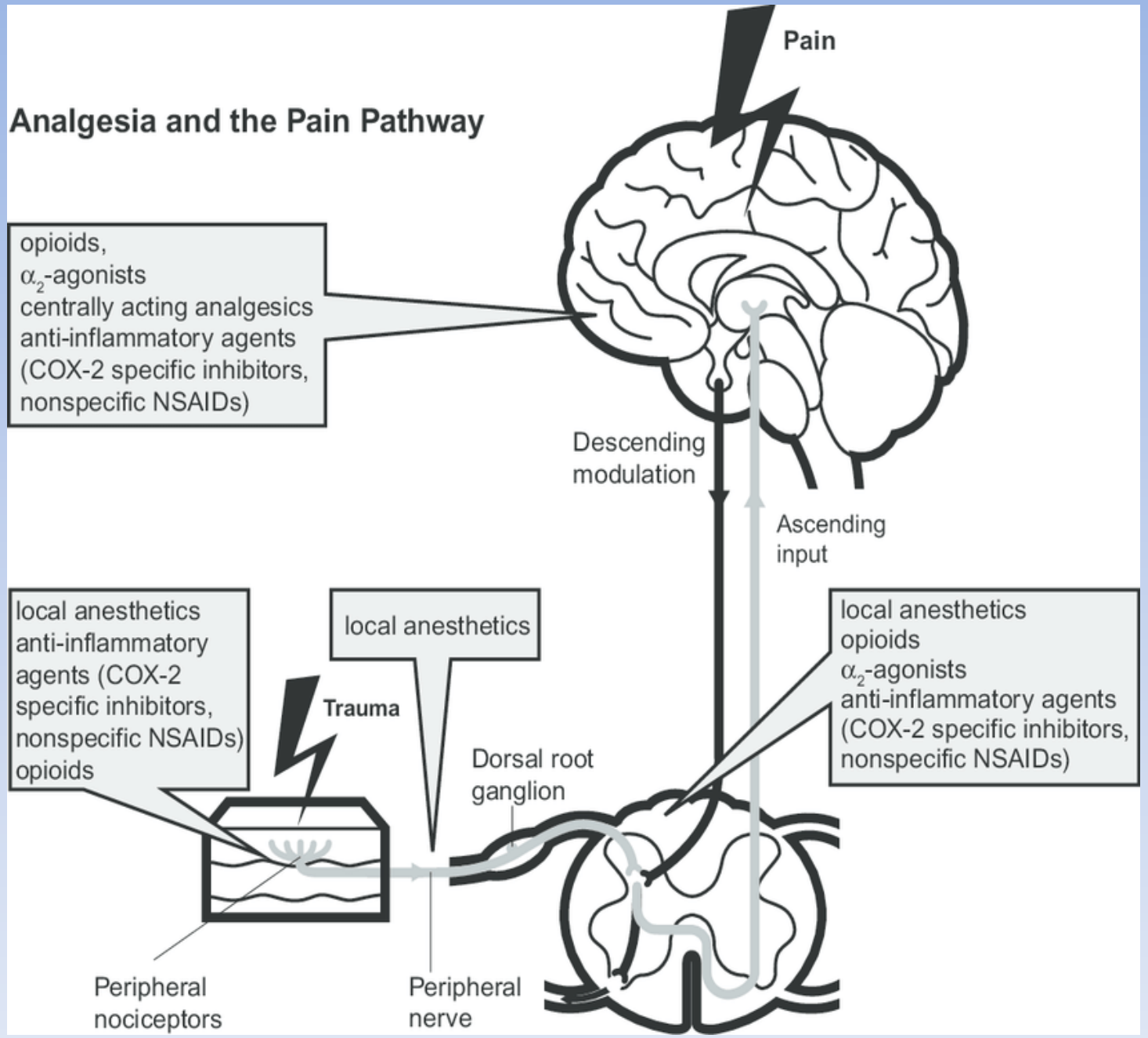
PCA


A PCA pump allows you to give yourself post-op pain medication as you need it.

Treatment of Pain

2- Peripheral and neuraxial nerve blocks.

- For acute and chronic pain
- Uses local anesthetics, steroids, alpha 2 agonists, and opioids,


Analgesia and the Pain Pathway
Pain
opioids,
α_2-agonists
centrally acting analgesics
anti-inflammatory agents
(COX-2 specific inhibitors,
nonspecific NSAIDs)
Descending
modulation
Ascending
input
local anesthetics
anti-inflammatory
agents (COX-2
specific inhibitors,
nonspecific NSAIDs)
opioids
local anesthetics
Trauma
Dorsal root
ganglion
local anesthetics
opioids
α_2-agonists
anti-inflammatory agents
(COX-2 specific inhibitors,
nonspecific NSAIDs)
Peripheral
nociceptors
Peripheral
nerve

Common blocks

Upper Extremity PNBs	Lower Extremity PNBs	Truncal Blocks
Cervical paravertebral	Subgluteal sciatic	Thoracic paravertebral
Interscalene	Femoral	Transverse abdominis plane
Interscalene	Popliteal	Ilioinguinal
Infraclavicular	Saphenous	
Axillary	Ankle	

Treatment of Pain

3- other tools for chronic pain

- Physiotherapy.
- Acupuncture.
- Cryoanalgesia.
- Radio-frequency ablation.
- Chemical neurolysis.

Opioids in a nutshell

BOX 31-1 *Classification of Opioid Compounds*

Naturally Occurring

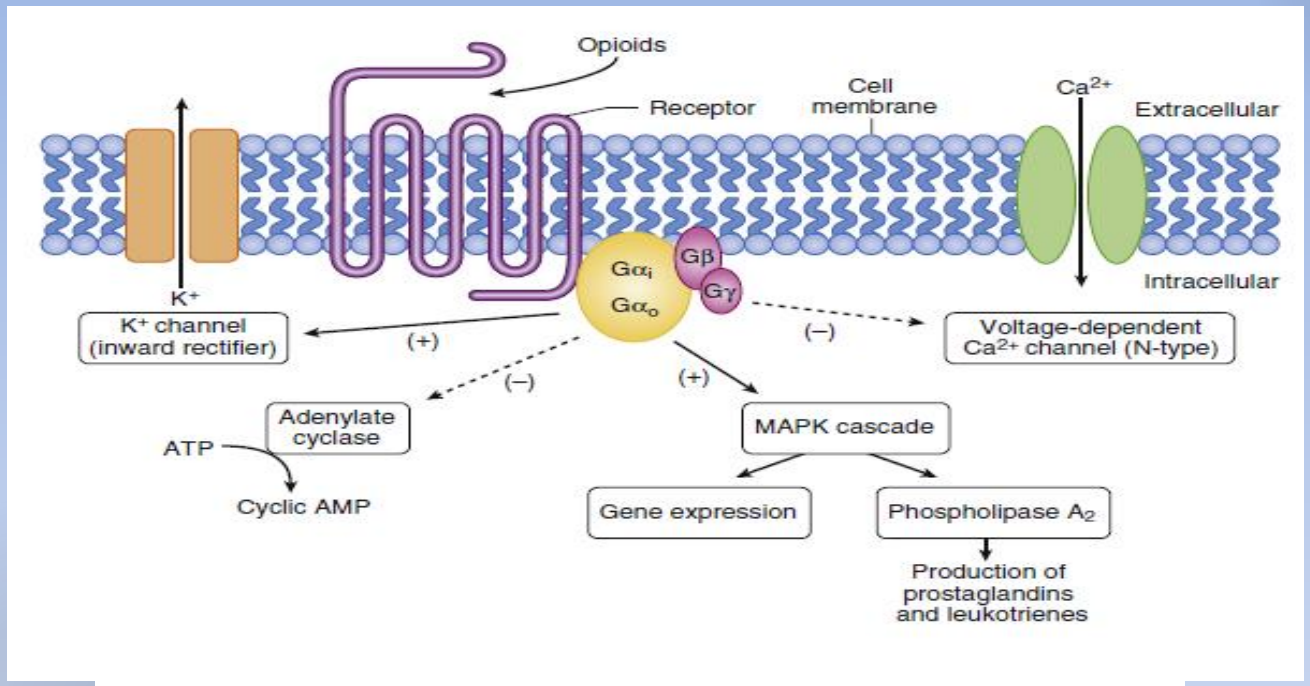
Morphine
Codeine
Papaverine
Thebaine

Semisynthetic

Heroin
Dihydromorphone, morphinone
Thebaine derivatives (e.g., etorphine, buprenorphine)

Synthetic

Morphinan series (e.g., levorphanol, butorphanol)
Diphenylpropylamine series (e.g., methadone)
Benzomorphan series (e.g., pentazocine)
Phenylpiperidine series (e.g., meperidine, fentanyl, sufentanil, alfentanil, remifentanil)



	μ	δ	κ
Agonist	Morphine, fentanyl, DAMGO	DPDPE, deltorphin,	Buprenorphine, pentazocine, U50488H
Antagonist	Naloxone, naltrexone	Naloxone, naltrindole	Naloxone, NorBNI

Opioids receptors

- opioids produce euphoria, tranquility, and other alterations of mood
- A significant feature of opioid analgesia is that it is not associated with loss of consciousness.
- Although nociceptive pain usually is responsive to opioid analgesics, neuropathic pain typically responds poorly to opioid analgesics and may require larger doses.

Effect on body systems

- 1-Miosis due to parasympathetic system activation
- 2- purities (Itching)
- 3- Bradycardia except
- meperdine (it has anticholinergic effects: 1- Mydriasis
- 2- no bradycardia and might even cause tachycardia

4- histamine release especially meperdine

5- vomiting and constipation

Hypercapnic responses	
hypoxic ventilatory drive	
ETCO2	
RR **********	
Tidal Volume	

Tolerance to opioids

- Tolerance develop most likely after long term use of opioids but can occur after short term use only.
- Tolerance to opioids might lead to hyperalgesia!!!!!!!
- Minimal tolerance to

1-meiosis

2- constipation

TABLE 31-5 PHYSICOCHEMICAL AND PHARMACOKINETIC DATA OF COMMONLY USED OPIOID AGONISTS

	Morphine	Fentanyl	Sufentanil	Alfentanil	Remifentanil
pK_a	8.0	8.4	8.0	6.5	7.1
% Un-ionized at pH 7.4	23	<10	20	90	67?
Octanol/H_2O partition coefficient	1.4	813	1778	145	17.9
% Bound to plasma protein	20-40	84	93	92	80?
Diffusible fraction (%)	16.8	1.5	1.6	8.0	13.3?
$t_{1/2\alpha}$ (min)	1-2.5	1-2	1-2	1-3	0.5-1.5
$t_{1/2\beta}$ (min)	10-20	10-30	15-20	4-17	5-8
$t_{1/2\gamma}$ (hr)	2-4	2-4	2-3	1-2	0.7-1.2
Vd_c (L/kg)	0.1-0.4	0.4-1.0	0.2	0.1-0.3	0.06-0.08
Vd_{ss} (L/kg)	3-5	3-5	2.5-3.0	0.4-1.0	0.2-0.3
Clearance (mL/min/kg)	15-30	10-20	10-15	4-9	30-40
Hepatic extraction ratio	0.6-0.8	0.8-1.0	0.7-0.9	0.3-0.5	NA

Morphine is principally metabolized by conjugation in the liver, but the kidney plays a key role in the extrahepatic metabolism of morphine.

- Onset: 1-2 min (IV)
- Peak effect: 3-5 min (IV) vs 20 min vs 90 minutes??? (different in multiple refernces)
- M6G accounts for nearly 10% of morphine metabolite and is a more potent μ-receptor agonist than morphine, with a similar duration of action.
- Especially in patients with renal dysfunction, the accumulation of M6G can lead to an increased incidence of adverse effects, including respiratory depression.

Fentanyl

- Fentanyl is relatively long acting, in large part because of this widespread distribution in body tissues.
- Norfentanyl, the primary metabolite
- Anesthetic induction is usually achieved by combining a loading dose of fentanyl (2 to 6 µg/kg)

Alfentanil

- At physiologic pH, alfentanil is mostly (90%) un-ionized because of its relatively low p*Ka* (6.5).
- Very fast onset

Sufentanil

- is twice as lipid soluble as fentanyl and is highly bound (93%) to plasma proteins, including α1-acid glycoprotein.
- some studies showed sufentanil is much better than morphine in decreasing M&Ms during and after cardiac surgeries.

Remifentanil

- remifentanil is structurally unique because of its ester linkages.
- Remifentanil's ester structure renders it susceptible to hydrolysis by blood- and tissue-nonspecific esterases that results in rapid metabolism and rapid reduction of blood concentrations after cessation of infusion
- Associated with emergence from remifentanil anesthesia, the need for alternative analgesic therapies should be anticipated, and these medications should be administered in a timely fashion.
- Remifentanil is not a good substrate for pseudocholinesterase and therefore is not influenced by pseudocholinesterase deficiency

TABLE 31-7 APPROXIMATE OPIOID LOADING (BOLUS) DOSES, MAINTENANCE INFUSION RATES, AND ADDITIONAL MAINTENANCE DOSES FOR TOTAL INTRAVENOUS ANESTHESIA

	Loading Dose (μg/kg)	Maintenance Infusion Rate	Additional Boluses
Alfentanil	25-100	0.5-2 μg/kg/min	5-10 μg/kg
Sufentanil	0.25-2	0.5-1.5 μg/kg/hr	2.5-10 μg
Fentanyl	4-20	2-10 μg/kg/hr	25-100 μg
Remifentanil	1-2	0.1-1.0 μg/kg/min	0.1-1.0 μg/kg

OTHER APPLICATIONS OF OPIOIDS

- Transdermal Therapeutic System
- Iontophoresis
- Transmucosal Drug Delivery (oropharynx and nasopharynx) (Sublingual, intranasal, inhaled, rectal)
- Extended-Release Epidural Morphine
- Orally:
- Despite the high first-pass metabolism of opioid analgesics

MEPERIDINE (PETHIDINE)

- Meperidine sometimes causes excitation of the CNS that is characterized by tremors, muscle twitches, and seizures largely caused by accumulation of a metabolite, normeperidine. (effect of renal failure)
- Has well-known local anesthetic properties.
- Meperidine (12.5 to 35 mg) is also effective for prevention and treatment of postoperative shivering

OPIOID ANTAGONISTS

- Clinically, opioid antagonists are used to reverse:
- 1-respiratory depression
- 2nausea and vomiting,
- 3- pruritus,
- 4-urinary retention
- 5-rigidity,
- 6- biliary spasm

- NALOXONE
- -it can enhance analgesia !!!!!
- Side effects (increases in heart rate and blood pressure) ,pulmonary edema)
- The onset of action of intravenous naloxone is rapid (1 to 2 minutes), and t½ and duration of effect are short, approximately 30 to 60 minutes.
- Also by Intratracheal administration
- Opioid reversal may be particularly hazardous in patients with pheochromocytoma or chromaffin tissue Tumors.
- Recurrence of respiratory depression after naloxone results from the short t½ of naloxone

Thank you