Pain

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Learning Objectives

- Define Pain.
- Describe The basic anatomy and physiology involved in pain transmission.
- Differentiate between nociception and pain experience.
- Differentiate between nociceptive and neuropathic pain.
- History, Examination and Assessment of Pain.
- Common Medications and Therapies for Pain.

Definition

- IASP, July 2020: Unpleasant sensory and emotional experience associated with -or resembling that associated with- actual or potential tissue damage.

1. Pain is always a personal experience. Influenced by biological, psychological, and social factors.
2. Through their life experiences, individuals learn the concept of pain.
3. A person's report of an experience as pain should be respected.
4. Pain has adverse effects on function and social and psychological well-being.
5. Verbal description is only one of several behaviors to express pain; inability to communicate does not negate that a human experiences pain.

Basic Terms

- Noxious: unpleasant.
- Noxious stimulus: A stimulus that is damaging or threatens damage to normal tissues.
- Nociceptor: A high-threshold sensory receptor of the peripheral somatosensory nervous system that is capable of transducing and encoding noxious stimuli.
- Nociception: The neural process of encoding noxious stimuli.
- Nociceptive pain: Pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors.
- Neuropathic pain: Pain caused by a lesion or disease of the somatosensory nervous system. (peripheral vs central).

Classification

There are several ways of classifying pain:

- By duration (acute (<12 weeks) vs chronic (> 12 weeks))
- By the underlying mechanism (nociceptive vs neuropathic) (sometimes mixed)
- By the physical origin (visceral vs somatic, referred pain)
- By its underlying cause (cancer, inflammatory, post-operative, mechanical pain)

Types of pain

Nociceptive pain

Somatic:

Sharp (somatic)

Throbbing

Ache

Localized to injury site

Visceral:

Dull, Cramping, Colicky

Poorly localized

Neuropathic pain

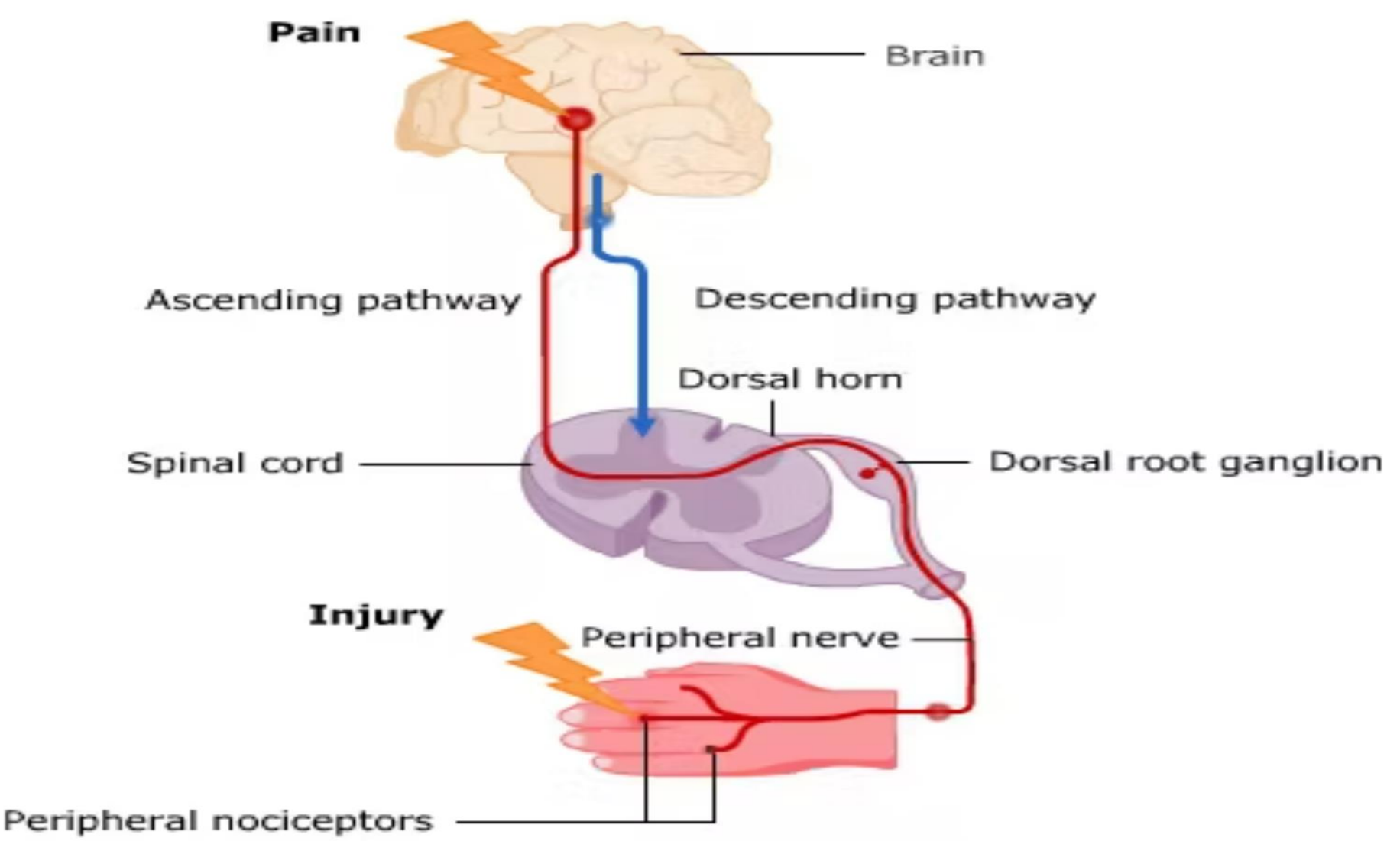
History of peripheral/central nerve damage

Systemic disease ex. DM

Poorly localized
Burning, shooting, crawling, electric shocks

Spontaneous and paroxysmal +/- paraesthesia, loss of sensation, weakness
Responds poorly to opioid.

Anatomy of pain



Physiology of Pain

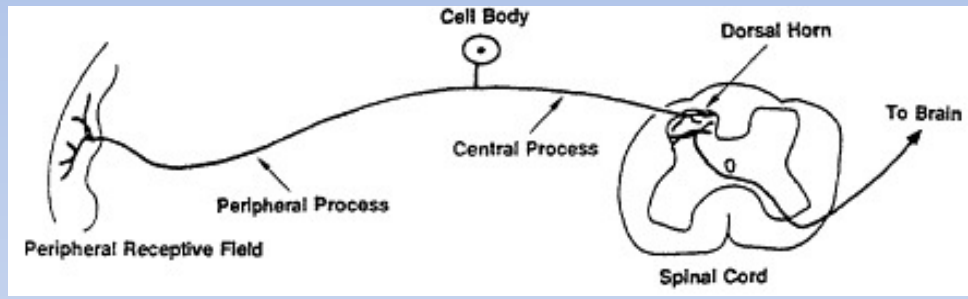
- 4 major processes:
- Transduction
- Transmission
- Modulation
- Perception

Transduction

- The processes by which tissue-damaging stimuli activate nerve endings (generating action potential) transmitted by C fibers and A-delta fibers.
- Mechanical (pressure, pinch), Heat, or Chemical.
- ATP, Bradykinin, PGE2, Na+, K+, H+, Serotonin → receptors → depolarize the cell membrane.
- Inflammation: TNF-alpha, IL-1B, IL-6, NGF → further activates C and A-delta fibers.

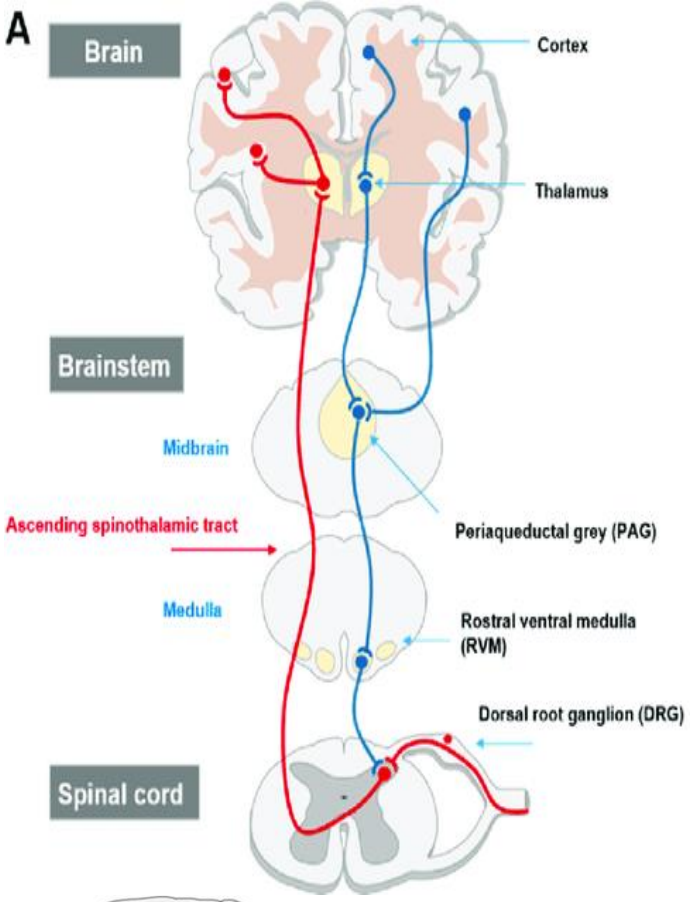
Transmission

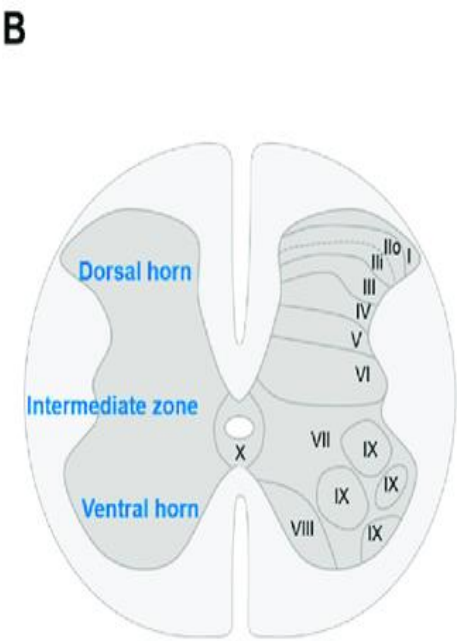
- Peripheral Nervous System: AP is propagated to the CNS by the primary afferent neuron.
- Each stimulus generates a pattern and frequency (code).

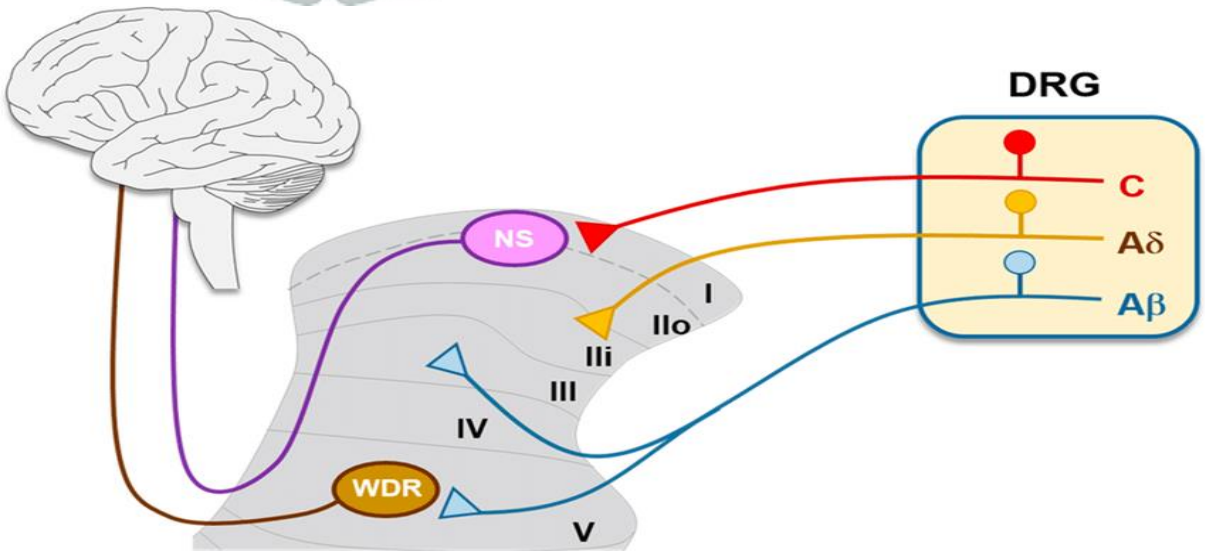


- Central Nervous System: 1st neuron will synapse with 2nd neuron in the dorsal horn of the spinal cord at Rexed laminae I and II.
  - Neurotransmitters: Substance P, Glutamate, and CGRP.
  - Receptors: APA, NMDA, and GPCR.
- Lateral and Medial Spinothalamic tract → thalamus → cortex.

Anatomy of pain

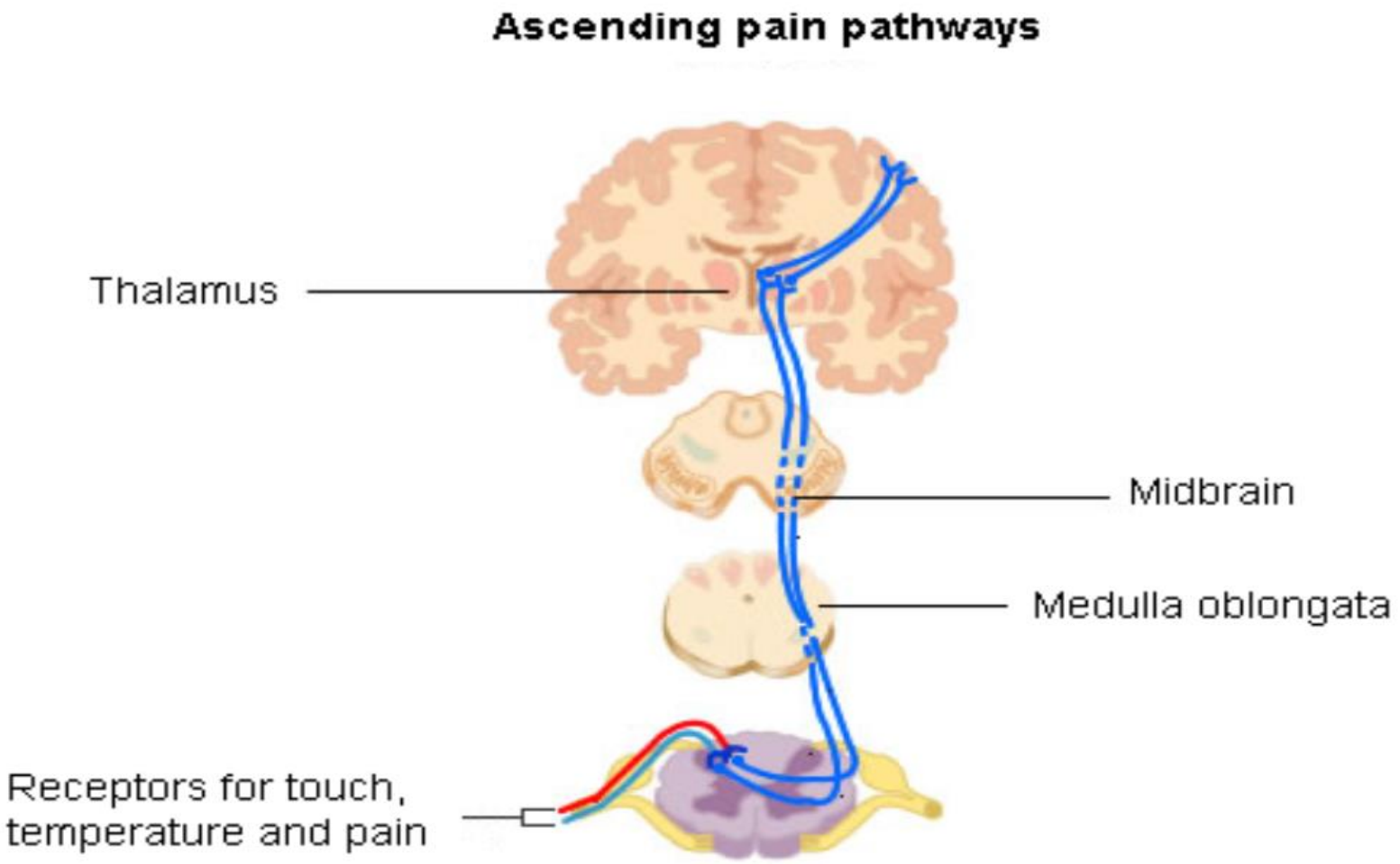






Anatomy of pain

Ascending pathways: The Spinothalamic tract

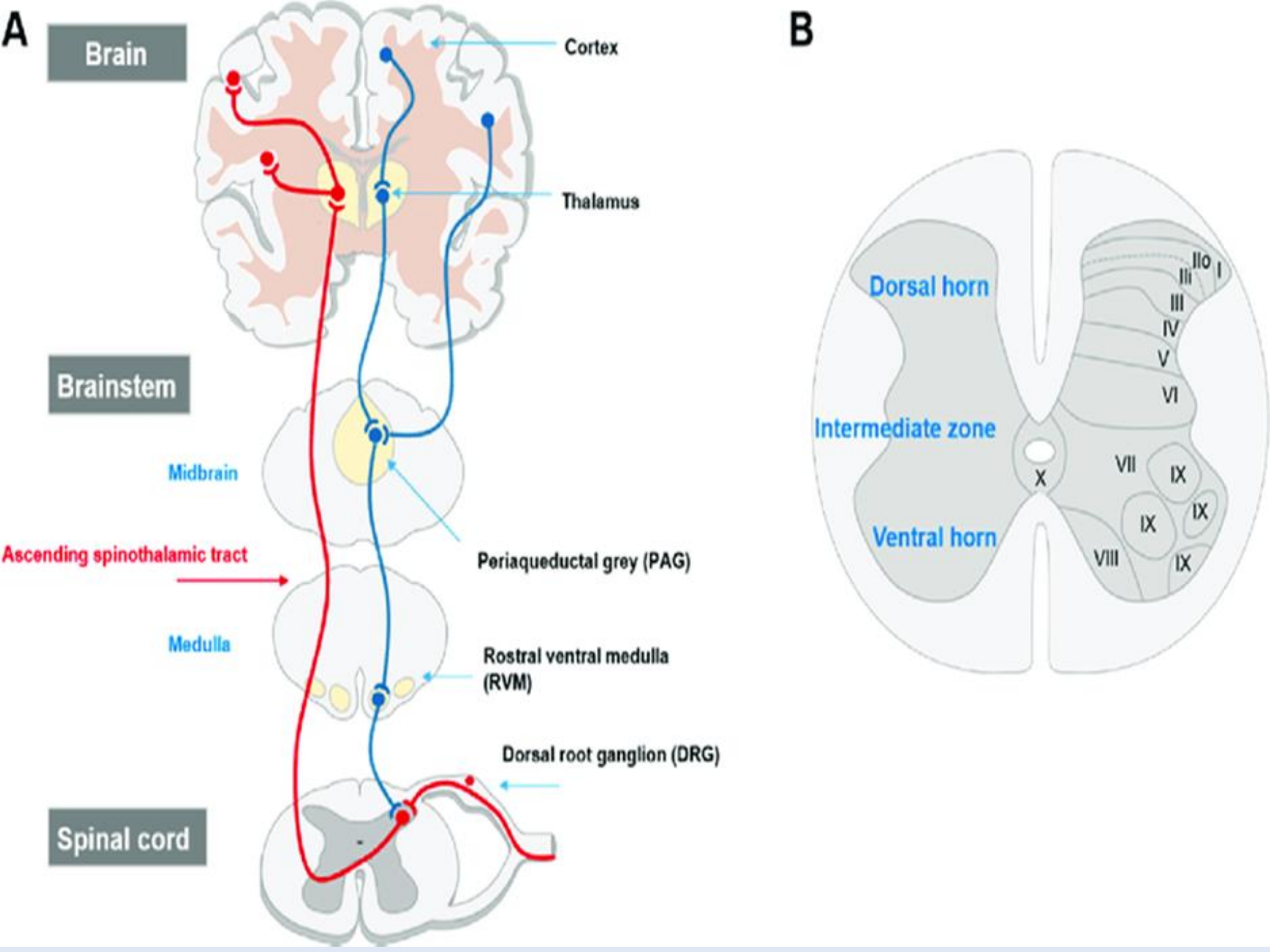


Perception and Modulation

- Perception: The subjective awareness produced by sensory signals; it involves the integration of many sensory messages into a coherent and meaningful whole.

- Modulation: adjustment of sensory signals to try and reduce the activity in the ascending pathways (mainly by action of descending pathways).

  - Endogenous opioids, serotonin, and Noradrenalin.


A
Brain
Cortex
Thalamus
Brainstem
Midbrain
Ascending spinothalamic tract
Periaqueductal grey (PAG)
Medulla
Rostral ventral medulla (RVM)
Dorsal root ganglion (DRG)
Spinal cord
B
Dorsal horn
Intermediate zone
Ventral horn
IIo
I
II
III
IV
V
VI
VII
IX
X
VIII

ACUTE PAIN

Acute pain

- Pain caused by noxious stimulation from injury, a disease process, and usually lasts less than 3-6 weeks.

- Alarm system, survival.

- Nociceptive: somatic: superficial (sharp, more localized)/ deep(less sharp (ache), less localized)

  visceral: diffuse, referred pain

Systemic response to acute pain

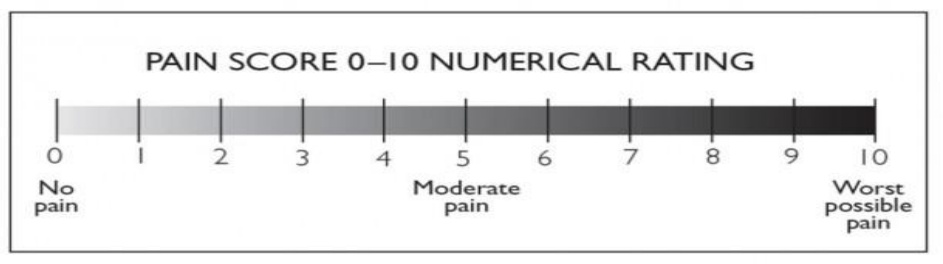
- Adversely affect perioperative morbidity and mortality
- **Cardiovascular:** Hypertension, tachycardia, enhanced myocardial irritability, may precipitate myocardial ischemia.
- **Respiratory:** Increase total body O2 consumption and CO2 production.
- **Gastrointestinal and urinary:** Ileus and urinary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

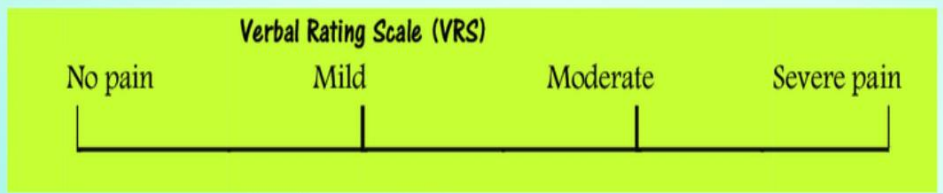
Taking a Patient History

- Location?
- What is the character of the pain (what does it feel like)?
- Onset? Abrupt vs. gradual
- Duration?
- Known cause? Ex. trauma?
- Relieving and aggravating factors?
- Pattern? Better or worse at a particular time of day/month?
- Constant vs. intermittent?
- Does it vary with position?
- Medications?

Assessment

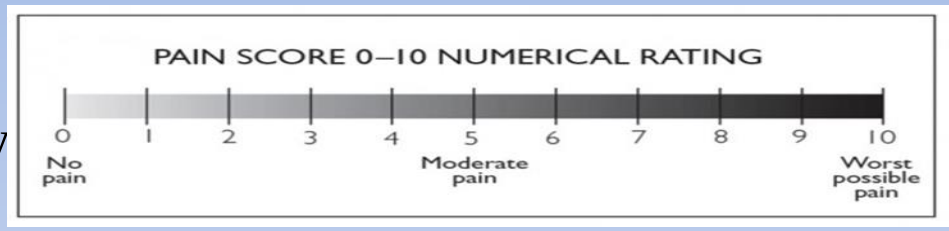
- **Pain Measurement (adults)**
  - Numerical rating scale (NRS)
  - Visual analog scale (VAS)
  - Verbal rating scale (VRS)





Assessment

- **Pain Measurement (pediatrics)**
  - Numerical rating scale (NRS), > 5-8y
  - Wong-Baker FACES rating scale
  - FLACC 2 months- 7 years



The FLACC pain scale

Sometimes it is difficult to assess pain in children who are non-verbal. The FLACC pain scale is a system that can help parents and professionals assess pain levels in children who have limited or no expressive communication. The diagram shows the categories for scoring. Zero, one or two points are given to each of the five categories: face, legs, activity, cry and consolability.

Interpreting the Behaviour Score

Each category is scored on the 0-2 scale, which results in a total score of 0-10.

0	relaxed and comfortable	4-6	moderate pain
1-3	mild discomfort	7-10	severe discomfort of pain or both

Categories	Score zero	Score one	Score two
F Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
L Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
A Activity	Lying quietly, normal position moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
C Cry	No crying (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
C Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

If a child is showing these behaviours, it doesn't necessarily mean that they are in pain as some of the behaviours measured by the FLACC scale can happen for other reasons. However, parents are advised to follow up high scores with a professional.

Reference

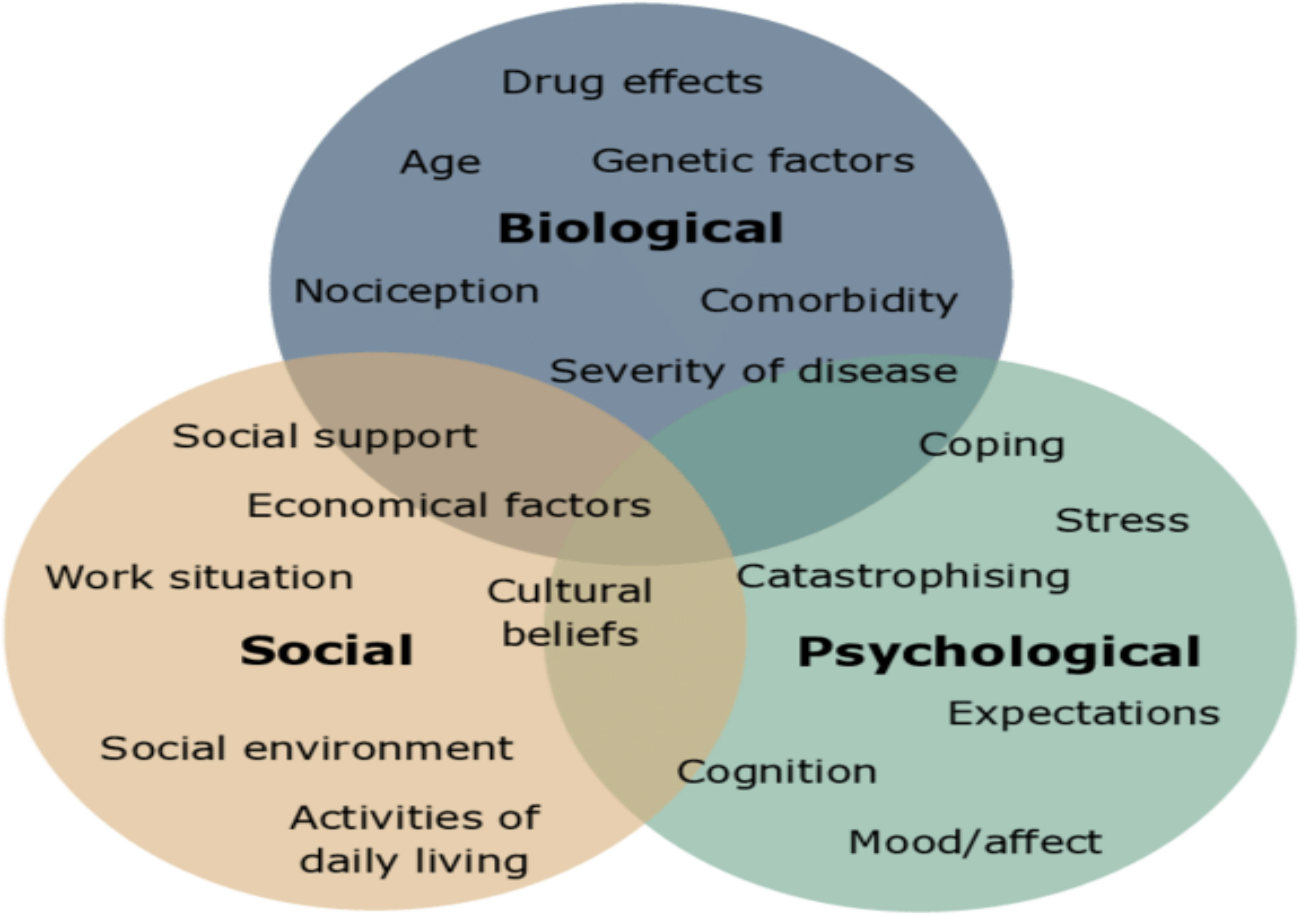
Merkel SI, Voepel-Lewis T, Shayevitz JR, Malviya S. (1997) The FLACC behavioural scale for scoring postoperative pain in young children. *Pediatric Nursing* 23(3), 293=297.

CHRONIC PAIN

Chronic pain

- Pain has persisted beyond tissue healing, > 12 weeks
- Chronic illness by itself.
- Affects Psychological aspects and Social aspects of the patient.
- Can be severe and limiting all life activities.

Biopsychosocial model of chronic pain



Assessment

- Requires multidimensional scales.
- Brief Pain Inventory (BPI) short form

Date: ____ /____ /____ Time: _____

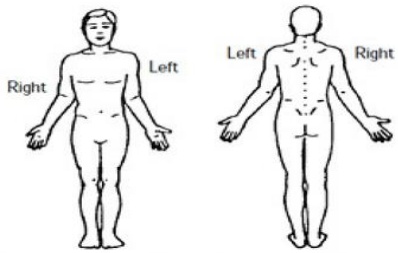
Name: _____ _____ _____

Last First Middle intial

1) Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today?

1. Yes 2. No

2) On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.



3) Please rate your pain by circling the one number that best describes your pain at its **worst** in the past 24 hours.

0 1 2 3 4 5 6 7 8 9 10
No pain — Pain as bad as you can imagine

4) Please rate your pain by circling the one number that best describes your pain at its **least** in the past 24 hours.

0 1 2 3 4 5 6 7 8 9 10
No pain — Pain as bad as you can imagine

5) Please rate your pain by circling the one number that best describes your pain on **average**.

0 1 2 3 4 5 6 7 8 9 10
No pain — Pain as bad as you can imagine

6) Please rate your pain by circling the one number that tells how much pain you have **right now**.

0 1 2 3 4 5 6 7 8 9 10
No pain — Pain as bad as you can imagine

7) What treatments or medications are you receiving for your pain?

_____

_____

8) In the past 24 hours, how much **relief** have pain treatments or medications provided? Please circle the one percentage that most shows how much relief you have received.

0% 10 20 30 40 50 60 70 80 90 100%
No relief — Complete relief

9) Circle the one number that describes how, during the past 24 hours, pain has **interfered** with your:

A. General activity

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

B. Mood

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

C. Walking ability

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

D. Normal work (includes both work outside the home and housework)

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

E. Relations with other people

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

F. Sleep

0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

G. Enjoyment of life

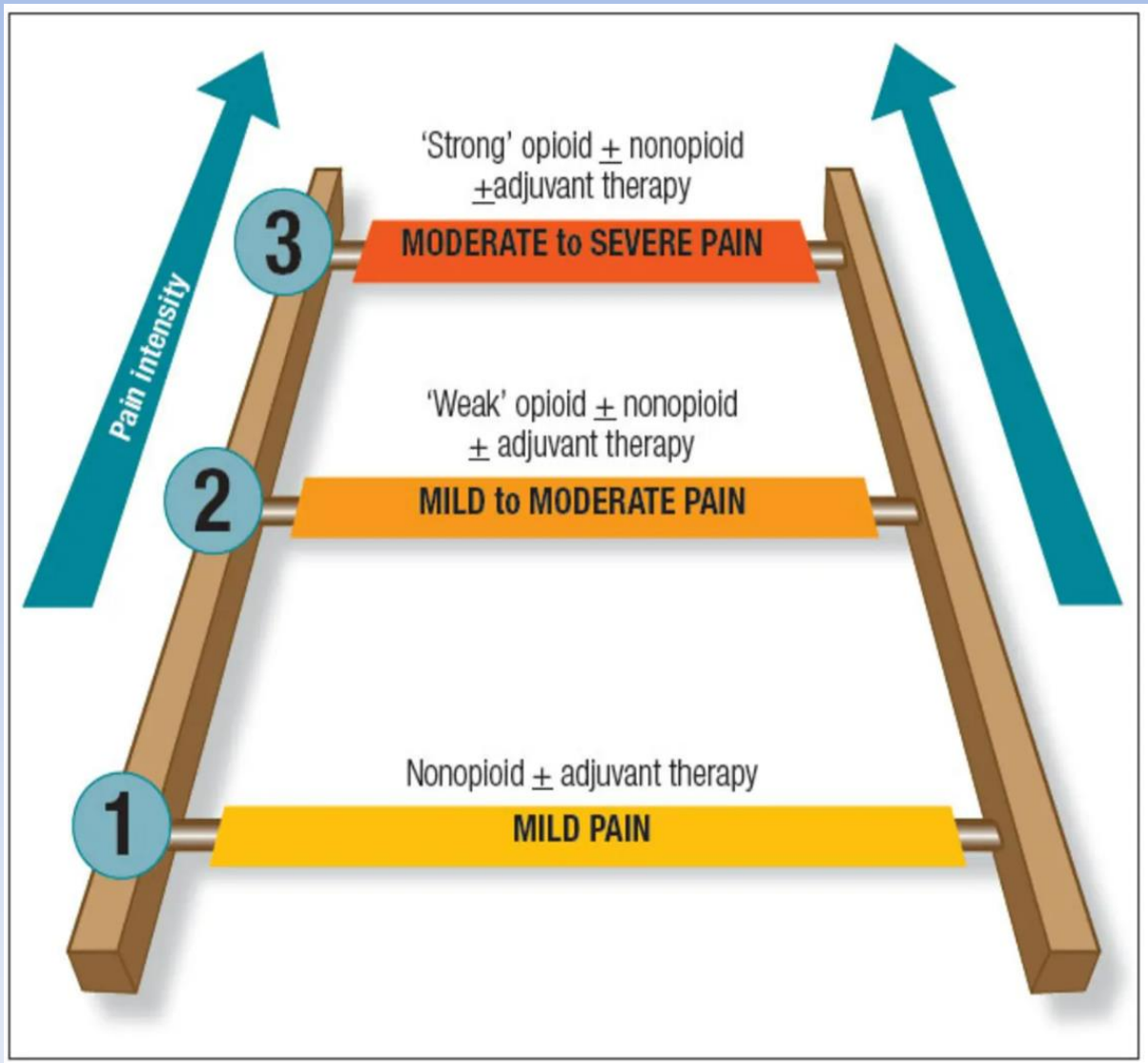
0 1 2 3 4 5 6 7 8 9 10
Does not interfere — Completely interferes

Treatment of Acute Pain

- Pharmacological
- Physical therapy and exercises
- Simple measures: ex. applying heat cold
- Electrical stimulation
- Acupuncture.

- WHO analgesic ladder

Paracetamol, NSAIDSs, Opioids, adjuvant meds.



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

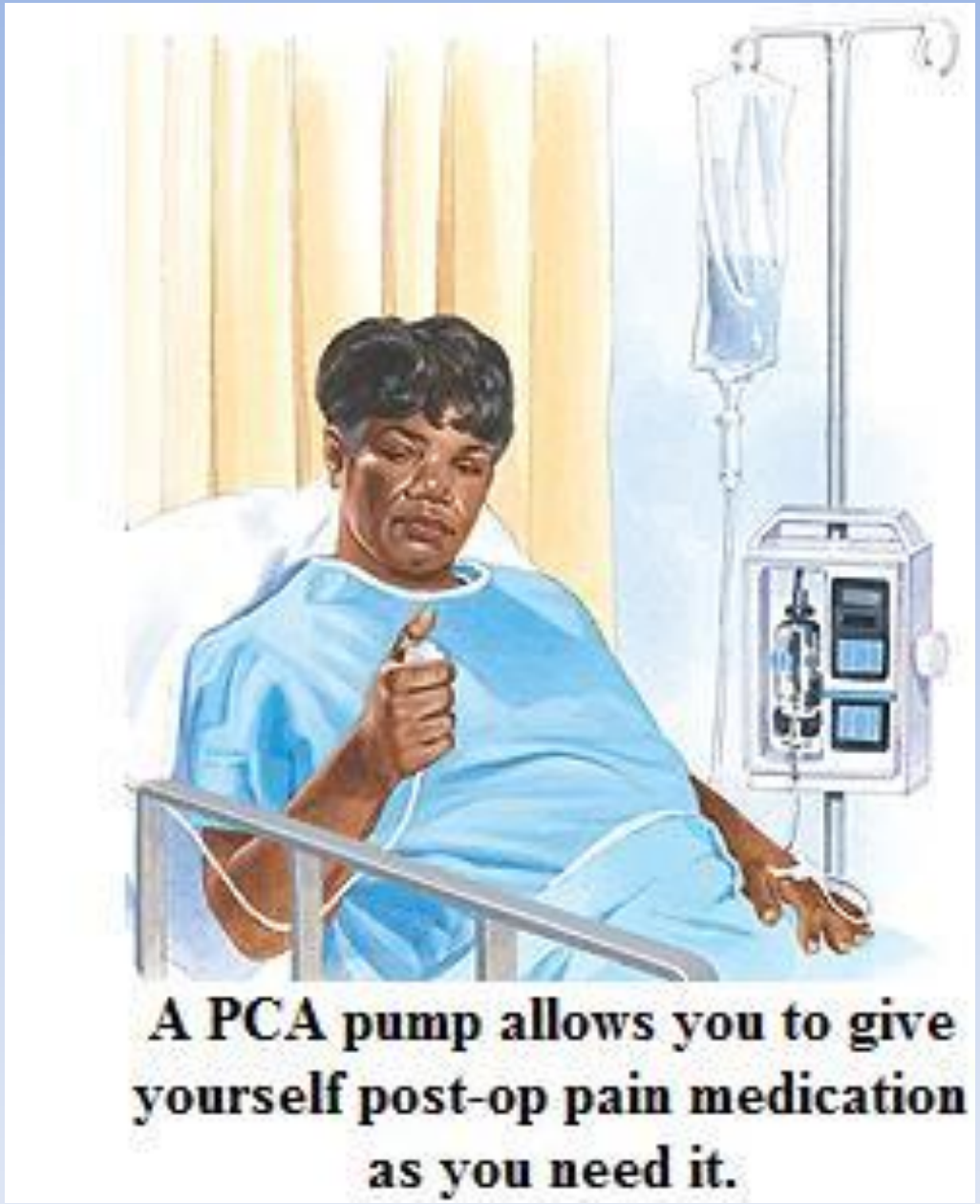
Mild Pain — Increasing Pain — Severe Pain

- 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

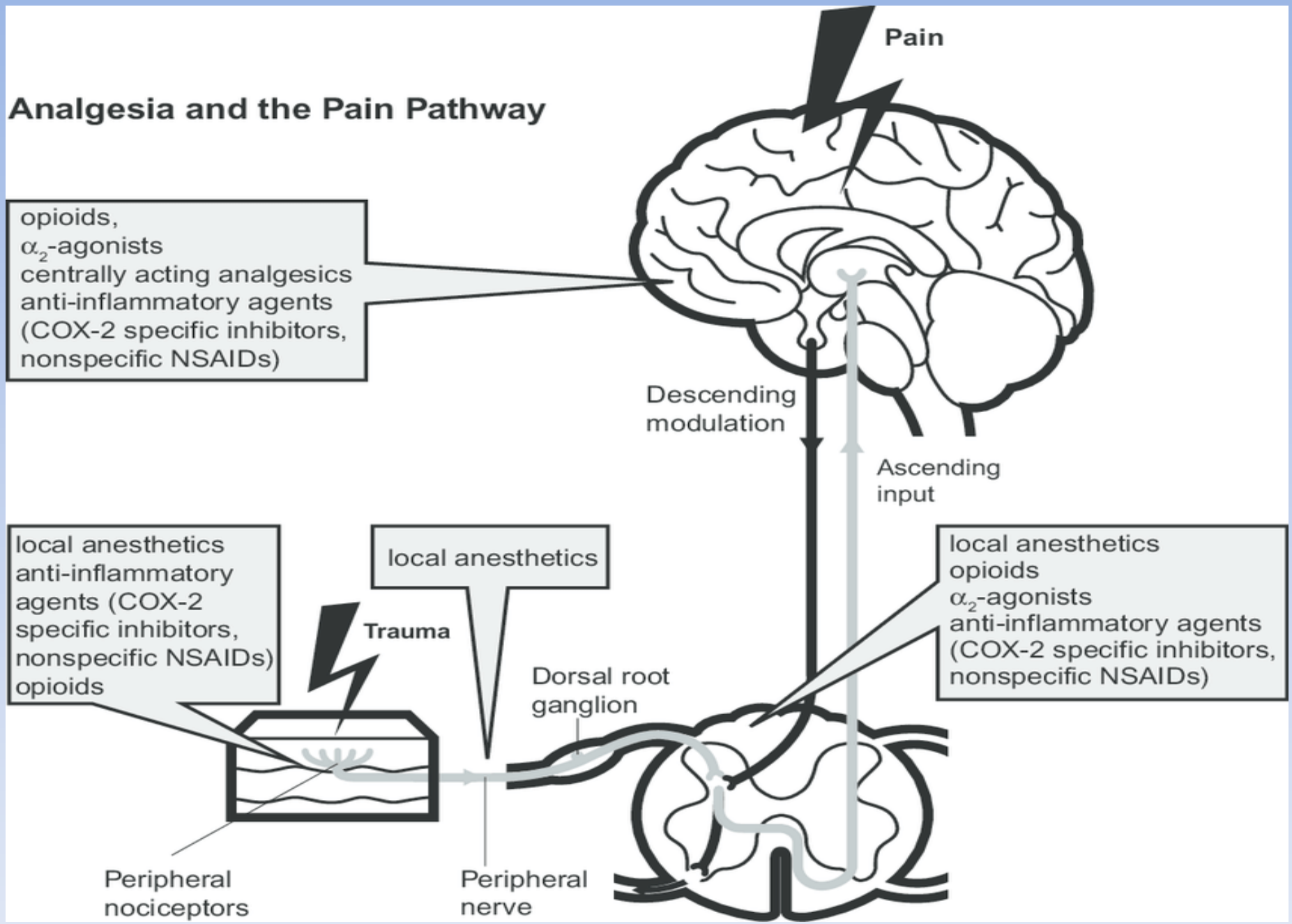
PCA


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

Peripheral and neuraxial nerve blocks.

- Uses local anesthetics and steroids +/- adjuvants

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	


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

Other modalities (chronic pain)

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

Opioids in a nutshell

BOX 31-1 *Classification of Opioid Compounds*

Naturally Occurring

Morphine
Codeine
Papaverine
Thebaine

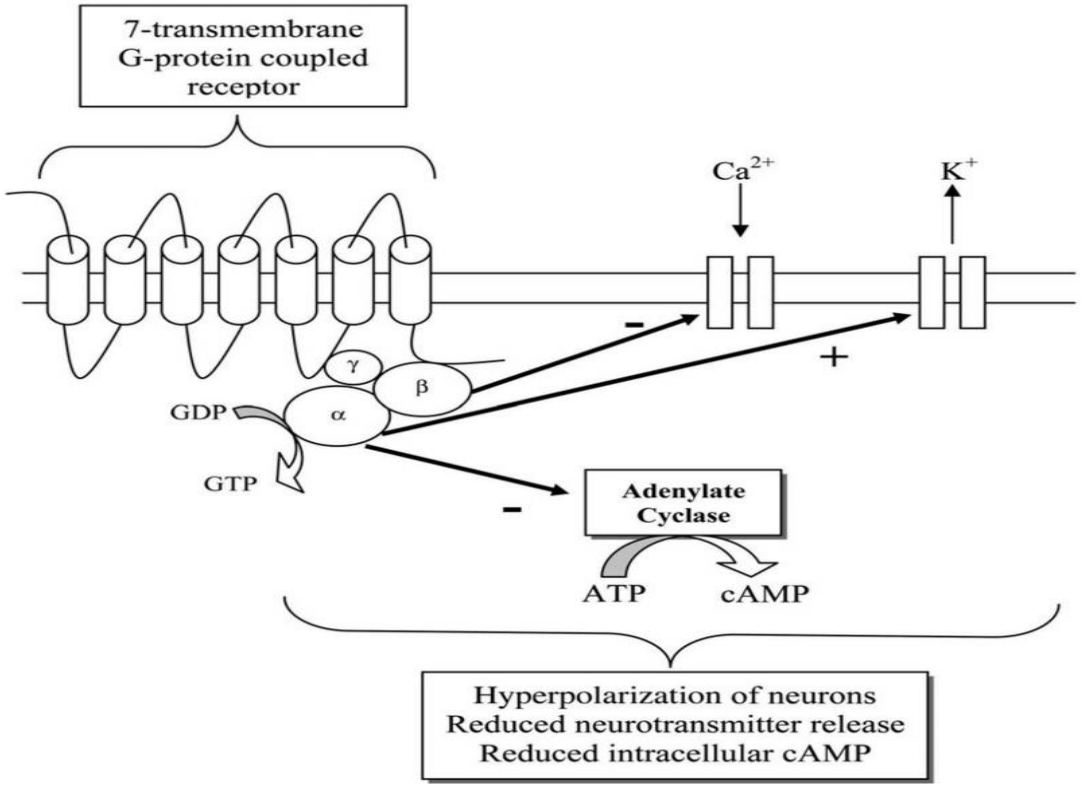
Semisynthetic

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)

Opioids receptors



Current NC-IUPHAR-Recommended Nomenclature[1]	Previous Nomenclature	Presumed Endogenous Ligands
μ, mu, or MOP	OP_3	β-endorphin (not selective) enkephalins (not selective) endomorphin-1[2] endomorphin-2[2]
δ, delta, or DOP	OP_1	enkephalins (not selective) β-endorphin (not selective)
κ, kappa or KOP	OP_2	dynorphin A dynorphin B α-neoendorphin
NOP	OP_4	nociceptin/orphanin FQ (N/OFQ)

Receptor	Clinical Effect	Agonists
μ	Supraspinal analgesia (μ_1) Respiratory depression (μ_2) Physical dependence Muscle rigidity	Morphine Met-enkephalin[2] β-Endorphin[2] Fentanyl
κ	Sedation Spinal analgesia	Morphine Nalbuphine Butorphanol Dynorphin[2] Oxycodone
δ	Analgesia Behavioral Epileptogenic	Leu-enkephalin[2] β-Endorphin[2]
σ	Dysphoria Hallucinations Respiratory stimulation	Pentazocine Nalorphine Ketamine

Effect on body systems

- Miosis due to parasympathetic system activation
- Purities (Itching)
- Bradycardia except for meperidine
- Histamine release
- Vomiting and constipation

Respiratory depression

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 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

- Onset: 1-2 min (IV)
- Peak effect: 30min
- Metabolized by conjugation in the liver, but the kidney plays a key role in the extrahepatic metabolism of morphine.
- M6G accounts for nearly 10% of morphine metabolite and is a more potent μ-receptor
- Renal dysfunction

Fentanyl

- Duration of 30-60 min after single IV injection
- Norfentanyl, the primary metabolite
- Anesthetic induction is usually achieved by combining a loading dose of fentanyl (2 to 6 µg/kg)

Alfentanil

- Faster onset than fentanyl.
- Less potent than fentanyl.

Sufentanil

- is twice as lipid soluble as fentanyl and is highly bound (93%) to plasma proteins, including α1-acid glycoprotein.

- More potent than fentanyl.

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

Routes of administartion

- Orally: Morphine, Buprenorphine (high first pass effect)
- Transdermal: Fentanyl
- Transmucosal: Buprenorphine, fentanyl
- Epidural: Morphine, fentanyl

OPIOID ANTAGONISTS

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

- NALOXONE

- 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.
- Recurrence of respiratory depression after naloxone results from the short t½ of naloxone

Thank you