Pain

DEPARTMENT OF ANESTHESIA AND INTENSIVE CARE .

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Learning Objectives

- Definition of Pain.
- The basic anatomy and physiology involved in pain transmission.
- Nociceptive and Neuropathic pain.
- History, Examination and Pain Assessment.
- Use of Opioids for Pain in acute condition .

Definition

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

1. Pain is always a personal experience. Influenced by biological, psychological, and social factors.
2. A person's report of an experience as pain should be respected.
3. Pain has adverse effects on function and social and psychological well-being.
4. 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

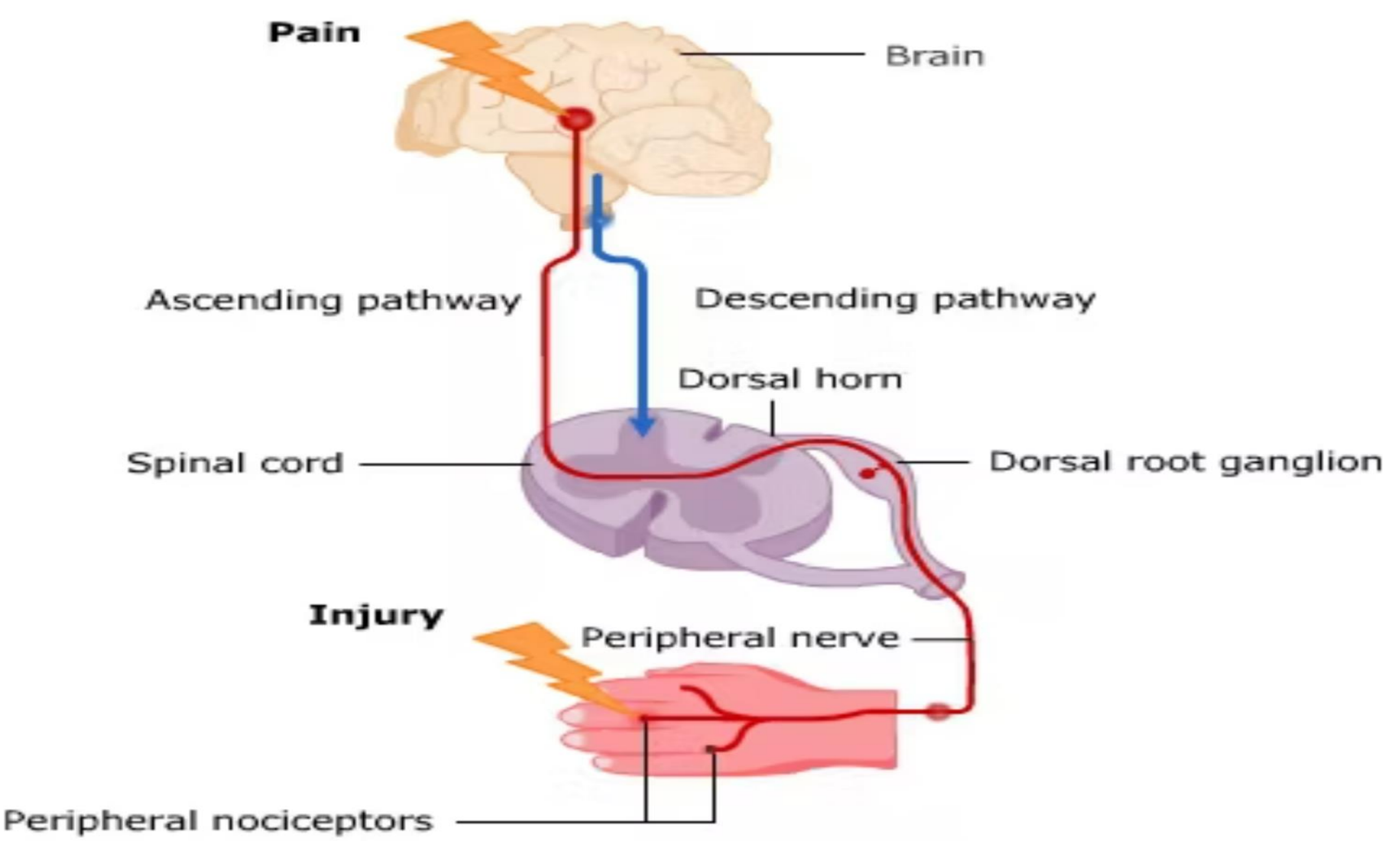
History of peripheral/central nerve damage

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

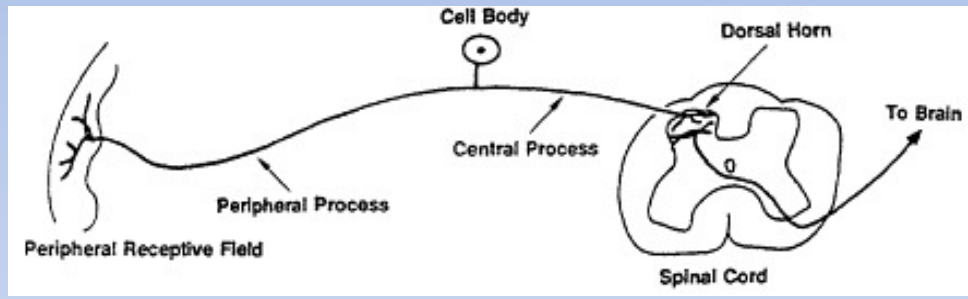
- 4 major processes:
- Transduction
- Transmission
- Modulation
- Perception

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.



- 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: AMPA, NMDA, and GPCR.

Perception and Modulation

- Perception: The subjective awareness produced by sensory signals; it involves the integration of many sensory messages (biopsychosocial) into a coherent and meaningful whole (brain process to decide if its pain or not).

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

  - Endogenous opioids, serotonin, and Noradrenalin.

ACUTE PAIN

Acute pain

- Pain caused by noxious stimulation from injury, a disease process, and usually lasts less than 6 months (some use 3 months).

- Alarm system, survival.

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

  visceral: diffuse, referred pain

Systemic response to acute pain

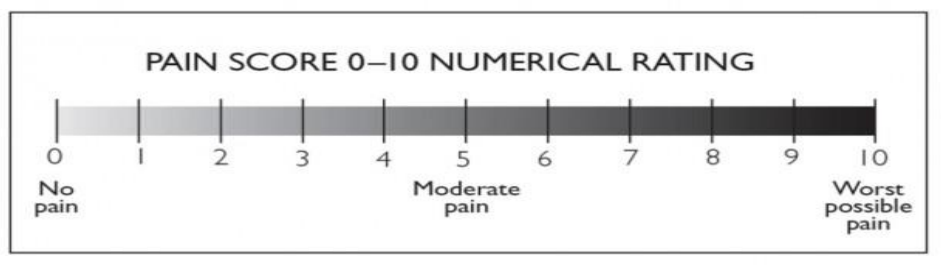
- Adversely affect perioperative morbidity and mortality
- **Cardiovascular:** Hypertension, tachycardia, enhanced myocardial irritability, may precipitate myocardial ischemia.
- **Respiratory:** Increase total body O2 consumption and CO2 production.
- **Gastrointestinal and urinary:** Ileus and urinary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

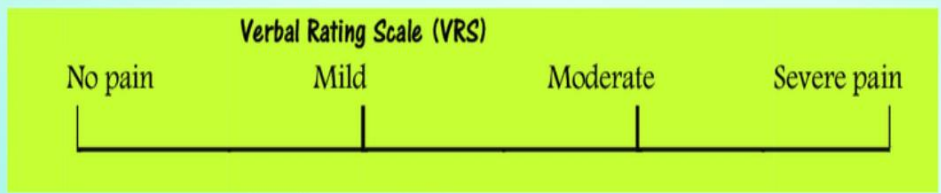
Taking a Patient History

- 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? Effectiveness of medications?

Assessment

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



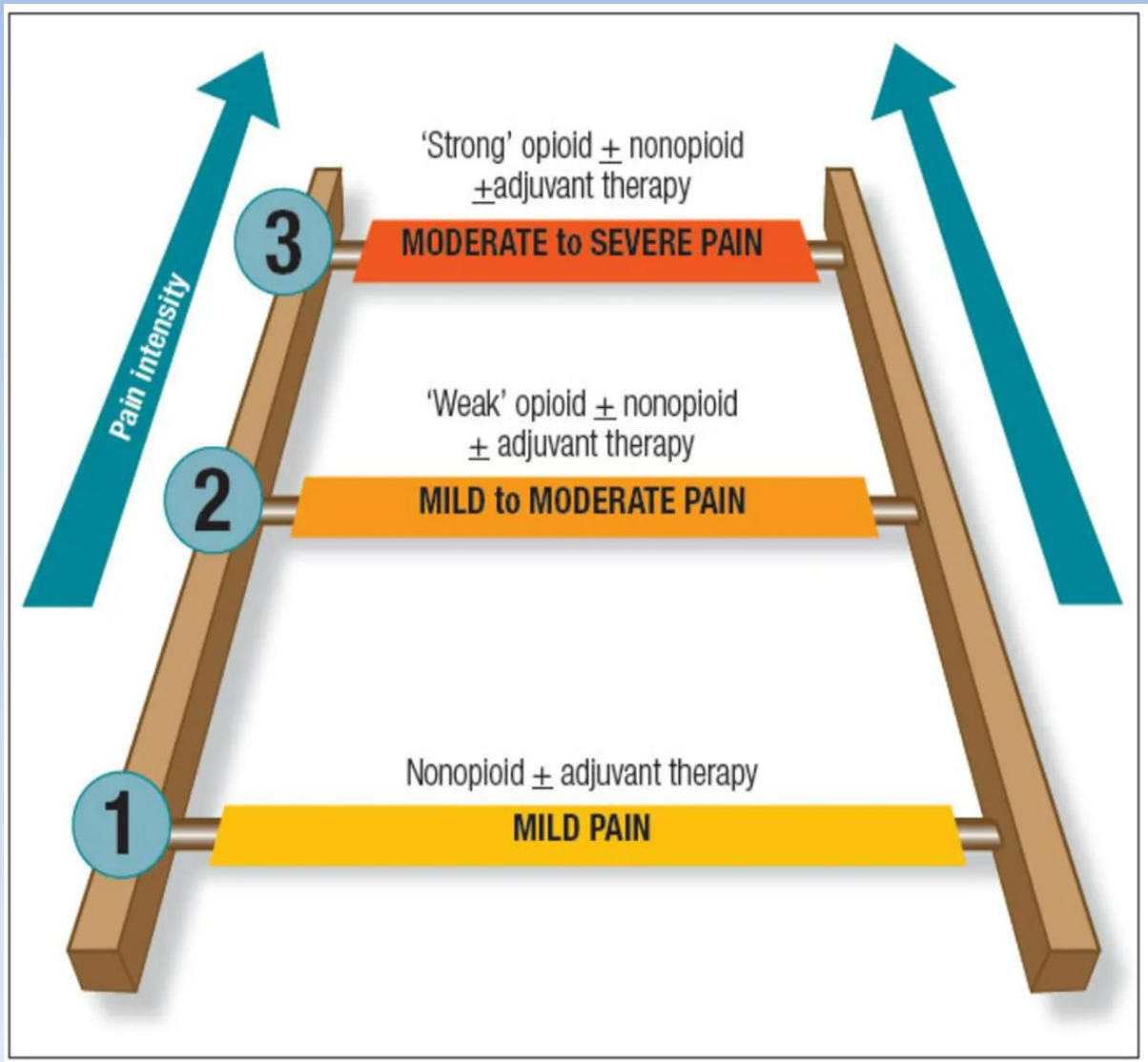


Treatment of Acute Pain

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

- Pharmacological
- WHO analgesic ladder

Paracetamol, NSAIDs, 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

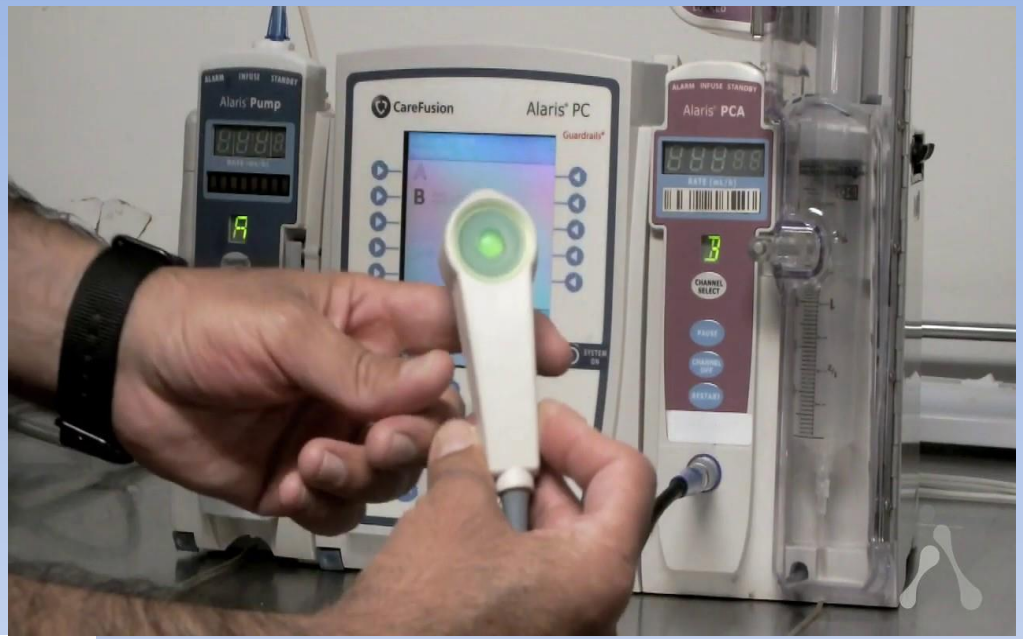
Mild Pain — Increasing Pain — Severe Pain

- 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


Alaris Pump
CareFusion
Alaris PC
Alaris PCA


PCA
1ml / 7min
VYGON

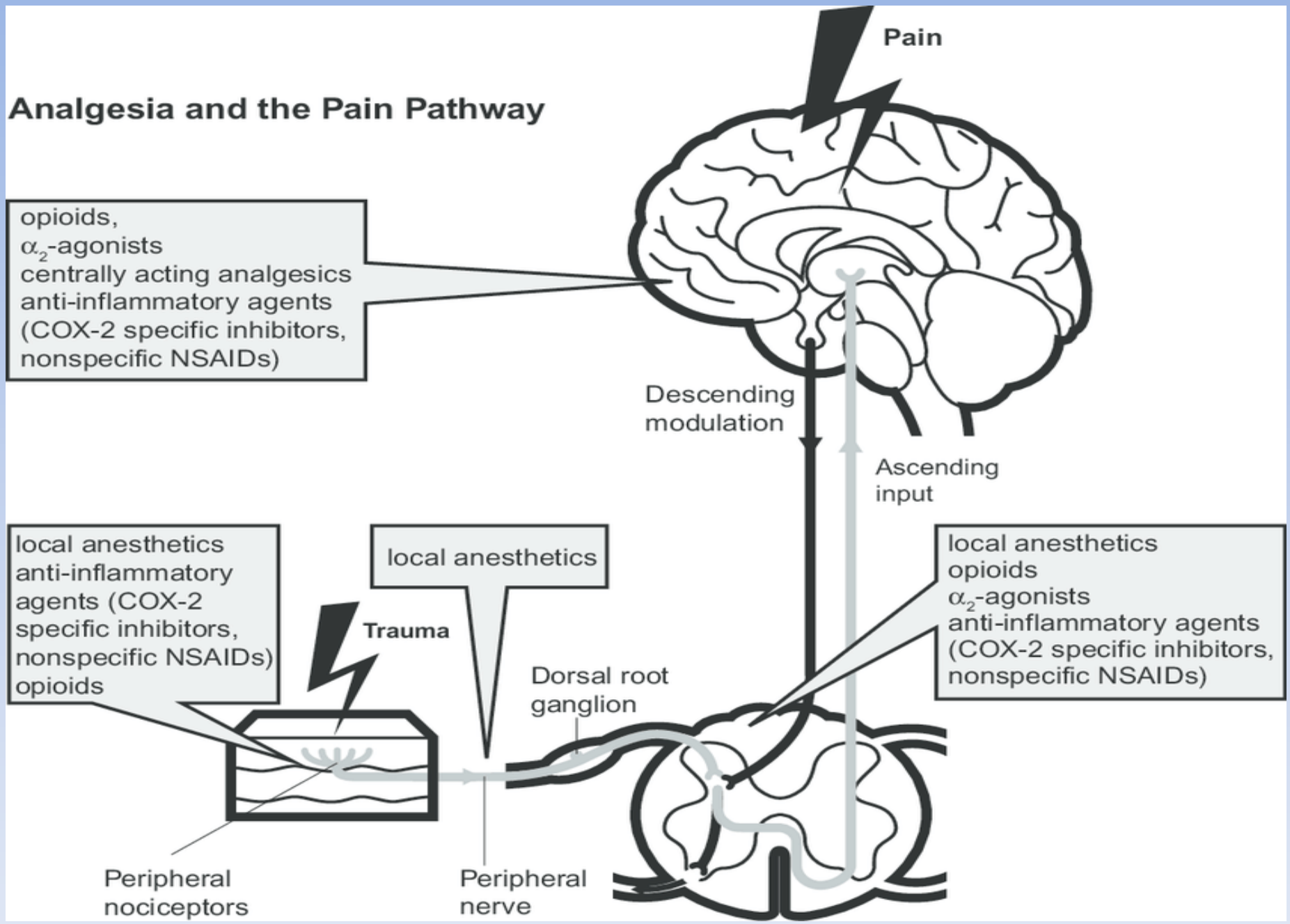

PCA
VYGON

Regional Anesthesia (nerve blocks)

Peripheral and neuraxial nerve blocks.

- Uses local anesthetics and steroids +/- adjuvants (ex. Ketamine,clonidine)

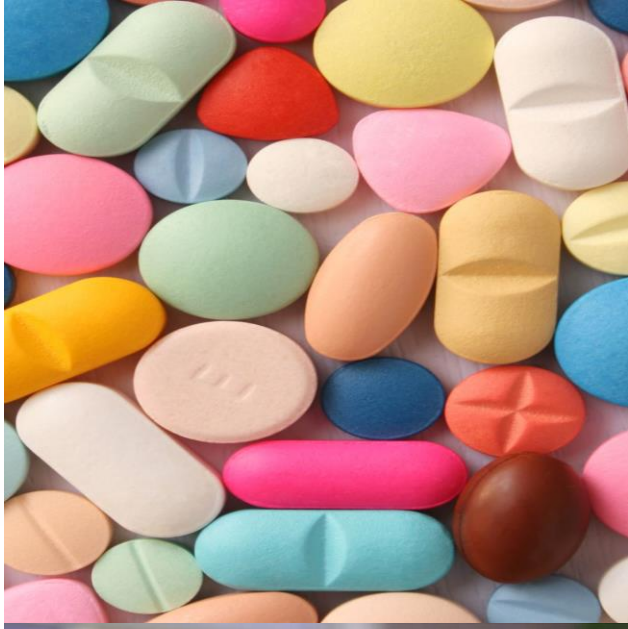
Upper Extremity PNBs	Lower Extremity PNBs	Truncal Blocks
Cervical paravertebral	Subgluteal sciatic	Thoracic paravertebral
Interscalene	Femoral	Transverse abdominis plane
Interscalene	Popliteal	Ilioinguinal
Infraclavicular	Saphenous	
Axillary	Ankle	


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

OPIOIDS

Opioid (narcotics)

- Opioids are main pain killers in acute postoperative pain (moderate to severe).
- Medications for analgesia intraoperatively.
- There is evidence to suggest that as long ago as 3000 BC the opium poppy, *Papaver somniferum*, was cultivated for its active ingredients.
- Morphine is commonly considered to be the archetypal opioid analgesic and the agent to which all other painkillers are compared.



Opioids in a nutshell

BOX 31-1 *Classification of Opioid Compounds*

Naturally Occurring

Morphine
Codeine
Papaverine
Thebaine

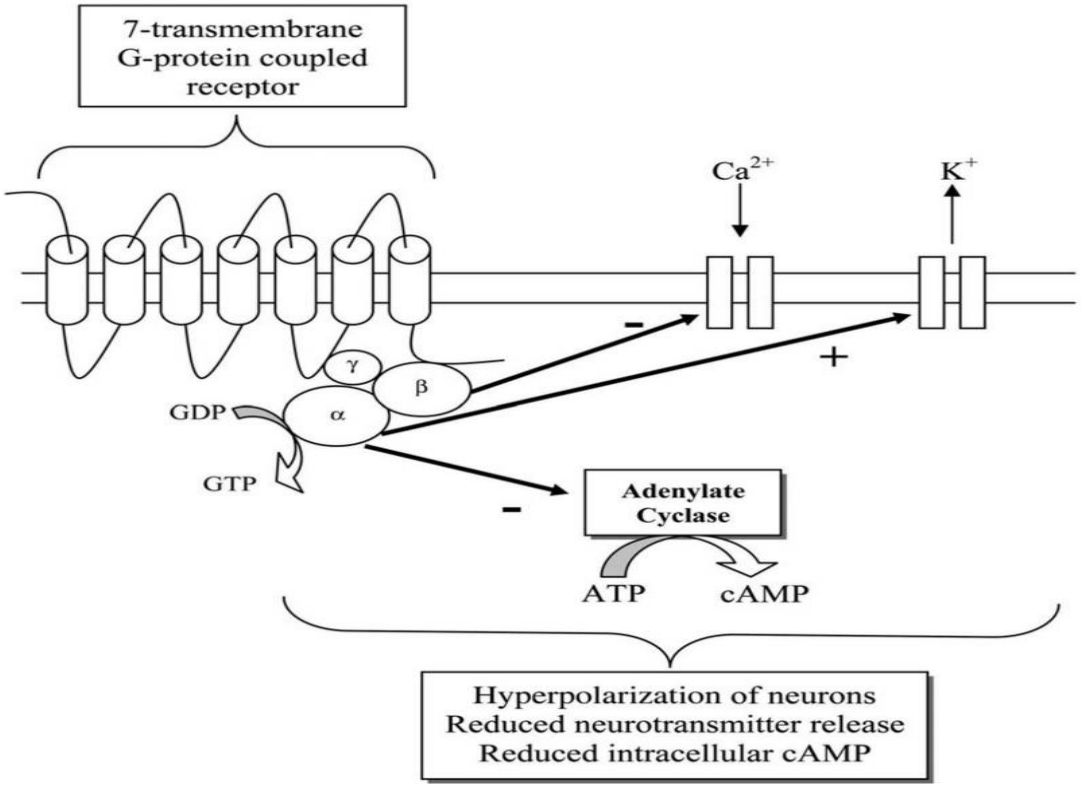
Semisynthetic

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

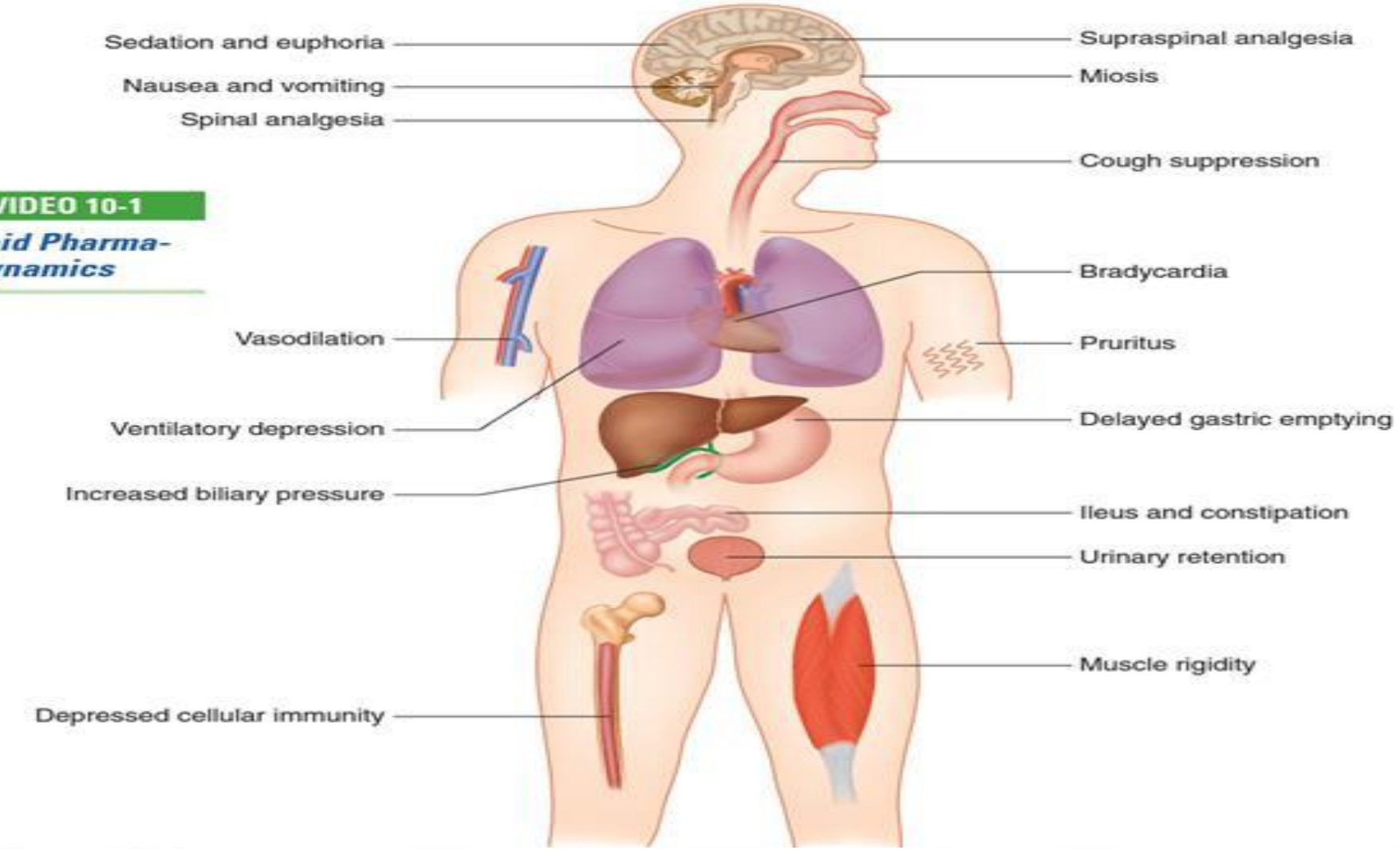
- Miosis due to parasympathetic system activation
- Purities (Itching)
- Bradycardia except for meperidine
- Histamine release
- Vomiting and constipation

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



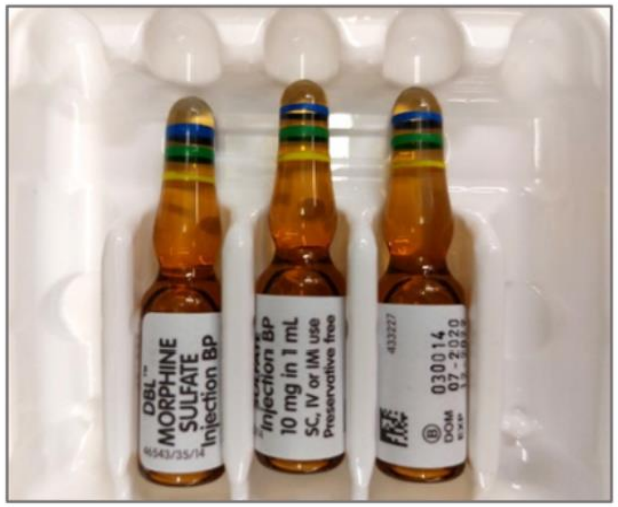
VIDEO 10-1

id Pharma-
namics

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
- Potency = 1 (reference for all opioids)

- 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

- Potency = 100x.
- 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) (6 is usually in cardiac anesthesia).

Alfentanil

- Faster onset than fentanyl.
- Less potent than fentanyl (5-10x less).
- Used for sedation in ICU in Europe.

Sufentanil

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

- More potent than fentanyl (10-12x of 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
- Main opioid for sedation in ICU in Jordan.

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