Cancer Pain
Chronic Pain

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PEACE
Beauty
LOVE
DREAMS
HOPE
Relief
JOY

Definition of pain

- The definition of pain proposed by International Assotiation for the Study of Pain:

  „Pain in an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage. Pain is always subjective”.

- Pain is always **subjective** – pain is what the patient says hurts. It is what the patient describes and not what others think it ought to be.

"Pain is whatever
the person says it is..."

- Margo McCaffery

Total pain

P — Physical pain: Osteopathic lesion, deep tissue or bone pain "tender"

A — Anxiety: rage, depression

I — Interpersonal interactions: family strains, isolation

N — Nonacceptance of the caregivers: doubting of their faith, sense of hopelessness

Classifications of pain

The various classifications of pain:

1. Temporal
2. Pathophysiological
3. Aetiological

Classifications 2

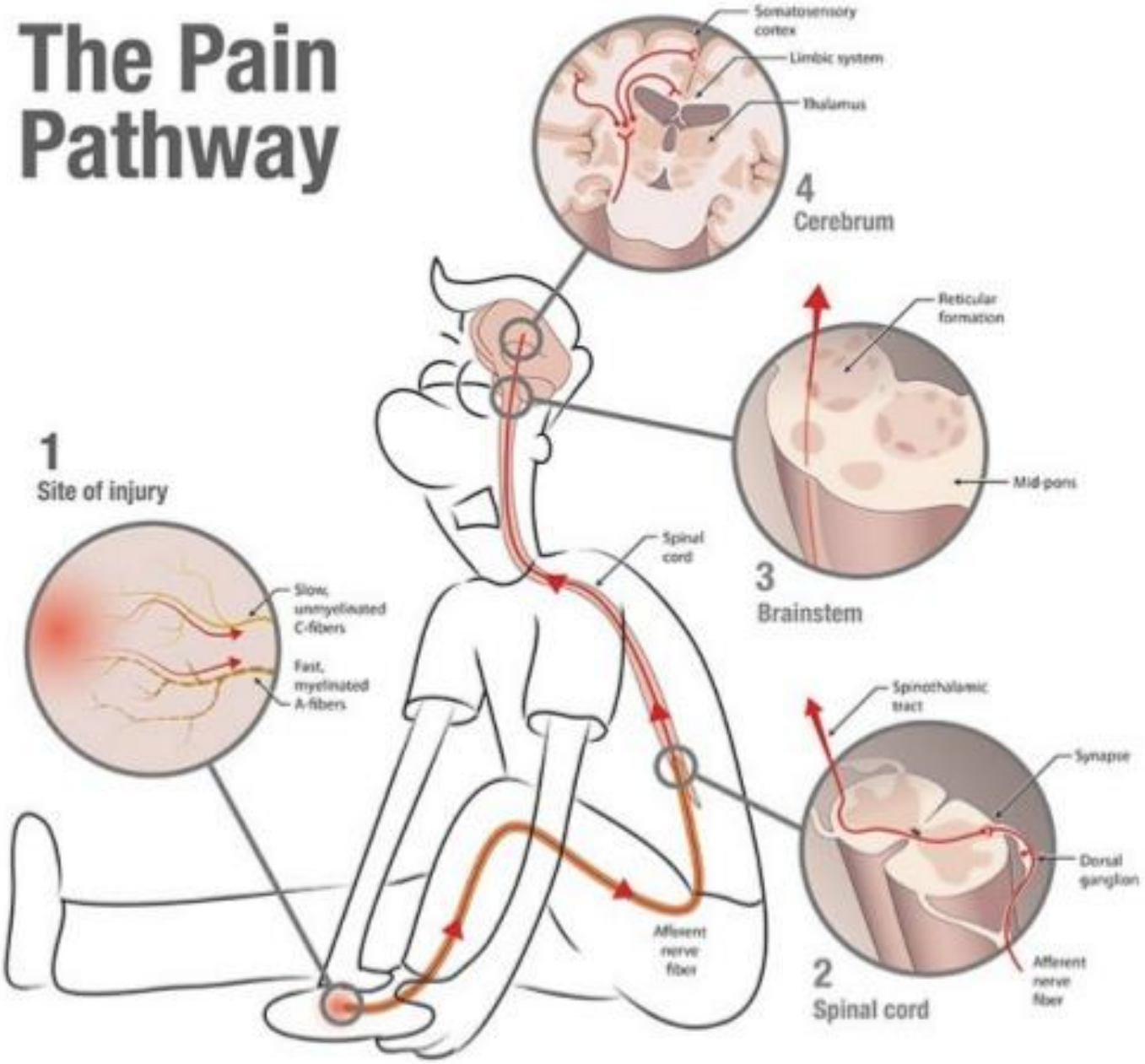
Temporal:

Acute pain – is usually due to a definable acute injury or illness (nociceptive cause), its onset is recognizable and its duration is limited and predictable. It may be accompanied by anxiety and clinical signs of sympathetic overactivity: tachycardia, tachypnoea, hypertension, sweating, pupillary dilatation and pallor. These signs are characteristic of suffering patient...

„obviously in pain”

Acute pain may indicate progression of cancer.

The Pain Pathway



Temporal classification

Chronic pain – results from a chronic pathological process.

When pain persists longer than 3 months.

It has a gradual or ill-defined onset, continues unabated and may become progressively more severe. The patient appears depressed and withdrawn, and as there are usually no signs of sympathetic overactivity, they are frequently labelled as…

„not looking like somebody in pain”

Patients with chronic pain have symptoms of depression with lethargy, apathy, anorexia and insomnia.

Aetiological classification

- Due to cancer or related disorders
- Due to diagnostic interventions
- Due to anticancer therapy

Pathophysiological classification

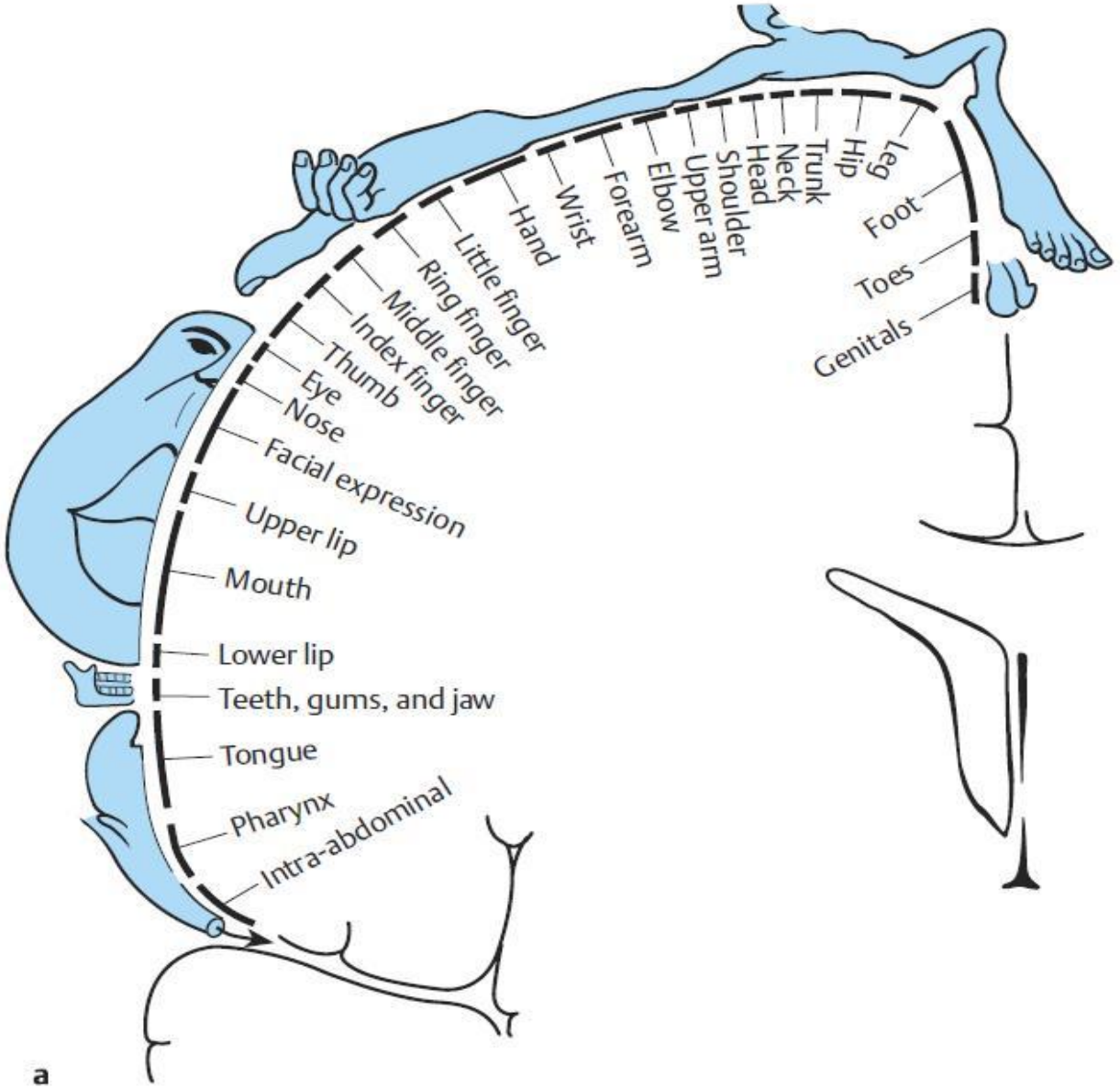
- **Nociceptive pain**

  - somatic (skin, soft tissue, muscle, bone, „body wall”)

  - visceral (internal organs)
- **Non-nociceptive pain**

  - neuropathic pain (central, peripheral)

  - psychogenic (psychological factors)



- **Relative sizes of the cortical representations of different parts of the body** in the human primary somatosensory cortical fields.

From: Penfield W and Rasmussen T. The Cerebral Cortex of Man, Macmillan, New York, 1950.

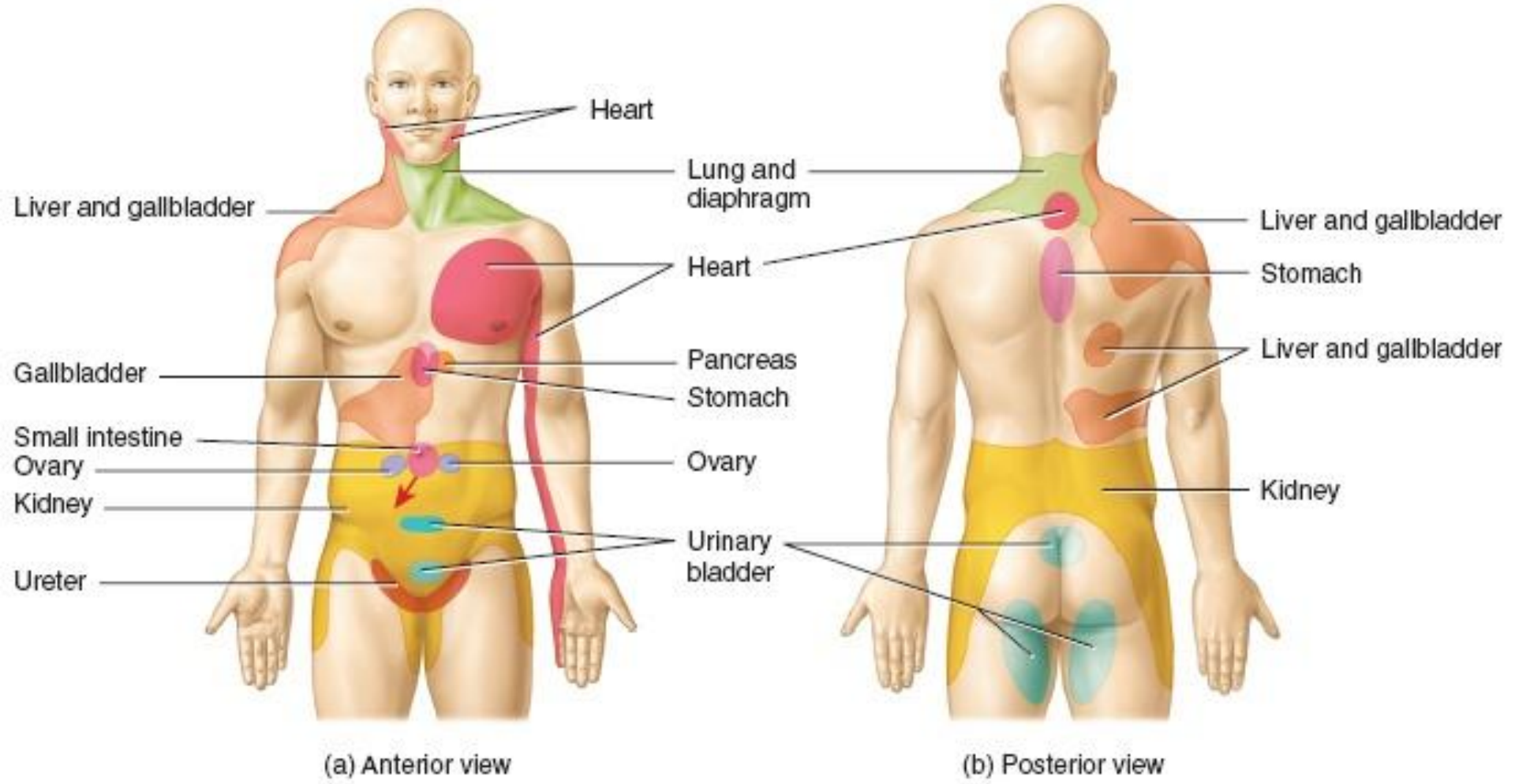
homunculus sensoricus

Nociceptive Pain

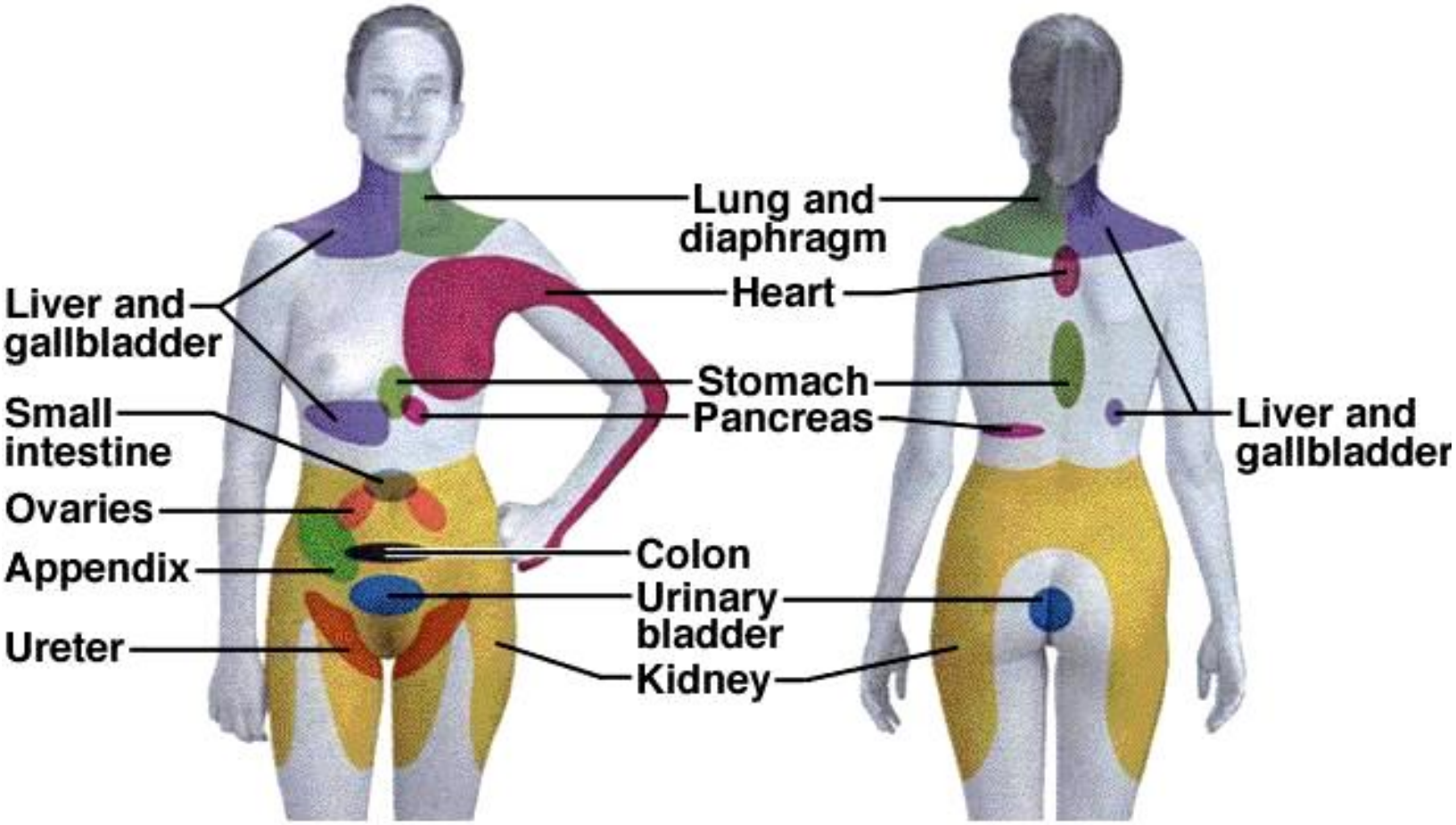
- Visceral Pain: Associated with internal organs.
  - Nature: Crampy, pressure, deep, dull to sharp, diffuse, referred.

- Somatic pain : Soft tissues/ myalgic.
  - Nature: Dull to sharp, throbbing, achy, localized

Referred pain



Referred pain



Neuropathic pain

- Damage or disfunction of peripheral or central nervous system
- Abnormal neural processing by P or CNS
- Patient description of neuropatic pain:

  burning, searing, itching, electric-like, tingling, shooting, stabbing, numb
- e.g., peripheral neuropathy, plexopathy, postherpetic neuralgia

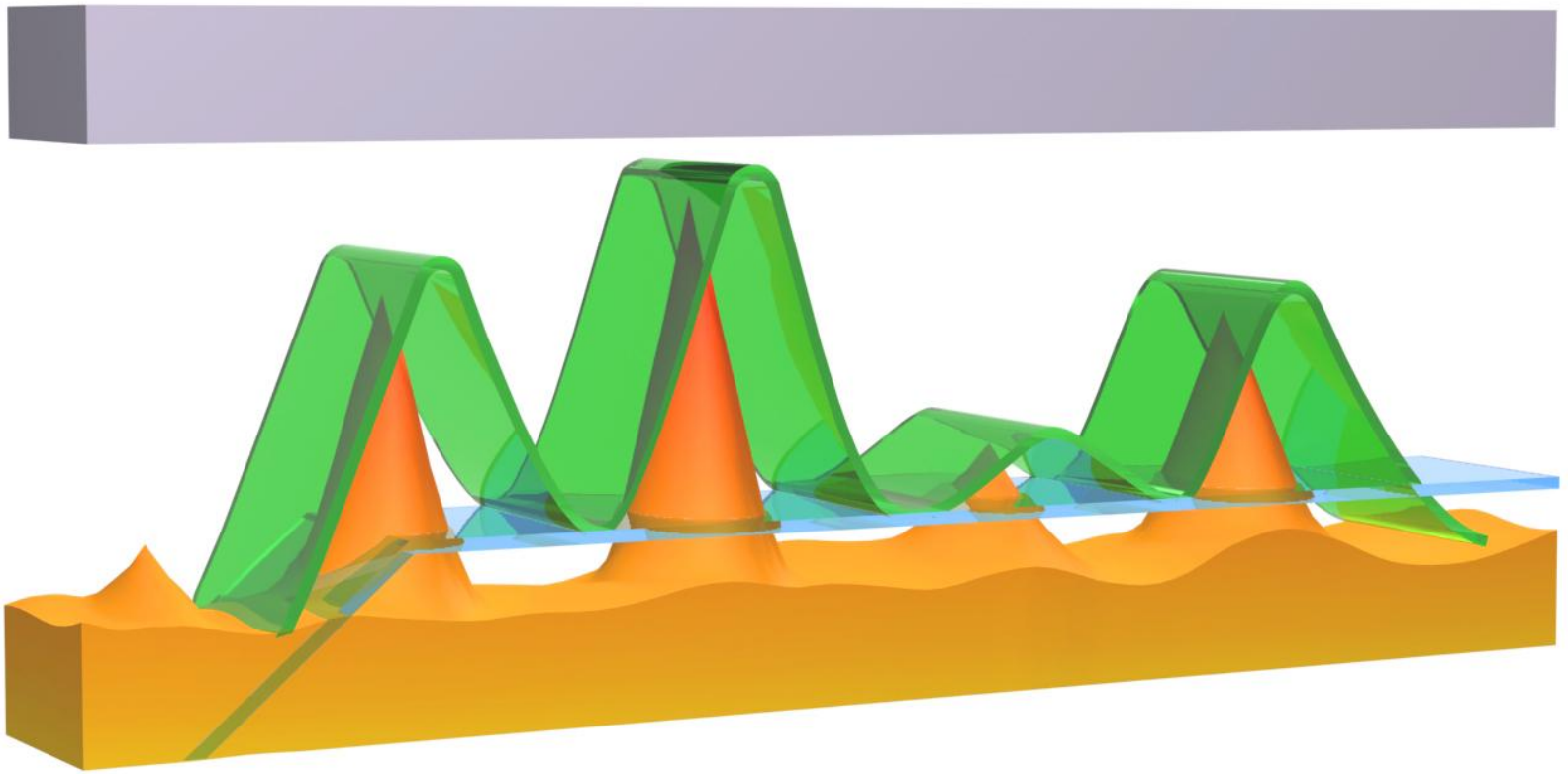
Summary

Understanding the pathophysiology leads to improved assessment and targeted management that will improve outcomes.

Pain assessment

- Location
- Description (type of pain)
- Change over time
- Severity (scales, 0-10)
- Effect of treatments
  - Benefits (+)
  - Unwanted effects (side effects) (-)

Change over time

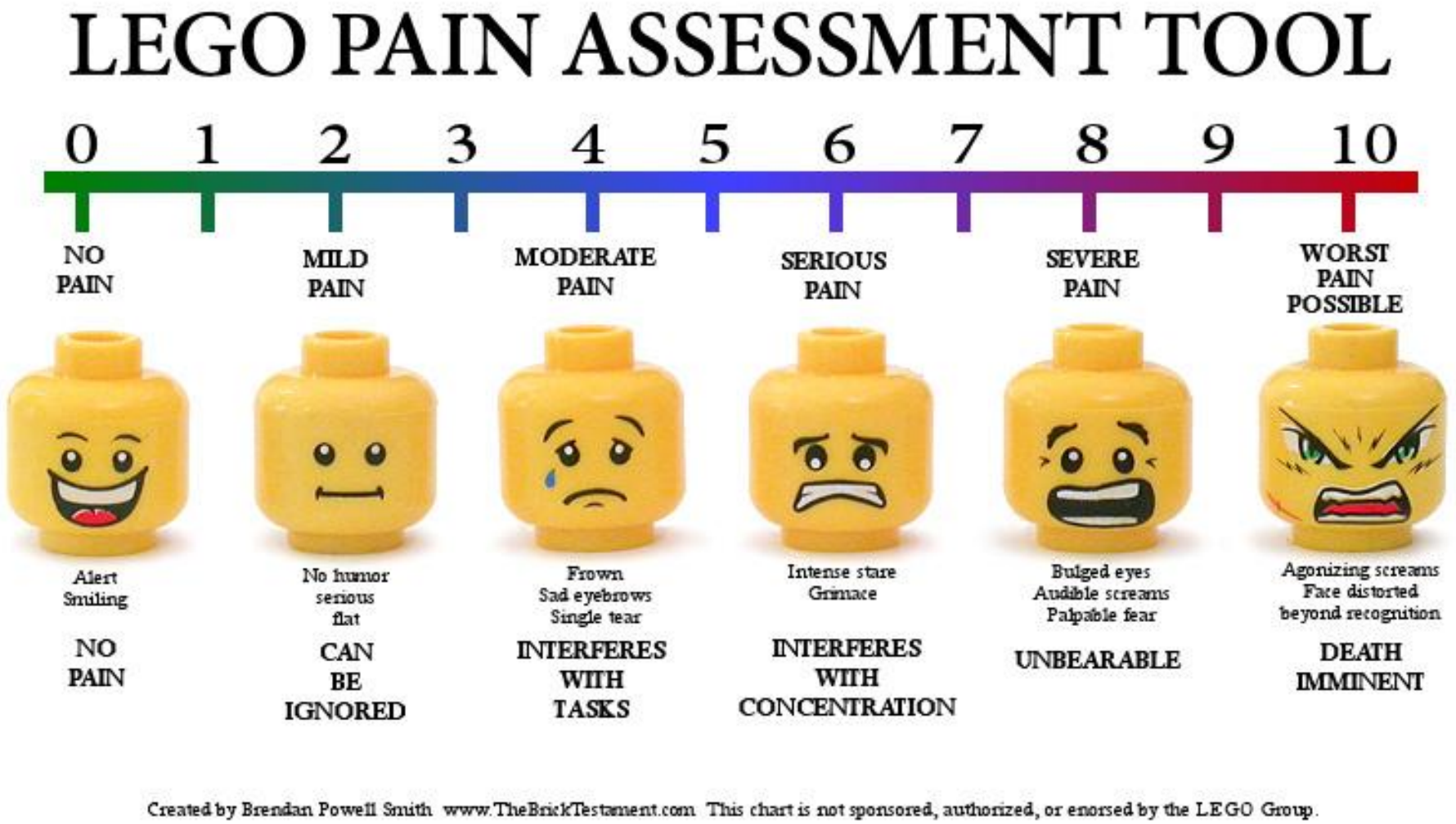


Pain assessment tools

Scale of pain:

- **NRS** (Numerical Rating Scale)
  - self reports
  - more for adults
  - patient with contact
  - from 0 to 10 (eleven-degree scale)
- **Verbal rating scale** (descriptive scale)
  - no pain, mild, moderate, severe, the worst

VAS – Visual Analog Scale



- more for children

Severity of pain (NRS/VAS)

- **Mild**: pain score 1 - 3
- **Moderate**: pain score 4 - 6
- **Severe**: pain score 7 - 10


Pain relief

Non-pharmacologic Pain Management

- Neurostimulation
- TENS
- Acupuncture
- Anesthesiology
- Nerve block
- Surgery
- Physical therapy
- Exercise
- Heat/cold
- Psychological approaches
- Cognitive therapies (relaxation, imagery, hypnosis)
- Biofeedback
- Behavior therapy
- Psychotherapy
- Complementary tx
- Massage therapy
- Art therapy
- Music therapy
- Aroma therapy

Pharmacologic Pain Management

The analgetics used to manage cancer-related pain can be divided into three categories:

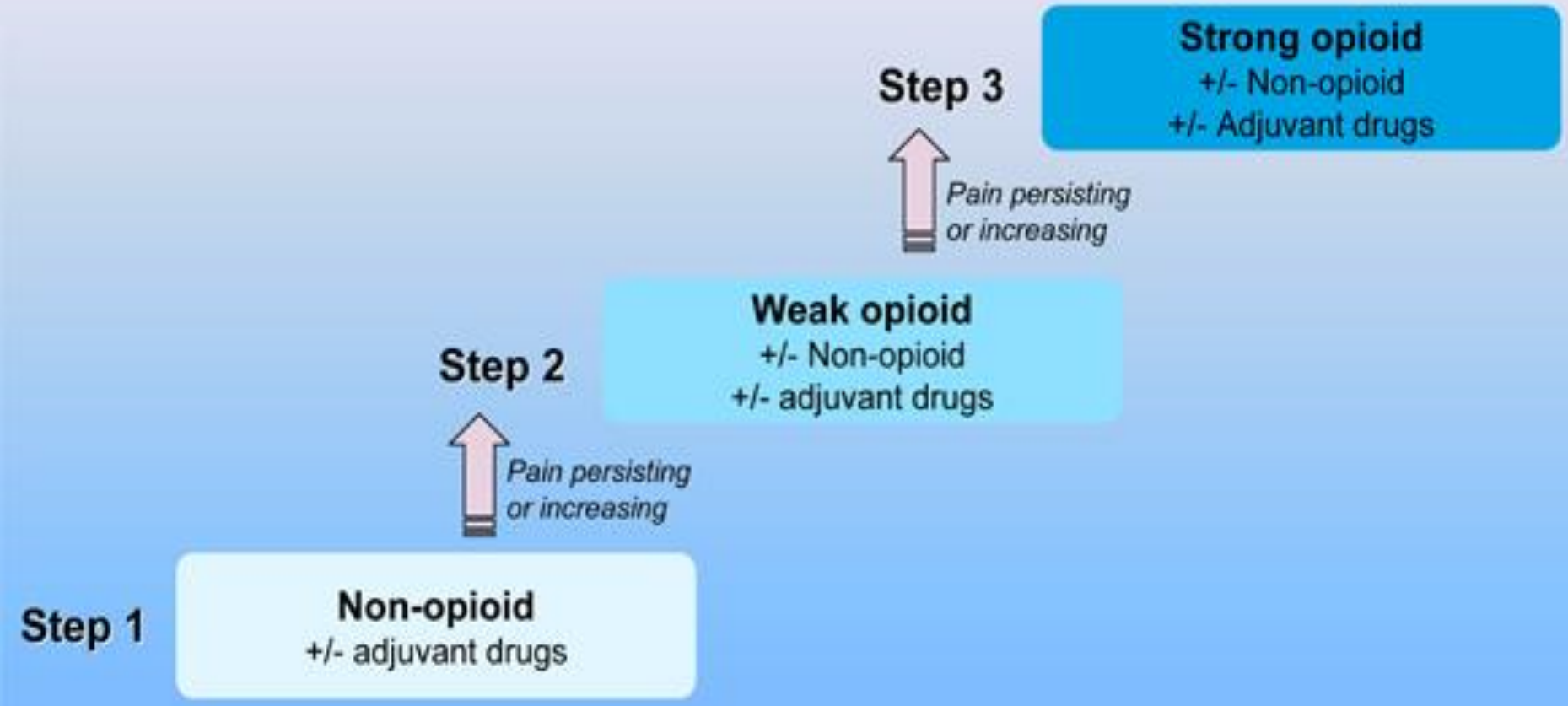
- Non-opioids medications such as acetaminophen (paracetamol) or nonsteroidal anti-inflammatory drugs (NSAIDs)
- Weak opiods medications such as codeine or strong opioids such as morphine
- Adjuvant medications such as tricyclic antidepressants (TCAs) and anti-epileptic drugs (AEDs)

Principles of the treatment of chronic pain according to the WHO

- **„by the mouth”**
  The oral route is preferred for all steps of the pain ladder.
- **„by the clock”**
  Cancer pain is continuous - analgesics should be given at regular intervals (every three to six hours), not on demand.
- **„by the ladder”**
  The WHO pain ladder is a framework for providing symptomatic pain relief. The three-step approach is inexpensive and 80-90% effective.
- ***For the individual***
- ***With attention to detail***

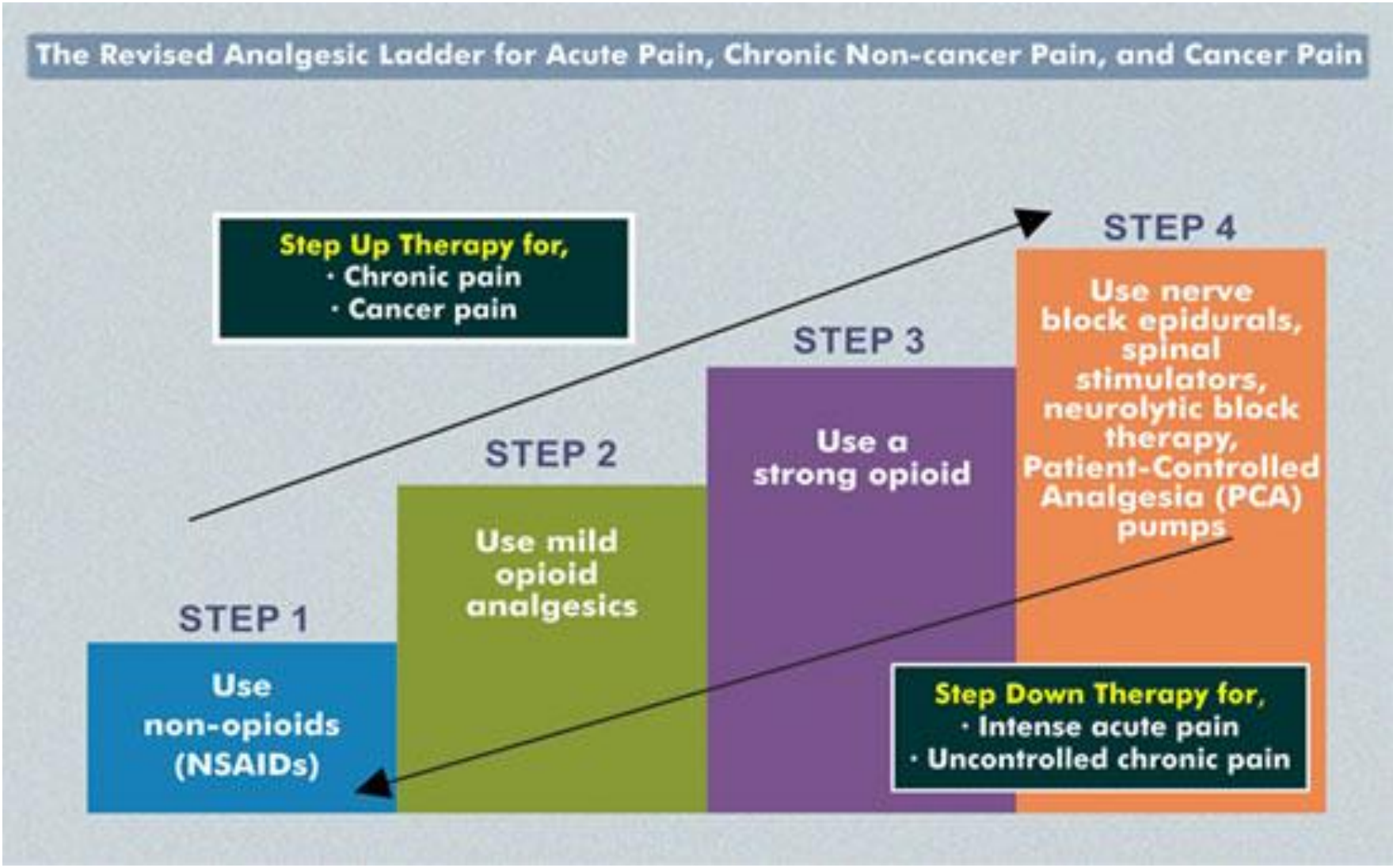
*** The WHO three-step analgesic ladder has been accepted and is used worldwide.**

World Health Organization Three Step Analgesic Ladder

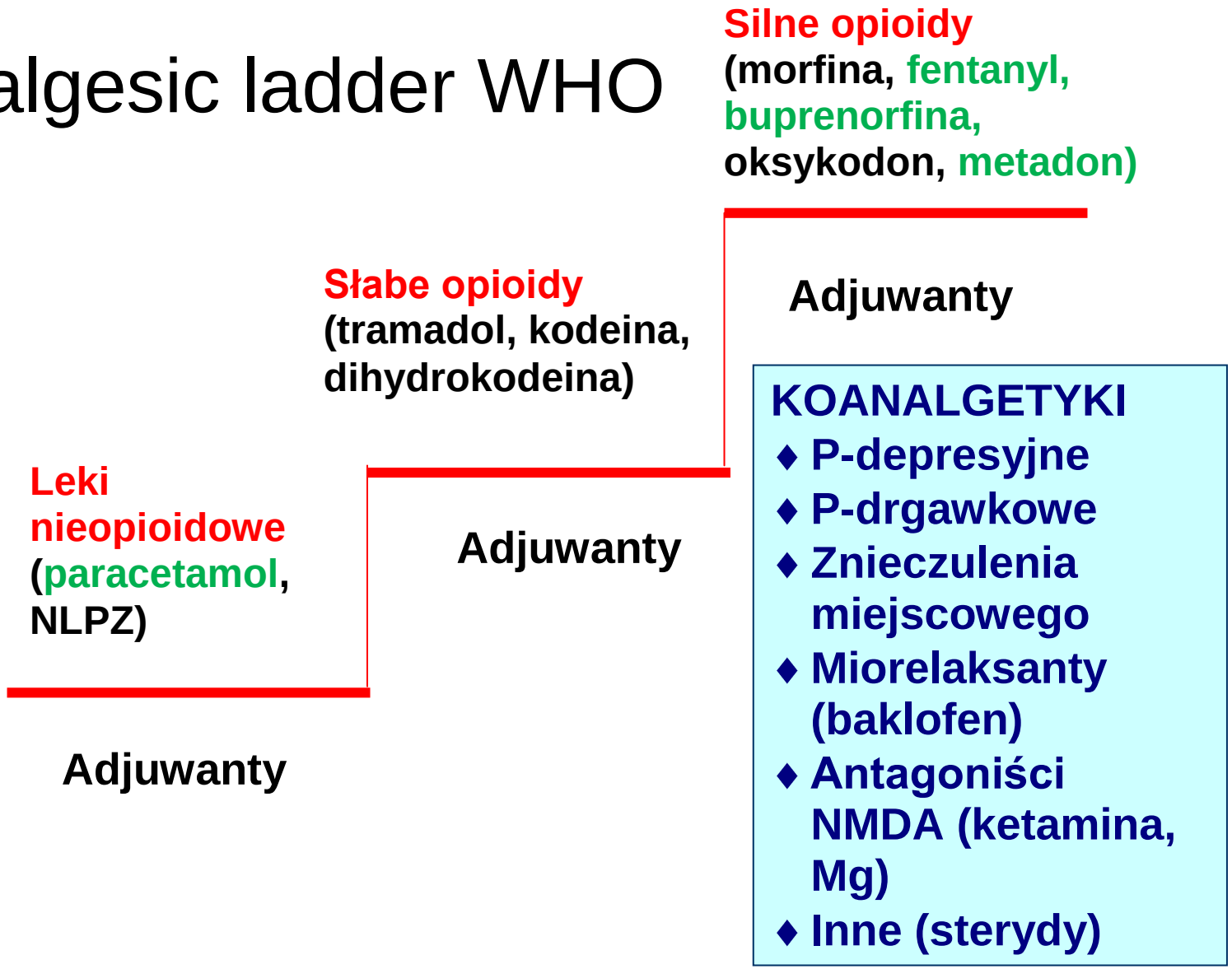


Non opioids include paracetamol, aspirin, ibuprofen, other NSAIDs - **Weak opioids** include tramadol, codeine, dihydrocodeine, dextropropoxyphene - **Strong opioids** include morphine, hydromorphone, oxycodone, fentanyl, buprenorphine - Adjuvants include carbamazepine, diazepam, prednisolone.

Reference: *Adapted from: Chapter 11 – Pain relief and palliative care. Three Step Analgesic Ladder. www.searo.who.int/linkFiles/Publications_ch11.pdf*


The Revised Analgesic Ladder for Acute Pain, Chronic Non-cancer Pain, and Cancer Pain
Step Up Therapy for,
· Chronic pain
· Cancer pain
STEP 1
Use non-opioids (NSAIDs)
STEP 2
Use mild opioid analgesics
STEP 3
Use a strong opioid
STEP 4
Use nerve block epidurals, spinal stimulators, neurolytic block therapy, Patient-Controlled Analgesia (PCA) pumps
Step Down Therapy for,
· Intense acute pain
· Uncontrolled chronic pain

Analgesic ladder WHO



* safe in renal failure

STEPS

- Step 1 – The first step of analgesic ladder is to use a non-opioid analgesic. Adjuvant drugs can be added to enhance analgesic efficacy. They may be used at any step.
- Step 2 – If pain persists despite the 1st step medications, then a mild low-potency opioid should be added (not substituted).
- Step 3 – If pain persists despite the 2nd step efforts, then strong opioids (high-potency) are initiated. The dose of the stronger opioid can be titrated upward according to the patient`s pain. There is no ceiling dose for strong opioid(s).

Equianalgesic opioid doses

- Morphine 1
- Buprenorphine x 100 (75-115)
- Fentanyl x 100 - 150
- Oxycodone x 1,5 - 2
- Methadone x 6 - 10
- Tamadol 1/10
- Codeine 1/10

Codeine

- Codeine is commonly prescribed for both its analgesic properties and antitussive effect.
- It can be one of the most constipating of all drugs and is sometimes used to control to diarrhea in opioid-tolerant cancer patients.
- Codeine is metabolized by the liver to its active metabolite – morphine.
- Approximately 10% of the Caucasian population has mutations in the hepatic enzyme (CYP2D6) and therefore cannot convert codeine to morphine, resulting in poor analgesic efficacy.

Tramadol

- T - codeine`s synthetic analogue is used in the treatment of cancer pain.
- It is a weak mu-receptor agonist effective for the treatment of mild to moderate pain states (including cancer).
- With activity via blocade of presynaptic reuptake of serotonin and norepinephrine, there is evidence that it works in neuropathic pain states.

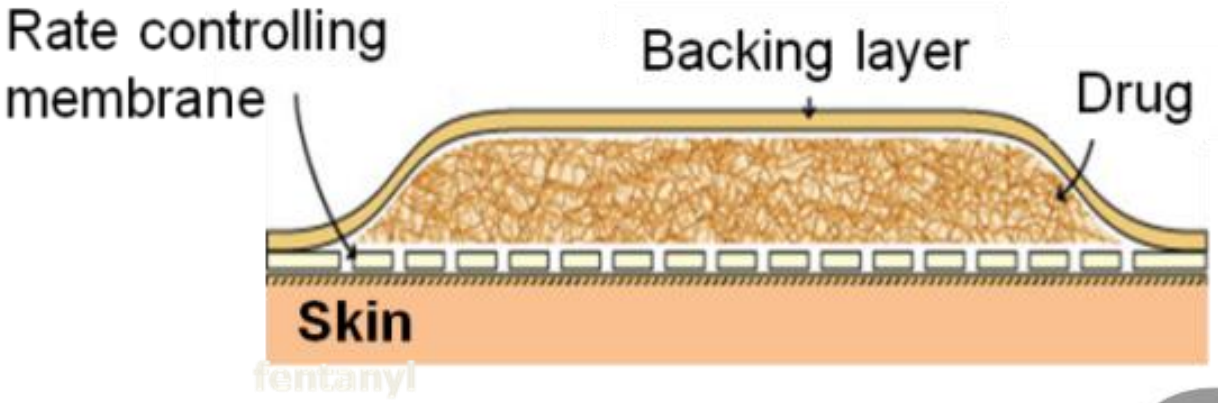
Morphine

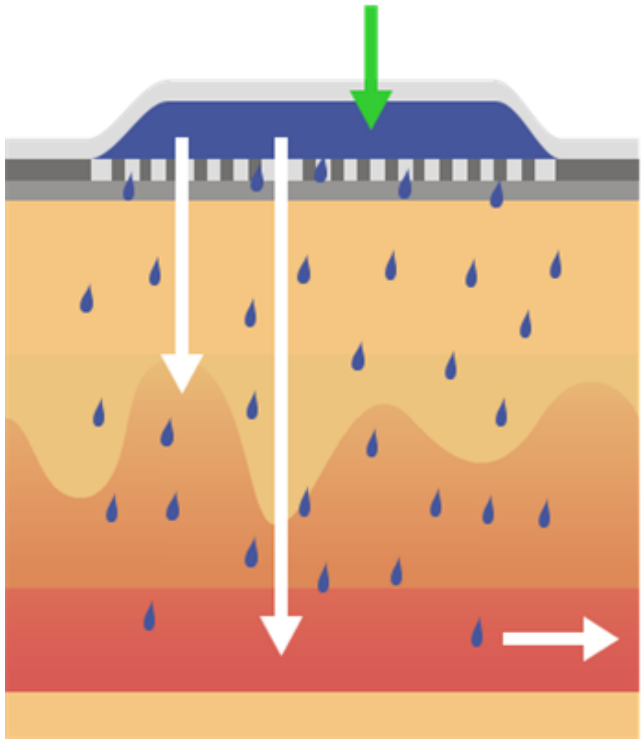
- MF is most widely used and prototype drug of this class.
- It is gold-standard drug avaliable in all countries and is valued for its low cost, ease of use, and analgesic potency.
- It is converted to morphine-3-glucuronide (M3G) and morphine-6-glucuronide (M6G) in the liver, acting on the mu receptor in CNS.
- M3G – has a very low affinity for opioids receptors, is ineffective as an analgesic, may be responsible for morphine`s observed neurotoxicity.
- M6G – has been implicated in opioid activity and side effects (e.g., sedation).
- Morphine`s duration of action is 2-4 hours (IR, immediate-release), 8 – 12 hours (SR, sustained-release or CR, controlled-release)
- Caution should be exercised when using morphine in patient with renal failure, as these compounds are excreted by the kidney.
- MF is available: oral, rectal, intravenous, intramuscular, subcutaneus, epidural, intrathecal preparations.

Fentanyl

- Fentanyl is a semisynthetic opid available in parenteral, transdermal and oral preparations.
- The sustained-release, transdermal form has been used successfully for stable pain.
- Once applied, it forms a depot under the skin and is slowly released into the circulation. This limits its use for emergency situations, though, since it takes up to 18 hours to reach peak (12-24 h).
- Each patch is changed every 72 hours (every 3 days).
- Oral transmucosal fentanyl has been approved for use in cancer patients with breakthrough pain, based on its rapid absorption via oral (buccal) mucosa and nasal musosa.

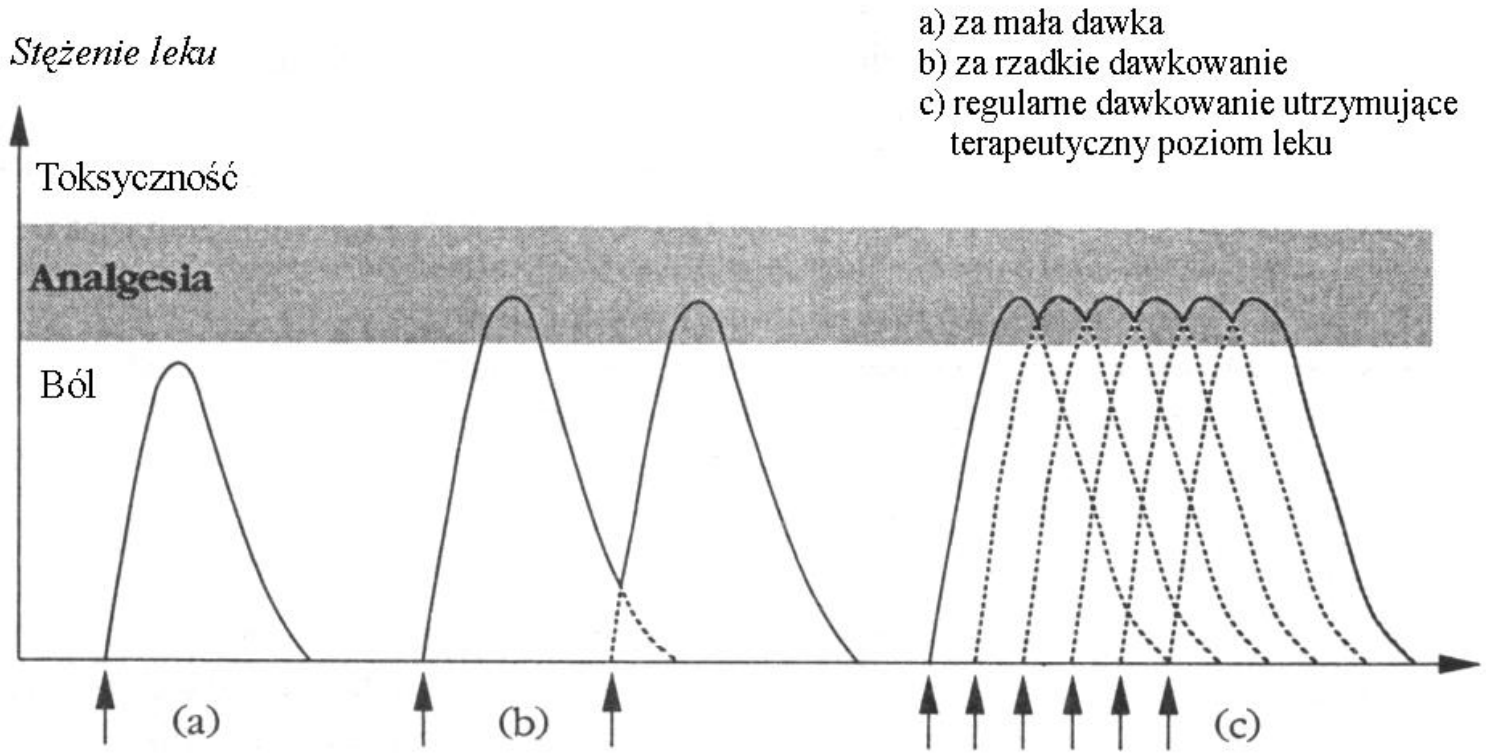
„catch the patch”





Remember basic principles:

- Use WHO pain ladder
- Take a careful drug history
- Know the pharmacology of the Rx
- "Start low, go slow"
- Regularly review the regimen
- Remember that drugs may cause illness



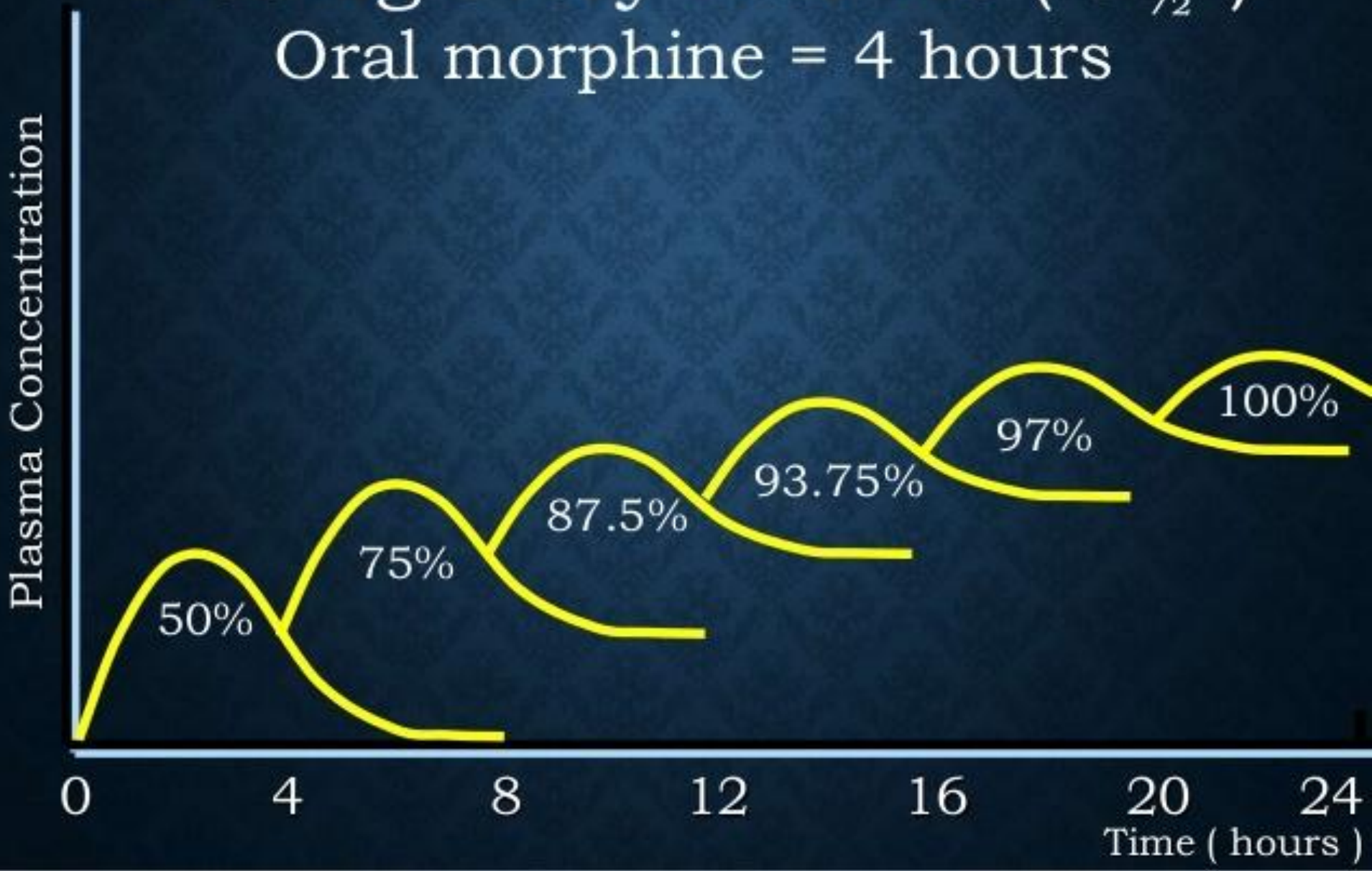
a) medication given in inadequate dosage

b) too infrequently will result in unrelieved pain

c) there regular scheduling of medications according to the duration of analgetic action will maintain therapeutic drug levels and prevent the recurrence of pain

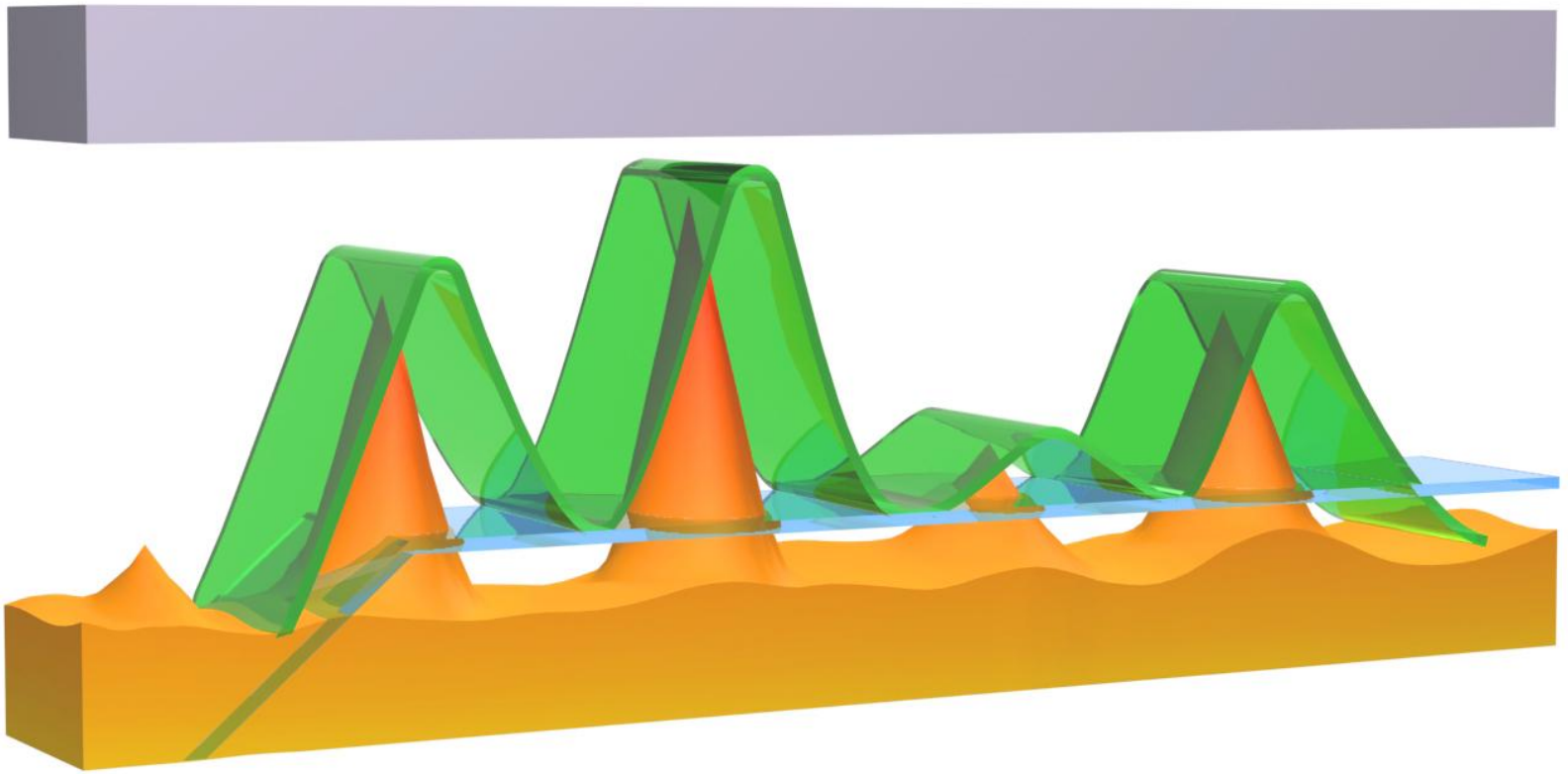
Dosing every half-life ($t_{1/2}$)

Oral morphine = 4 hours



Steady state after 5 half-lives ≈ 20 hours

Change over time… BTP



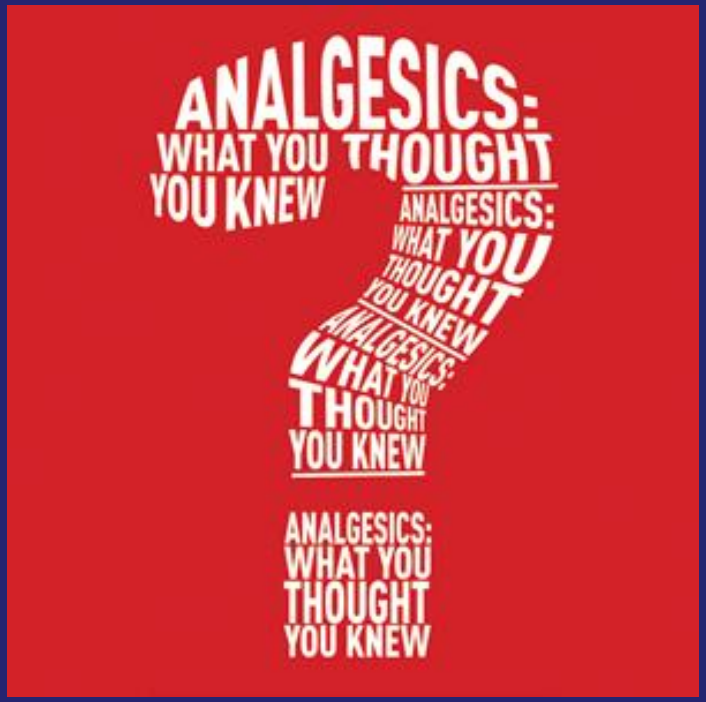
Breakthrough pain (BTP)

- **BTP: a transient exacerbation of pain that occurs either spontaneously, or in relation to a specific predictible or unpredictible trigger, despite relatively stable and adequately controlled background pain.**

- Breakthrough pain (BTP) is a fact of life for many cancer patients. But pain experts are now finding that these sudden, temporary flares of severe pain can affect people with noncancerous conditions as well.

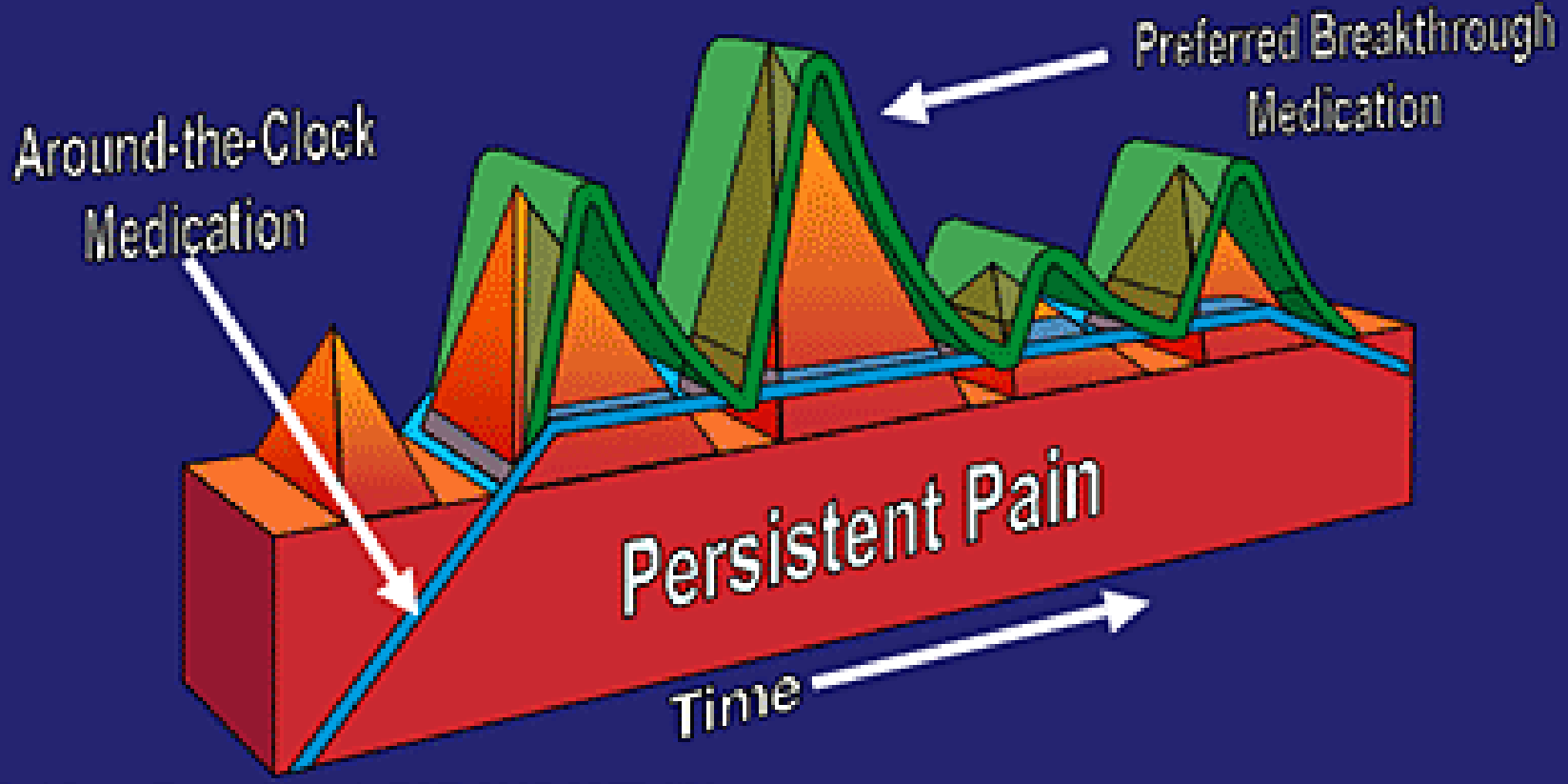
Pain

- *Persistent (*or chronic baseline) *pain* and *breakthrough pain (BTP)* are distinct entities that should be addressed individually



Breakthrough Pain Medication

- An analgesic with
  - Rapid onset of action (within minutes of administration)
  - Short duration of action (around 30 minutes)

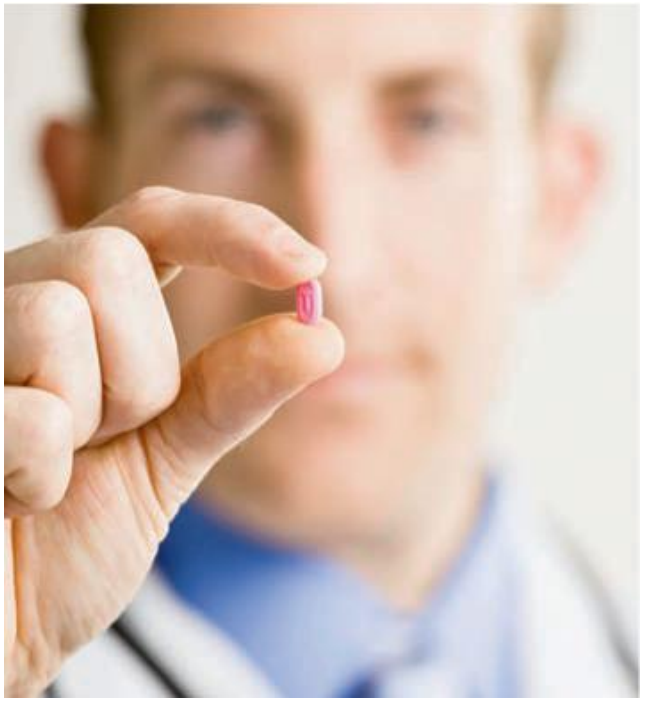


Modified from Bennett et al. *P&T.* 2005;30(5):296.

Types of BTP

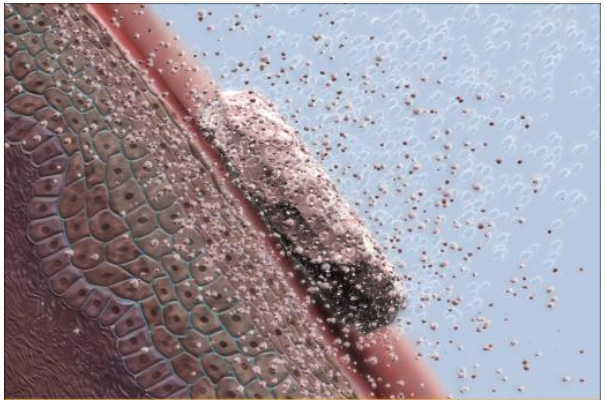
- incidental pain
- idiopathic pain
- *„end-of-dose failure (pain)”*

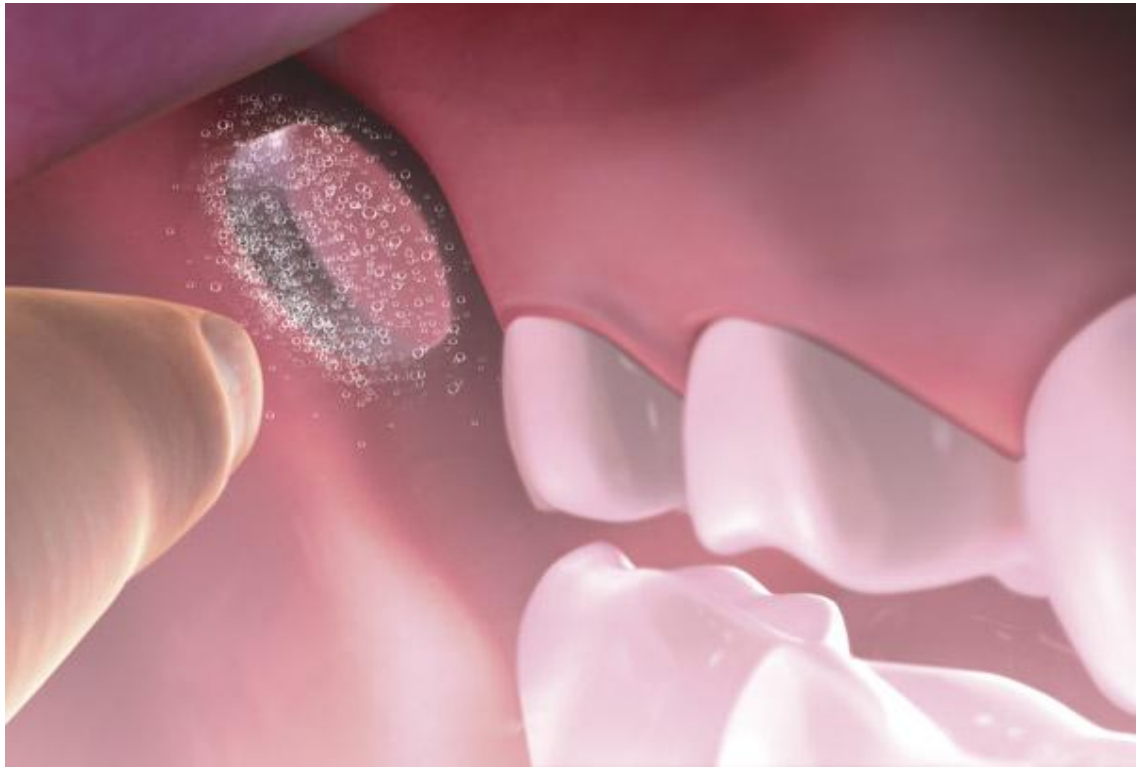
  *it occurs with great regularity



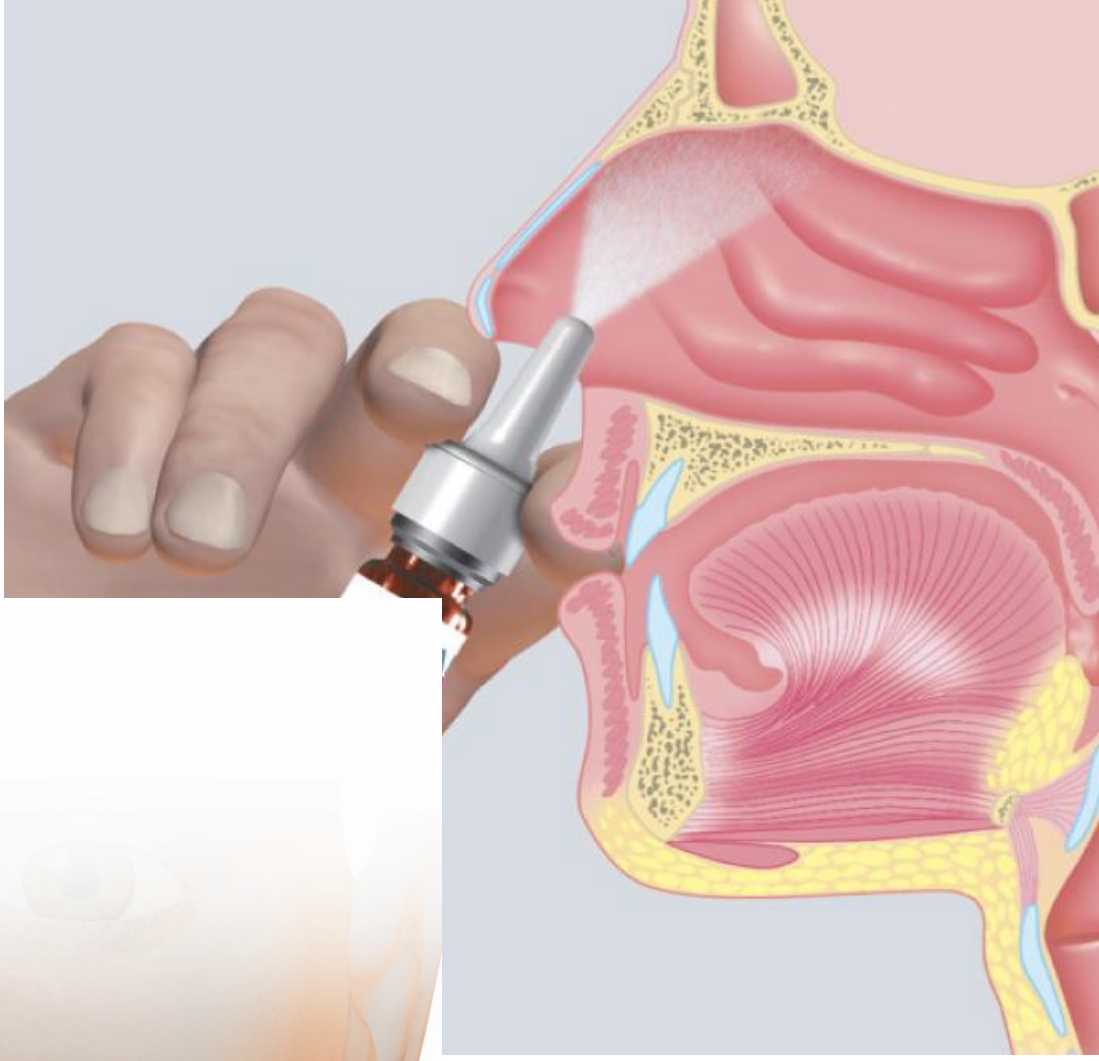
Simmonds M.A. Management of Breakthrough pain due to cancer. Oncology, 1999 :13:1103-1108.

Fentanyl buccal tablets
(correct administration)*





Intranasal fentanyl spray



Manage side-effects opiates:

- Constipation
- Tolerance to nausea and sedation develops in 3-7 days.
- Use adjuvant (coanalgesic) agents with opioid:
  - Tricyclic antidepressants
  - Corticosteroids
  - Anticonvulsants
  - Muscle relaxants
  - Stimulants

Opioids in neuropathic pain treatment

- we can use them!
- in cancer pain we use them earlier because of other types of pain
- oxycodone (polineuropathy after bortezomib)
- *Claudio Cartoni, Gregorio Antonio Brunetti et al. Controlled-release oxycodone for the treatment of bortezomib-induced neuropathic pain in patientswith multiple myeloma. Support Care Cancer, Springer-Verlag 2012*

Used drugs

Drug	Mean daily doses (mg)	No. of patients	Mean NRS	Mean intensity of side effects	Global patient evaluation
Gabapentin	1,800	17	9.3	Mild	Not effective
Pregabalin	300	11	7.9	Slight	Not effective
Gabapentin+tramadol	1,200 220	4	8.4	Mild	Not effective
Pregabalin+tramadol	175 250	6	6.8	Slight	Slightly effective
Amitriptyline+tramadol	75 150	8	8.6	Mild	Not effective

Results

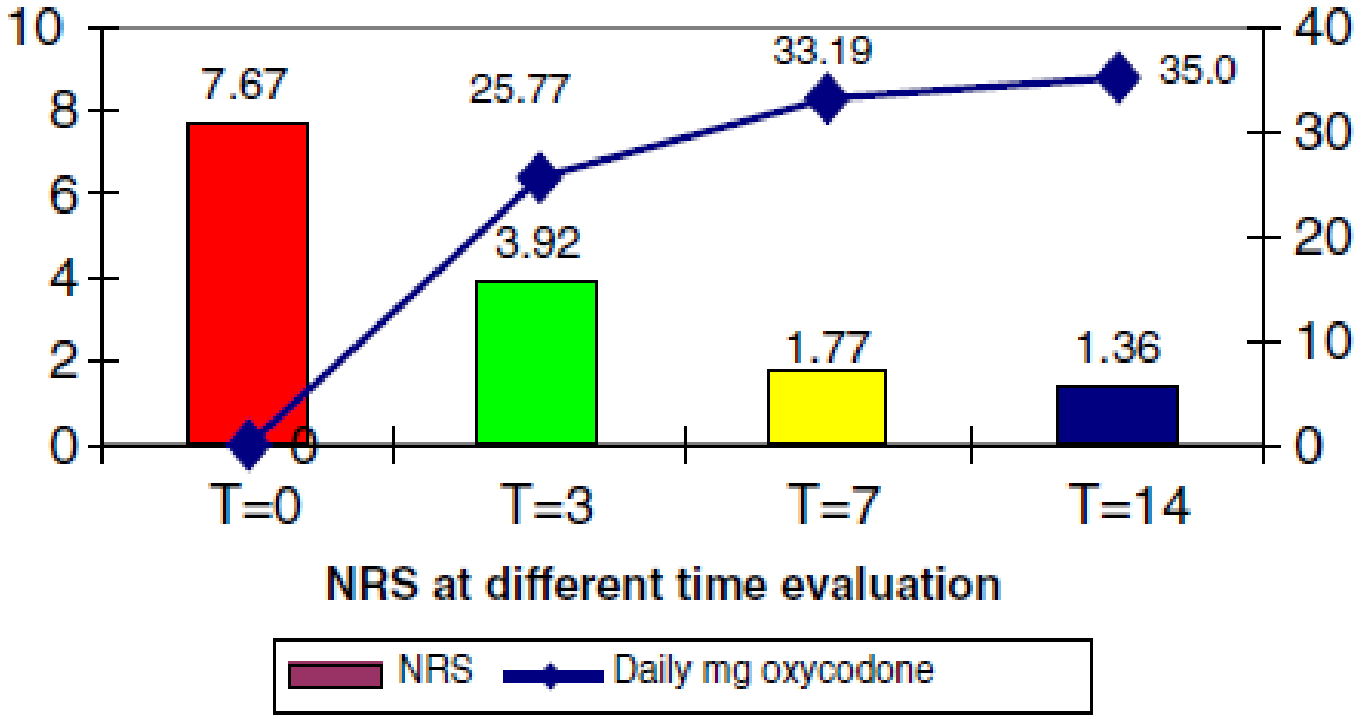
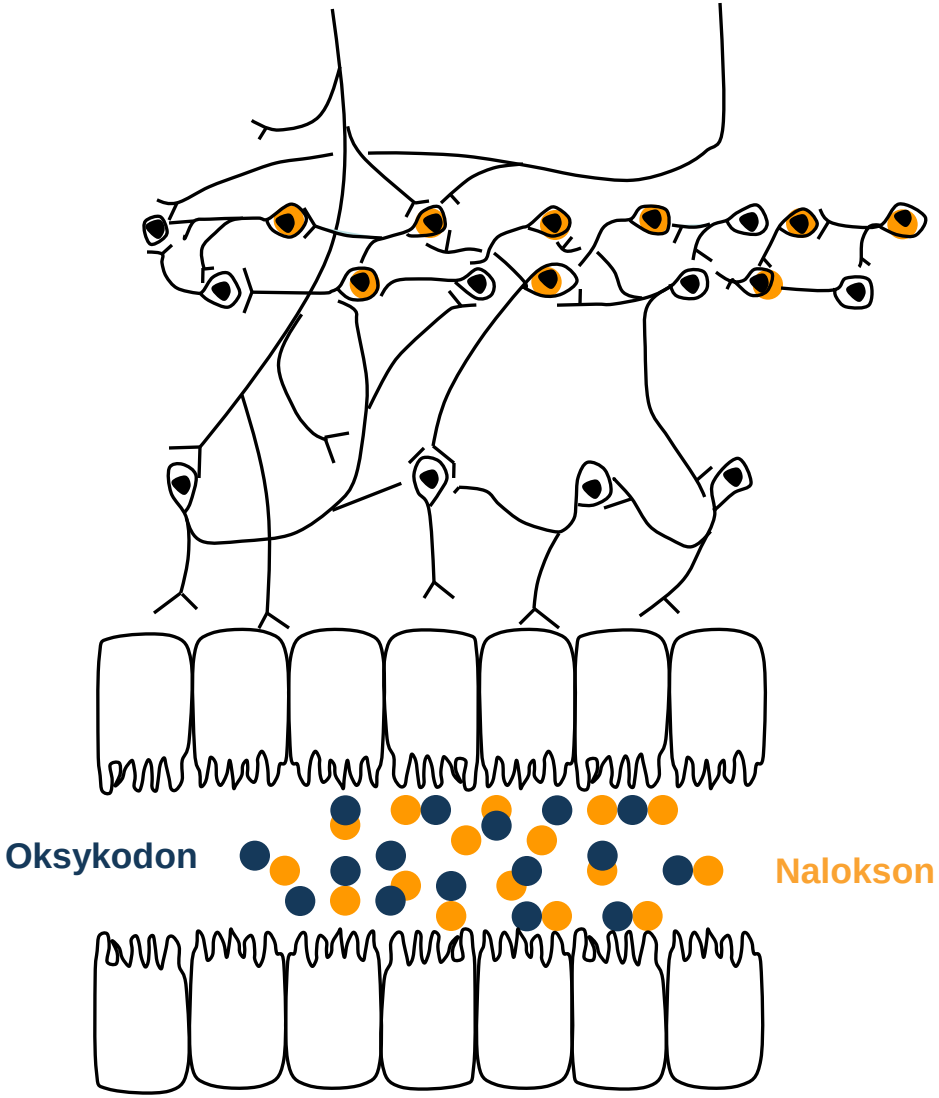


Fig. 1 Relationship between pain and oxycodone CR dosage

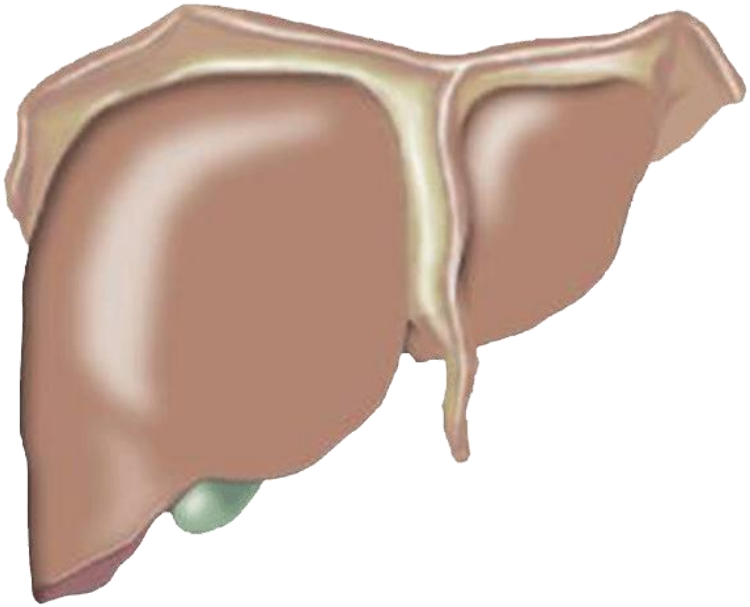
Oxycodone + naloxone in the intestine



TARGIN®
OXYCODONE/NALOXONE

Dane w dokumentacji

Liver as an important place of metabolism



Oksykodon

Nalokson

Oksykodon

Nalokson

De Schepper HU et al. Neurogastroenterol Motil 2004; 16: 383–94
Heiskanen T et al. Clin Pharmacol Ther 1998; 64:603–611


YOU ARE LEAVING
PAIN
ENJOY THE JOURNEY!