

PANCREATIC PAIN MANAGEMENT

Univerza v Ljubljani



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Pain Classification

Pancreatic Pain

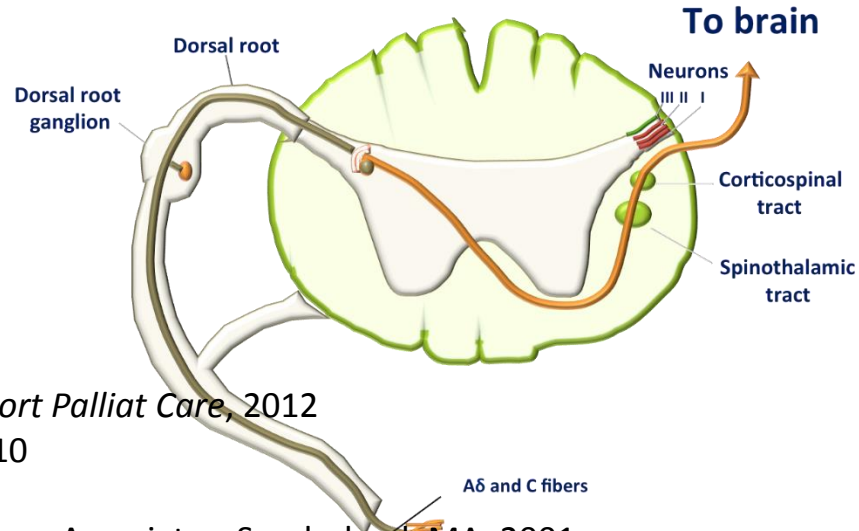
- time course: acute / chronic
- site of origin: somatic, visceral
- type of pain: nociceptive / neuropathic
- intensity: mild, moderate, severe, intorelable
- underlying cause for pain: malignant / non-malignant

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Visceral Pain

- transferred through thinly myelinated A δ -fibres and unmyelinated C-fibres
- 50 – 90% of primary afferent neurons are 'silent' and become mechanosensitive after inflammation



Sikandar and Dickenson, *Curr Opin Support Palliat Care*, 2012

Dubin and Patapoutian, *J Clin Invest*, 2010

Fields HL *et al.*, *Neurobiol Dis*, 1998

Williams and Purves, *Neuroscience*. Sinauer Associates; Sunderland, MA: 2001

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Visceral Pain

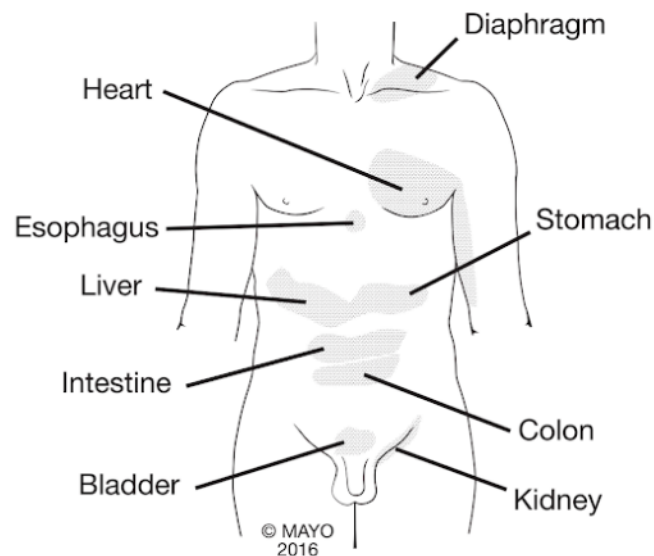
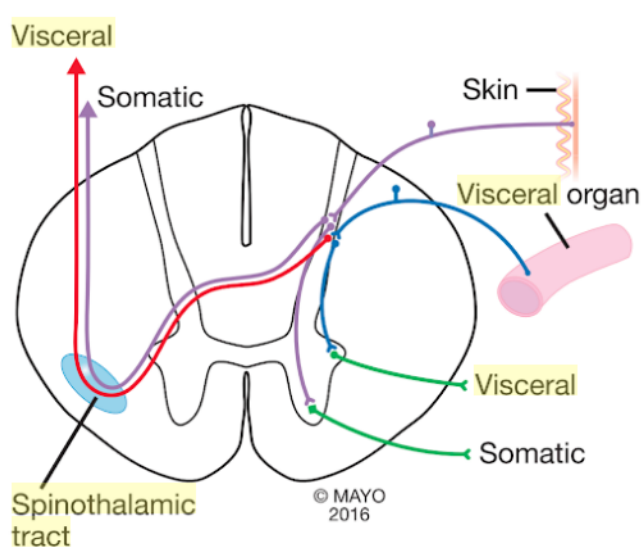
- caused by tension (stretch), ischemia and inflammation
- poorly localized with referral to somatic structures
- produces nonspecific regional or whole-body motor responses
- produces strong autonomic responses
- leads to sensitization of somatic tissues
- produces strong affective responses
- gradual increment of pain sensations: discomfort, malaise, pain

Sikandar and Dickenson, *Curr Opin Support Palliat Care*, 2012

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Viscerosomatic convergence



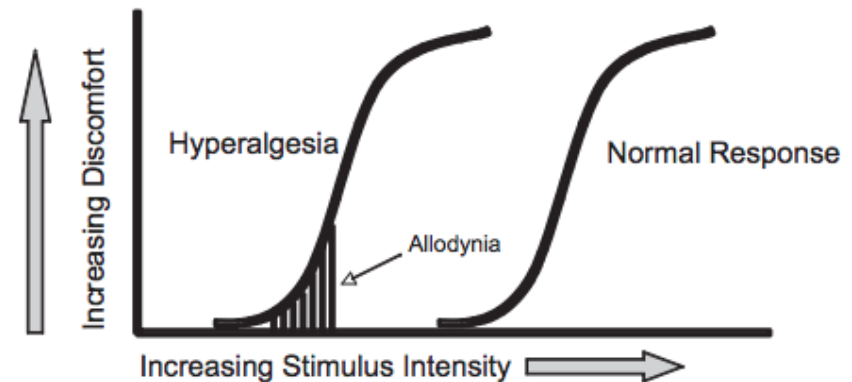
Benarroch, Cutsforth-Gregory and Flemming (2017). Mayo Clinic Medical Neurosciences: Organized by Neurologic System and Level. Oxford, UK: Oxford University Press.

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Sensitization and visceral pain

- visceral pain involves visceral hyperalgesia
- increased sensitivity has two causes:
 1. A change of sensory neurons in the viscera; they respond more intensely to naturally occurring stimuli
 2. An enhanced sensitivity of the sensory pathways in the brain that mediate sensations from the viscera
- both processes are known as “sensitization”
 - peripheral sensitization occurs in the viscera
 - central sensitization occurs in the brain

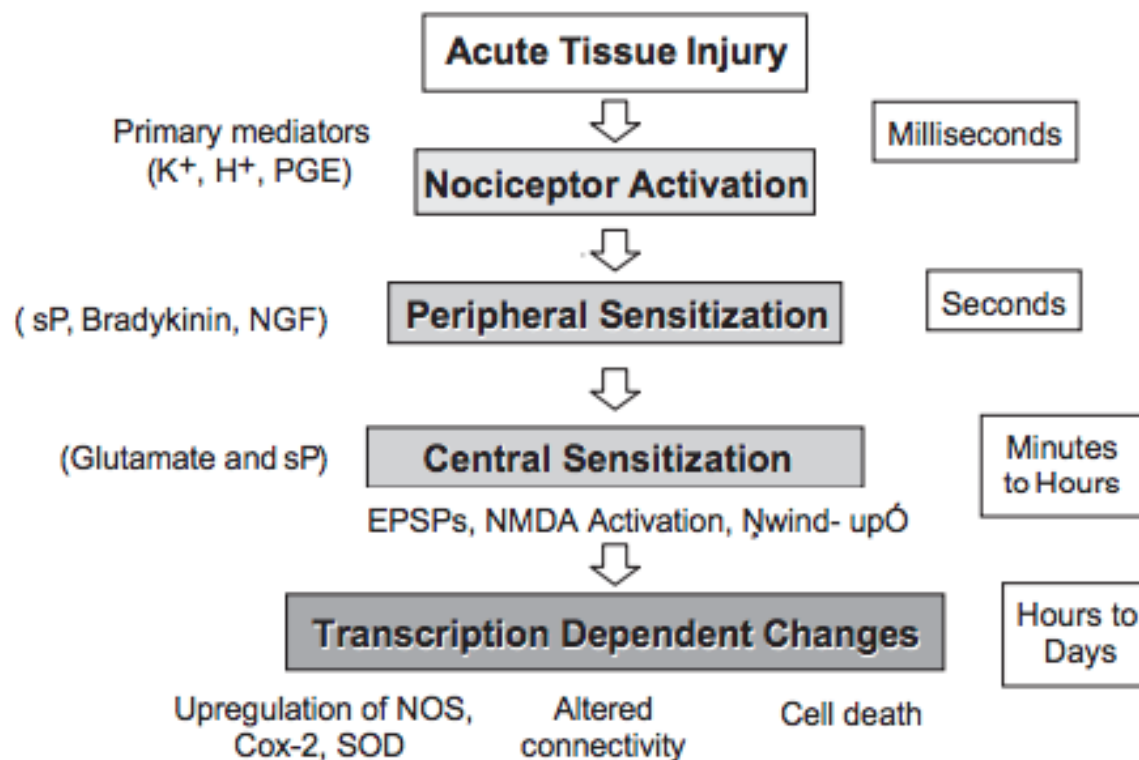


McClain (2010). Primary and secondary hyperalgesia. In Sinatra, Jahr & Watkins-Pitchford (Eds.), *The Essence of Analgesia and Analgesics*, Cambridge: Cambridge University Press.

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Sensitization and visceral pain - timeline



McClain (2010). Primary and secondary hyperalgesia. In Sinatra, Jahr & Watkins-Pitchford (Eds.), The Essence of Analgesia and Analgesics, Cambridge: Cambridge University Press.

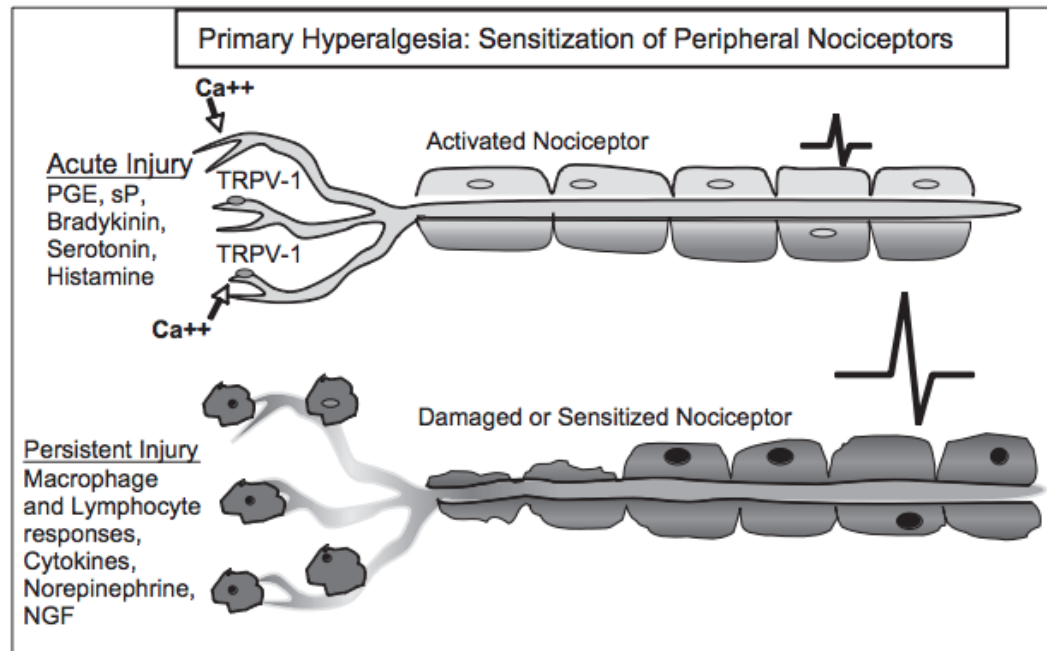
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Peripheral sensitization (primary hyperalgesia)

- persistent noxious stimulation of visceral nociceptors
 - inflammatory mediators
 - ectopic activity
 - noxious stimuli

- hyperalgesia



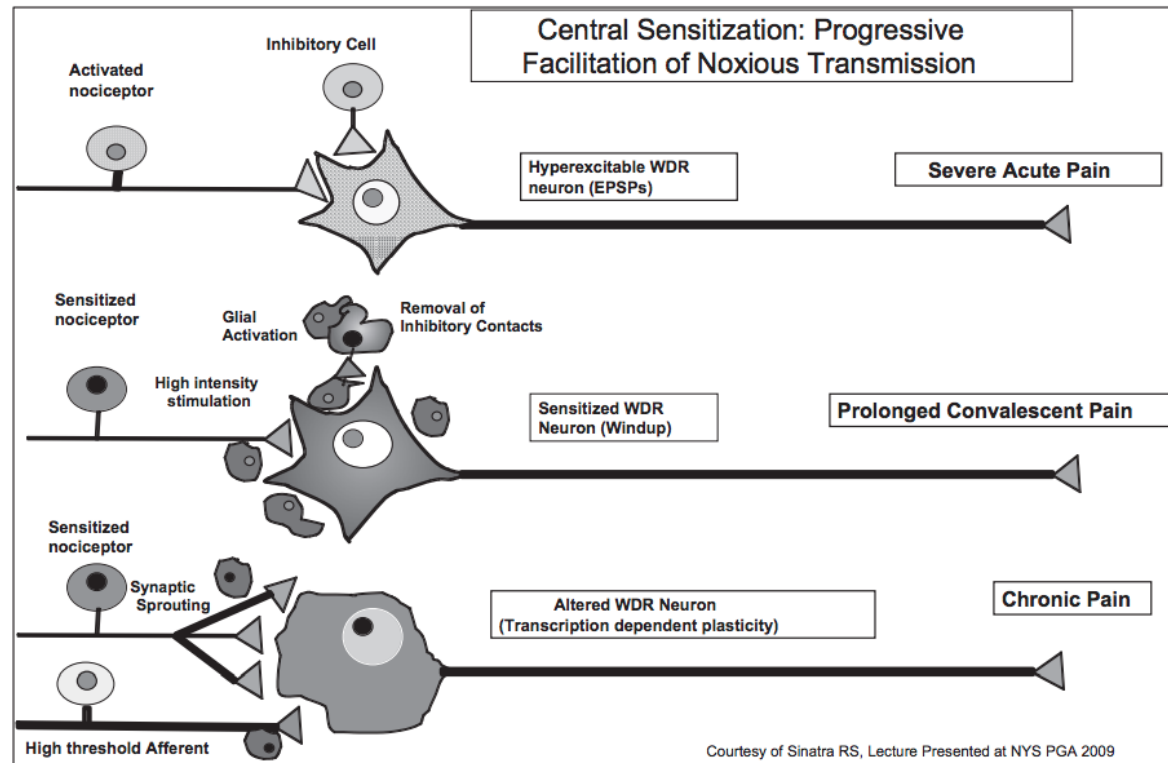
McClain (2010). Primary and secondary hyperalgesia. In Sinatra, Jahr & Watkins-Pitchford (Eds.), The Essence of Analgesia and Analgesics, Cambridge: Cambridge University Press.

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Central sensitization (secondary hyperalgesia)

- sensitized peripheral nociceptors stimulate second order neurons in dorsal horn
- wind up
- transcription dependent plasticity



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Neuropathic pain

LESION INVOLVES NOCICEPTIVE PATHWAY!

Disease process

- Infection/Inflammation
- Neurotoxicity
- Tumor infiltration
- Metabolic abnormality

Trauma

- External injury
- Nerve compression
- Inflammation

Therapeutic interventions

- Surgery
- Chemotherapy
- Irradiation

Genetic predisposition

- Inherited neurodegeneration
- Metabolic/ endocrine abnormalities

Campbel and Meyer,
Neuron, 2007

Hansson, *European Journal
of Pain*, 2002

Dvorkin et al. *Arch Neurol*,

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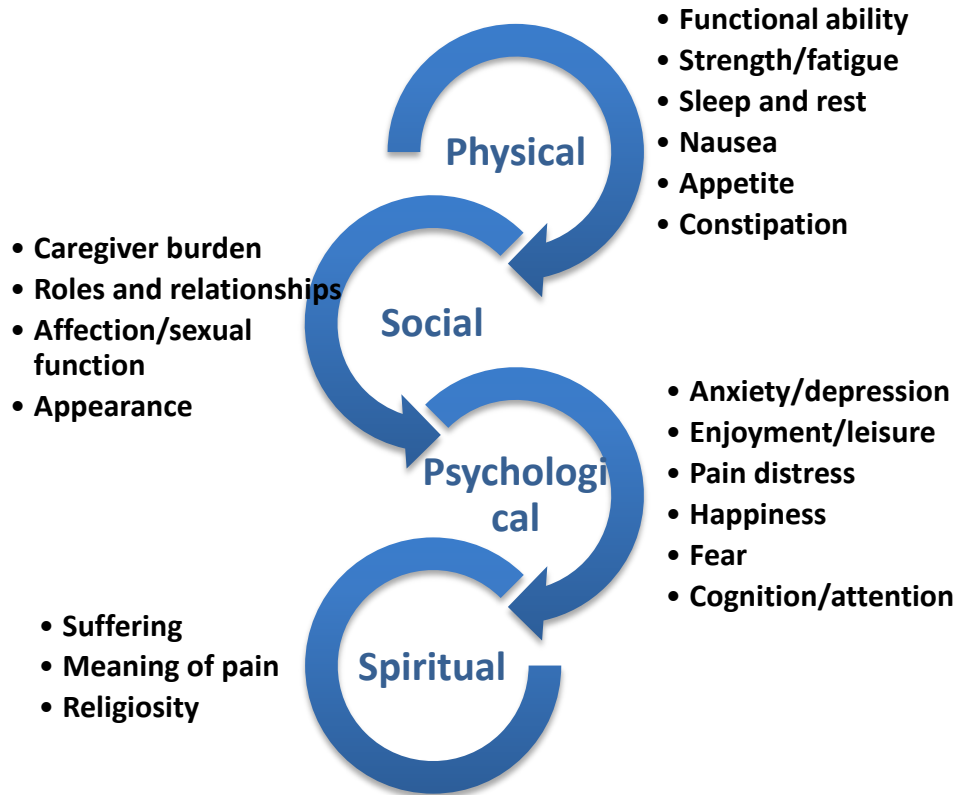
Neuropathic pain

- persistent /short episodes
- burning / electrical
- combined with hyperalgesia and allodynia
- intensified at night

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Impact of pain on the quality of life



Adapted from Ferrell et al. *Oncol Nurs Forum*. 1991;18:1303–9.

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Pain management strategies

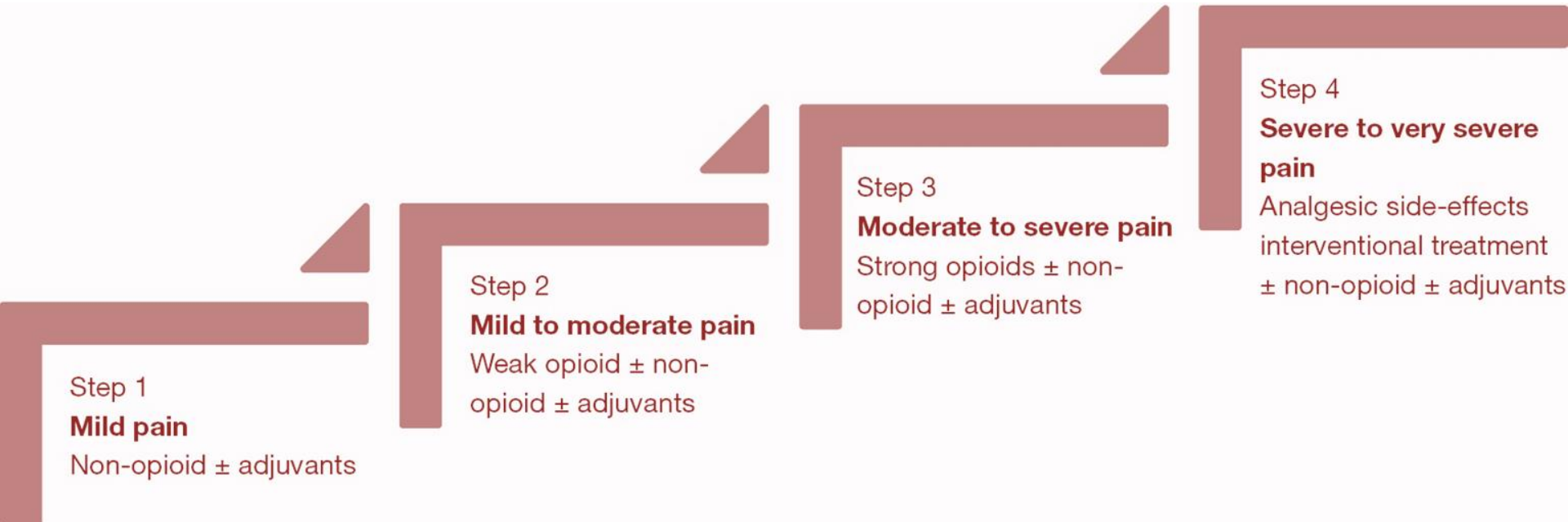
- multimodal
- individualized
- medical therapy
 - pharmacological
 - non-pharmacological
- patient's collaboration
- family support

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Pain management strategies

PHARMACOLOGICAL – WHO ladder



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Pain management strategies

PHARMACOLOGICAL – WHO ladder

- simple analgetics
 - paracetamol
 - (NSAIDs)
 - metamizol
 - adjuvant analgesics
 - anxiety, depression: antidepressants (TCA, SSRI, SNRI)
 - abdominal cramps: antispasmodics, benzodiazepines
 - neuropathic pain: pregabalin, gabapentin, amitriptyline, duloxetine
 - inadequately controlled pain (unconventional treatment): ketamine, lidocaine, cannabinoids
- 
- Step 1
Mild pain
Non-opioid ± adjuvants

Working group for the International (IAP – APA – JPS – EPC) Consensus Guidelines for Chronic Pancreatitis, Pancreatology. 2017

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Pain management strategies PHARMACOLOGICAL – WHO ladder

- opioids



- adjuvant analgesics:

- anxiety, depression: antidepressants (TCA, SSRI, SNRI)
- abdominal cramps: antispasmodics, benzodiazepines
- neuropathic pain: pregabalin, gabapentin, amitriptyline, duloxetine
- inadequately controlled pain (unconventional treatment): ketamine, lidocaine, cannabinoids

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Adjuncts for pancreatic pain

- pancreatic enzymes supplements
- antioxidants
- octreotide

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Pain management strategies PHARMACOLOGICAL – intravenous therapy

- **NON-OPIOIDS** metamizol 2,5 g /12h
NSAID Neodolpasse 250 ml / 12 h
- **OPIOIDS** piritramide
- **ADJUVANT ANALGETICS** lidocaine 100 mg / 50 ml
infusion 15 ml/h (3 h)

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Pain management strategies

PHARMACOLOGICAL – oral therapy

- **NON-OPIOIDS**
 - metamizol 1000 mg / 8 h or 40 drops / 8
NSAID – if not contraindicated
- **OPIOIDS** long-acting slow-release opioid
tramadol, tapentadol, oxycodone, oxycodone / naloxone, morphine,
fentanyl
- **ADJUVANT ANALGETICS (NEUROPATHY)** pregabalin, amitriptyline,
duloxetine...

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Pain management strategies

INVASIVE AND NON-PHARMACOLOGICAL MEDICAL THERAPY

- endoscopic therapy (+ ESWL, sphincterotomy, stenting)
- surgical treatment
- neurolytic interventions
 - celiac plexus blocks
 - splanchnic nerve ablation
 - spinal cord stimulation
 - transcranial magnetic stimulation
- lifestyle changes: alcohol / smoking abstinence
- support groups
- psychological (behavioral) interventions, hypnosis

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Pain management goals

NON-MALIGNANT CHRONIC PAIN

- education: lifestyle changes, life with moderate pain (VAS 5 – 6)
- non-pharmacological pain treatments
- pharmacological pain treatment: non-opioids combined with lowest dose opioids (< 120 mg morphine / day)

MALIGNANT CHRONIC PAIN:

- pain relief (VAS < 3) - no maximum opioid dose

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Pain management strategies for chronic pancreatic pain

INTERDISCIPLINARY APPROACH

- gastroenterologist
- anesthesiologist – algologist
- abdominal surgeon
- dietician
- physical medicine and rehabilitation (PM)
physiotherapist
- psychologist / psychiatrist
- social worker



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THANK YOU



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