REGISTRATION

Natural Ingredient and Chronic Pain

DIAGNOSIS OF MIXED PAIN

NUTRITION AND NATURAL INGREDIENTS FOR PAIN MANAGEMENT

28 March 2025

P&G Health

Pain 香港疼痛學會 The Hong Kong Pain Society

Diagnosis of Mixed Pain
+/- Management

Dr. LAW Man Shun,
President of Hong Kong Pain Society

P&G Health

Pain
香港疼痛學會
The Hong Kong Pain Society

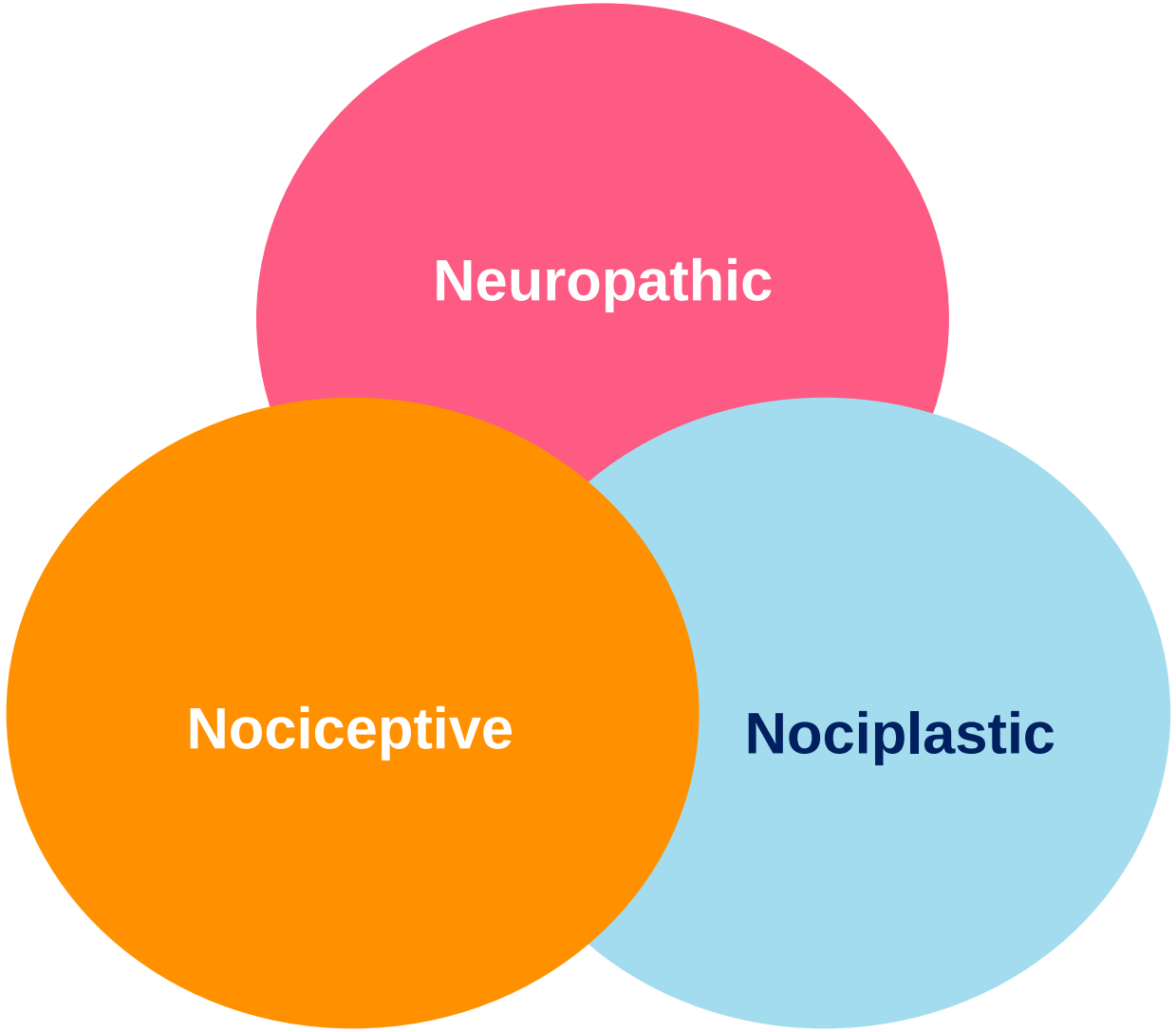
Disclosure

What is Mixed Pain?

Mixed pain consensus:

Mixed pain is a complex overlap of the different known pain types

(nociceptive, neuropathic, nociplastic) in any combination



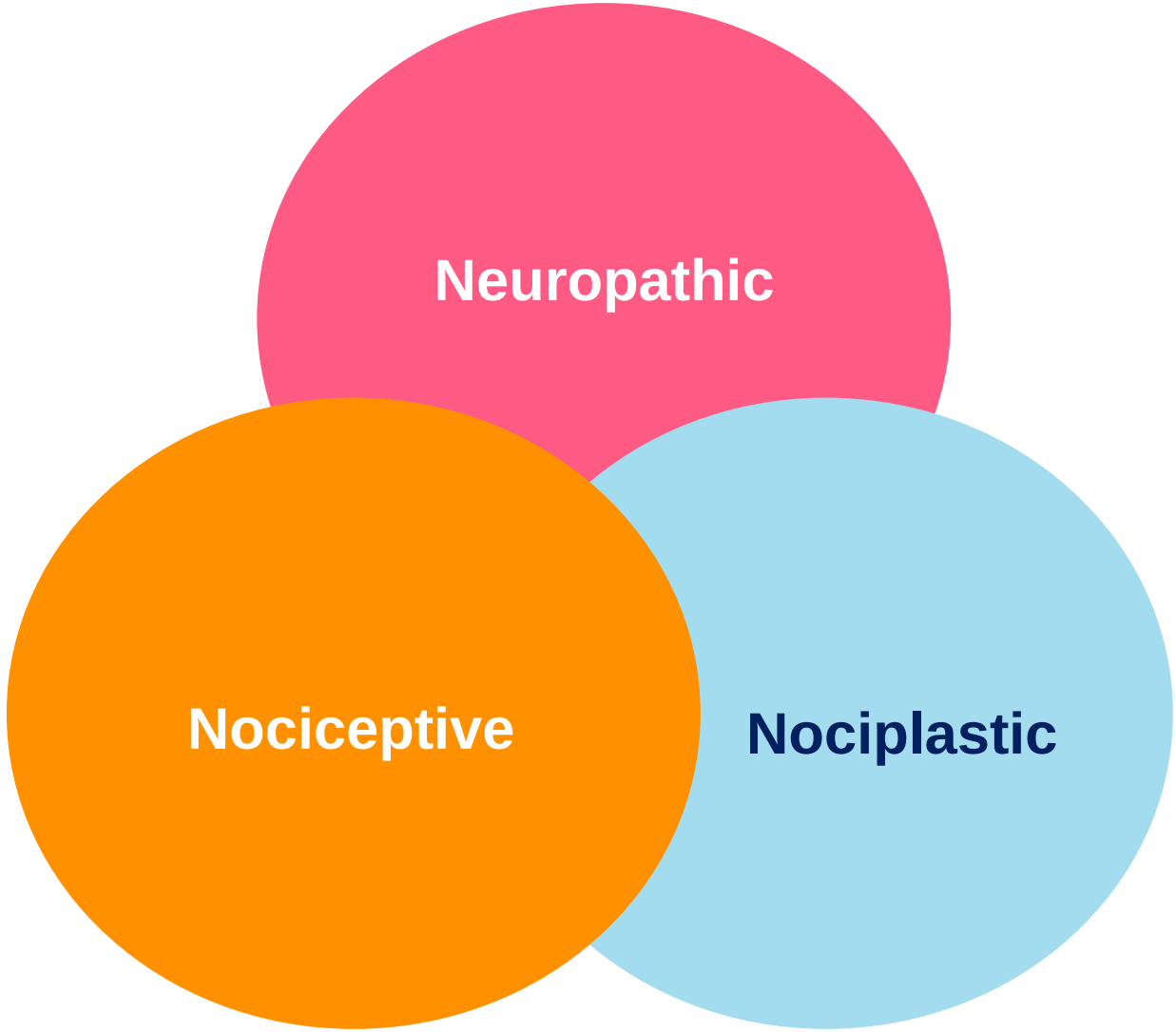
Reference: Freynhagen, R. et al: Curr Med Res Opin. 2019 Jun;35:1011-1018.

What is Mixed Pain?

Mixed pain consensus:

- Simultaneously and/or concurrently to cause pain in the same body area.

- Either mechanism may be more clinically predominant at any point of time.

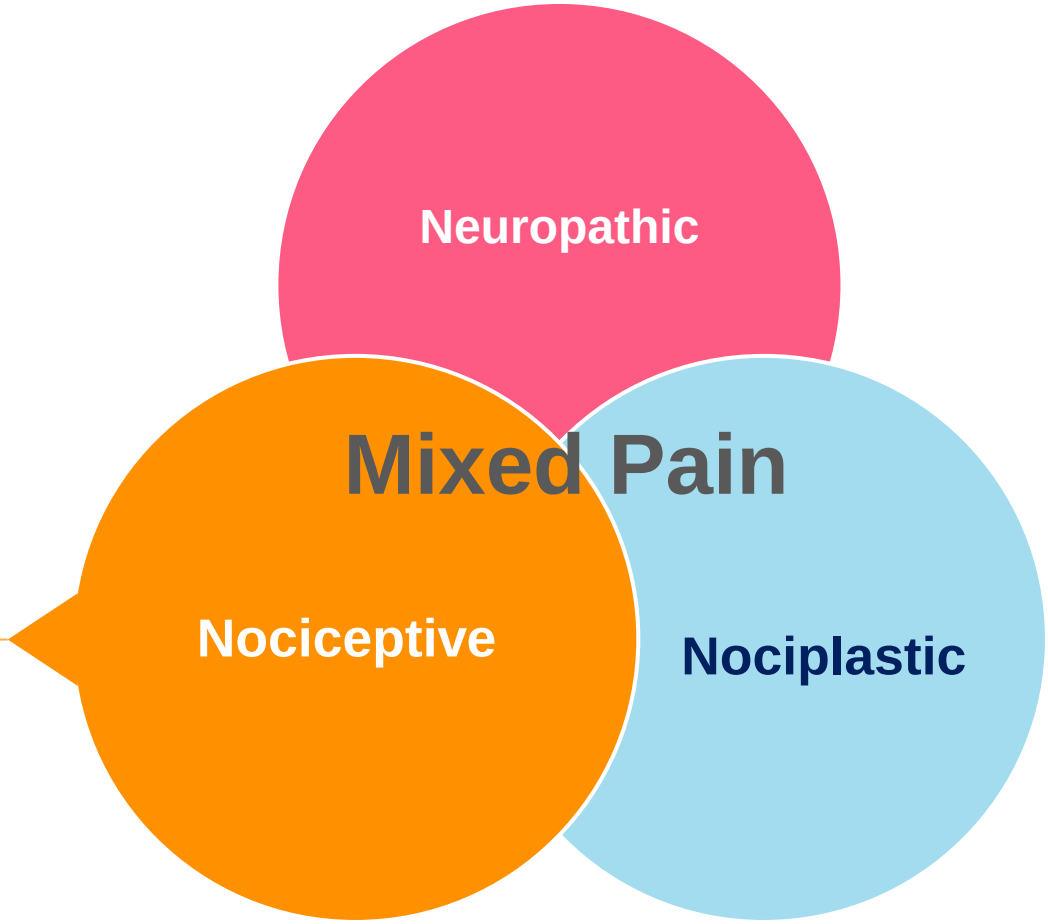


Reference: Freynhagen, R. et al: Curr Med Res Opin. 2019 Jun;35:1011-1018.

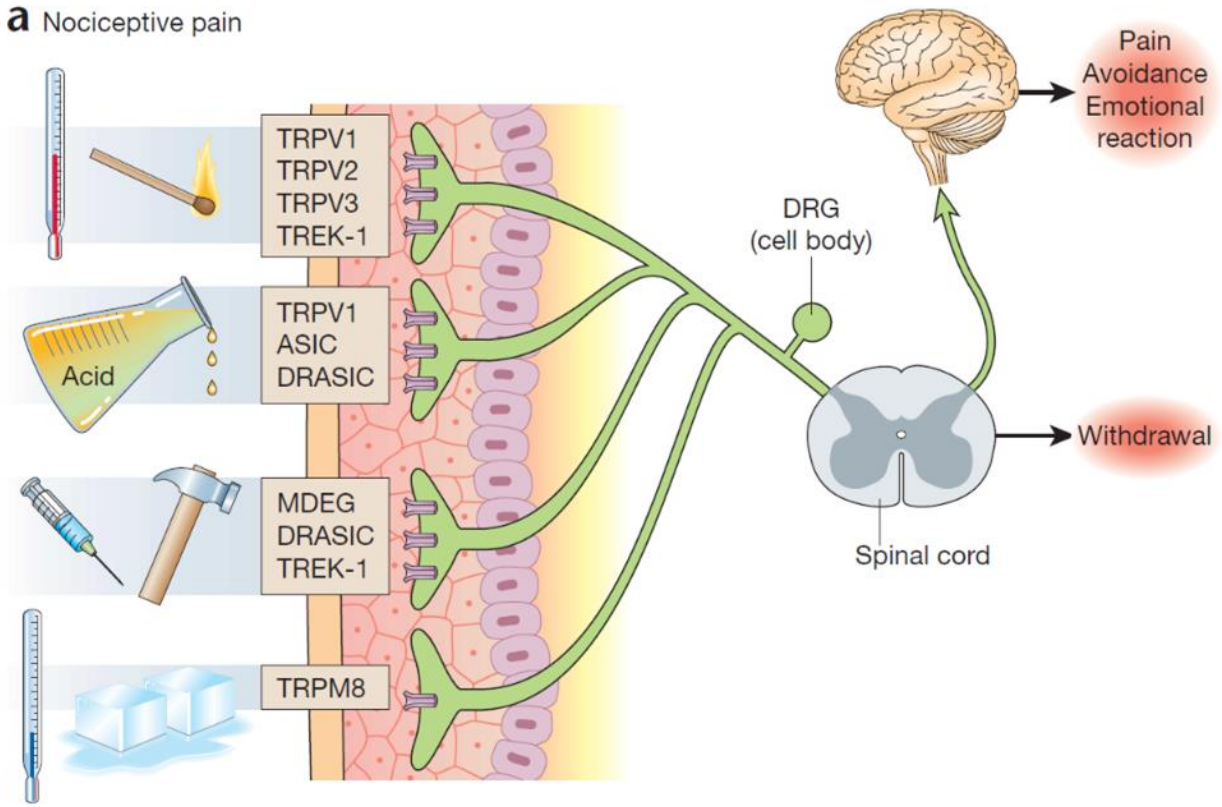
Different types of pain

"pain that arises from actual or threatened damage to non-neural tissue and is due to activation of nociceptors"[1]

Related to acute inflammation

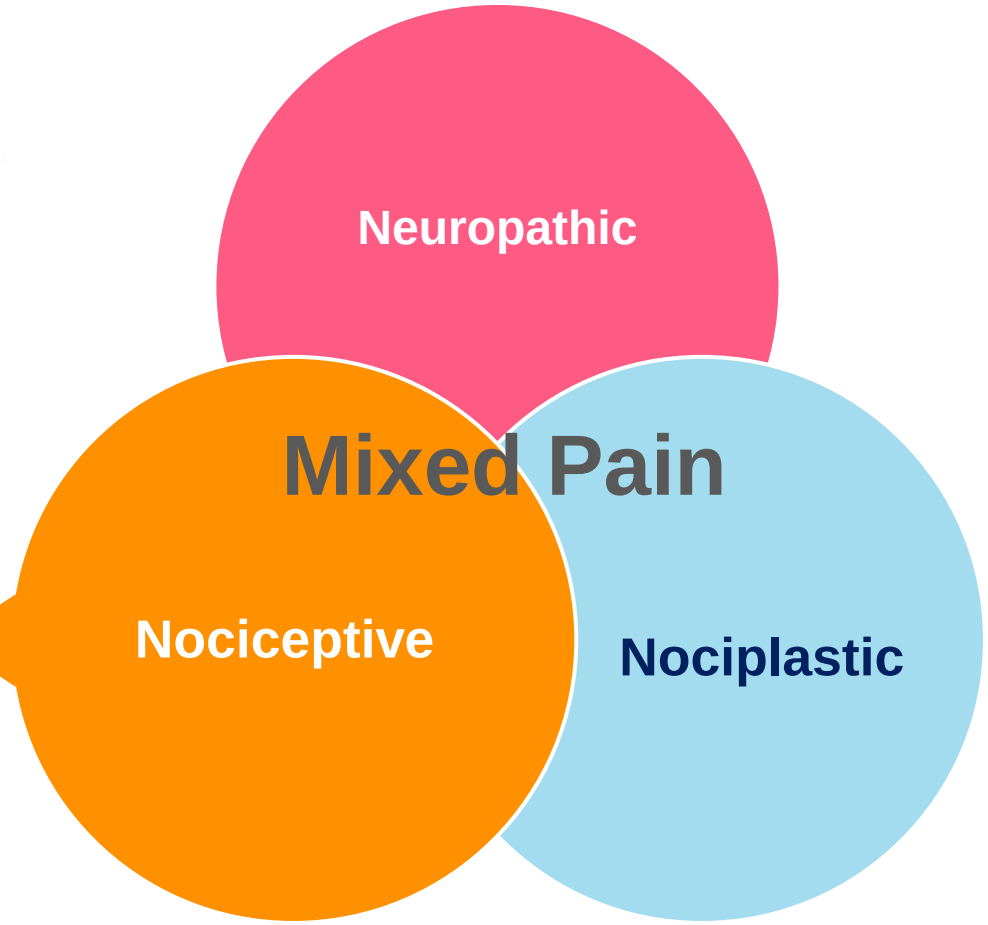


References: **1.** Freynhagen, R. et al: Curr Med Res Opin. 2019 Jun;35:1011-1018. **2.** Savvas S, et al. Pain Management Guide (PMG) Toolkit for Aged Care, 2nd Edition. Sydney: National Ageing Research Institute, Melbourne and Australian Pain Society; 2021. 84p.

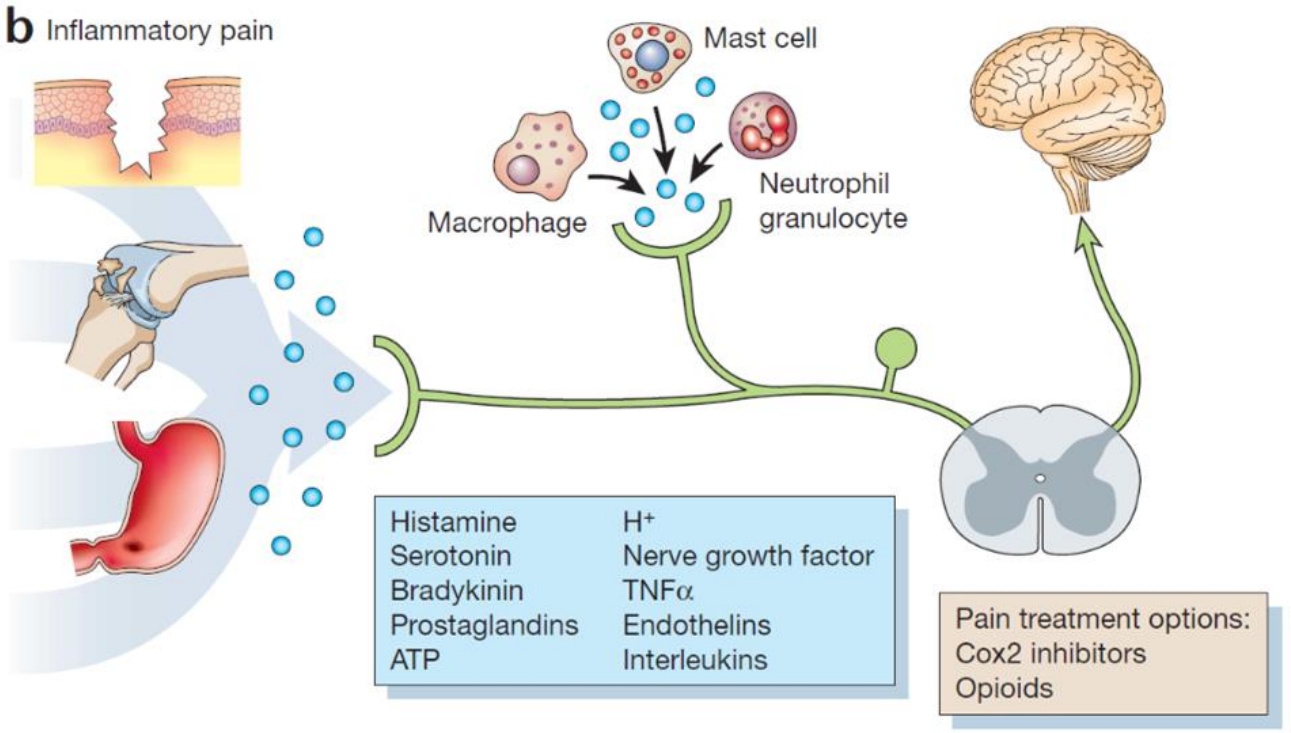


"pain that arises from actual or threatened damage to non-neural tissue and is due to activation of nociceptors"[1]

Related to acute inflammation[2]

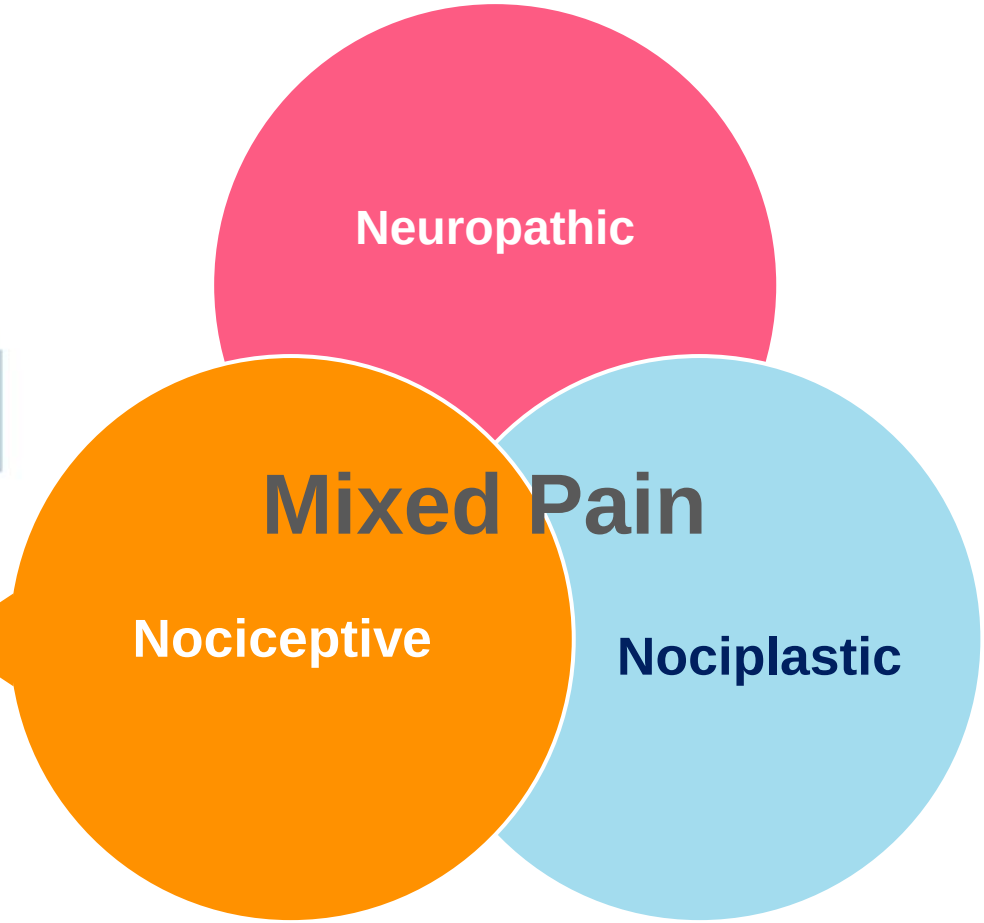


References: **1.** Freynhagen, R. et al: Curr Med Res Opin. 2019 Jun;35:1011-1018. **2.** Savvas S, et al. Pain Management Guide (PMG) Toolkit for Aged Care, 2nd Edition. Sydney: National Ageing Research Institute, Melbourne and Australian Pain Society; 2021. 84p.

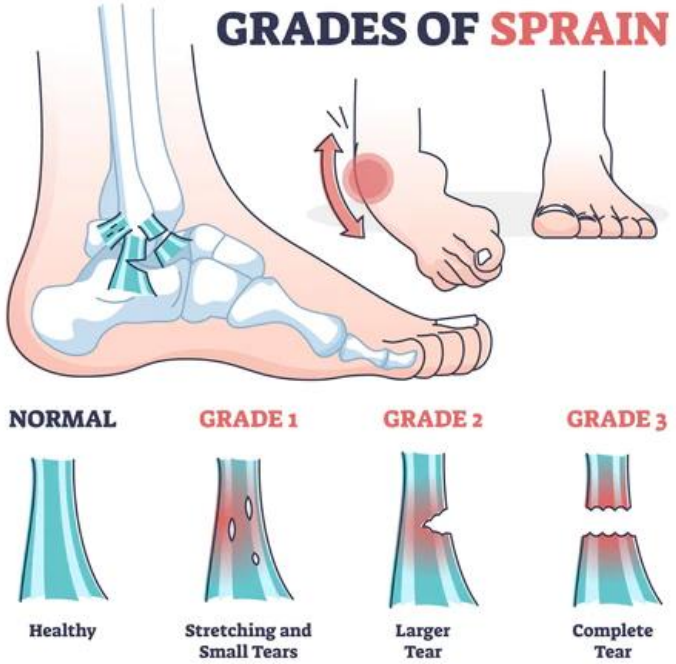


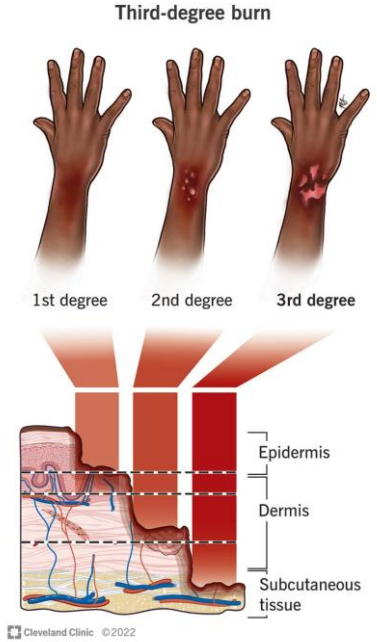
"pain that arises from actual or threatened damage to non-neural tissue and is due to activation of nociceptors"[1]

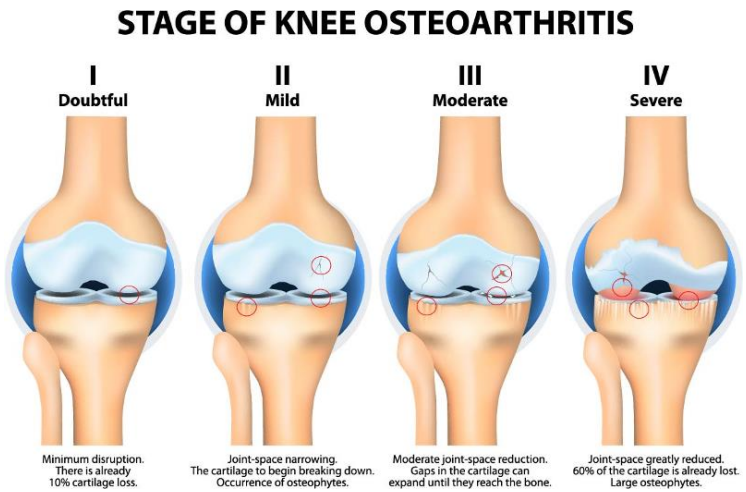
Related to acute inflammation[2]



References: **1.** Freynhagen, R. et al: Curr Med Res Opin. 2019 Jun;35:1011-1018. **2.** Savvas S, et al. Pain Management Guide (PMG) Toolkit for Aged Care, 2nd Edition. Sydney: National Ageing Research Institute, Melbourne and Australian Pain Society; 2021. 84p.

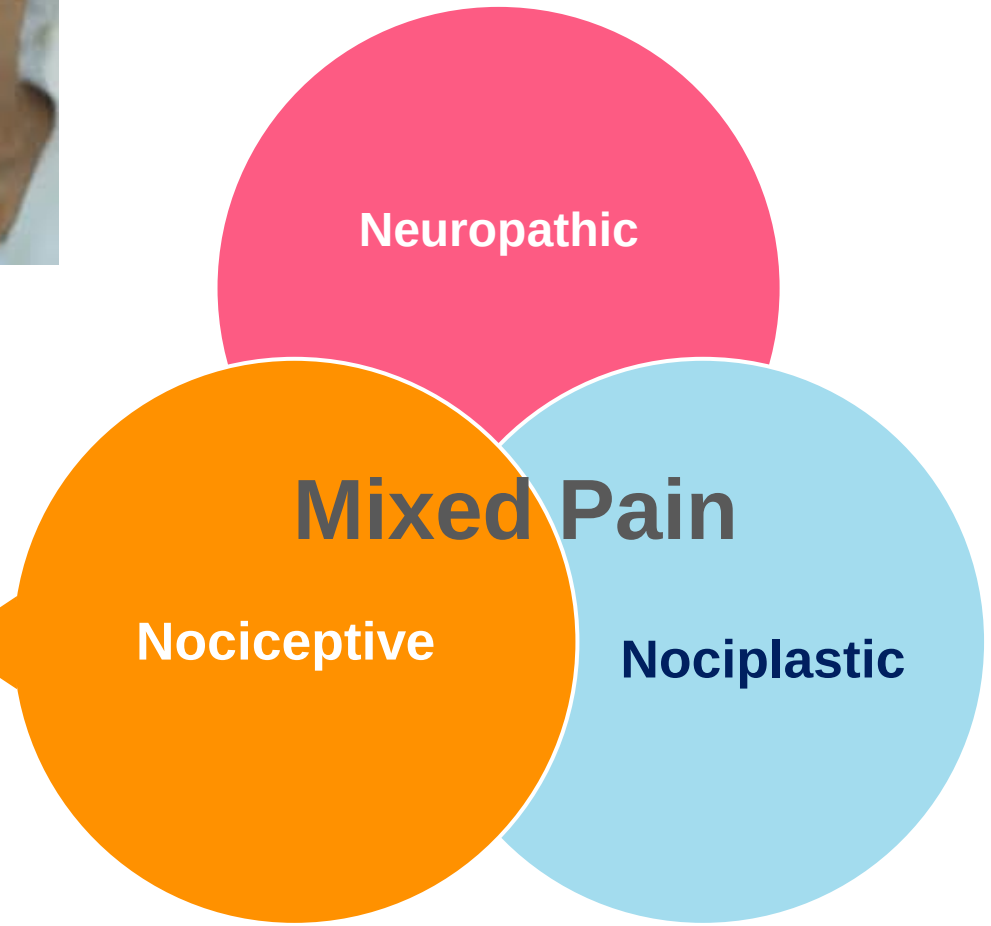


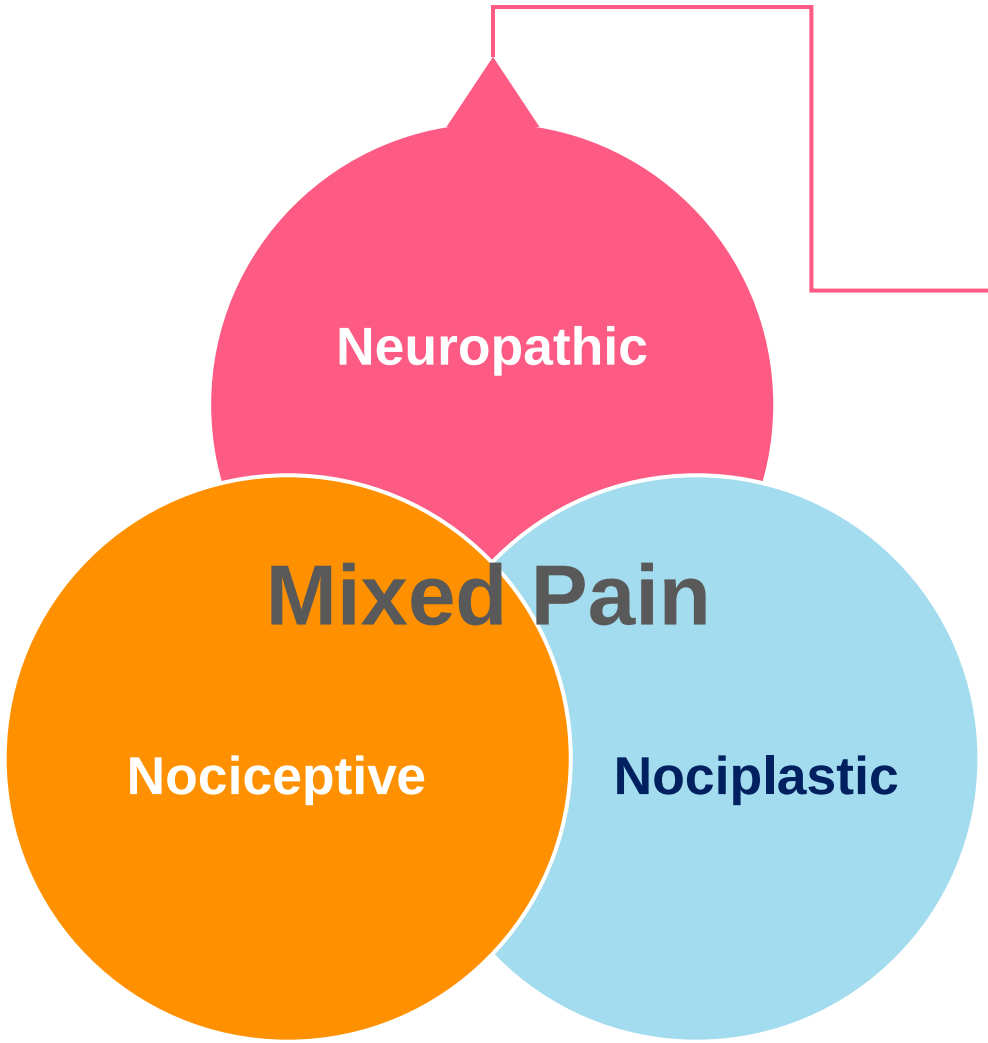




"pain that arises from actual or threatened damage to non-neural tissue and is due to activation of nociceptors"[1]

Related to acute inflammation[2]





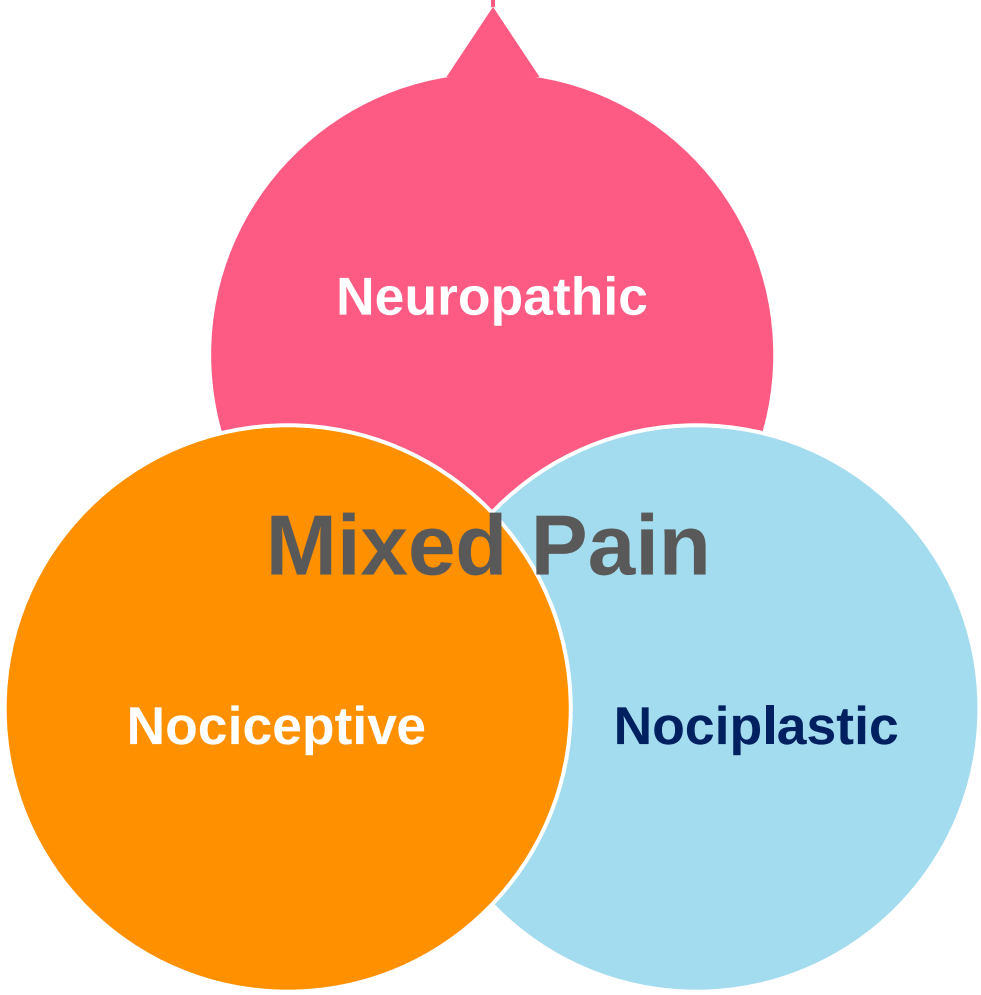
"Pain arising as a direct consequence of a lesion or disease affecting the somatosensory system"[1]

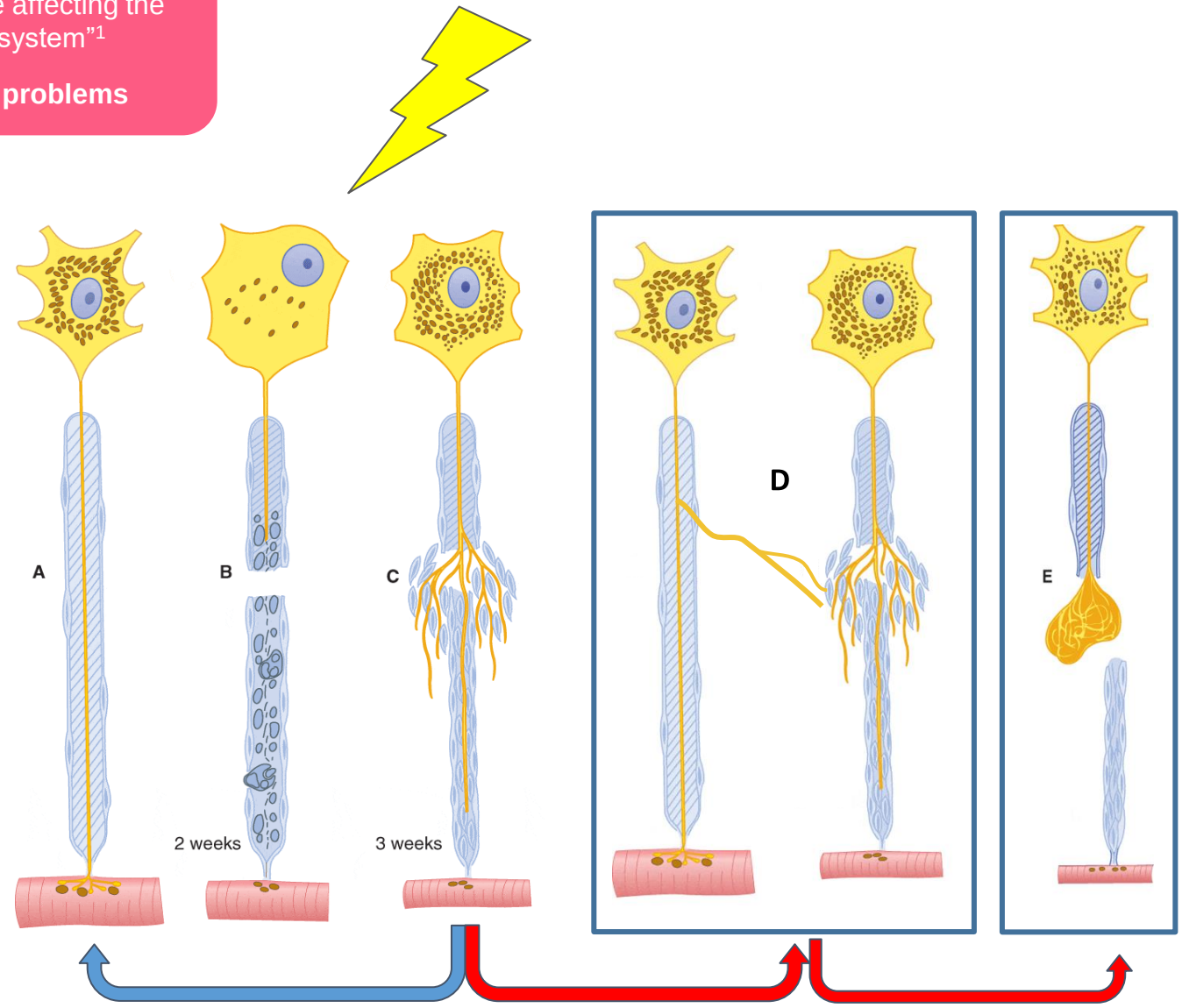
Related to nerve problems

References: **1.** Freynhagen, R. et al: Curr Med Res Opin. 2019 Jun;35:1011-1018. **2.** Savvas S, et al. Pain Management Guide (PMG) Toolkit for Aged Care, 2nd Edition. Sydney: National Ageing Research Institute, Melbourne and Australian Pain Society; 2021. 84p.

"pain arising as a direct consequence of a lesion or disease affecting the somatosensory system"[1]

Related to nerve problems

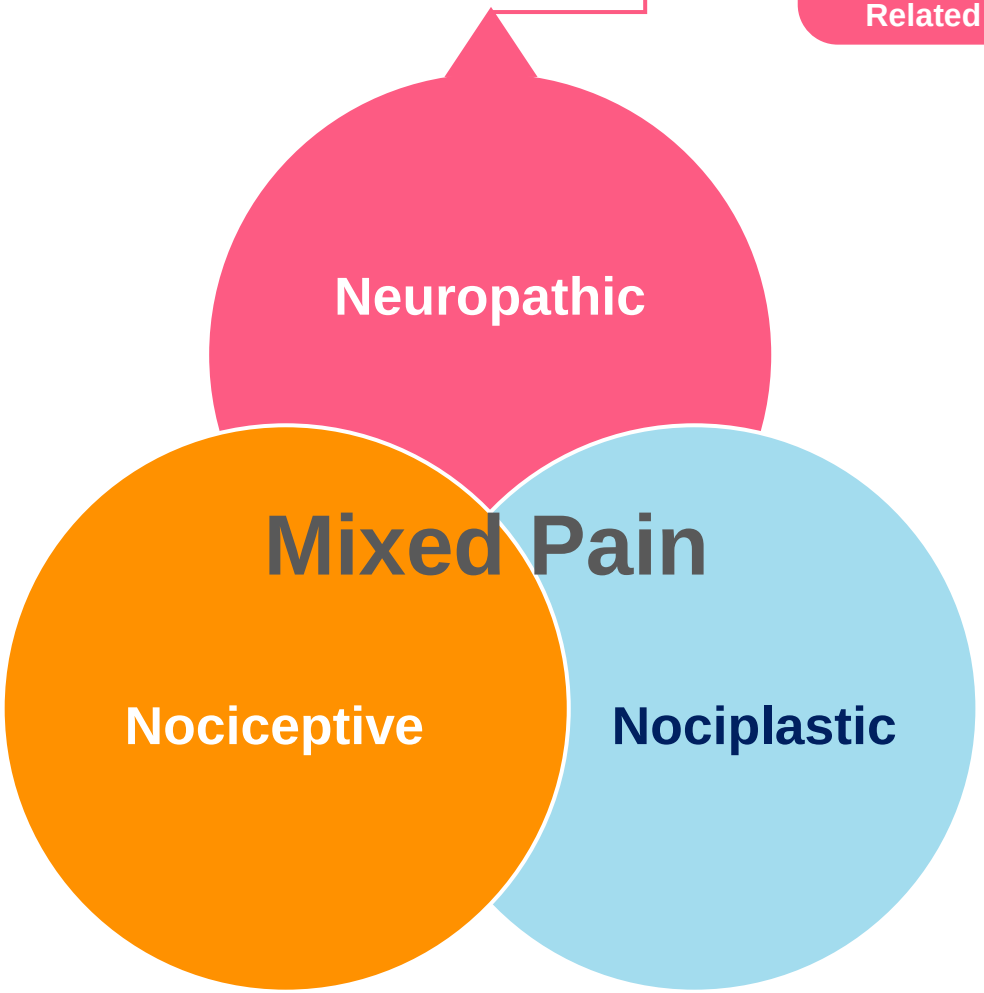


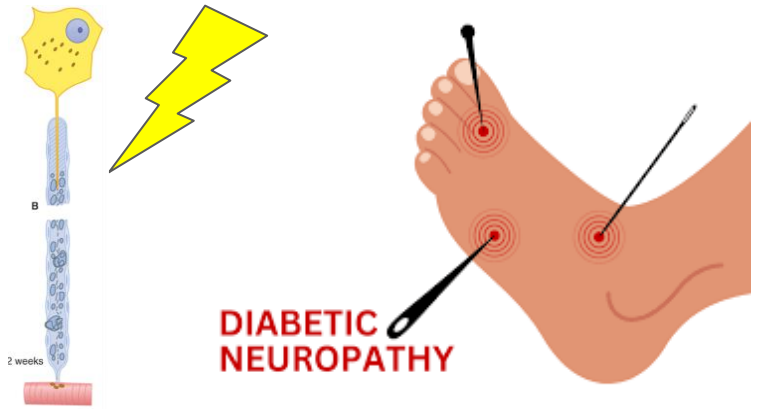


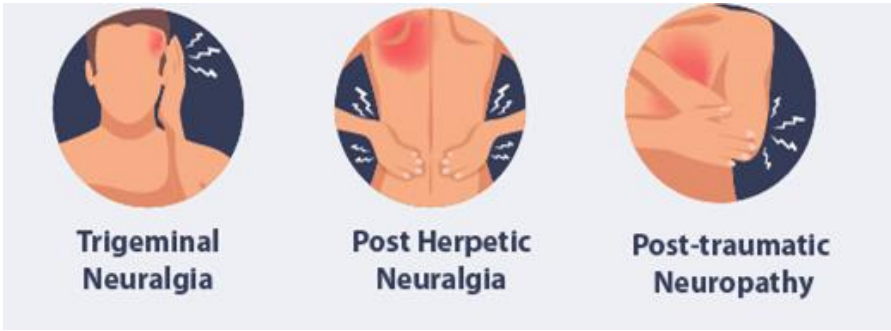
References: **1.** Freynhagen, R. et al: Curr Med Res Opin. 2019 Jun;35:1011-1018. **2.** Savvas S, et al. Pain Management Guide (PMG) Toolkit for Aged Care, 2nd Edition. Sydney: National Ageing Research Institute, Melbourne and Australian Pain Society; 2021. 84p.

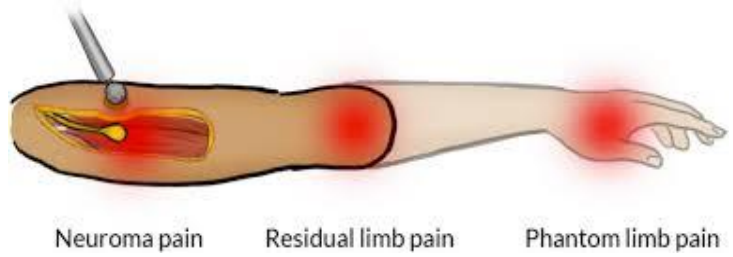
"pain arising as a direct consequence of a lesion or disease affecting the somatosensory system"[1]

Related to nerve problems

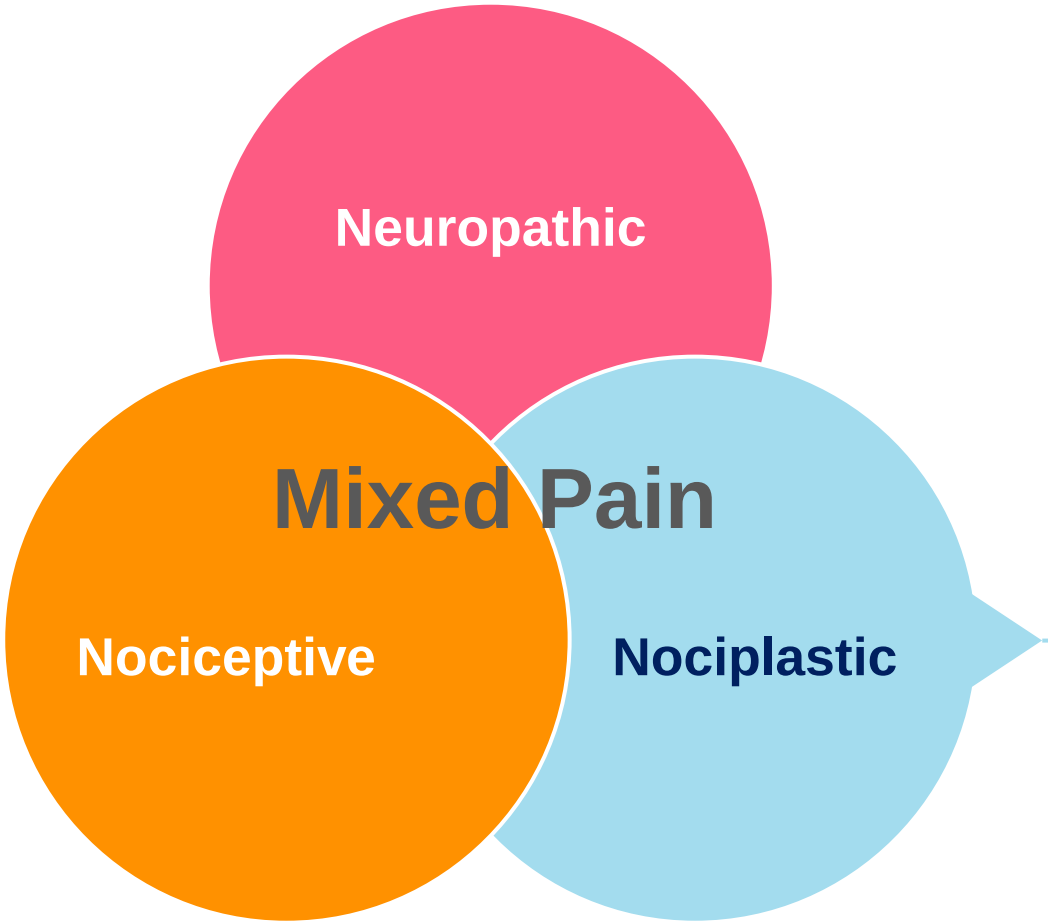






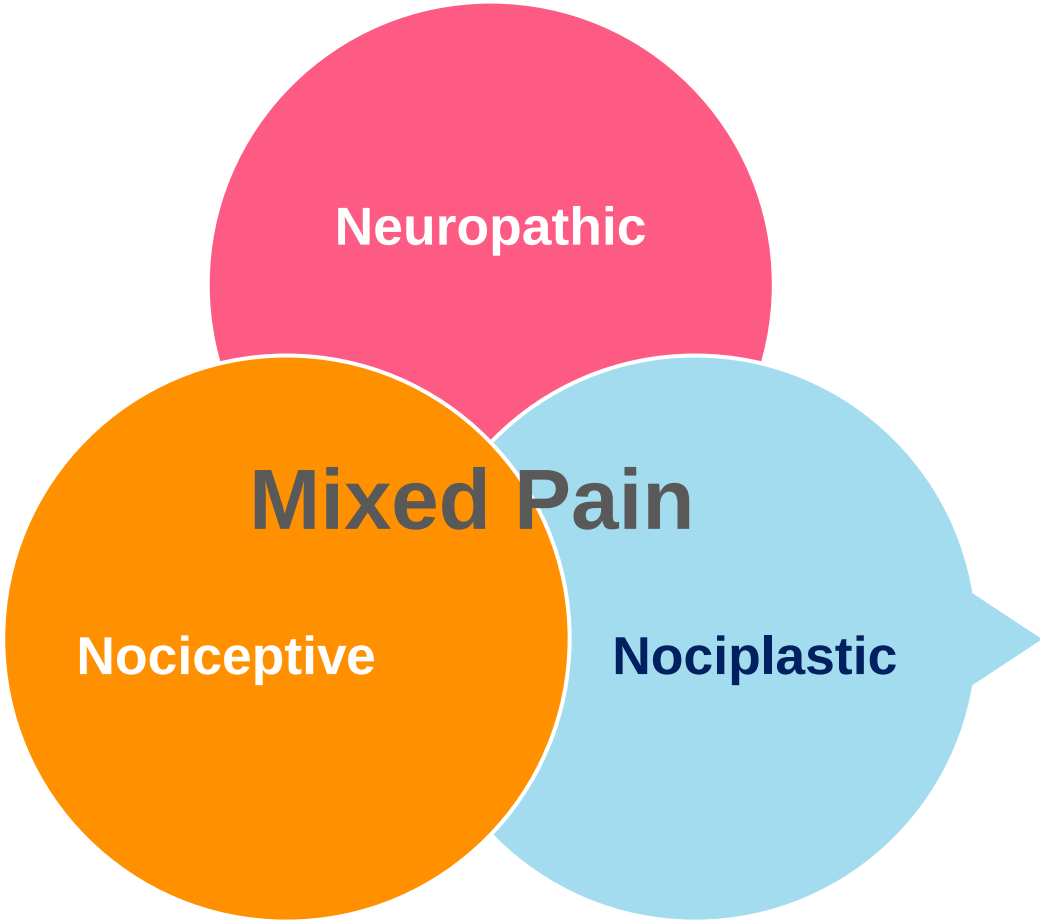


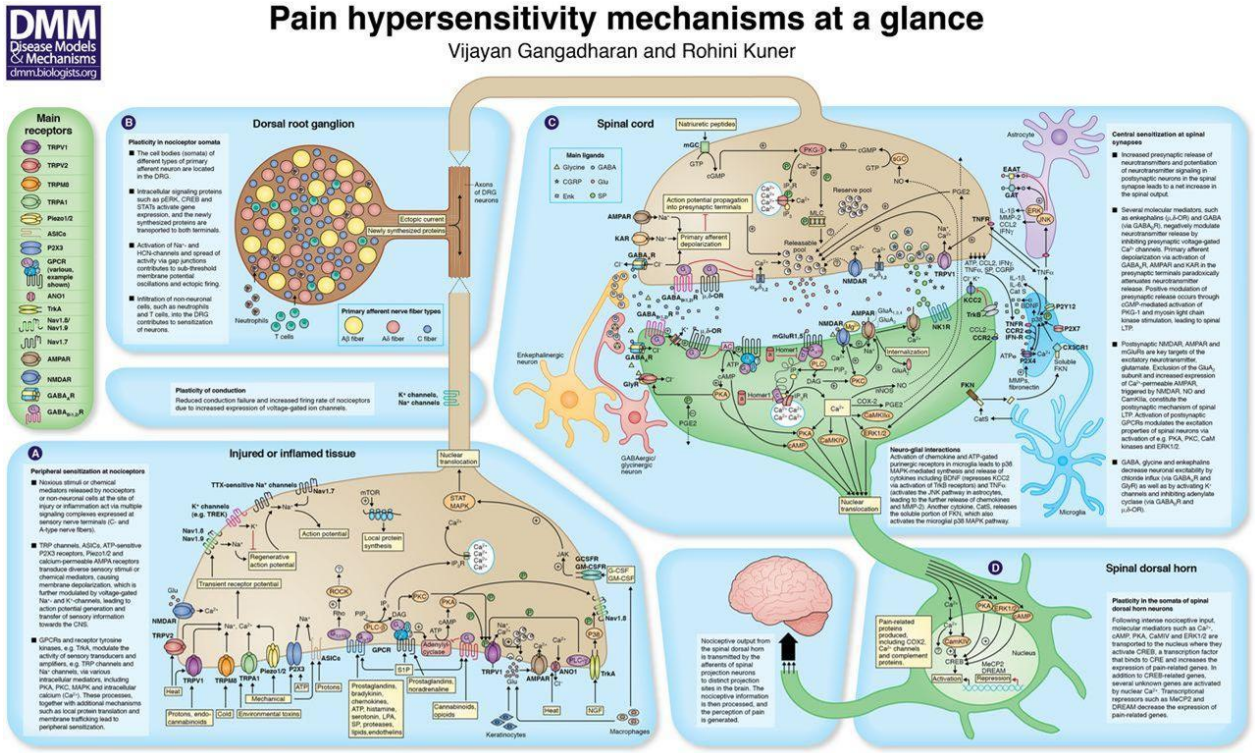
Post Chemo/RT/ Surgical/ Trauma
Nerve entrapment



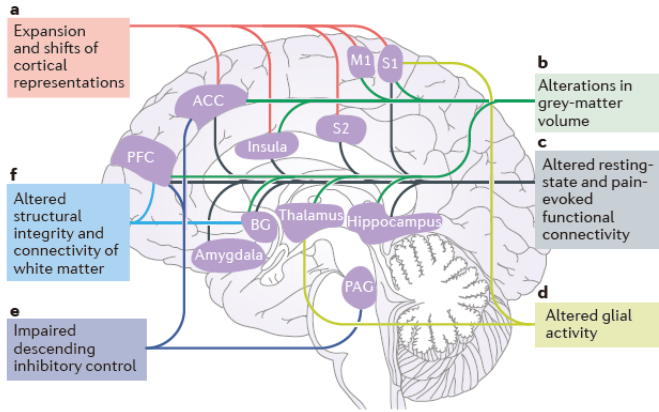
"pain that arises from **altered nociception** despite **no clear** evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain"[1]

References: **1.** Freynhagen, R. et al: Curr Med Res Opin. 2019 Jun;35:1011-1018. **2.** Savvas S, et al. Pain Management Guide (PMG) Toolkit for Aged Care, 2nd Edition. Sydney: National Ageing Research Institute, Melbourne and Australian Pain Society; 2021. 84p.

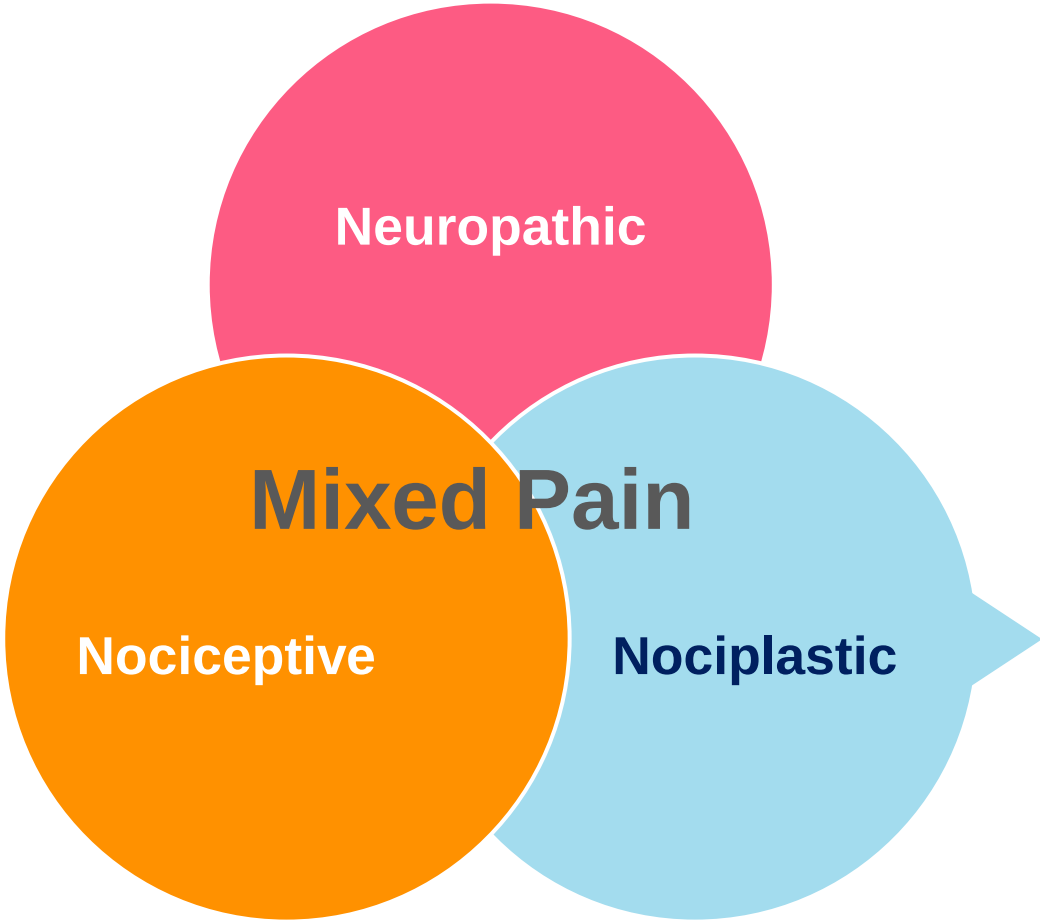


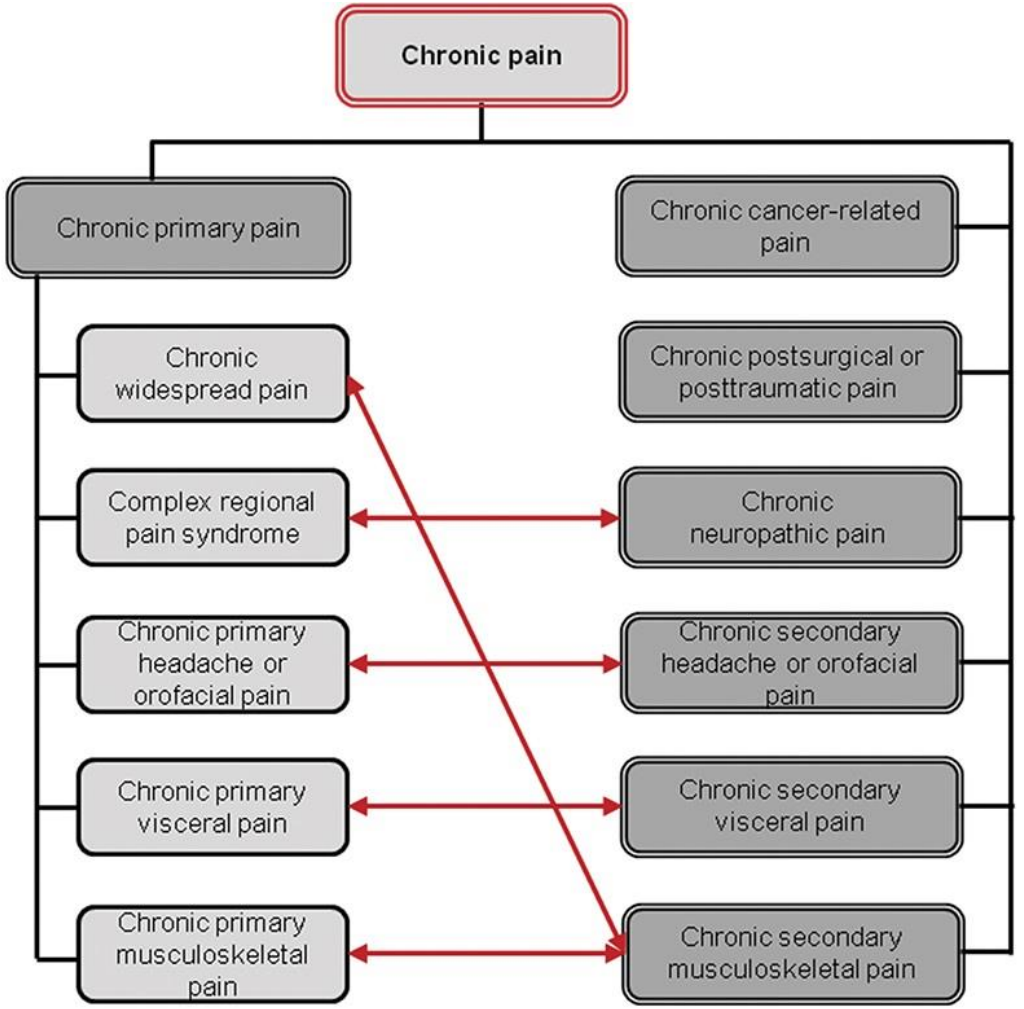


"pain that arises from **altered nociception** despite **no clear** evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain"[1]



References: **1.** Freynhagen, R. et al: Curr Med Res Opin. 2019 Jun;35:1011-1018. **2.** Savvas S, et al. Pain Management Guide (PMG) Toolkit for Aged Care, 2nd Edition. Sydney: National Ageing Research Institute, Melbourne and Australian Pain Society; 2021. 84p.



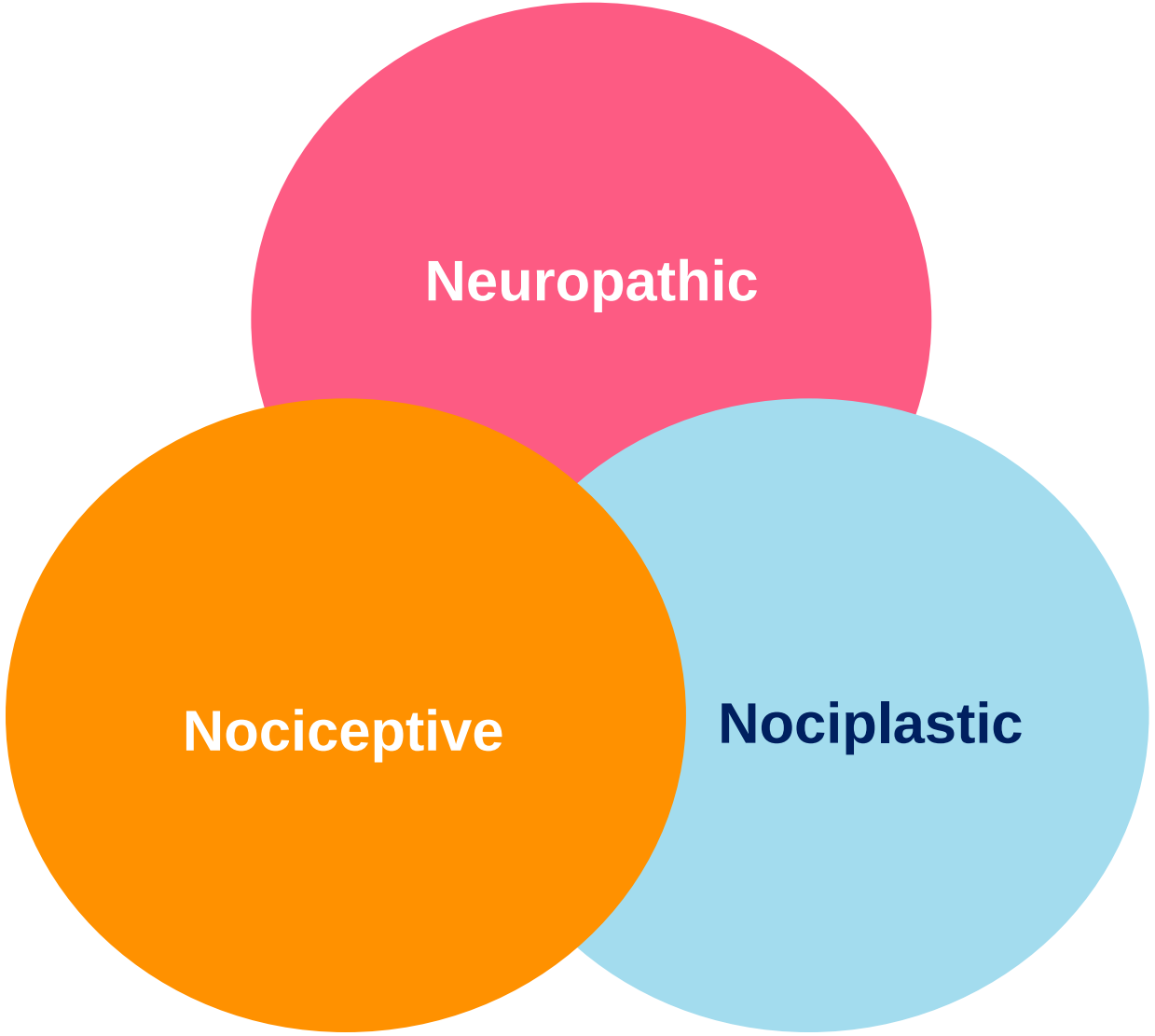


Chronic secondary pain syndromes

"pain that arises from **altered nociception** despite **no clear** evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain"[1]

What is Mixed Pain?

Mixed pain was the most common pain condition (59.3%) in a cross-sectional study, followed by nociceptive pain (31.8%) and neuropathic pain (8.9%).

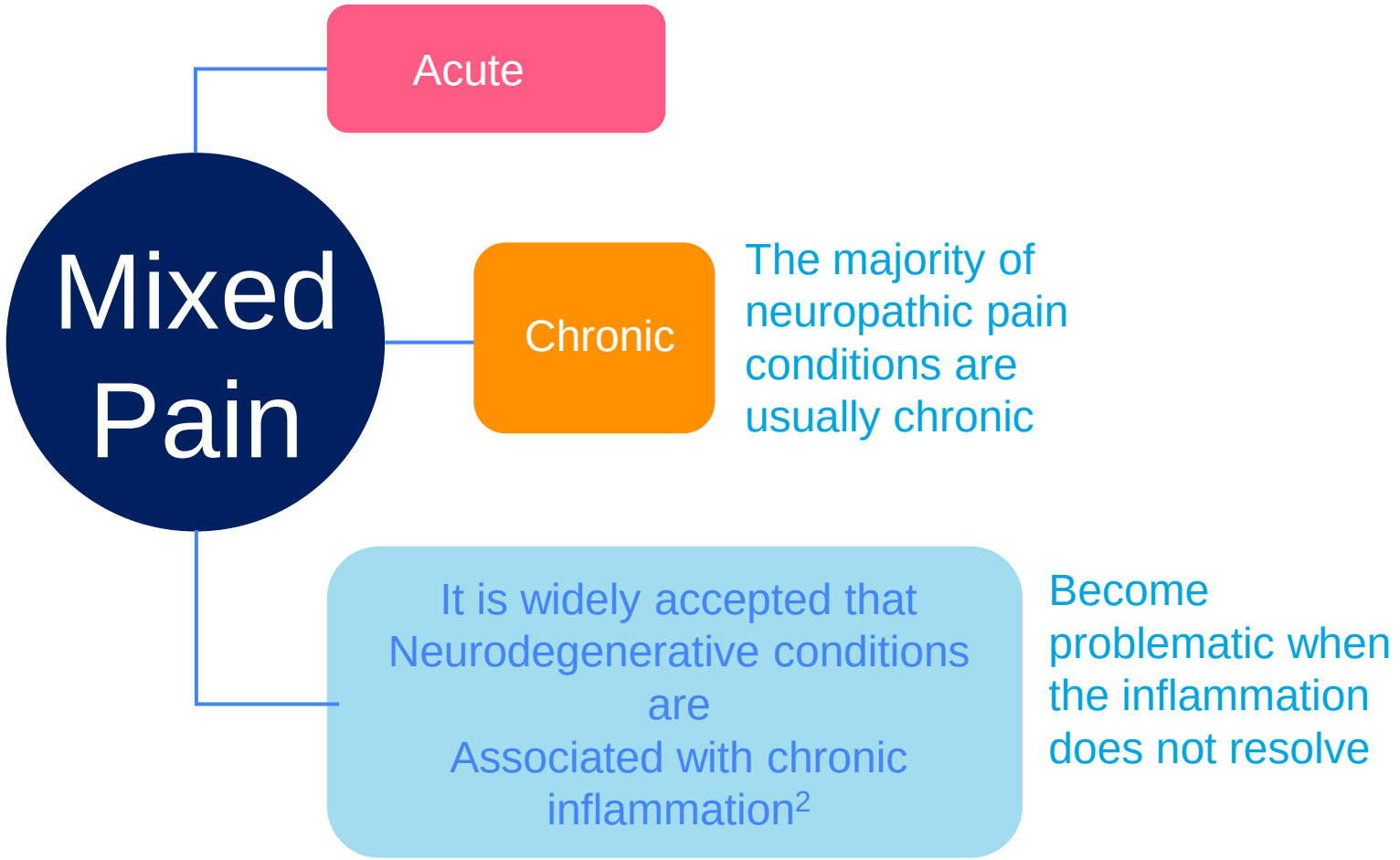


Reference: Freynhagen, . et al: Curr Med Res Opin. 2019 Jun;35:1011-1018.

Mixed pain is Associated with Chronic Pain

Mixed pain can manifest as acute or chronic.

However, it is particularly prevalent in chronic pain cases.[1]

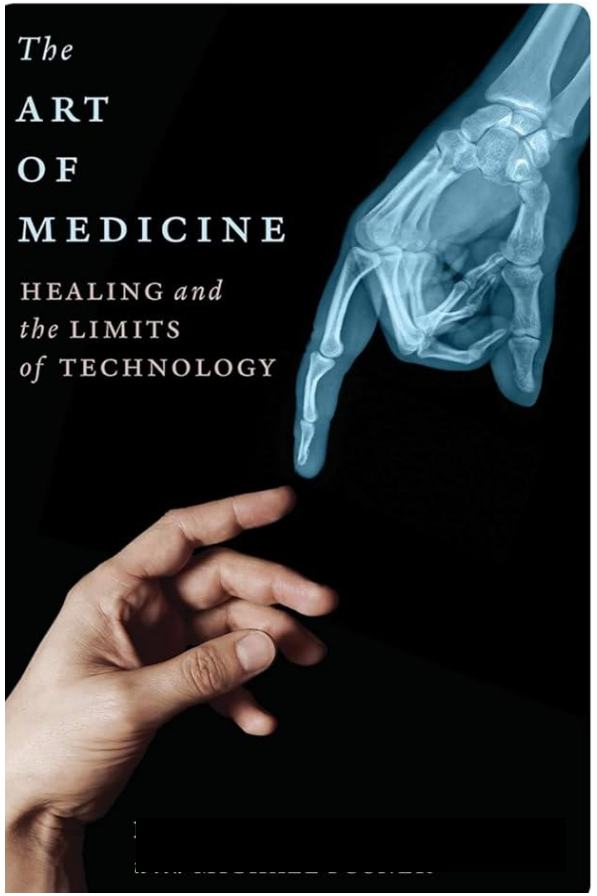


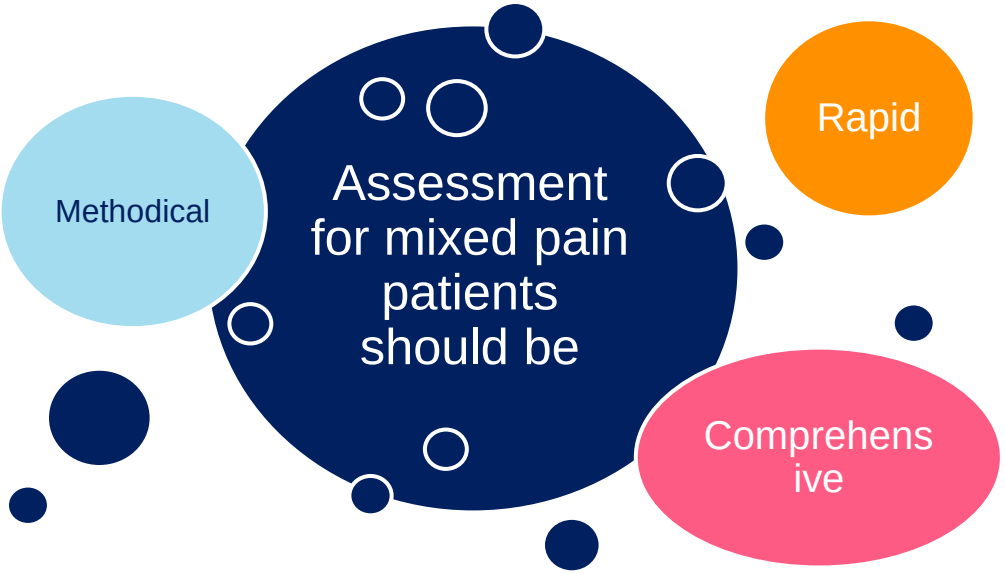
References: **1.** Freynhagen R, et al: Curr Med Res Opin. 2019 Jun;35(6):1011-1018. **2.** Safieh-Garabedian B,et al. Neurosci Lett. 2019;702:61-65.

Categorised the type of pain is Necessary

Timely & Accurate categorization is crucial for treatment, which would benefit mixed pain patients by improving their health outcomes and quality of life.

- **History**
- **Physical examination**
- **+/- investigation**



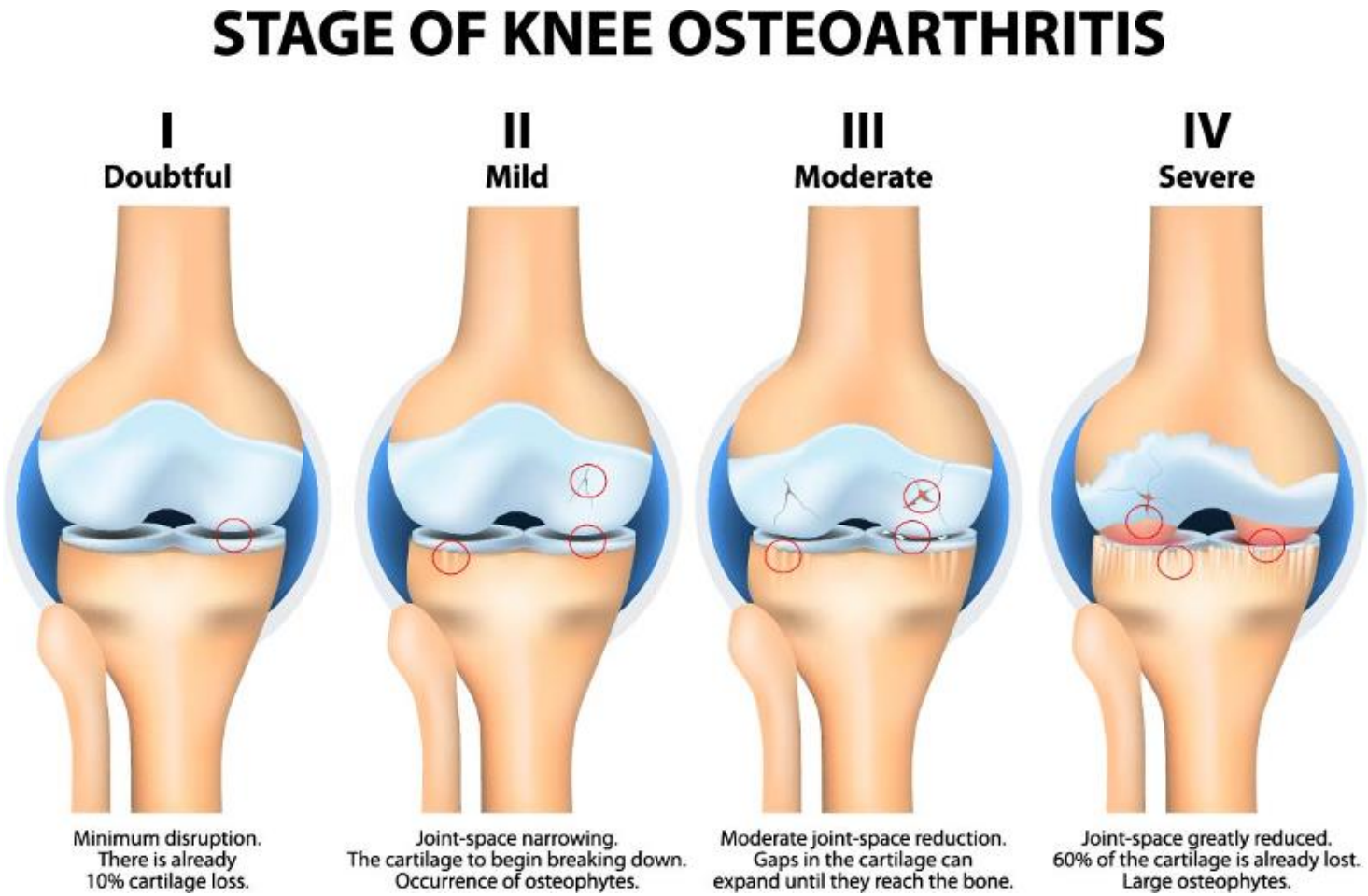


Reference: Freynhagen R, et al. Curr Med Res Opin. 2020;36:2037-2046.

Categorised the type of pain

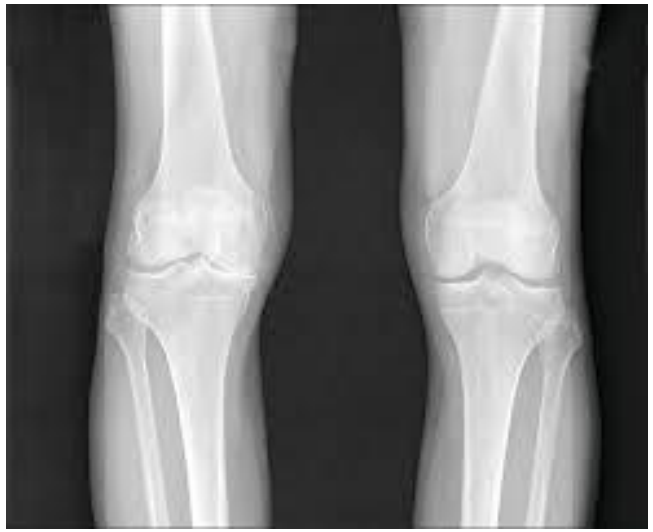
	Nociceptive	Neuropathic	Nociplastic
History	Injury/ OA/ degenerative	Injury of nerve	Without injury (Primary Pain)/ Sensitization process
	Acute/ Chronic	Acute/ Chronic	Chronic
	Mechanical/ Movement	Spontaneous/ Evoked	Any
	Sharp	Stabbing/ Burning/ Electricity/ Numbing	Any
	Well localized	Distribution of nerve	Wide spread
			Cognitive symptoms
Physical examination	Normal nervous system	-ve = dysfunction of nervous system	
	Local pathology	+ve = allodynia / hyperalgesia	Evoke pain hypersensitivity - lower pain threshold/ 1or 2 hyperalgesia
			Wide spread
Investigation	Imaging / NCT / Diagnostic block / Questionnaire		

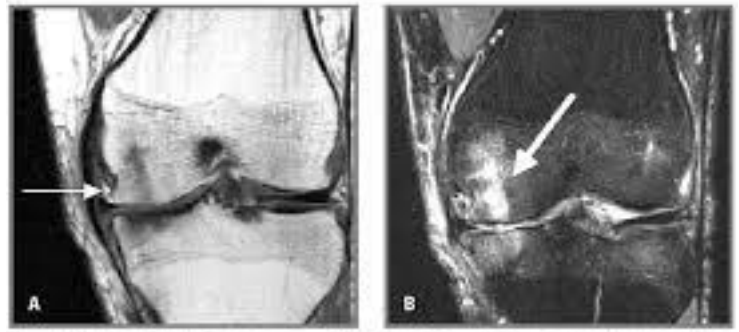
OA knee


STAGE OF KNEE OSTEOARTHRITIS
I
Doubtful
Minimum disruption.
There is already
10% cartilage loss.
II
Mild
Joint-space narrowing.
The cartilage to begin breaking down.
Occurrence of osteophytes.
III
Moderate
Moderate joint-space reduction.
Gaps in the cartilage can
expand until they reach the bone.
IV
Severe
Joint-space greatly reduced.
60% of the cartilage is already lost.
Large osteophytes.

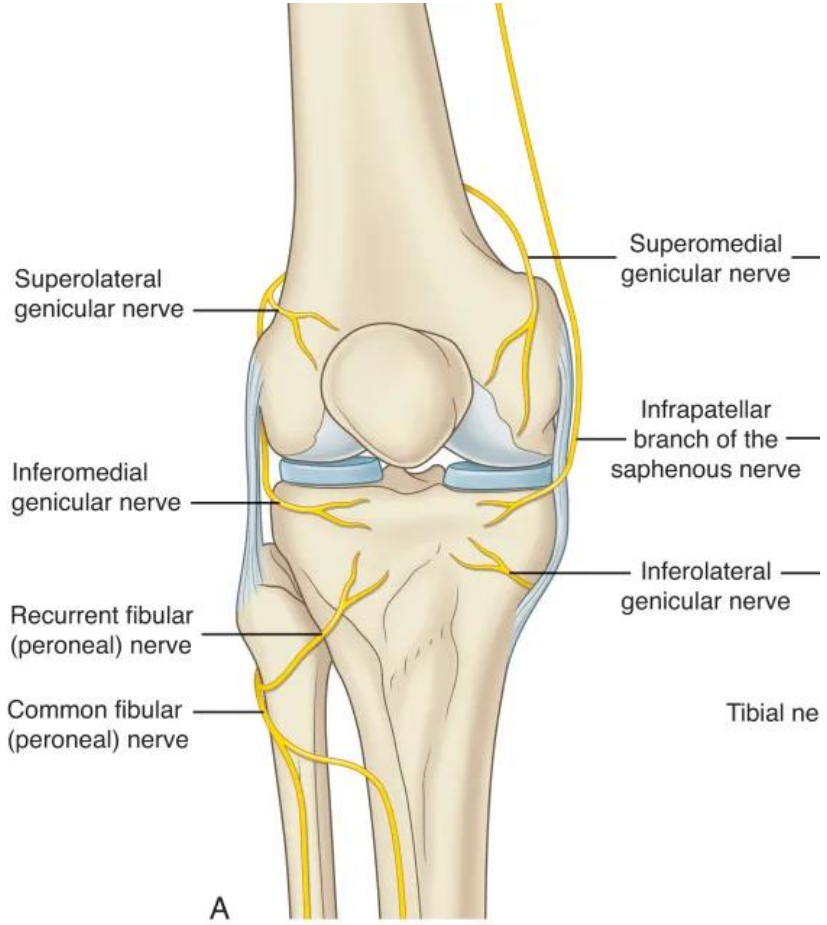
Pain in OA knee

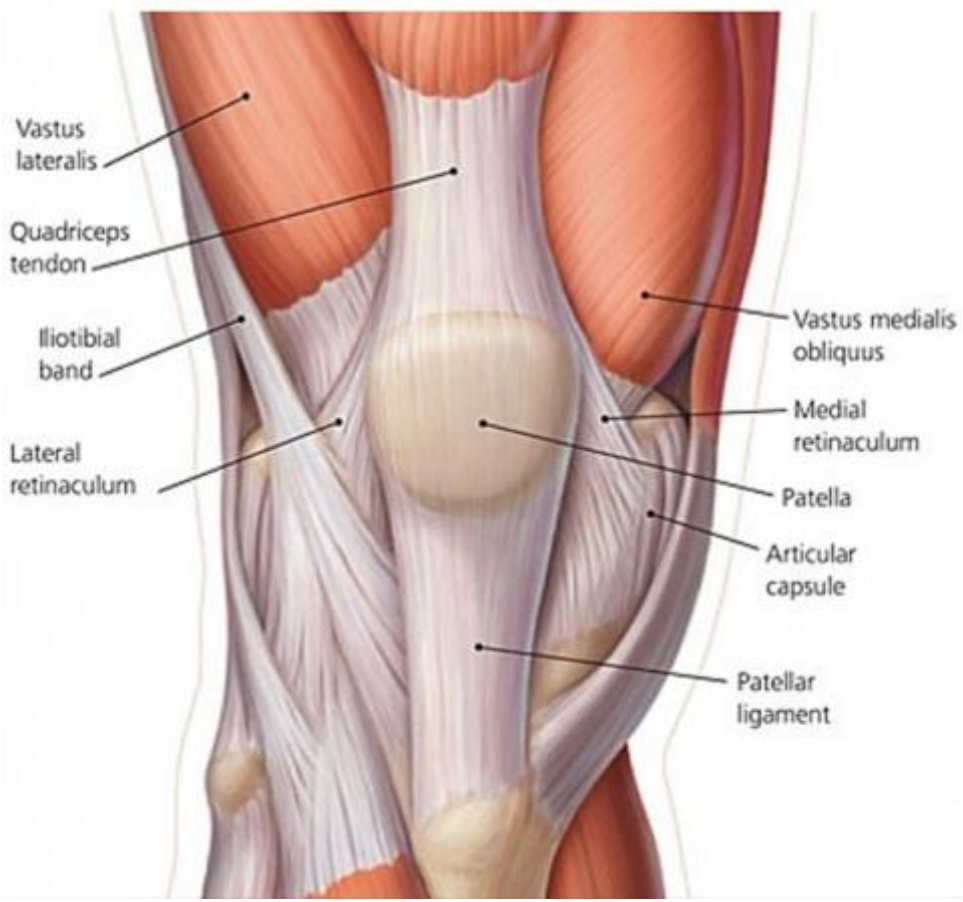
- Discordance of X ray and pain
- 20% knee pain and 10% hip pain - normal appearance of X Ray
- MRI of OA knee - address the soft tissue part of pain
  - Bone marrow lesion - 2-5X increase likelihood of pain
  - Synovitis - 3-10X increase in likelihood of pain





Pain in OA knee





Neuropathic pain component

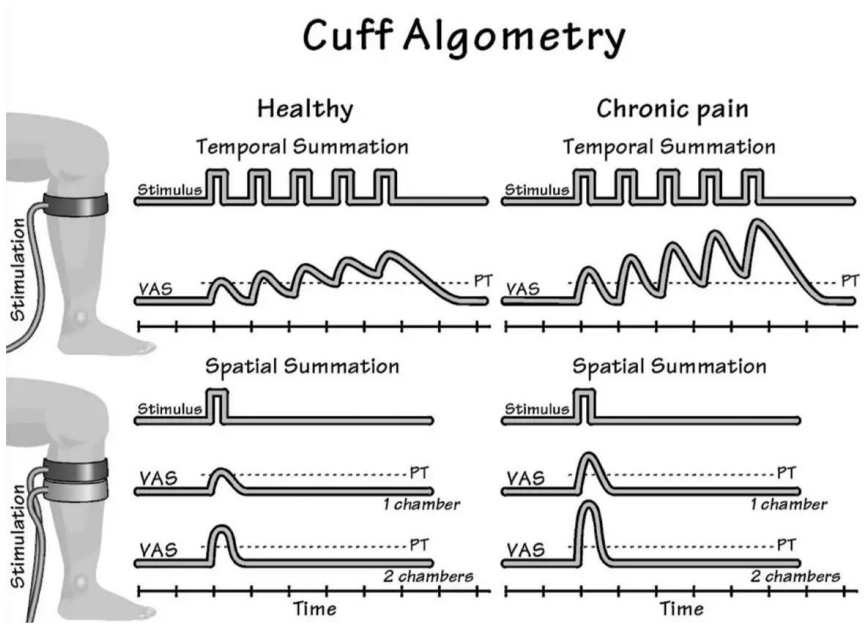
Pain in OA knee

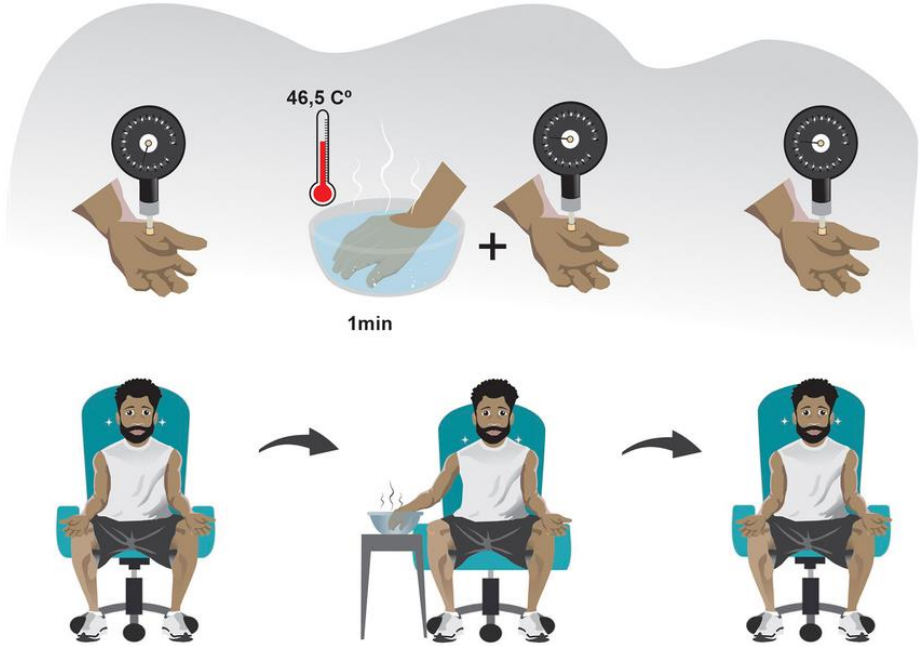
Nociplastic pain component

<u>Central sensitization of OA knee</u>

QST to demonstrate the signs of central sensitization:

- Pressure pain sensitivity
- Temporal summation of pain
- Conditioned pain modulation





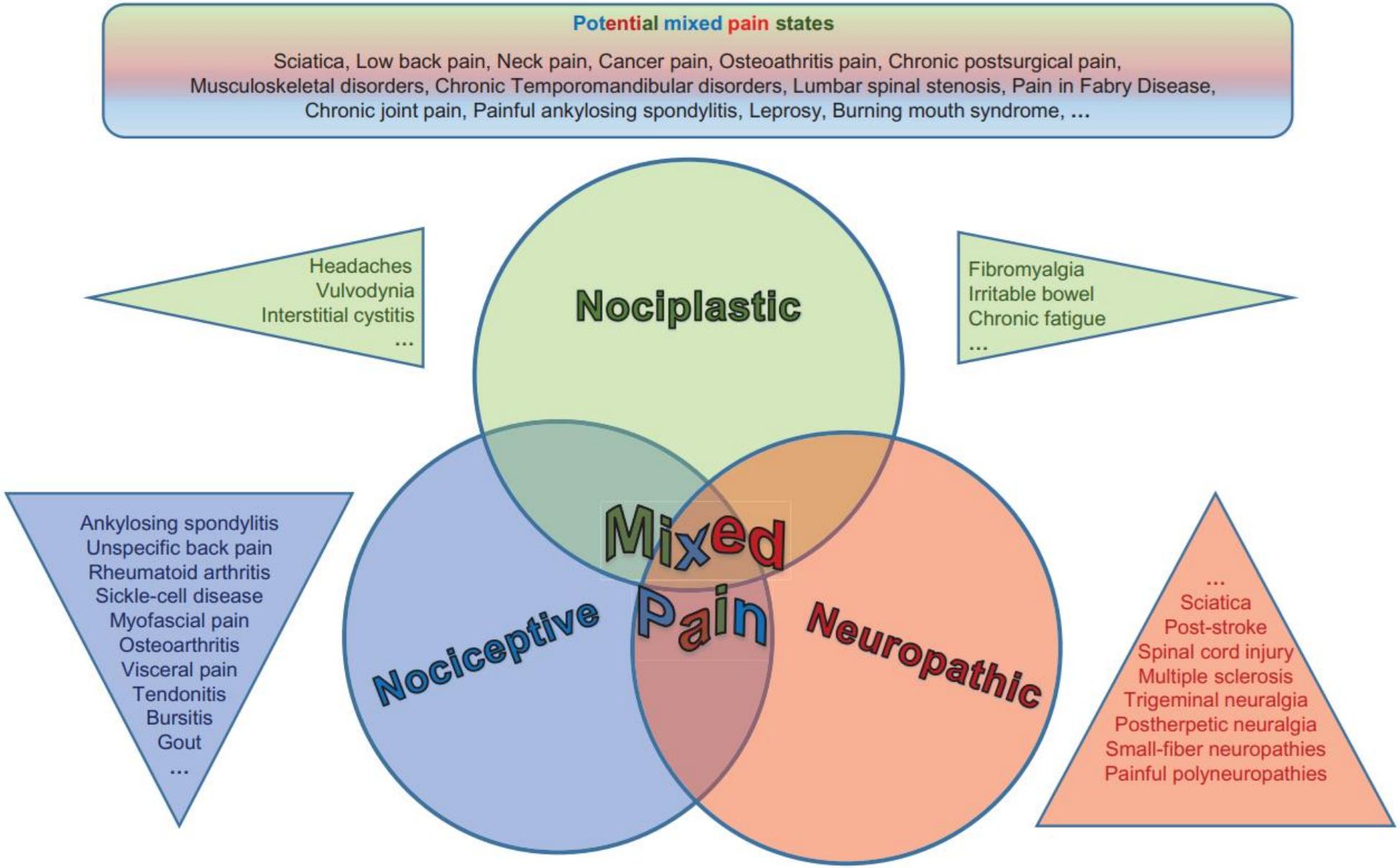


Figure 1. The three different types of pain defined by the IASP give rise to overlap which can be acknowledged as "mixed pain" (Freynhagen©). Conditions described as "mixed pain" in the literature share a common characterization of manifesting clinically with a substantial overlap of the different known pain types.

Screening Tool – 9 Question Survey

- 9 Question Survey is proposed for the diagnosis of mixed pain
- 9 simple key questions are included to provide a framework for identifying the predominant pain mechanisms within the patients
- With the answer of the pain questionnaire and the complement of essential detailed physical examination, it leads to a clearer diagnostic picture

Reference: Freynhagen R, et al. Curr Med Res Opin. 2020;36:2037-2046.

Key question	Reply elements that may indicate presence of nociceptive pain (NP)	Reply elements that may indicate presence of neuropathic pain (NeP)	Reply elements that may indicate presence of mixed pain (MP)	Evaluating our case: what could be the key type of pain?
1. Where exactly do you feel your pain? Can you mark the painful areas in this pain drawing?	Pain localized to one body area	Pain in more than one body area; pain following a clear dermatomal area; generalized pain	Pain in more than one body area; pain following a clear dermatomal area; generalized pain	Initialy: low back > leg pain (NP); Lately: lumbar radiculopathy with electric shocks (NeP) ∑ **suggestive of mixed pain**
2. What words would you use to describe your pain?	Use of the following verbal descriptors: Aching, deep, dull, squeezing, internal intense deep pressure, feeling of tense muscles	Use of the following verbal descriptors: Burning, numbness, stabbing, shooting, prickling, tingling, like pins and needles, like crawling ants, pain in a numb area	Mixed use of pain descriptors for both, nociceptive and neuropathic pain	Mix of NP & NeP verbal pain descriptors; Final Score of painDETECT: 20 → A NeP component is likely (>90%) ∑ **suggestive of mixed pain**
3. How long have you been experiencing your pain?	Pain of acute duration	Pain of chronic duration	Pain of chronic duration	Overall 8 months, but for 7 months only pseudo-radicular back pain (NP), then since 1 month radiculopathy (NeP) ∑ **suggestive of mixed pain**
4. On a scale of 0 to 10, how intense is your pain at rest and during movement?	NRS score of 5 to 7 (moderate pain)	NRS score of up to 10 when experiencing electric shock–like pain (severe pain)	NRS score of up to 10 when experiencing electric shock–like pain (severe pain)	Moderate back pain (NP); Severe leg pain (NeP) ∑ **suggestive of mixed pain**
5. Do you feel pain more on movement or more at rest?	Pain more on movement	Spontaneous pain at rest	Pain both on movement and at rest	Pain more at movement (NP) but spontaneously shooting pain at rest (NeP) ∑ **suggestive of mixed pain**
6. Is your pain related to any identifiable cause? How did it start and develop?	Pain that developed as a response to an identifiable injury or trigger	Pain that seemed to have developed spontaneously	-	Primarily degenerative processes led to NP. Over time it is overlapped by symptoms of radiculopathy (NeP). ∑ **suggestive of mixed pain**
7. What have you done to treat your pain?	Pain reduction with non-selective NSAIDs, COX-2 inhibitors, corticosteroid injections, opioids, tramadol	Pain reduction with alpha-2-delta ligands, tricyclic antidepressants, serotonin-noradrenaline reuptake inhibitors, opioids, tramadol	Some response to anti-nociceptive agents and anti-neuropathic agents, with incomplete pain relief	Incomplete positive response to NSAIDs and COX-2 (NP), incomplete positive response to weak opioids (NP + NeP) and alpha-2-delta ligands (NeP). ∑ **suggestive of mixed pain**
8. Has your pain caused you psychological distress?	Any kind of pain may lead to psychological distress over time. However, with NP, symptoms seem to be less pronounced	A strong positive response; more pronounced depressive symptoms, anxiety symptoms, sleep disturbances	A strong positive response; depressive symptoms, anxiety symptoms, sleep disturbances	Answer reflects a tendency of rising psychological distress within the last weeks (NP + NeP) ∑ **suggestive of mixed pain**
9. Have you experienced any other symptoms or changes which have worried you?	Symptoms that indicate the presence of acute or chronic inflammation	Symptoms that indicate nervous system involvement	Overlap of symptoms which show both nervous system involvement and presence of acute or chronic inflammation	Answer reflects symptoms which might indicate acute or chronic inflammation (NP); no red flags ∑ **suggestive of nociceptive pain**

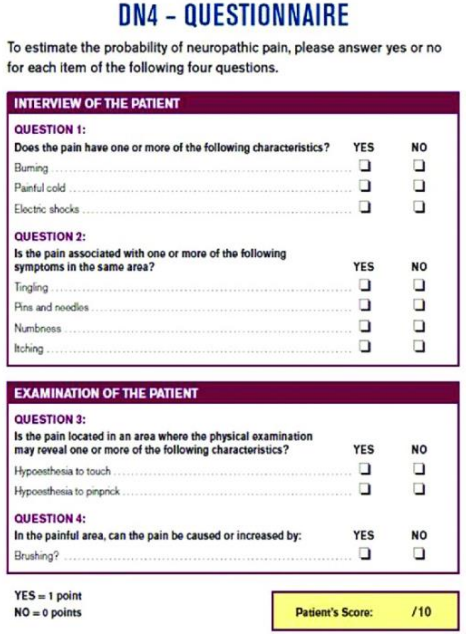
Reference: Freynhagen R, et al. Curr Med Res Opin. 2020;36:2037-2046.

Screening Tools of Neuropathic Component

Other than 9 Question Survey, these brief and useful screening tools are also assessment ways for patients:

Douleur Neuropathique 4 Questions (DN4)

A total score of ⩾4 (out of a maximum of 10) indicates neuropathic pain



DN4 – QUESTIONNAIRE

To estimate the probability of neuropathic pain, please answer yes or no for each item of the following four questions.

INTERVIEW OF THE PATIENT

QUESTION 1:
Does the pain have one or more of the following characteristics? YES NO
Burning ❑ ❑
Painful cold ❑ ❑
Electric shocks ❑ ❑

QUESTION 2:
Is the pain associated with one or more of the following symptoms in the same area? YES NO
Tingling ❑ ❑
Pins and needles ❑ ❑
Numbness ❑ ❑
Itching ❑ ❑

EXAMINATION OF THE PATIENT

QUESTION 3:
Is the pain located in an area where the physical examination may reveal one or more of the following characteristics? YES NO
Hypoesthesia to touch ❑ ❑
Hypoesthesia to pinprick ❑ ❑

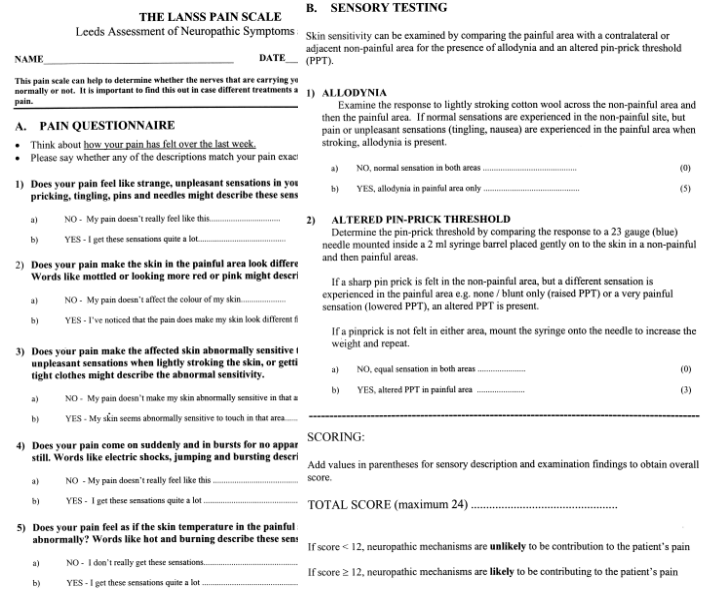
QUESTION 4:
In the painful area, can the pain be caused or increased by: YES NO
Brushing? ❑ ❑

YES = 1 point
NO = 0 points

Patient's Score: /10

Leeds Assessment of Neuropathic Symptoms and Signs (LANSS)

A LANSS score of ⩾12 (out of a maximum of 24) indicates neuropathic pain



THE LANSS PAIN SCALE
Leeds Assessment of Neuropathic Symptoms

NAME_____ DATE___

This pain scale can help to determine whether the nerves that are carrying ye normally or not. It is important to find this out in case different treatments a pain.

A. PAIN QUESTIONNAIRE

- Think about how your pain has felt over the last week.
- Please say whether any of the descriptions match your pain exac

1) Does your pain feel like strange, unpleasant sensations in you pricking, tingling, pins and needles might describe these sens
a) NO - My pain doesn't really feel like this.....
b) YES - I get these sensations quite a lot.....

2) Does your pain make the skin in the painful area look differe Words like mottled or looking more red or pink might descri
a) NO - My pain doesn't affect the colour of my skin.....
b) YES - I've noticed that the pain does make my skin look different fi

3) Does your pain make the affected skin abnormally sensitive unpleasant sensations when lightly stroking the skin, or getti tight clothes might describe the abnormal sensitivity.
a) NO - My pain doesn't make my skin abnormally sensitive in that a
b) YES - My skin seems abnormally sensitive to touch in that area.....

4) Does your pain come on suddenly and in bursts for no appar still. Words like electric shocks, jumping and bursting descri
a) NO - My pain doesn't really feel like this .....
b) YES - I get these sensations quite a lot .....

5) Does your pain feel as if the skin temperature in the painful abnormally? Words like hot and burning describe these sens
a) NO - I don't really get these sensations.....
b) YES - I get these sensations quite a lot .....

B. SENSORY TESTING

Skin sensitivity can be examined by comparing the painful area with a contralateral or adjacent non-painful area for the presence of allodynia and an altered pin-prick threshold (PPT).

1) ALLODYNIA
Examine the response to lightly stroking cotton wool across the non-painful area and then the painful area. If normal sensations are experienced in the non-painful site, but pain or unpleasant sensations (tingling, nausea) are experienced in the painful area when stroking, allodynia is present.
a) NO, normal sensation in both areas ..... (0)
b) YES, allodynia in painful area only ..... (5)

2) ALTERED PIN-PRICK THRESHOLD
Determine the pin-prick threshold by comparing the response to a 23 gauge (blue) needle mounted inside a 2 ml syringe barrel placed gently on to the skin in a non-painful and then painful areas.

If a sharp pin prick is felt in the non-painful area, but a different sensation is experienced in the painful area e.g. none / blunt only (raised PPT) or a very painful sensation (lowered PPT), an altered PPT is present.

If a pinprick is not felt in either area, mount the syringe onto the needle to increase the weight and repeat.
a) NO, equal sensation in both areas ..... (0)
b) YES, altered PPT in painful area ..... (3)

SCORING:

Add values in parentheses for sensory description and examination findings to obtain overall score.

TOTAL SCORE (maximum 24) .....

If score < 12, neuropathic mechanisms are **unlikely** to be contribution to the patient's pain

If score ≥ 12, neuropathic mechanisms are **likely** to be contributing to the patient's pain

PainDETECT Questionnaire

Total score ⩾19: likely neuropathic component; ⩽12: unlikely neuropathic component; between is uncertain

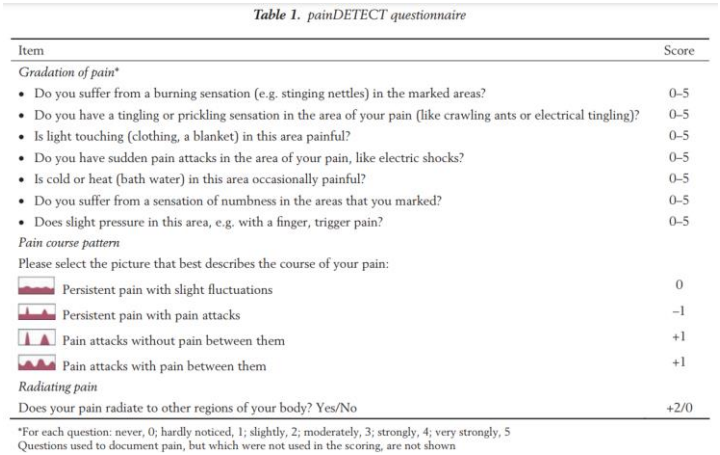


Table 1. painDETECT questionnaire

Item	Score
*Gradation of pain**	
• Do you suffer from a burning sensation (e.g. stinging nettles) in the marked areas?	0–5
• Do you have a tingling or prickling sensation in the area of your pain (like crawling ants or electrical tingling)?	0–5
• Is light touching (clothing, a blanket) in this area painful?	0–5
• Do you have sudden pain attacks in the area of your pain, like electric shocks?	0–5
• Is cold or heat (bath water) in this area occasionally painful?	0–5
• Do you suffer from a sensation of numbness in the areas that you marked?	0–5
• Does slight pressure in this area, e.g. with a finger, trigger pain?	0–5
Pain course pattern	
Please select the picture that best describes the course of your pain:	
Persistent pain with slight fluctuations	0
Persistent pain with pain attacks	−1
Pain attacks without pain between them	+1
Pain attacks with pain between them	+1
Radiating pain	
Does your pain radiate to other regions of your body? Yes/No	+2/0

*For each question: never, 0; hardly noticed, 1; slightly, 2; moderately, 3; strongly, 4; very strongly, 5
Questions used to document pain, but which were not used in the scoring, are not shown

Reference: Hamdan A, et al. SAGE Open Med. 2024;12:20503121231218985.

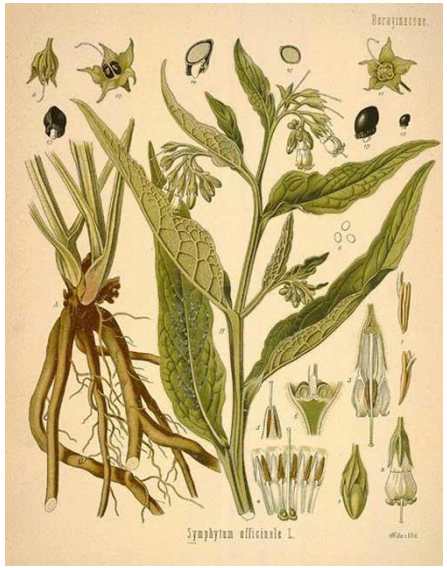
Management

How to treat different type of pain?

		Nociceptive	Neuropathic	Nociplastic
Pharmacological	Opioid	Acute - ✔ , Chronic - ✗	✗	✗
Multimodal	NSAID (Steroid)	Acute - ✔ , Chronic - ✗	✗	✗
Multimodal	Antineuropathic pain	✗	✔ poor response unsatisfactory NNT v.s. NNH	±✔ even less evidence empirical tx
Non-pharmacological	PT/ OT	✔	±✔	±✔
Multidisciplinary	Psychological (CP)/ Rehabilitation (PN)/	✔	✔	✔✔
Multidisciplinary	Sleep/ Diet/ Ex/ BO			
Multidisciplinary	Complementary e.g. TCM			
Multidisciplinary	Supplement			
	Pain intervention	Selective	Selective	Selective

Comfrey Root Extract - Alternative to NSAID

- Has been used for the treatment of painful muscle and joint complaints
- Clinically proven to have below actions:



Anti-inflammation

Relieve swelling of muscles and joints

Relieve pain

Promotion of callus formation

Reference: Staiger C. Wien Med Wochenschr. 2013;163:58-64.

Efficacy on different pain

Back Pain		OA
Average reduction of pain intensity on active standardized movement **95.2%** Comfrey extract group **V.S.** **37.8%** Placebo group ($p < 0.001$)		The variable of the Western Ontario and McMaster Universities Osteoarthritis Index score Decreased by **54.7%** Comfrey extract group **V.S.** Decreased by **10.7%** Placebo group ($p < 0.001$)

Abbreviations: OA=Osteoarthritis.

Reference: Staiger C. Wien Med Wochenschr. 2013;163:58-64.

Acupuncture

Andrew J. Vickers et al. Acupuncture for chronic pain: update of an individual patient data meta-analysis
J Pain. 2018 May; 19(5): 455–474.

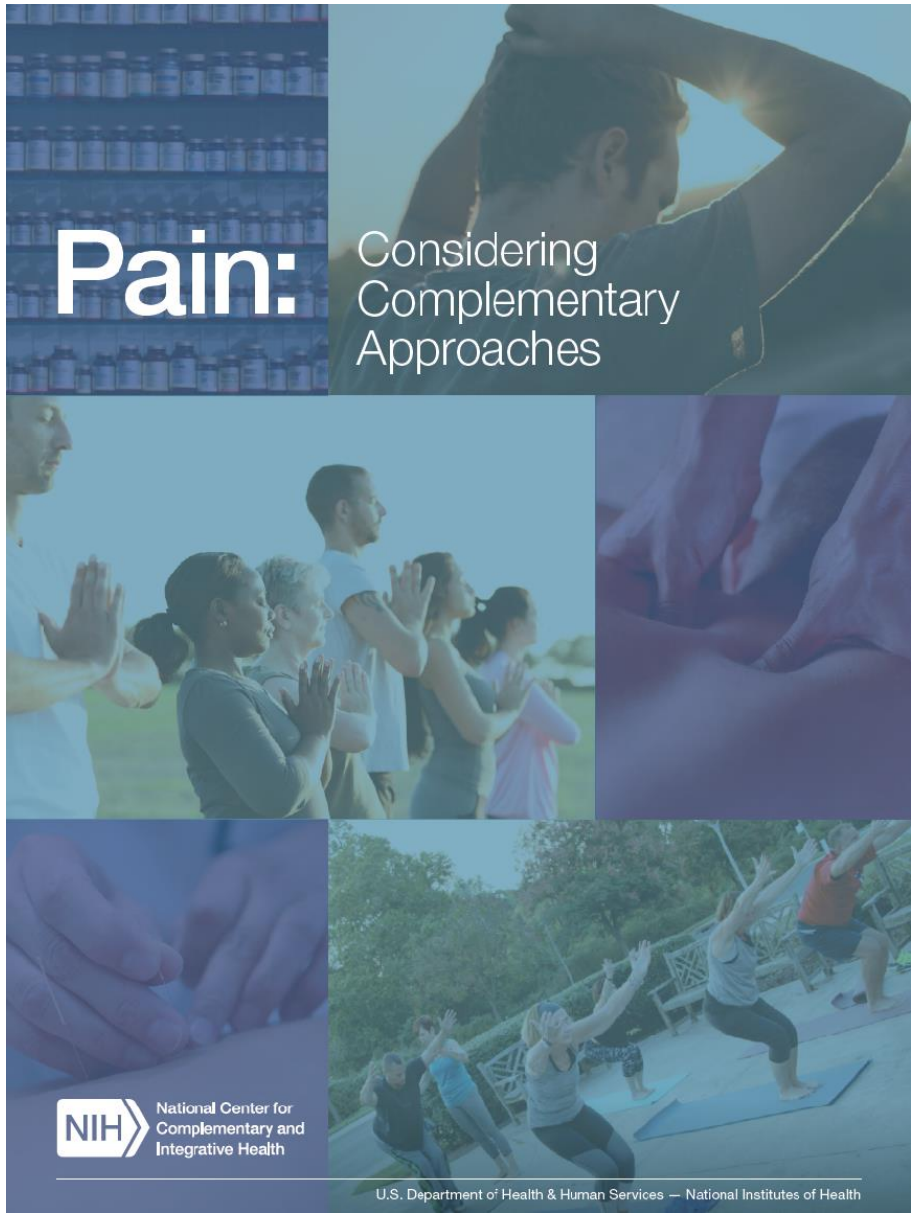
Andrew J. Vickers et al. Acupuncture for chronic pain: individual patient data meta-analysis.
Arch Intern Med. 2012; 172:1444–1453.

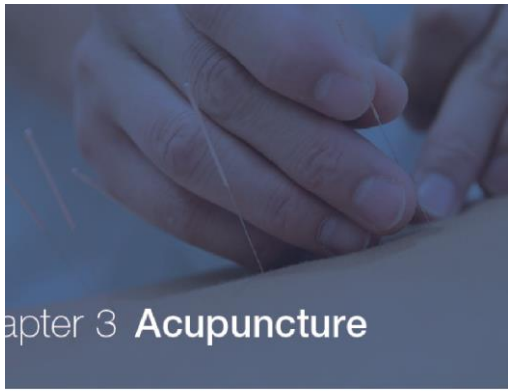
on behalf of the Acupuncture Trialists' Collaboration

searched MEDLINE and

the Cochrane Central Registry of Controlled Trials randomized trials published up until December 31, 2015.

Secondary analyses


Pain:
Considering Complementary Approaches
NIH
National Center for Complementary and Integrative Health
U.S. Department of Health & Human Services — National Institutes of Health


apter 3 Acupuncture


Chapter 8 Tai Chi

Regenerative Medicine

Cryotherapy

Stimulation

VR

Scrambler therapy

Art therapy

Radiofrequency ablation

Aroma

Cognitive behavioural therapy


THE HONG KONG 香 港 醫 訊
MEDICAL DIARY
www.fmshk.org
VOL.21 NO.1 January 2016
Pain Medicine
July 2025
Pain
香 港 疼 痛 學 會
The Hong Kong Pain Society


The Hong Kong Pain Society
Annual Scientific Meeting 2023
9 December 2023
Hong Kong Convention and Exhibition Centre
PAIN
Integrative Pain Care
Pain ASM
Sep 2025
for more information.
Please click HERE to view the preliminary programme.
For enquiry, please contact
HKPS ASM 2023 Meeting Secretariat
c/o International Conference Consultants Ltd.
Tel: (852) 2559 9973
Email: hkpsasm@icc.com.hk
Organized by:
Supporting Organization:
Pain
香 港 疼 痛 學 會
The Hong Kong Pain Society

End