

# Management of Cancer Pain

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# Prevalence of pain

- 30% diagnosis
- 50% during active tumor oriented therapy
- 70-90% advanced and terminal stages

# Reality

Many patients suffer from unrelieved pain!!!!

- Focusing on the cause, pain itself is overlooked....
- Poor assessment
- Lack of knowledge
- Fear of
  - addiction
  - tolerance
  - adverse effects

# Let's treat our first patient...

L.B.

- 58 y man
- Dg.: NSCLC (lung cancer), bone metastases,
- 3 series of standard chemotherapy were given
- Coming to our office with pain 6/10 in his back, with episodes of 9/10 irradiating to left leg on some movement
- Medication: He is taking Ibuprofen 400mg 4-5 tbl daily without any effect

# Assessment:

- History
- Presenting complaint - describing pain:
  - Intensity
  - Type
  - Irradiation
  - Breakthrough pain:
    - provoking moments, duration, relief
- Physical examination
- Imaging...

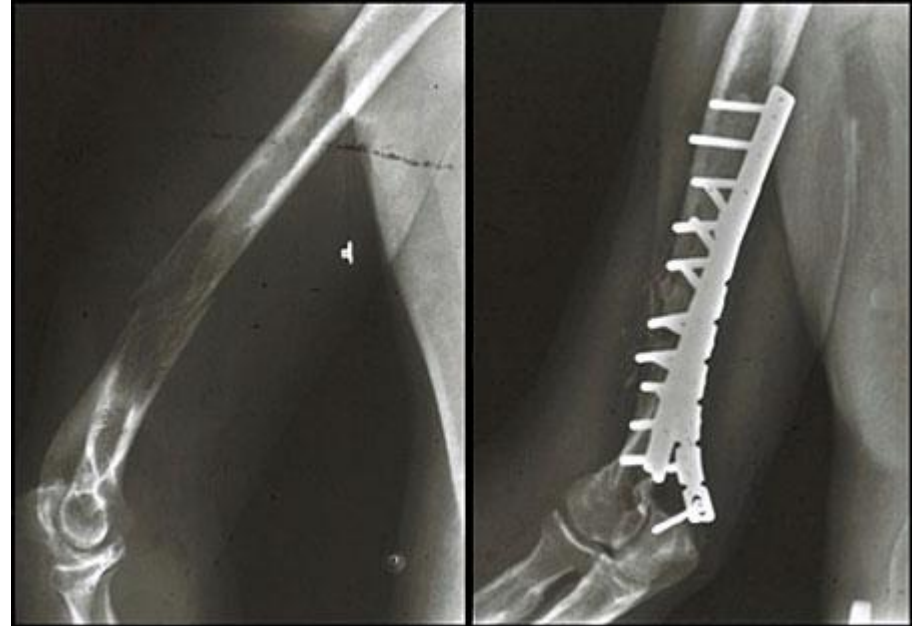
# Imaging

- X-ray image
- CT
- MRI
- Nuclear medicine:
  - Bone scan with  $^{99m}\text{Tc}$
  - SPECT/CT
  - PET, PET/CT – not for bone metastases

# X-ray

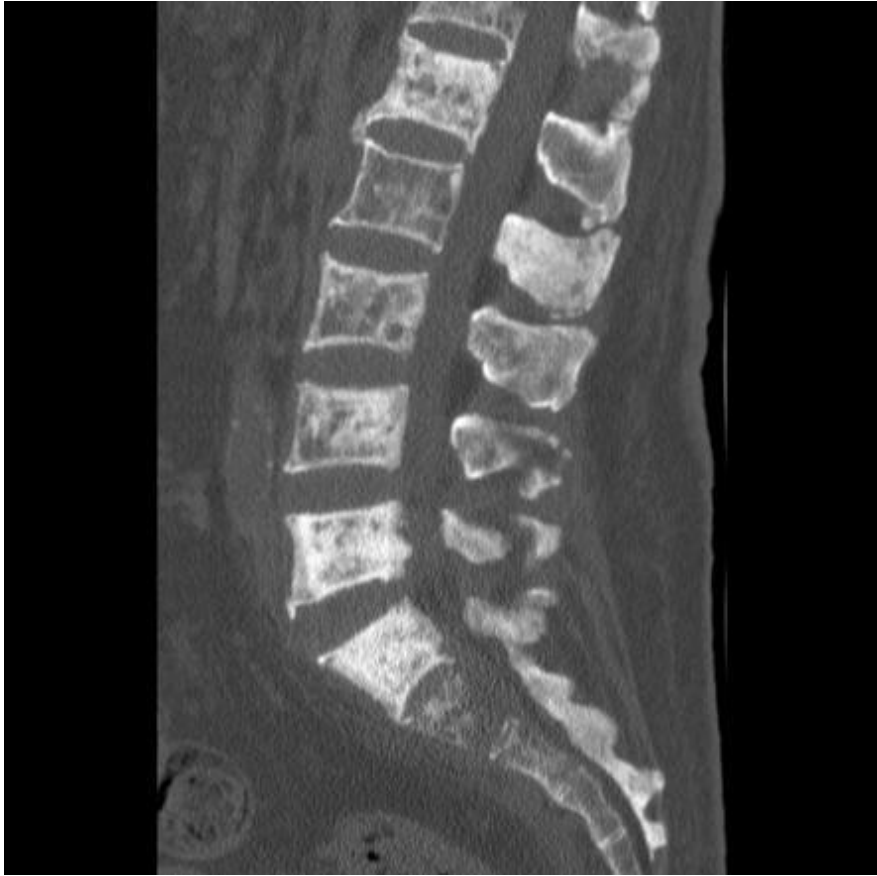


# X-ray

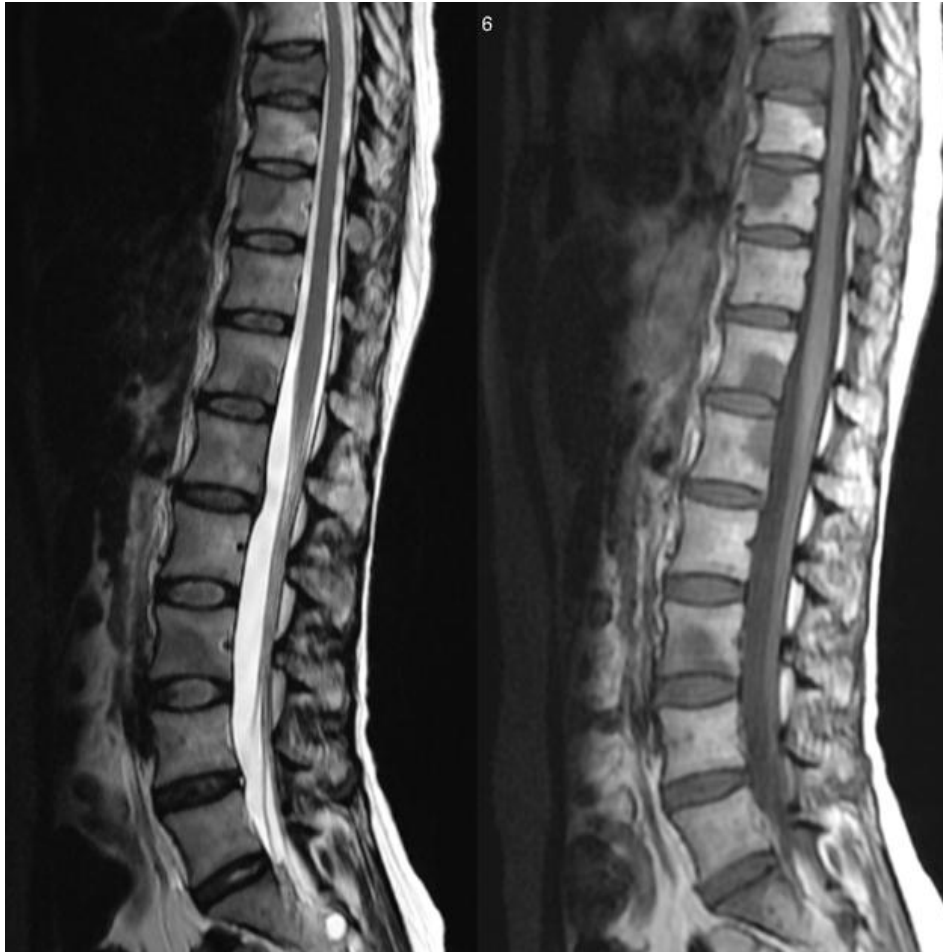




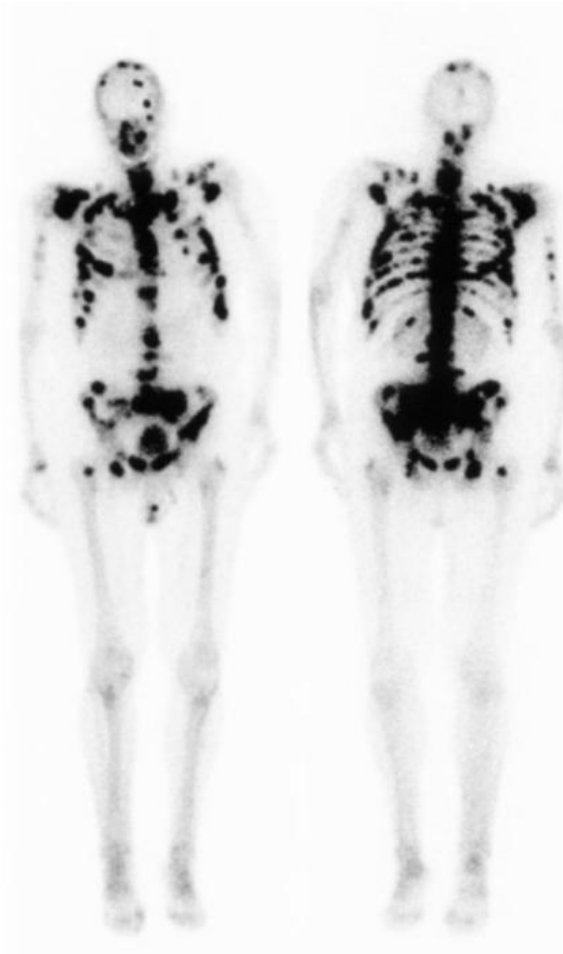
CT



# MRI



# bone scan (scintigraphy)



# Types of pain

- ▶ **Nociceptive pain:**
  - Irritation of nociceptors caused by local tissue damage (inflammation, ischemia, infiltration by tumor)
- ▶ **Neuropathic pain:**
  - **Central Nervous System:**
    - Spinal cord or root compression (pathological fracture of the vertebrae)
  - **Peripheral Nervous System:**
    - Plexus infiltration
    - Herpes Zoster
    - Chemotherapy itself (paclitaxel)
- ▶ **Combination (mixed)**

L.B.

- How would you characterize the pain

L.B.

- How would you manage the pain?

# WHO ladder

		<b>III. Severe pain</b>
	<b>II. Moderate pain</b>	<b>Strong opioids</b> - morphine - hydromorphone - oxycodone - fentanyl - buprenorphine
<b>I. Mild pain</b>	<b>Mild opioids</b> - dihydrocodein(DHC) - tramadol(Tramal)	
<b>Non-opioid analgesics</b> - paracetamol/acetaminophen - NSAIDs(diclofenac, metamizol, ibuprofen) - COX2 pref. (nimesulid)	+/- non-opioids	+/- non-opioids
+/- co-analgesics		

# Non-opioids



- ▶ Paracetamol/acetaminophen
- ▶ NSAIDs
  - diclofenac(Veral)
  - metamizol(Novalgin)
  - Ibuprofen(Motrin)
- ▶ COX2 pref.
  - nimesulid(Aulin, Coxtral)
- ▶ Adverse effects:
  - GI toxicity
  - Nefrotoxicity
  - Thrombocytes aggregation - bleeding
  - Hepatotoxicity (nimesulid, acetaminophen)
  - Agranulocytosis



# Opioids for moderate pain

## ▶ Tramadol (Tramal, Tralgit)

- + immediate/sustained release tablets available
- nausea, vomiting, weakness, sedation
- Ceiling dose at 400mg daily

## ▶ Dihydrocodein (DHC continus)

- Ceiling dose at 240mg

# L.B. medication

- Tramadol SR 100mg 1-0-1
- Eventually Metamizol 500mg every 8hours or Nimesulide 100 mg 1-0-1 (or paracetamol 1000mg TID)
- Tramadol IR 50mg as a rescue every 6hours

What are you going to do next?

- He underwent irradiation 5 x 4Gy to the vertebrae Th 11 – L3
- After that just residual pain
- He was taking Tramadol SR 0-0-1 for 3 months

## ...L.B.

- 4 months later – progression of lung cancer in bone, liver
- ...strong low back pain and right epigastrium pain despite tramadol 400 mg/D + metamizol 3000 mg/d
- What would you do?

# Strong opioids

- Opioid receptor agonists (CNS, PNS, lung, lymphocytes..)
- Effect/ adverse effects are dose dependent
- Individual dose „titration“
- Drug of choice for severe cancer pain (prognosis is not relevant)

# Strong opioids

## Postoperative, ICU setting (parenteral)

- sufentanyl
- piritramide (Dipidolor)
- pethidine (Dolsin)

## Chronic pain (oral, transdermal)

- morphine
- hydromorphone
- oxycodone
- fentanyl
- buprenorphine
- tapentadol

# Forms of Opioids

- Long-acting
  - Tablets (morphine, oxycodone, hydromorphone)
  - Transdermal patches (fentanyl, buprenorphine)
- Short-acting
  - Morphine s.c., i.v.
  - Tablets po
  - Buccal tablets – fentanyl (Effentora)
  - Nasal spray - fentanyl (Instanyl)
  - Sublingual tablets (Lunaldin)

# V.B.

- Cancer progressed in spine, pelvis and lymph nodes

What opiates did we choose ?

- Fentanyl patches 25ug/h → 75ug/h every 72hours
- Morphine p.o. 20mg tablets 2-3x daily

What side effects could we expect?

- V.B. presented with:
  - Fatigue, sleepiness, weakness, worse concentration
  - Obstipation, nausea, loss of appetite

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**TABLE 1. Opioid-related Side Effects<sup>3</sup>**

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**Neurologic**

Delirium

Hallucination

Sedation

Myoclonus

Hyperalgesia

Muscle rigidity

Seizures

Headaches

**Cardiopulmonary**

Respiratory depression

Noncardiogenic

pulmonary edema

Bradycardia

Hypotension

Cardiac dysrhythmias

**Immunologic**

Immune suppression

**Gastrointestinal**

Nausea and vomiting

Constipation

Xerostomia

Gastroesophageal reflux disease

Obstruction of the common bile duct

**Urologic**

Altered kidney function

Urinary retention

Peripheral edema

**Endocrinologic**

Hypogonadism/sexual dysfunction

Osteoporosis

**Dermatologic**

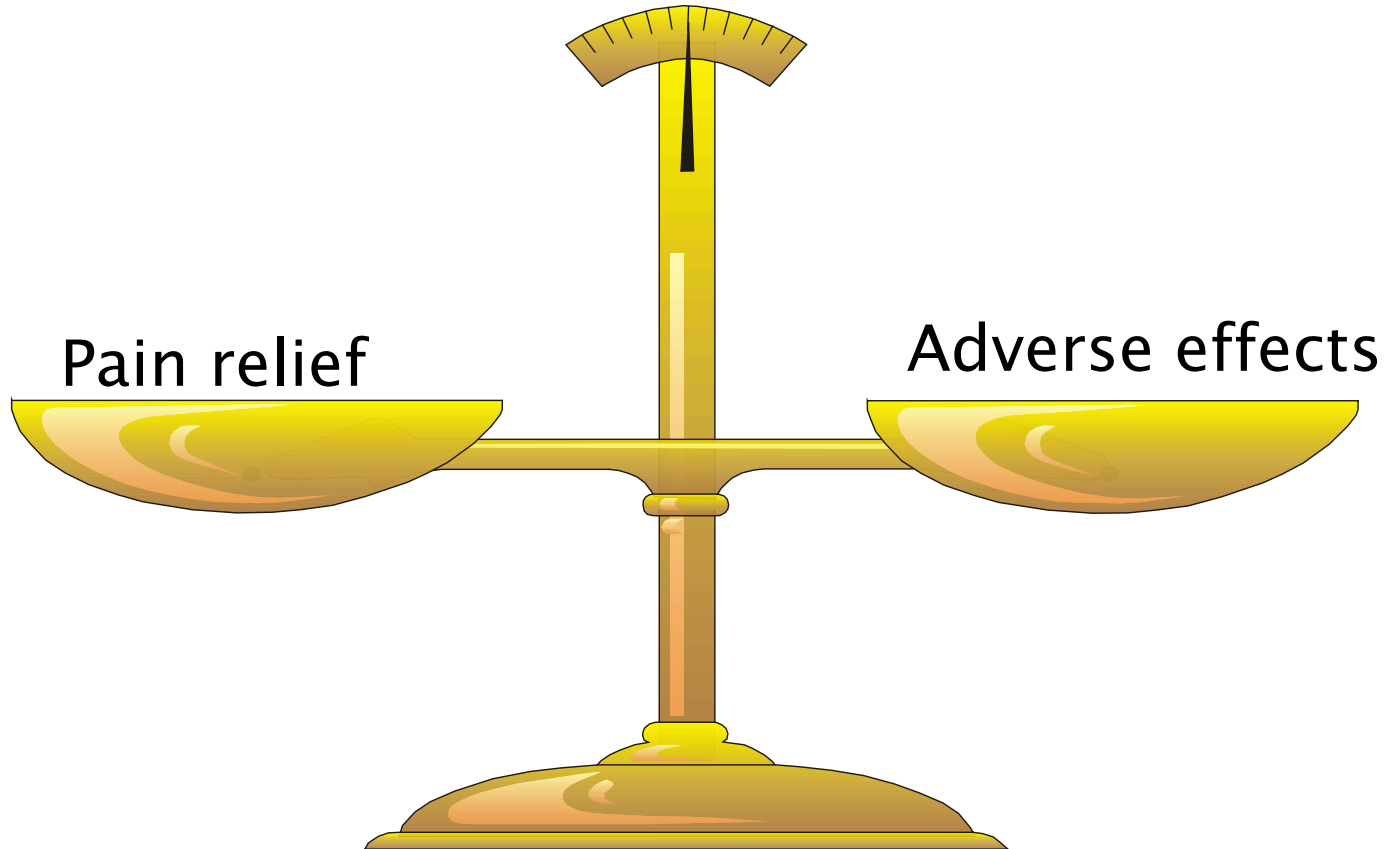
Pruritus

Diaphoresis">

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# Balance



# Nausea and Vomiting

▶ Transitory, usually disappears after 5-10 days

▶ Stimulation of CTZ

- **anti-D2:**

  - haloperidol* 0.5mg-2mg q6-12h

  - triethylperazin (Torecan):* 6,5mg q8h

  - metoclopramide (Degan):* 10 mg q6h

  - ↑EPS (especially combination with AD)

- **5-HT3:**

  - ondasetron (Zofran):* 8 mg, \$, antipsychotic effect?

  - olanzapine (Zyprexa)*

▶ Gastric stasis (vomiting)

- *metoclopramide (Degan)*

# Sedation

- Common at start, tolerance develops
- D/C of contributing medications: antihistamines, antidepressants, anxiolytics,
- Dose reduction, invasive methods of opioids application
- Opioids rotation

# Constipation

- Common, tolerance doesn't develop
- Laxatives
  - *Osmotic: Lactulose*
  - *Stimulants: picosulphate(Gutalax)*
  - .....
- Oxycodon/Naloxon (TARGIN)
- Methylnaltrexon(Relistor)
  - S.c. injection q48h
  - Antagonist of the opioid receptors in the gut, but no effect on central opioid receptors

# Respiratory depression

- Rare in chronic pain management
- Tolerance usually develop
- D/C benzodiazepines
- Naloxone
  - – if less than 8 breaths / minute
  - - systemic withdrawal syndrome

# General recommendations in management of the side-effects:

- (1) Balance the doses of systemic opioids (use rescue medication)
- (2) Manage actively the adverse effects of opioids
- (3) Opioid rotation
  - Equianalgesic** dose minus 20-30% (lower tolerance to the new opioid)
  
- (4) Change the route of administration

- Opioids are safe and effective
- Side effects are manageable

# Neuropathic pain

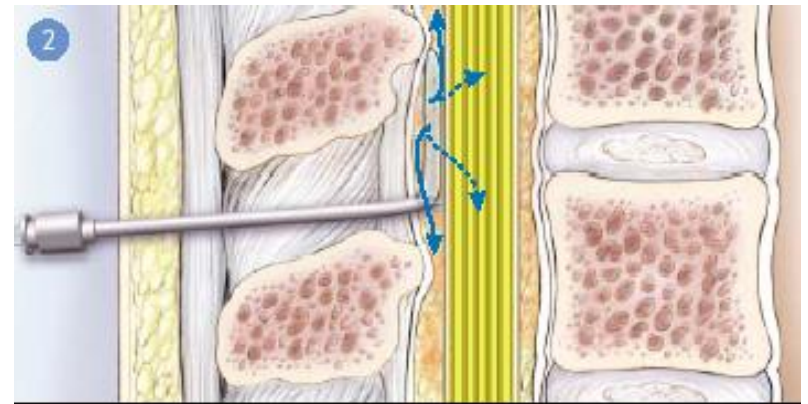
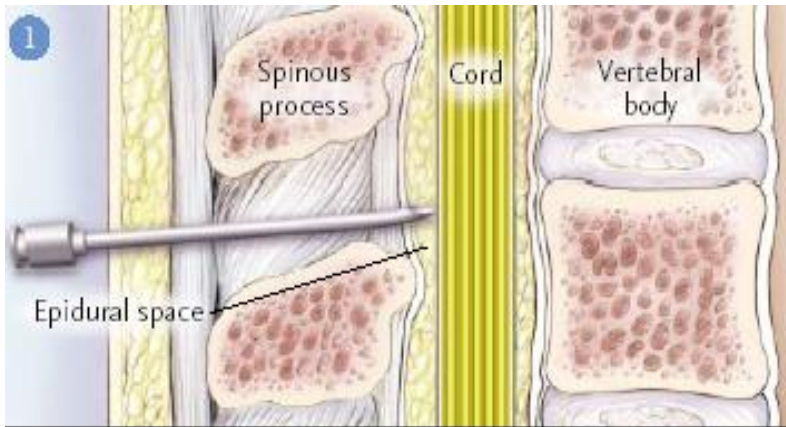
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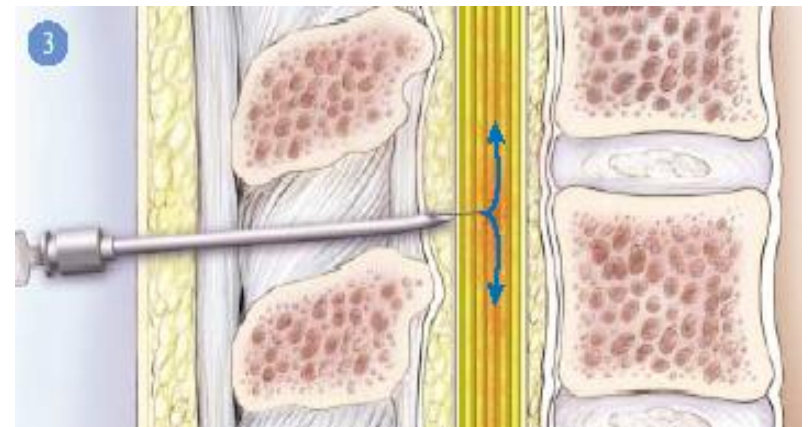
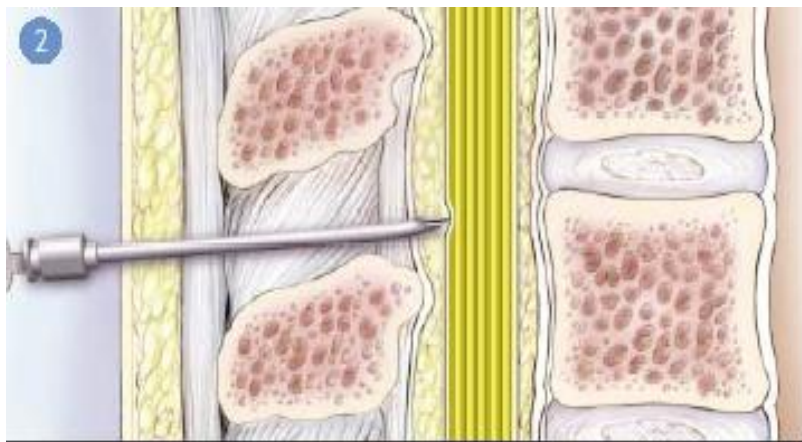
# Co-analgesics for neuropathic pain

- Antidepressants
  - TCA (Amitryptilin, Nortryptilin, Dosulepin)
- Anticonvulsants (Gabapentin, Pregabalin, Carbamazepine)
- Corticosteroids (Dexamethasone)
  - Especially in case of root/spine cord compression

## Epidural delivery



## Subarachnoidal delivery



- Use mixture of opioid + anaesthetics (bupivacaine, mesocaine)



# V.B.

- Continual infusion to the epidural catheter
- Morphine 5ml(20→50mg) + Bupivacaine 1%  
5ml + saline solution 10ml v=2-3ml/h
- Effect:
  - no pain
  - some level of sedation

# V.B.

- In August symptoms of chronic sepsis
- Worsening of pain
- CT: huge abscess invading gluteal muscles, both lesser and greater pelvis on the right



# Summary

- Cancer pain is manageable
- Need of comprehensive assessment
- Comprehensive intervention
  
- Opioids are safe and effective drugs for the management of severe cancer pain
- Side effects are manageable