Every day is a gift from God. There is no guarantee of tomorrow

Breast cancer

Pain Management

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↑survival→↑ complications

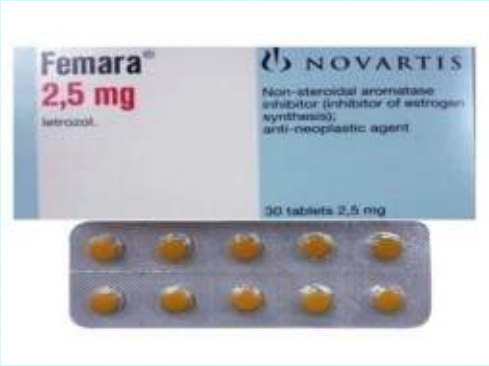
- As a consequence of advancements in diagnostic procedures and treatments available, the rate of survival of patients has increased. Hence, it is expected that the population susceptible to develop pain as a complication would increase

incidence

- The variation observed in rates of incidence as well as mortality due to breast cancer, is due to a number of contributing factors like age, race, socio-economic status, life style, reproductive history, family history, *etc*[1].
- Patgophysio-anatoico-socio-economico-cultru-spiritual and psycho …

- **etiology of cancer pain**

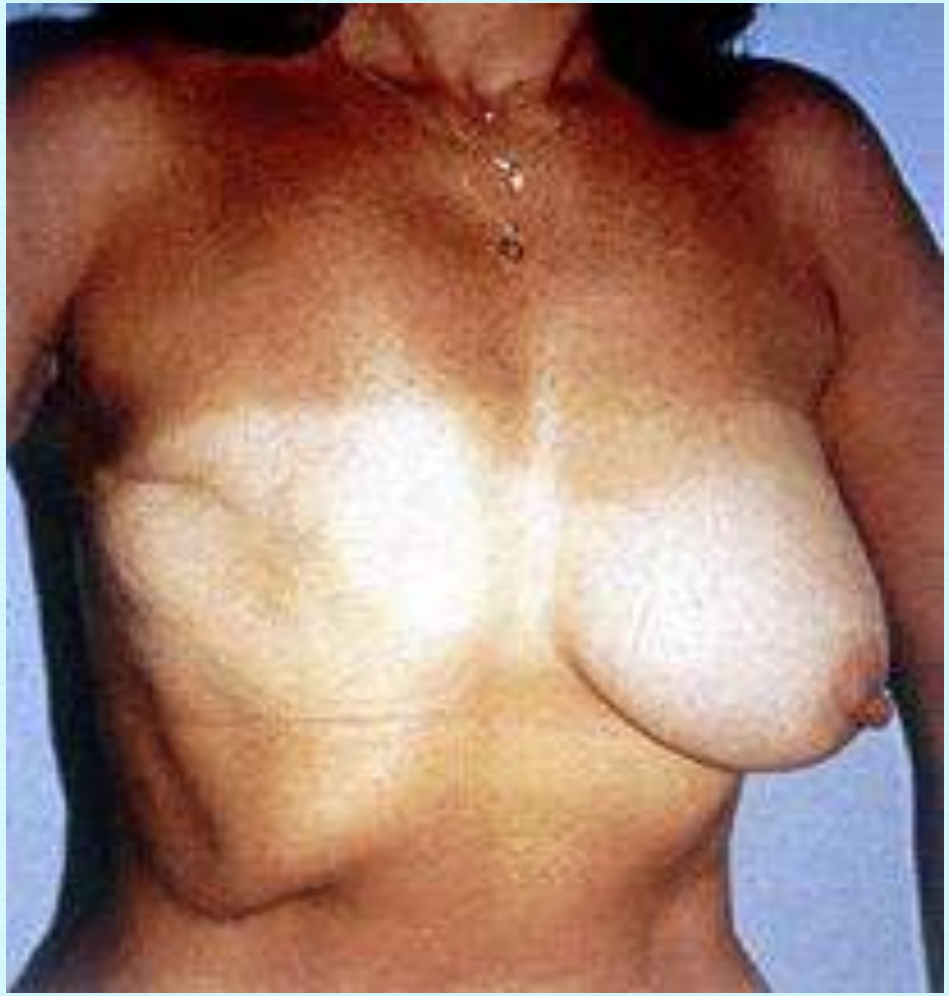
- multi-factorial.
- It may arise due to *(i)* cancer itself due to release of inflammatory mediators or due to metastases to distant tissues including bones and neuronal tissue.
- *(ii)* Cancer treatment. Sensory neurons are degenerated after chemotherapy and lead to neuropathic pain.
- Radiotherapy induced pain arises as a result of microvascular changes and nerve compression.
- The main causes for surgery induced pain are damage to the intercostobrachial nerves and neuroma formation.
- Estrogen deficiency caused by aromatase inhibitors leads to arthralgias.
- What does tamoxifen do to the body?
- Tamoxifen. Tamoxifen **blocks estrogen from connecting to the cancer cells and telling them to grow and divide**. While tamoxifen acts like an anti-estrogen in breast cells, it acts like an estrogen in other tissues, like the uterus and the bones. Because of this, it is called a selective estrogen receptor modulator (SERM)
- .
- What are the best aromatase inhibitors?
- In addition to being the most potent non-steroidal AI, **letrozole** is the only AI that has demonstrated superior efficacy in both the neoadjuvant and adjuvant settings compared with tamoxifen.
- breakthrough cancer pain (BTcP)



Chronic pain following breast surgery

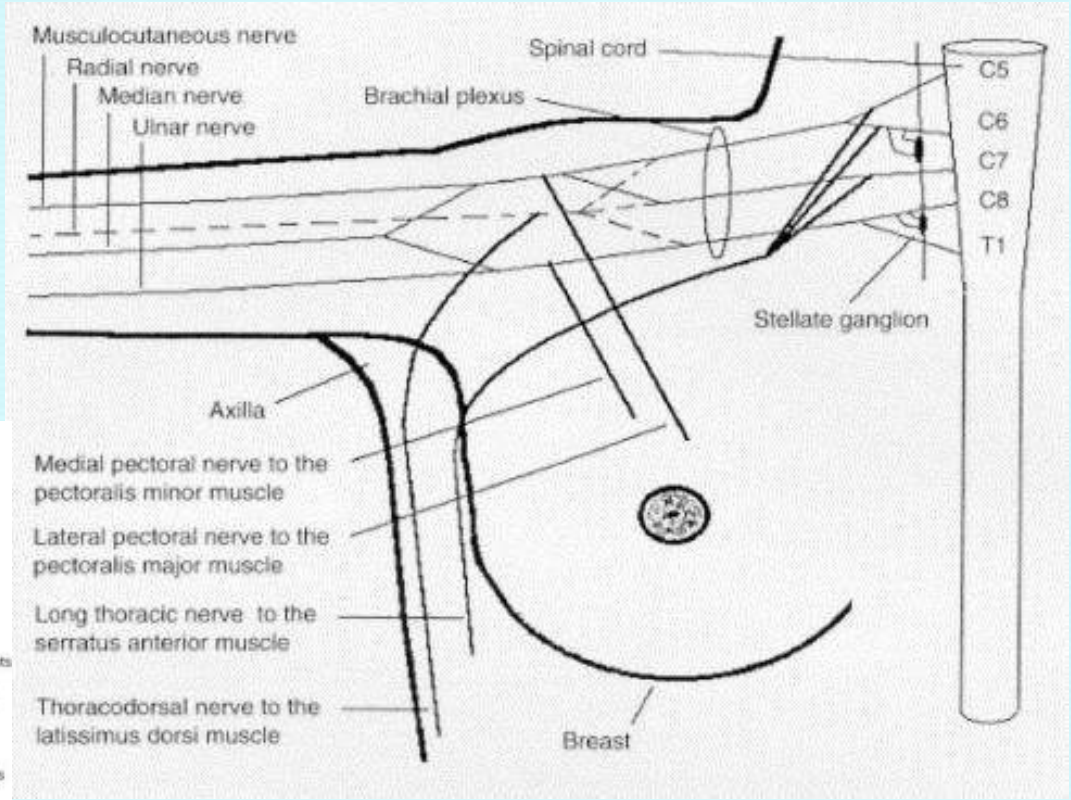
- ✓ Breast cancer surgery (overall): ~50%
- ✓ Mastectomy:(lumpectomy) ~50%
- ✓ Breast conserving surgery: ~50%
- ✓ Breast augmentation:(reconstruction)10-40%
- ✓ Abnormal sensory (neuropathic) symptoms: ~80%
- ✓ Phantom breast pain: ~5-10%

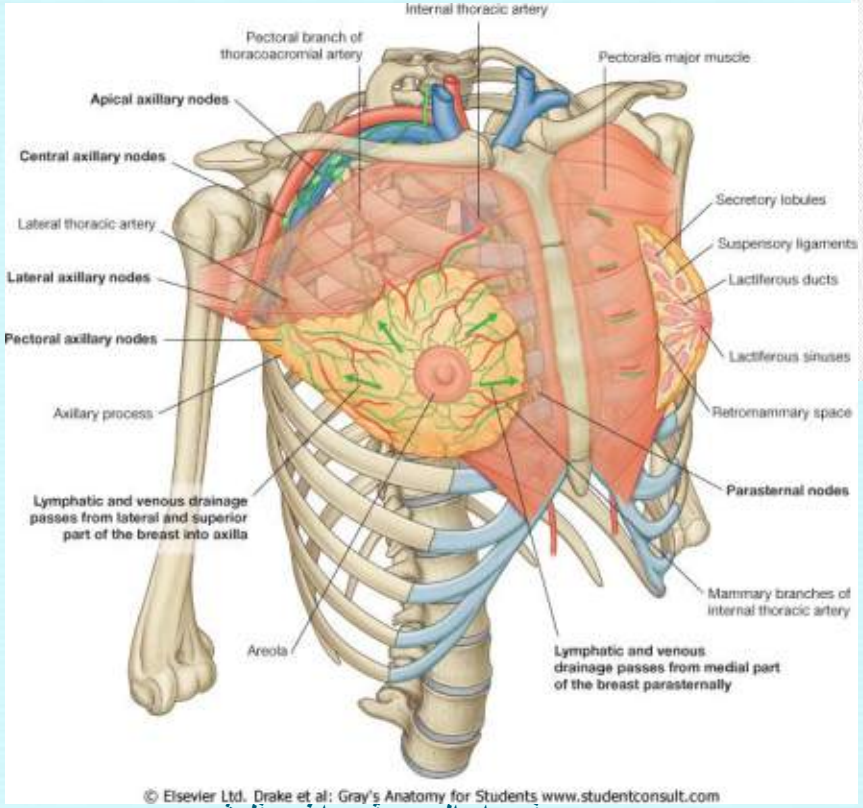
- ✓ Remove one or more lymph nodes from axillary area



Features of chronic pain after breast surgery

- ✓ Daily pain 50%
- ✓ Moderate-mild (≤4/10) 90%
- ✓ Severe %10-40
- ✓ Site: -Breast or chest wall 70%
  -Axilla or arm 60%
  -Regional (neck & shoulder) 50%
  -Other sites (widespread) 40%





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Chronic pain syndromes

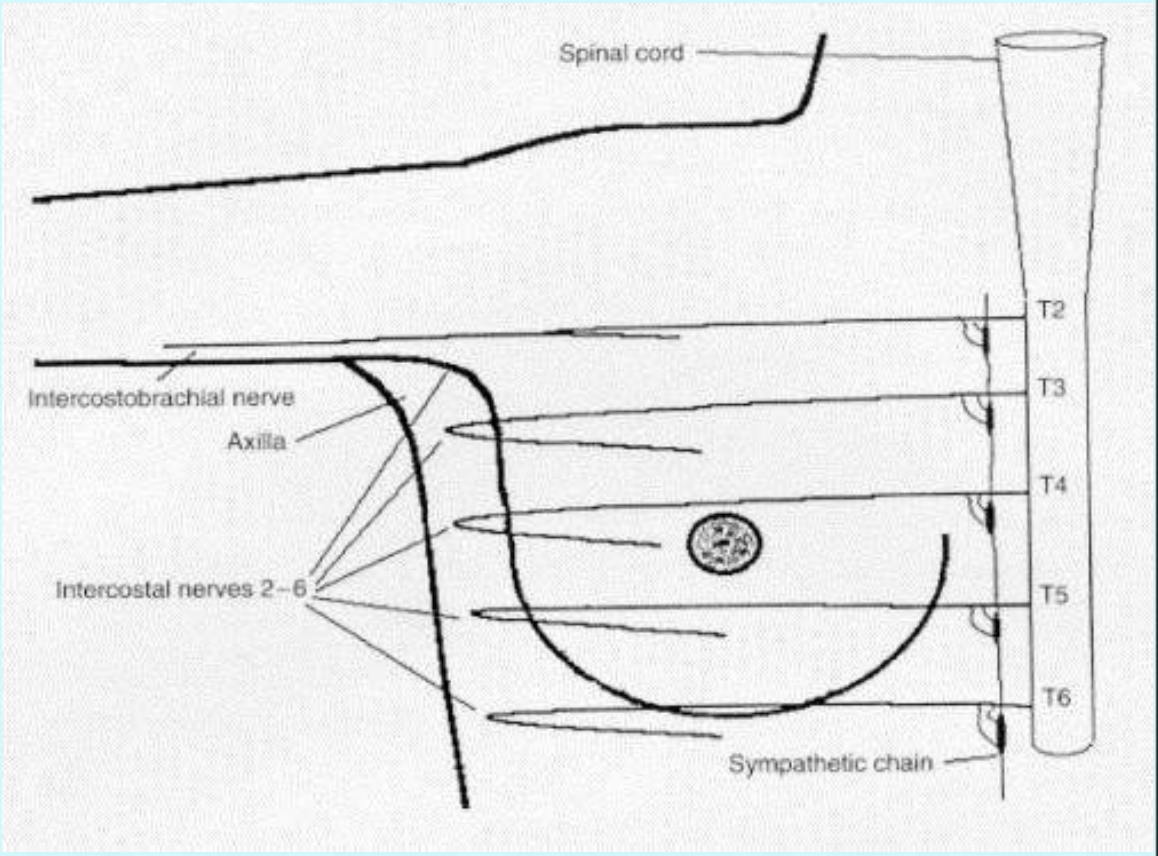
- **Post-mastectomy pain syndrome :**
- ('neuropathic pain')

  -Inter-costo-brachial neuralgia (axillary dissection)

  -'Scar pain' (neuroma)30-50%
- **Phantom breast pain**

- **Reconstructive (flap/implant) surgery**

  -No difference in pain; mastectomy alone ± plastics
- pain due to other nerve injury



Scar pain' (neuroma)

- It can happen after any type of breast surgery, including a lumpectomy (wide local excision), mastectomy, lymph node removal and breast reconstruction. **The pain is usually caused by bruising, stretching or damage to nerves during surgery or when scar tissue forms**

Scar pain' (neuroma)

- in their literature review of 23 studies, Post Breast Surgery Pain Syndrome is pain that occurs after any breast surgery, is of at least moderate severity, possesses neuropathic qualities, is located in the ipsilateral breast/chest wall, axilla, and/or arm, lasts **at least 6 months or later**, occurs at least 50% of the time.
- Treatment: multimodal approach

Phantom breast syndrome/pain/STUMP ?!

- Phantom breast syndrome is **a type of condition in which patients have a sensation of residual breast tissue and can include both non-painful sensations as well as phantom breast pain**. The incidence varies in different studies, ranging from approximately 30% to as high as 80% of patients after mastectomy. Neuropathic type.
- Treatment: **(anticonvulsants), such as gabapentin. Antidepressants, such as amitryptyline or Cymbalta (duloxetine) and neural blockade**

Chronic pain syndromes after mastectomy

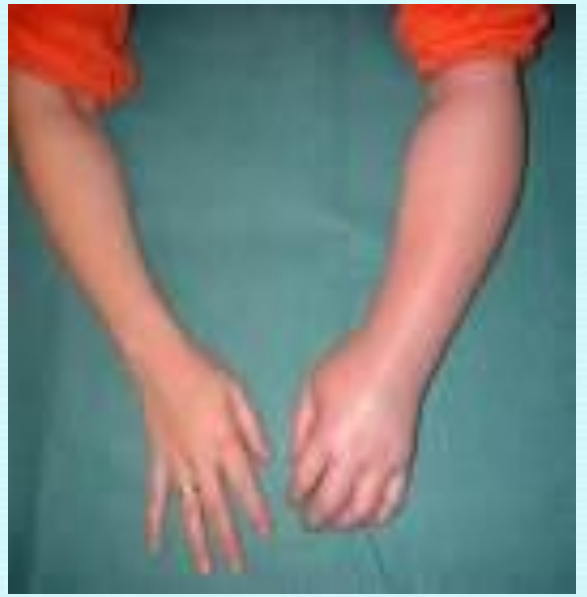
- **Secondary pain syndromes (arm, shoulder)**

  -'Frozen shoulder'

  -Neck & shoulder myofascial pain (trigger points)

  -Lymphoedema

  -Complex Regional Pain Syndrome



- **Cancer pain syndromes**

  -Local invasion, metastases

  -Treatment effects (chemo-neuropathies)

Neuropathic pain (nerve pain)

Neuropathic pain descriptors

- ❑ 'Electrical'
- ❑ Burning, shooting, stabbing

'Positive' signs & symptoms

- ❑ Allodynia
  (touch, pressure, cold pain)
- ❑ Dysesthesiae
- ❑ Phantom sensations

'Negative' signs & symptoms

- ❑ Numbness
- ❑ Anaesthesia dolorosa

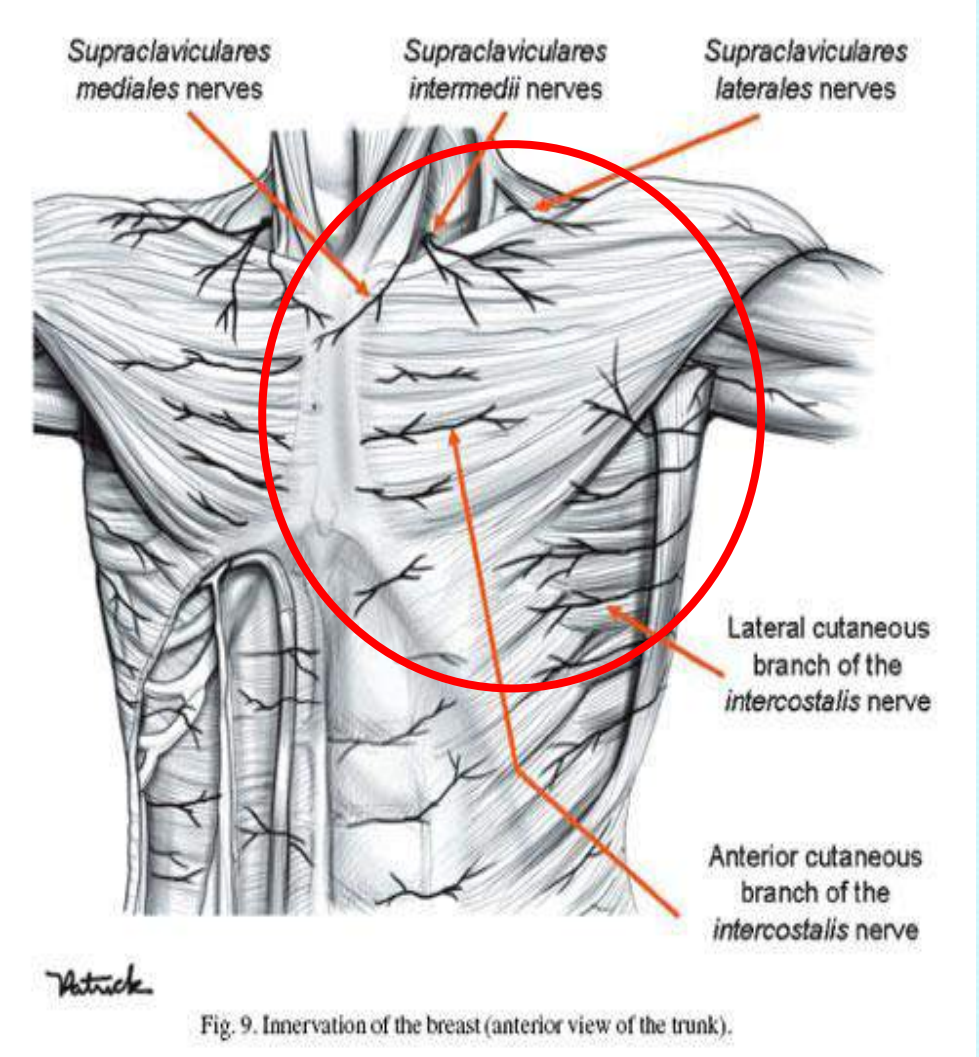


Fig. 9. Innervation of the breast (anterior view of the trunk).

Risk factors for chronic pain

- High BMI
- Younger age
- Pre-op pain (breast, widespread pain, fibromyalgia)
- Severe acute post-operative pain (>6/10)
- Complex surgery: revision, reconstruction
- Nerve injury: axillary dissection *vs* sentinel node
- Radiotherapy (chemotherapy)
- Limb immobilization (frozen shoulder, CRPS)
- Lymphoedema

Risk factors for chronic pain: Psychosocial 'Yellow Flags'(CHAMPS)

- Catastrophic thinking (hypervigilance, ruminating)
- Anxiety, depression
- Medically-focused
- Passive coping style
- Single (poor social support)

Prevention of chronic pain

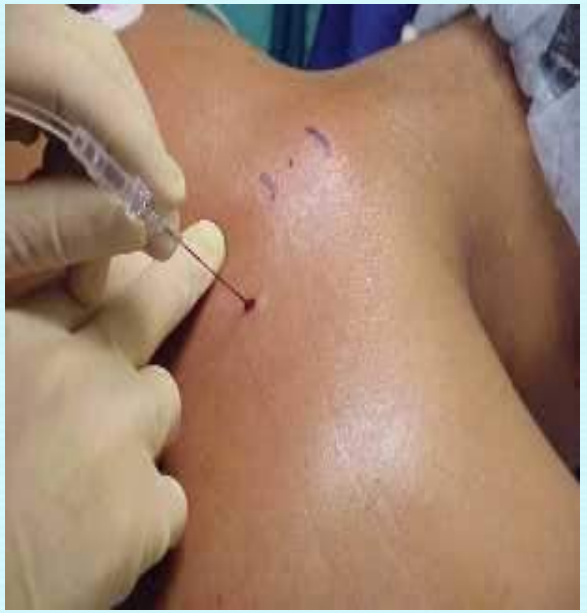
- Avoid 'unnecessary' surgery & re-operations (cosmetic?)
- Surgical technique (minimally invasive, nerve sparing)
- Screen & monitor at 'risk patients'
- 'Preventive analgesia' techniques
- Multidisciplinary rehabilitation

Preventive analgesia techniques

- Multimodal analgesia

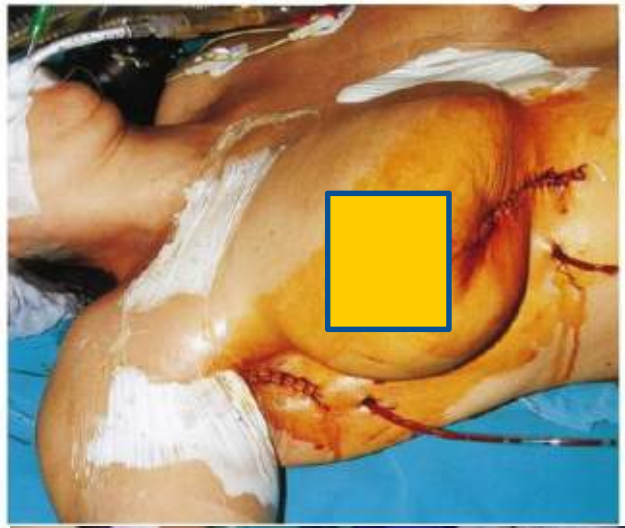
- Paracetamol
- Parecoxib or celecoxib
- Neuropathic pain drugs

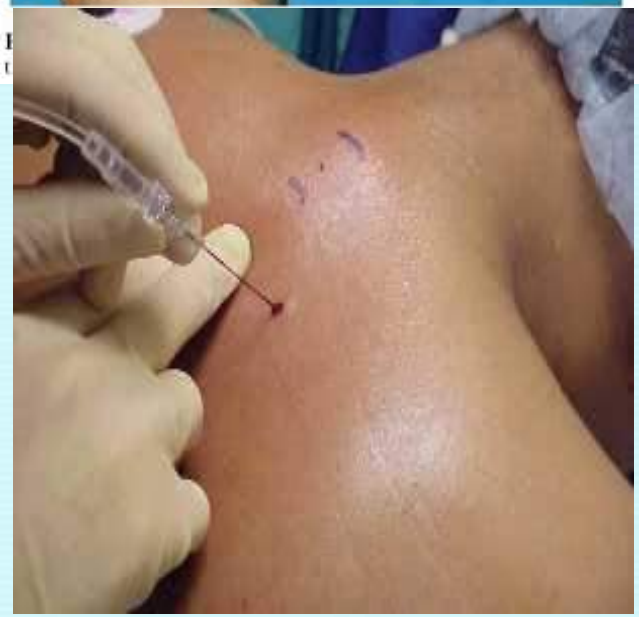
- Pregabalin
- Tramadol or tapentadol



Preventive analgesia techniques

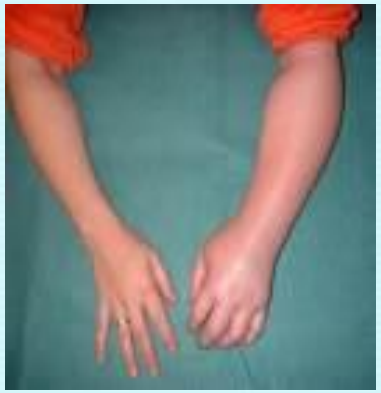
- Local anaesthetic infiltration
- EMLA cream
- Paravertebral block
- Epidural
- IV Lignocaine infusion
- IV Dexmedetomidine





Breast pain management checklist

- Provide education & information about breast pain
- Always ask about neuropathic pain & phantom sensations
- Test for allodynia, DN4Q
- Check for lymphoedema
- Check for shoulder pain & stiffness
- Check for Complex Regional Pain Syndrome (CRPS)



Interview questions for the patient:

Question 1: Does your pain have one or more of the following characteristics?

	Yes (1)	No (0)
1. Burning		
2. Cold is painful		
3. Electric shocks		

Question 2: Is the pain associated with one or more of the following symptoms in the same area?

	Yes (1)	No (0)
4. Tingling		
5. Pins and needles		
6. Numbness		
7. Itching		

Examination of the patient:

Question 3: Is the pain located in an area where the physical examination had one or both of the following characteristics?

	Yes (1)	No (0)
8. Hypoaesthesia to touch		
9. Hypoaesthesia to pinprick		

Hypoaesthesia: decreased sensitivity

Question 4: In the painful area, can the pain be caused or increased by:

	Yes (1)	No (0)
10. Brushing		
Total score =		

Total score ≥ 4: 90% probability of neuropathic pain.

Breast pain management checklist

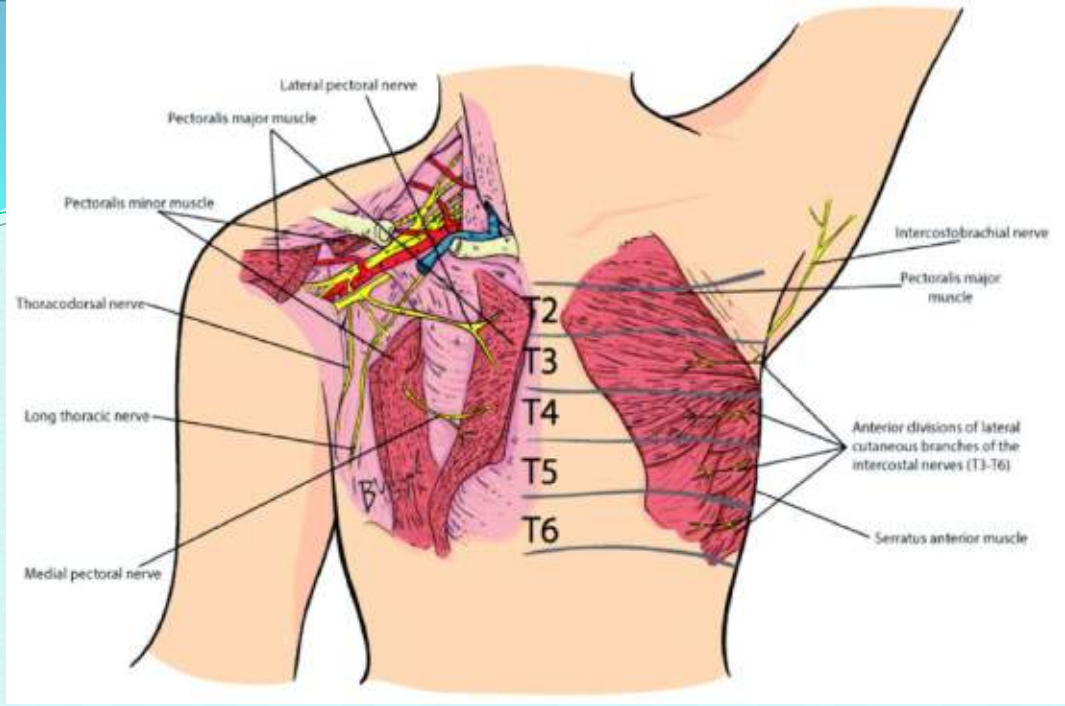
- Check for 'red flags' (TINT) (tumor: cancer recurrence, infection, neurpathic pain, trauma;lymphoedema)
- Check 'yellow flags' (CHAMPS)
- Indentify those at risk of chronic pain & disability
- Early referral to a pain management clinic
- Start multimodal analgesia (drugs or/and intervention)

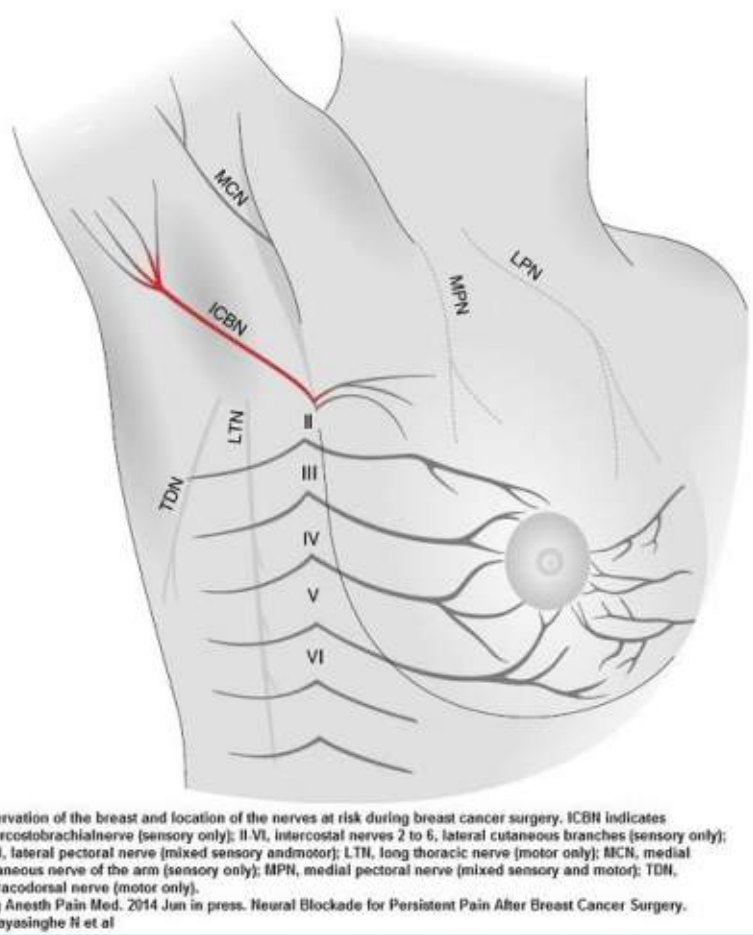
Breast pain management checklist

- Start Vitamin C 1000 mg/d & Vitamin E 500IU/d for 2M
- Physiotherapy (TENS, trigger points)
- Keep shoulder & arm moving
- Scar or neuroma injections
- Shoulder injections
- Lignocaine patches
- Nerve blockade/interventional techniques
- Behavioural pain management & social support

CHOICES FOR PAIN CONTROL

- Administration of opioids via IV, IM, or IV PCA routes
- Thoracic epidural analgesia
- Paravertebral blocks
- Intercostal nerve blocks
- Intrapleural catheter
- Pectoralis Plane Blockade
- Serratus Plane Blockade
- Cryoanalgesia has been used

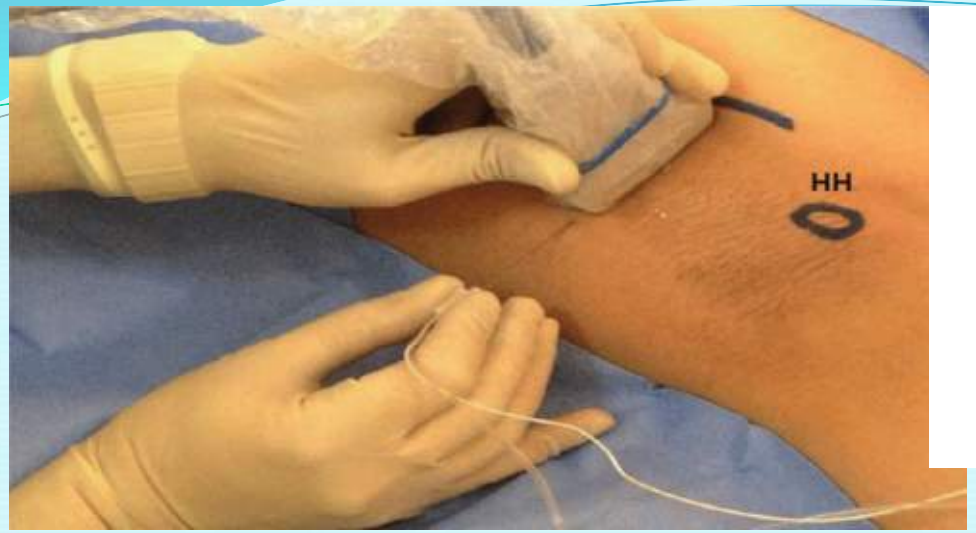


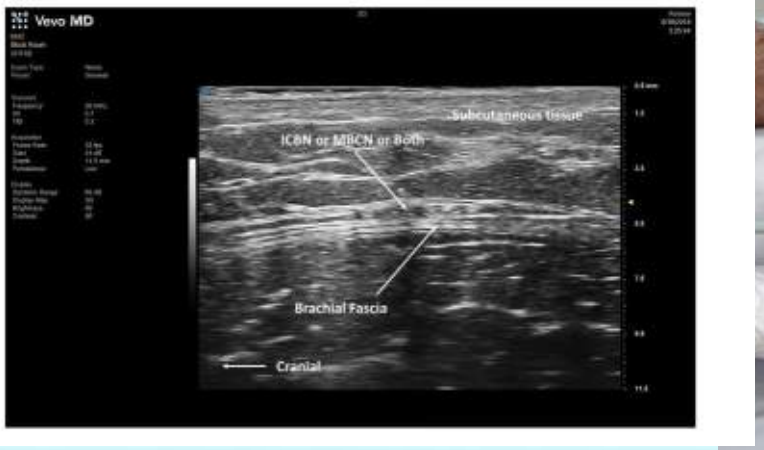


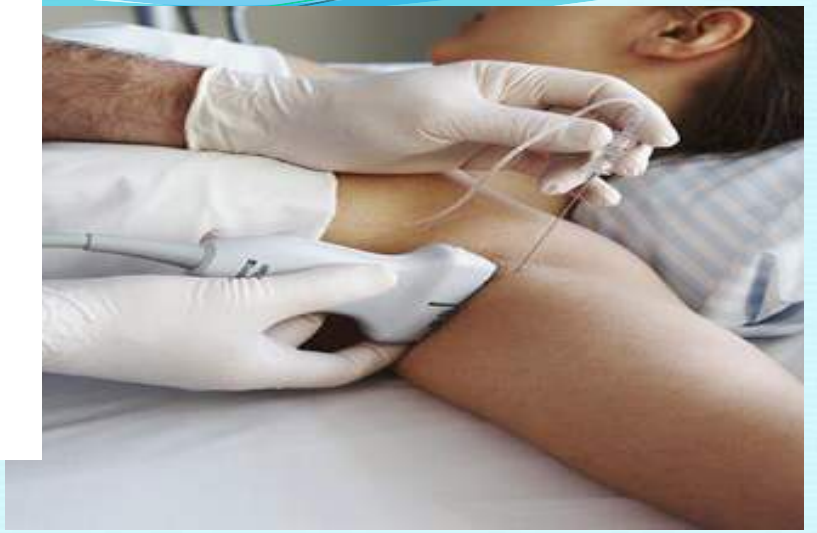
Innervation of the breast and location of the nerves at risk during breast cancer surgery. ICBN indicates intercostobrachialnerve (sensory only); II-VI, intercostal nerves 2 to 6, lateral cutaneous branches (sensory only); LPN, lateral pectoral nerve (mixed sensory andmotor); LTN, long thoracic nerve (motor only); MCN, medial cutaneous nerve of the arm (sensory only); MPN, medial pectoral nerve (mixed sensory and motor); TDN, thoracodorsal nerve (motor only).
Reg Anesth Pain Med. 2014 Jun in press. Neural Blockade for Persistent Pain After Breast Cancer Surgery. Wijayasinghe N et al

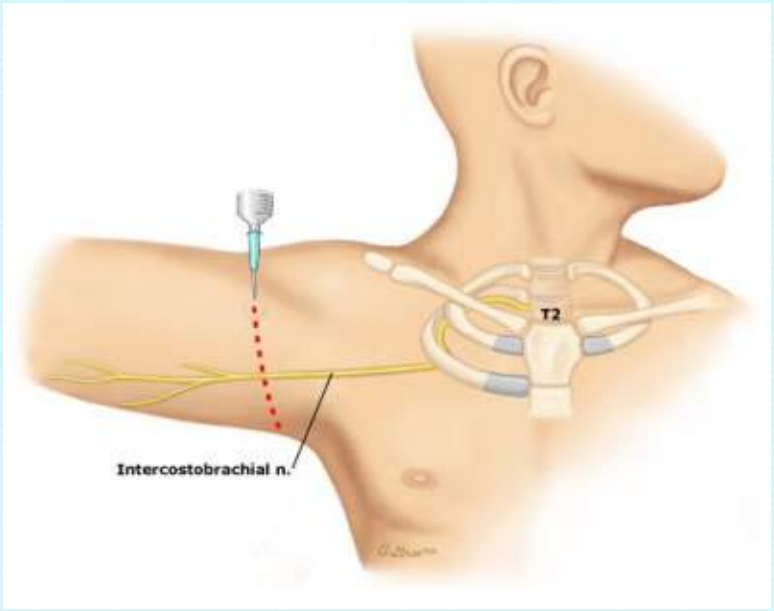
- Inter-costo-brachial neuralgia (axillary dissection)
  The intercostobrachial nerve (ICBN) is (**this** nerve is a **sensory nerve)a cutaneous nerve that provides sensation to the lateral chest wall, medial aspect of the upper arm, and the skin of the axilla and tail of breast. Classically originating from the lateral cutaneous branch of the second intercostal nerve.**

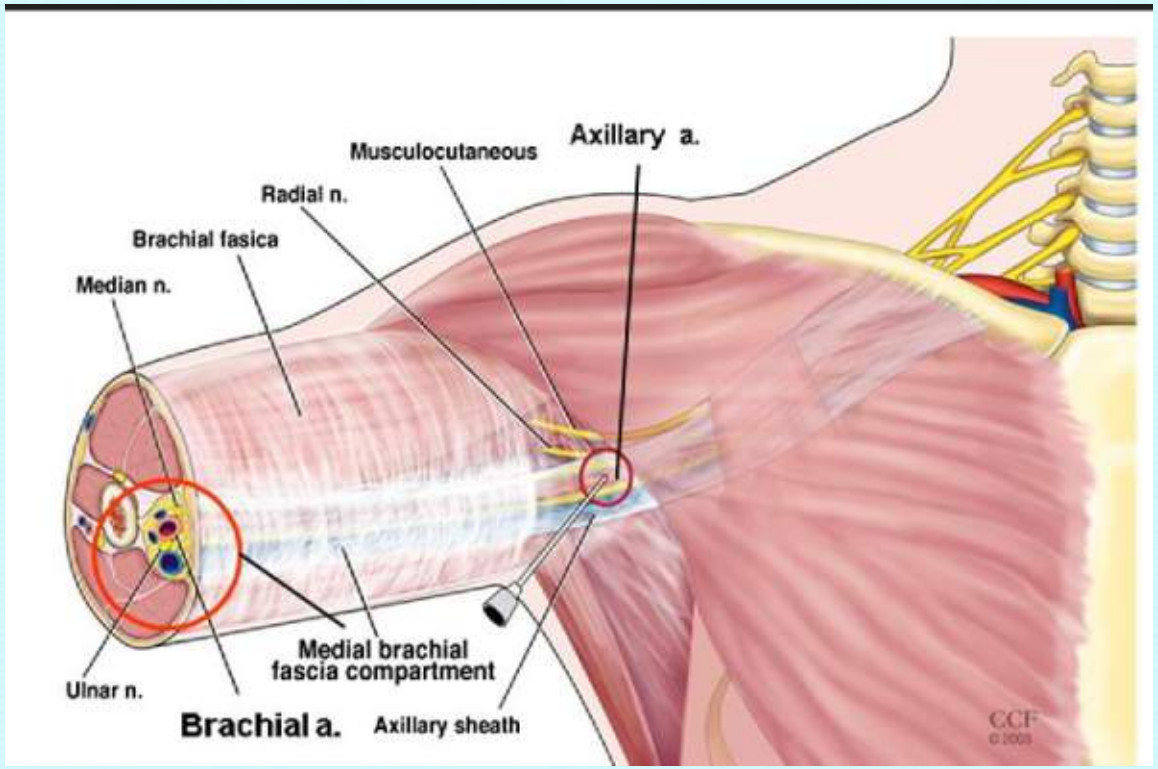
Inter-costo-brachial nerve blockade











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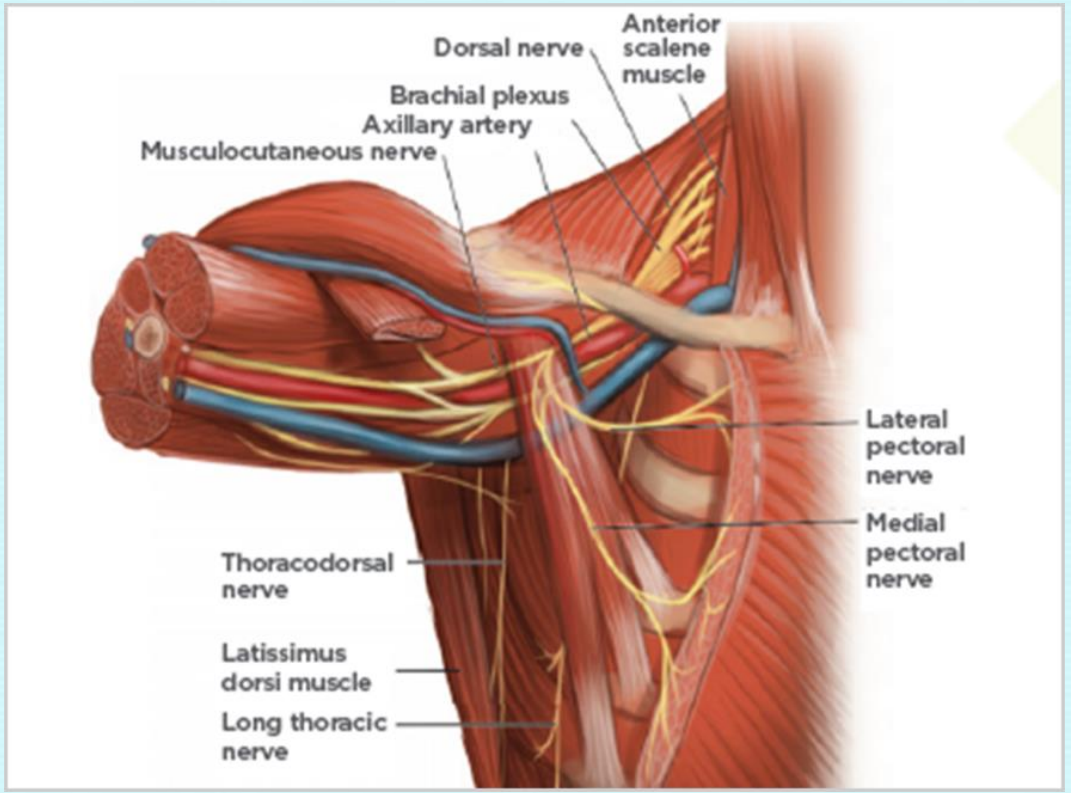
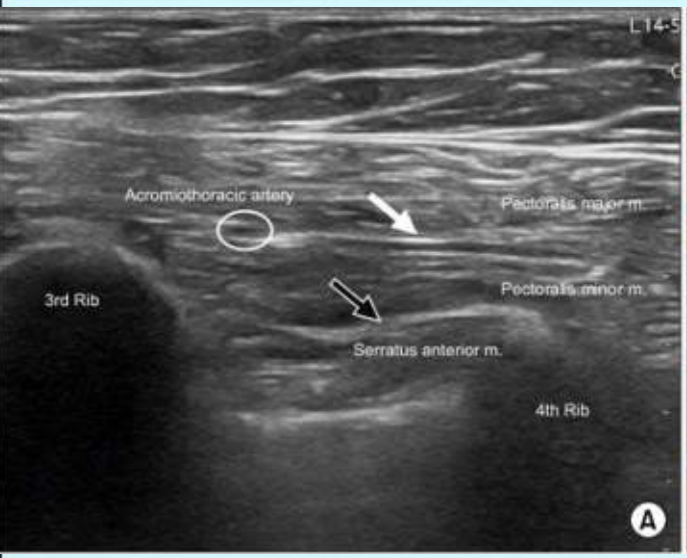
Pectoralis Plane Blockade

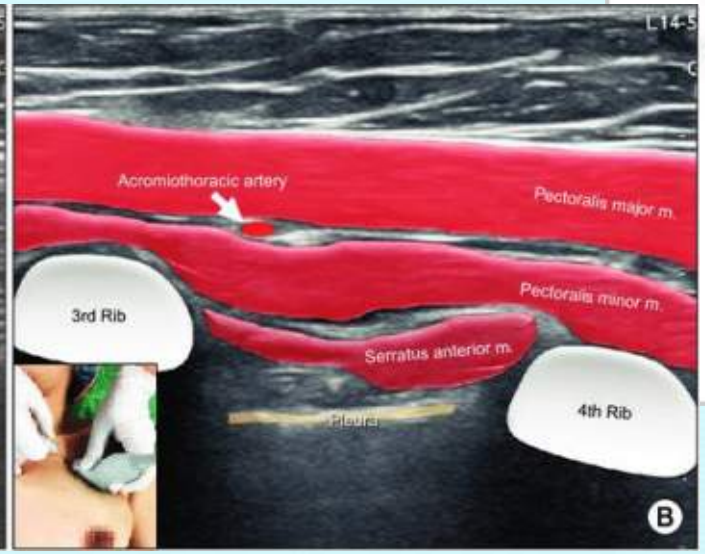
PECS I block Devised to anesthetize the medial and lateral pectoral nerves, which innervate the pectoralis muscles
PECS II block Extends the block to provide blockade of the upper intercostal nerves

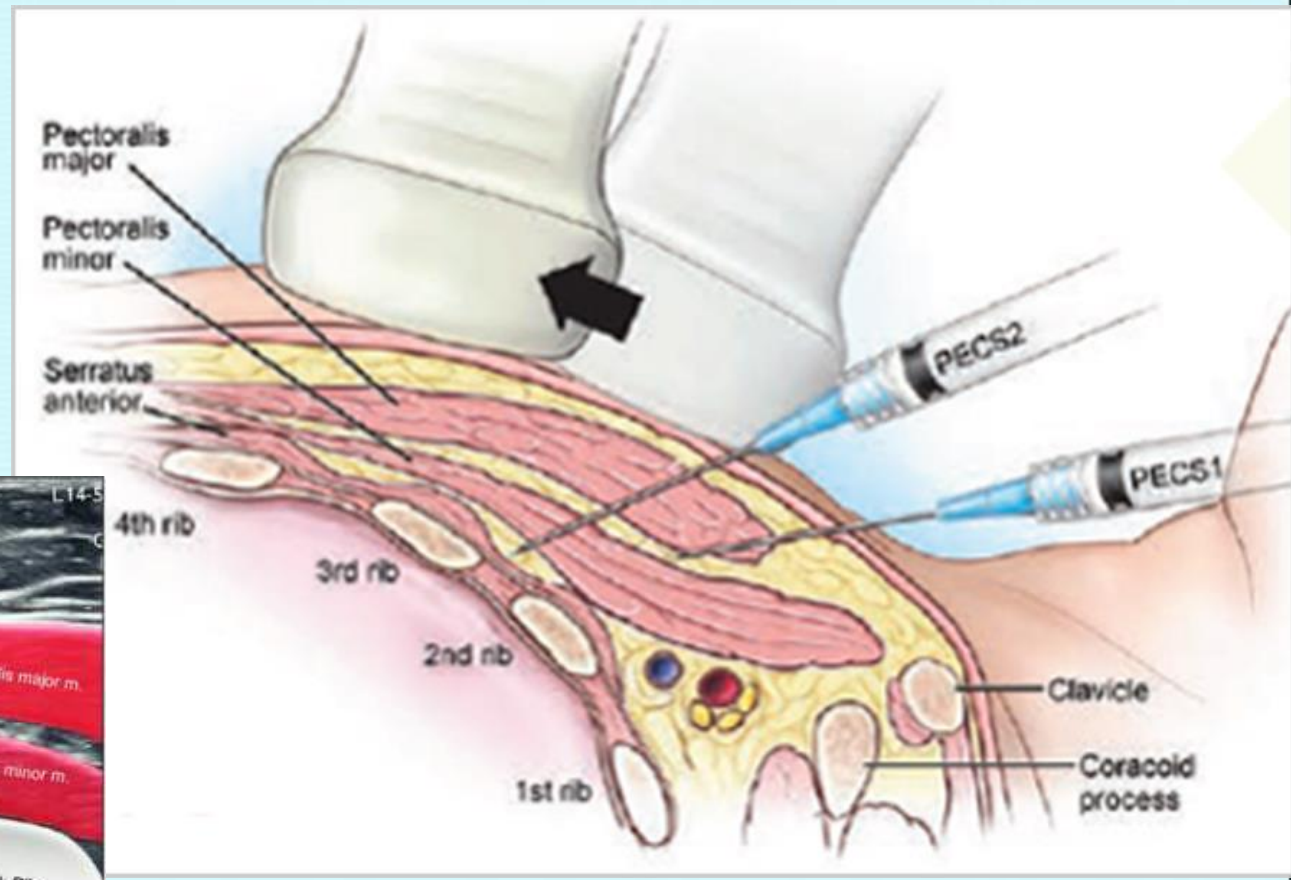


PECS I bloc: Injection between pectoralis major and minor muscles

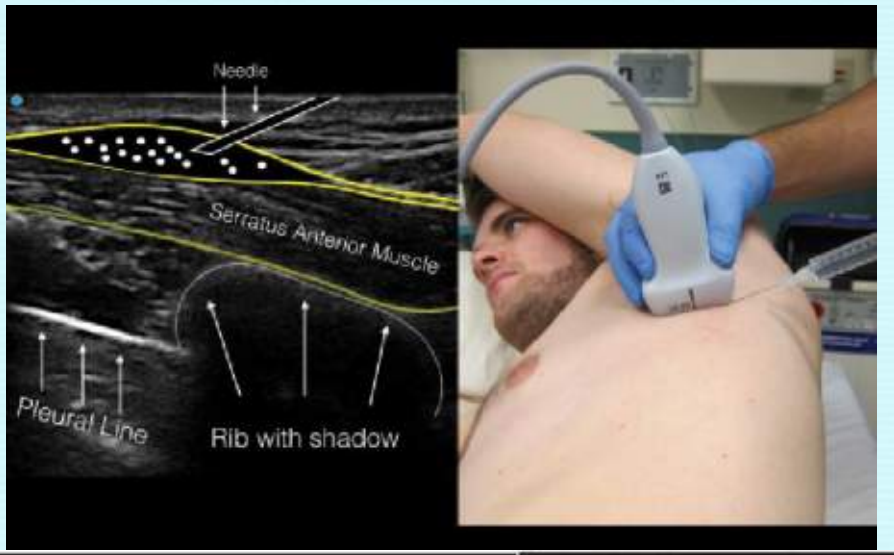
PECS II block: Injection between the pectoralis muscles and a second injection between the serratus anterior and pectoralis minor muscles

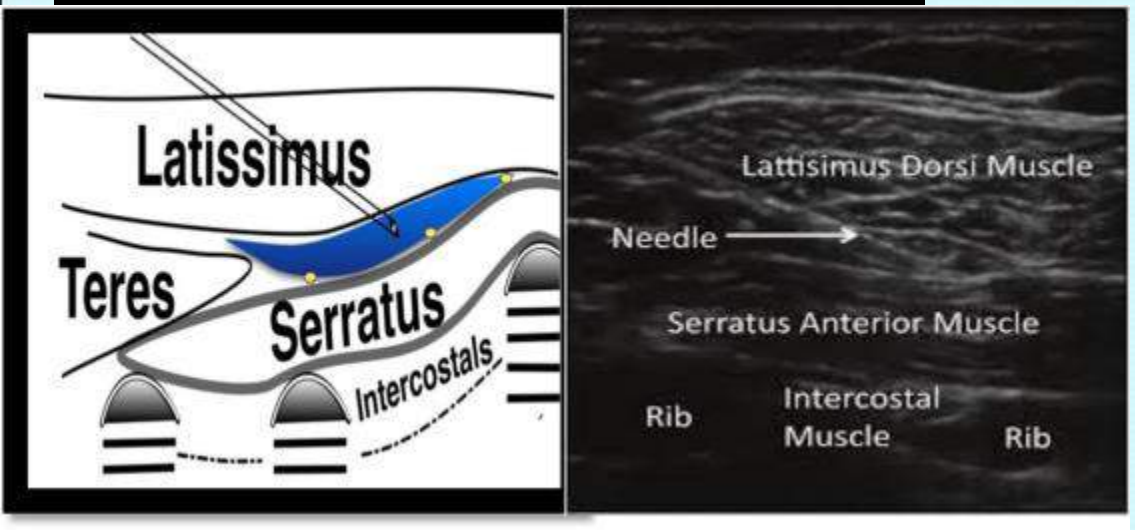


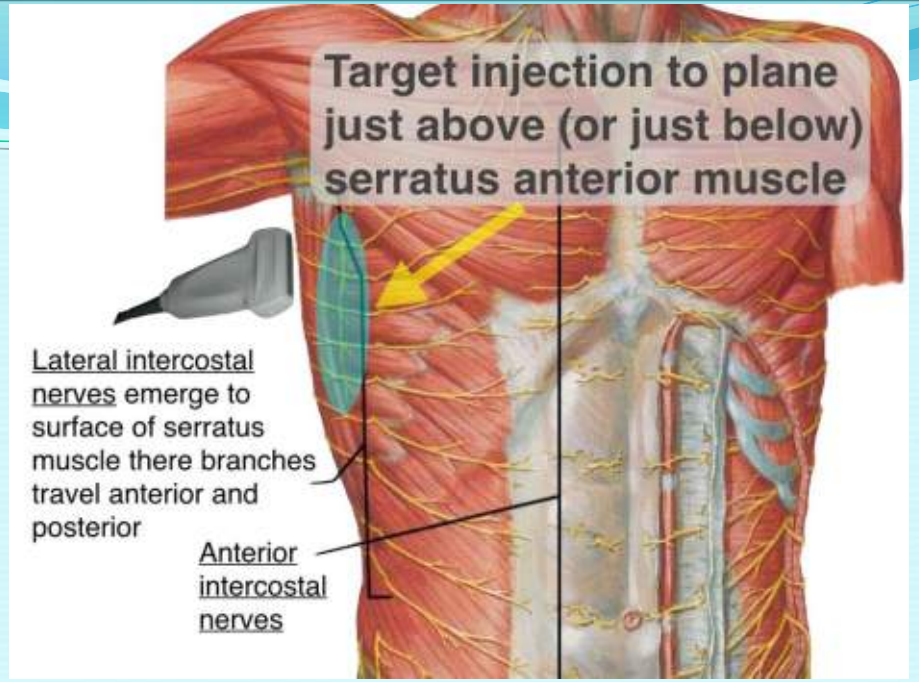


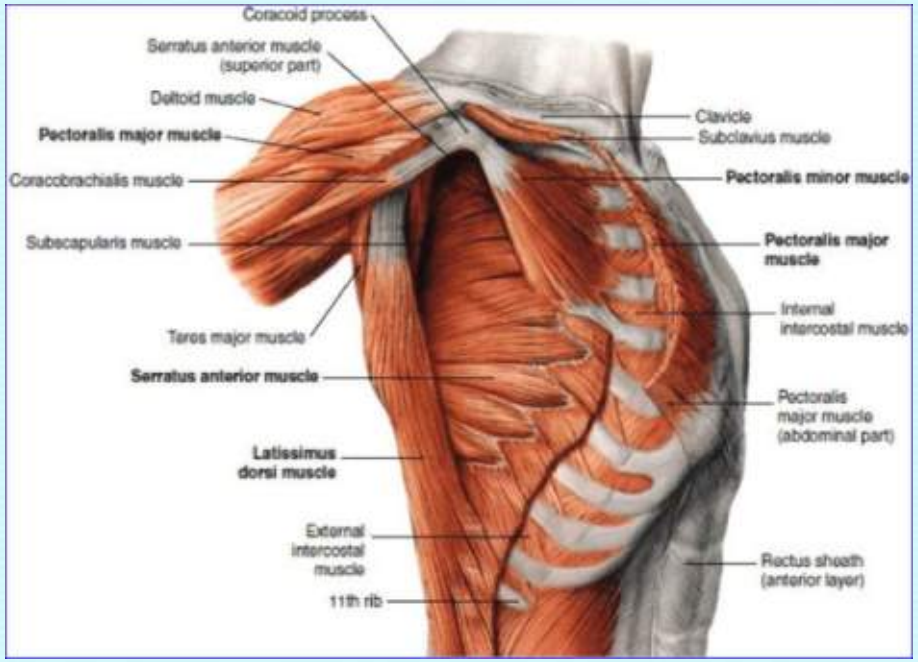


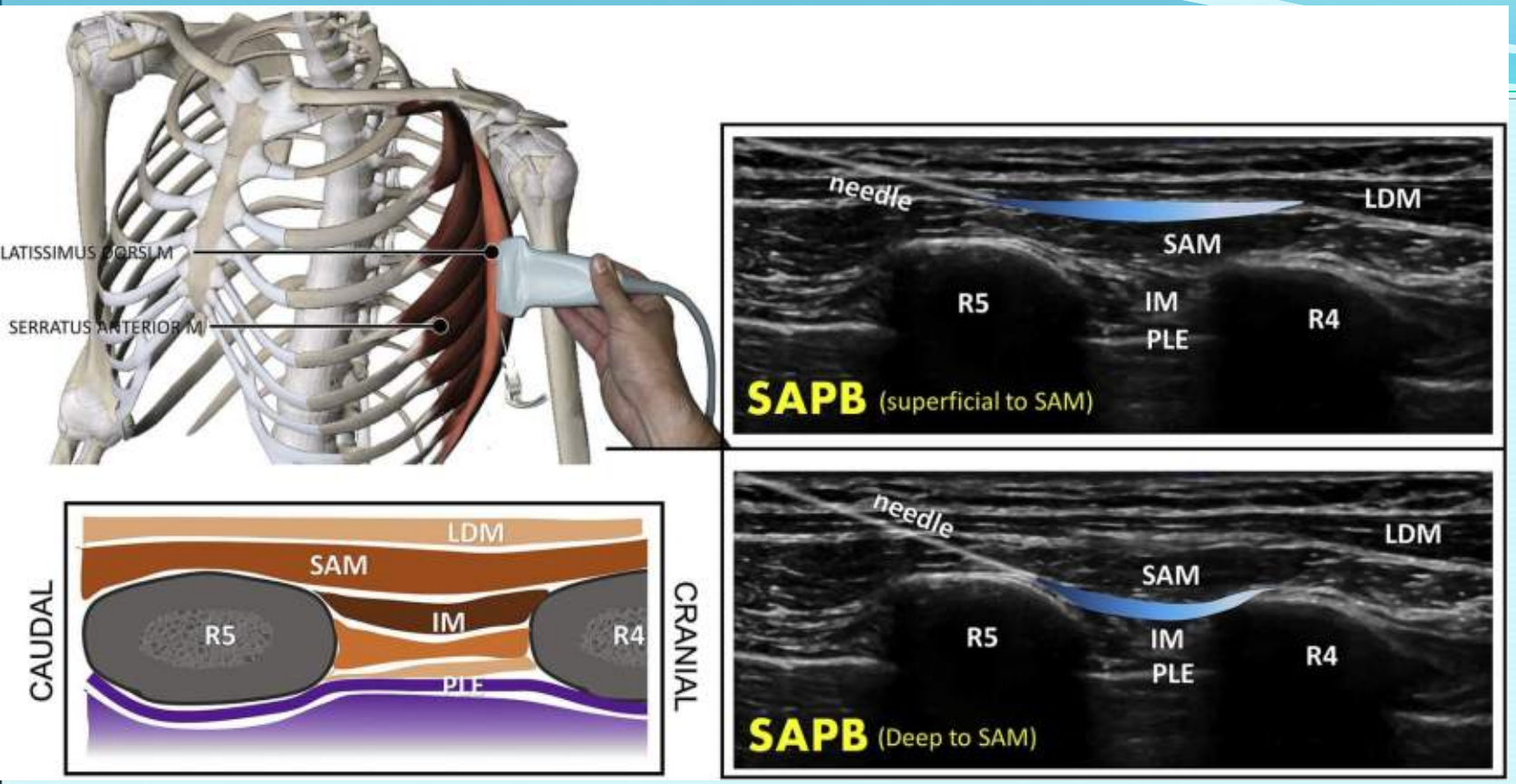
Serratus Plane Blockade

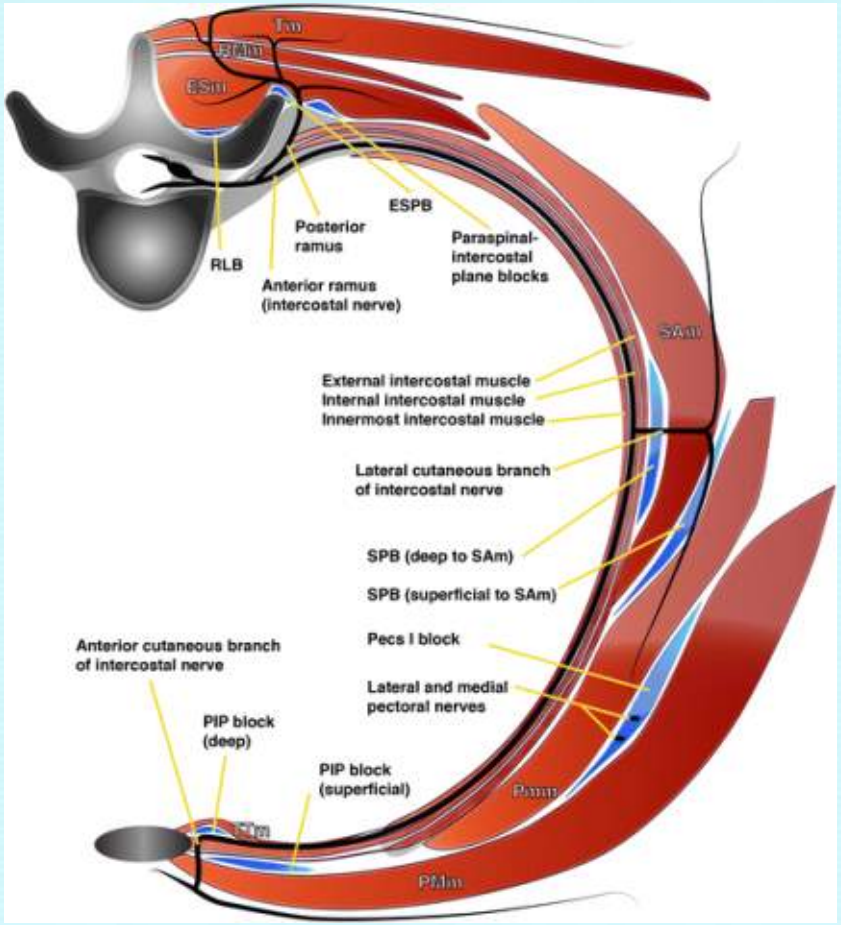




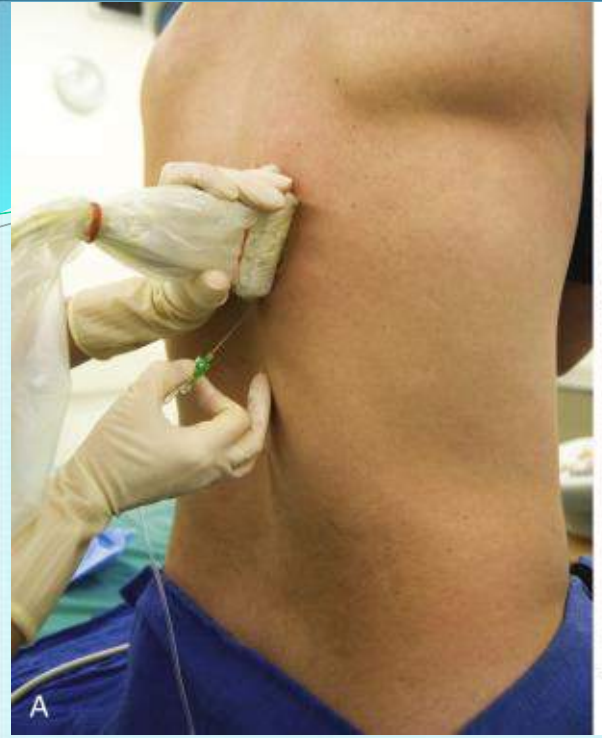


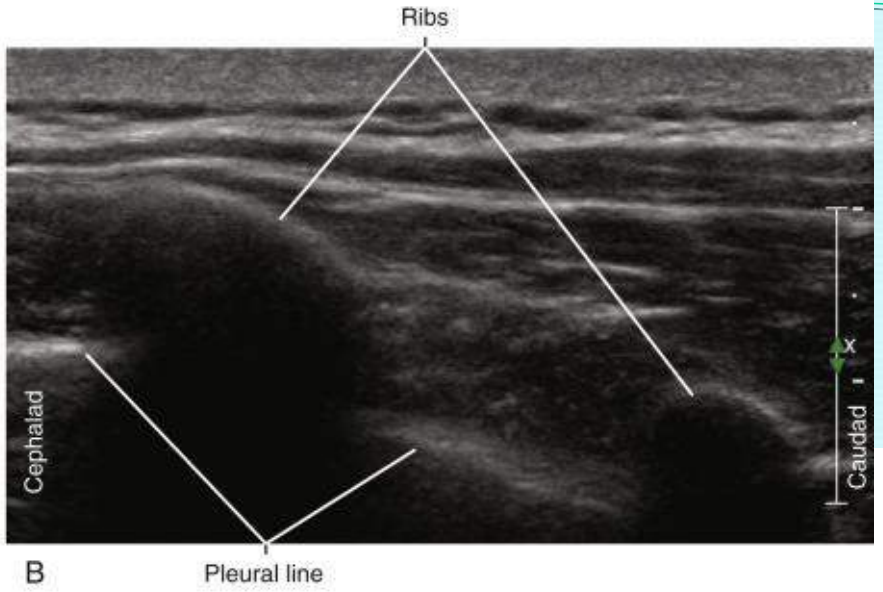


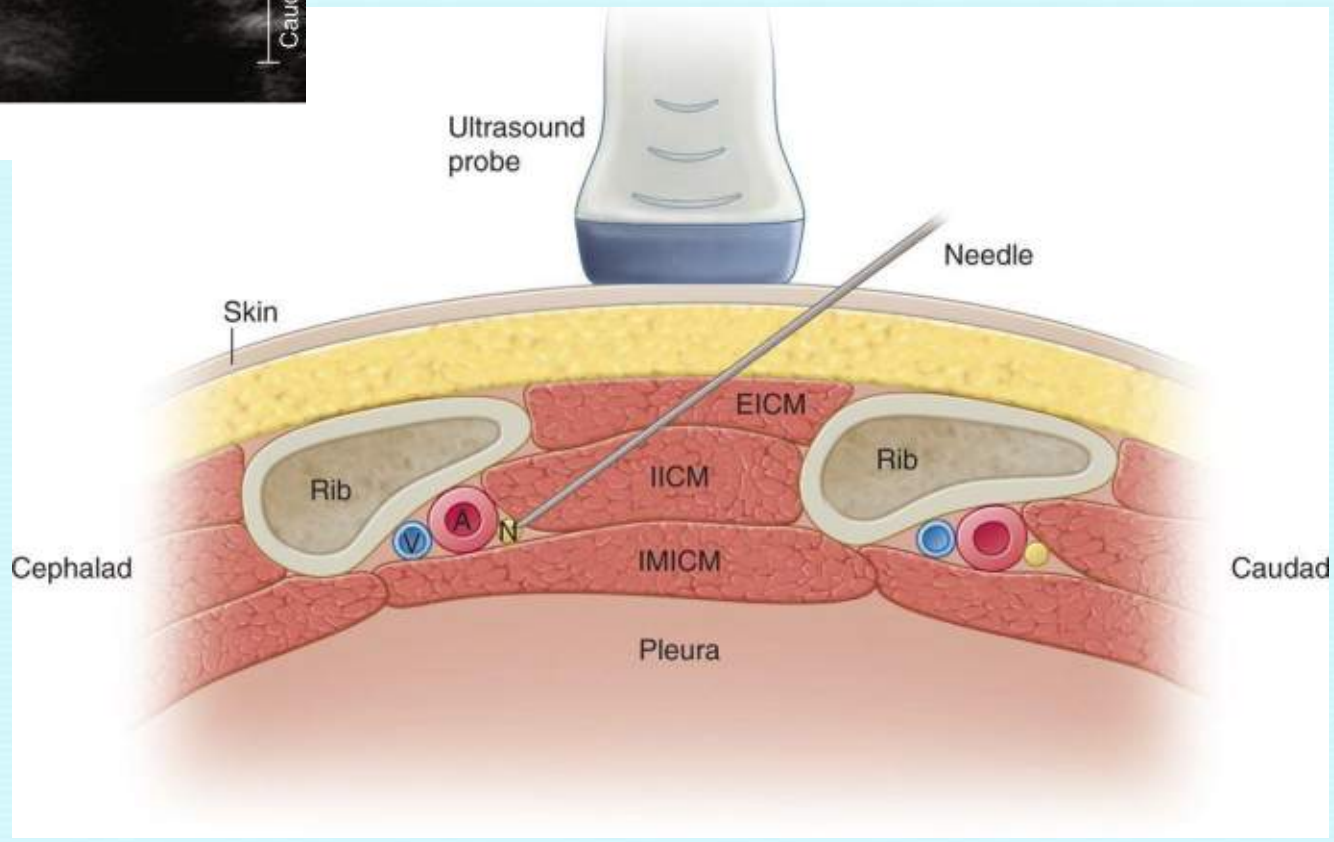

LATISSIMUS DORSI M
SERRATUS ANTERIOR M
needle
LDM
SAM
R5
IM
PLE
R4
SAPB (superficial to SAM)
needle
LDM
SAM
R5
IM
PLE
R4
SAPB (Deep to SAM)
CAUDAL
CRANIAL
LDM
SAM
IM
R5
R4
PLE


ESPB
Posterior ramus
Paraspinal-intercostal plane blocks
RLB
Anterior ramus (intercostal nerve)
External intercostal muscle
Internal intercostal muscle
Innermost intercostal muscle
Lateral cutaneous branch of intercostal nerve
SPB (deep to SAm)
SPB (superficial to SAm)
Pecs I block
Anterior cutaneous branch of intercostal nerve
Lateral and medial pectoral nerves
PIP block (deep)
PIP block (superficial)

Intercostal nerve blockade







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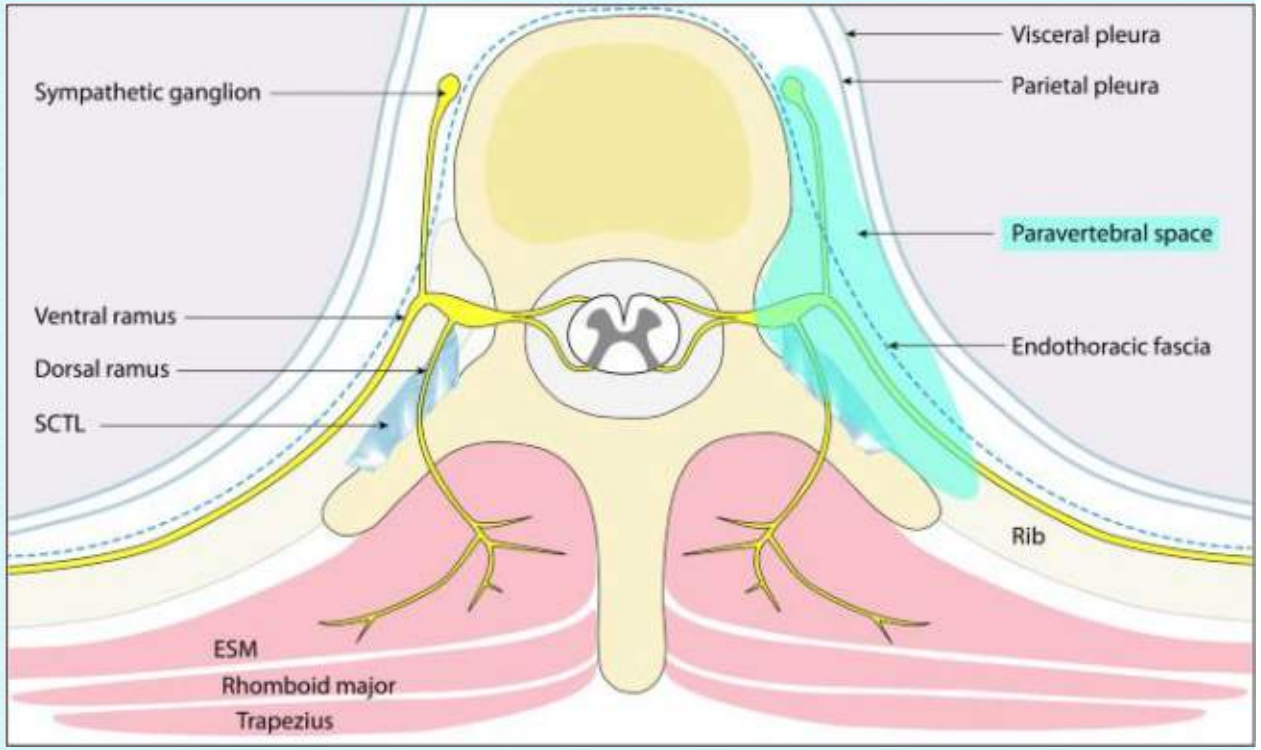
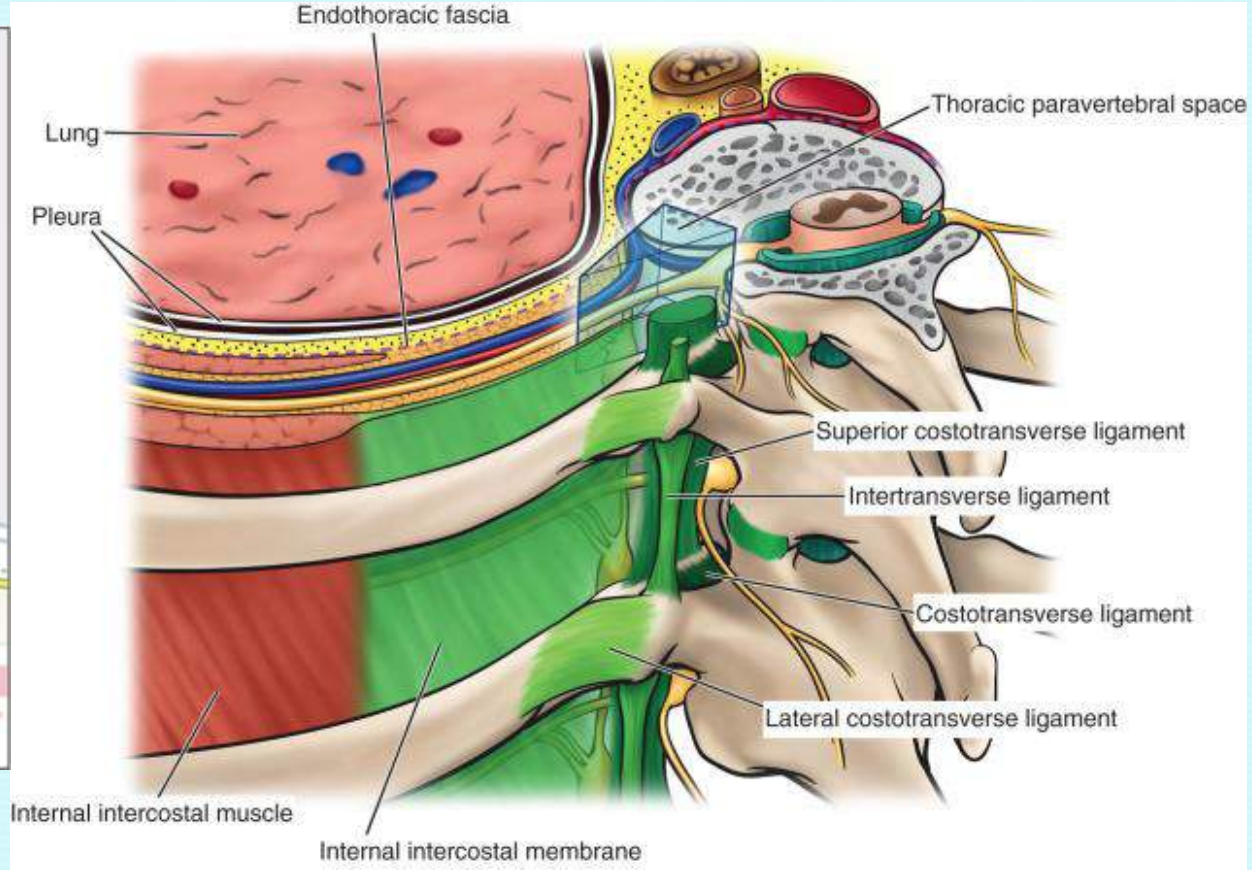
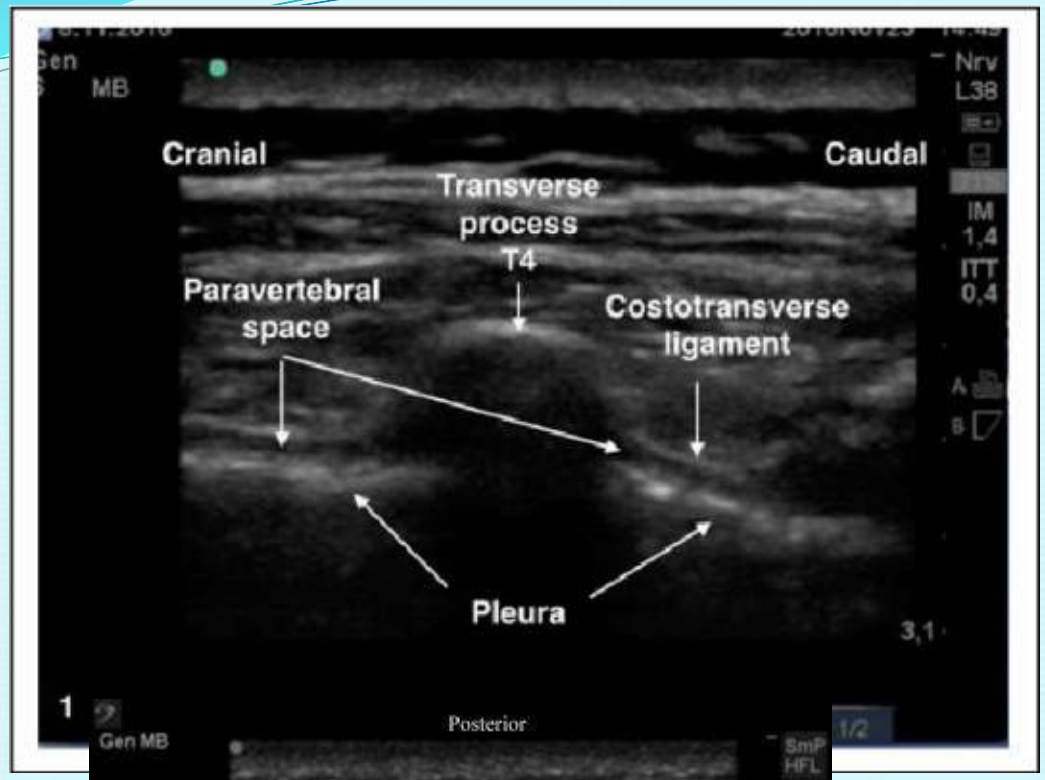
- Thoracic paravertebral nerve block technique reduces post-operative pain and lessens the chances of developing chronic mastectomy pain syndrome. It helps in pain relief and improves the quality of life of breast cancer patients after surgery when combined with glucocorticoids

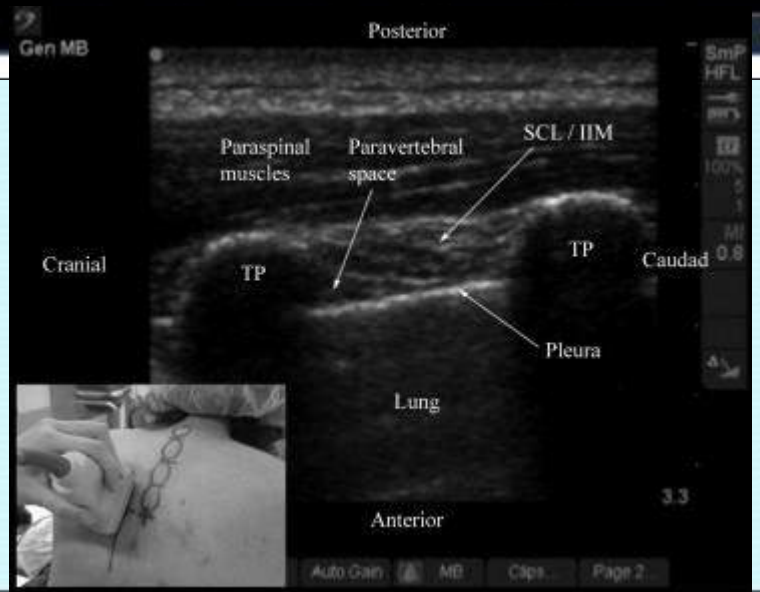


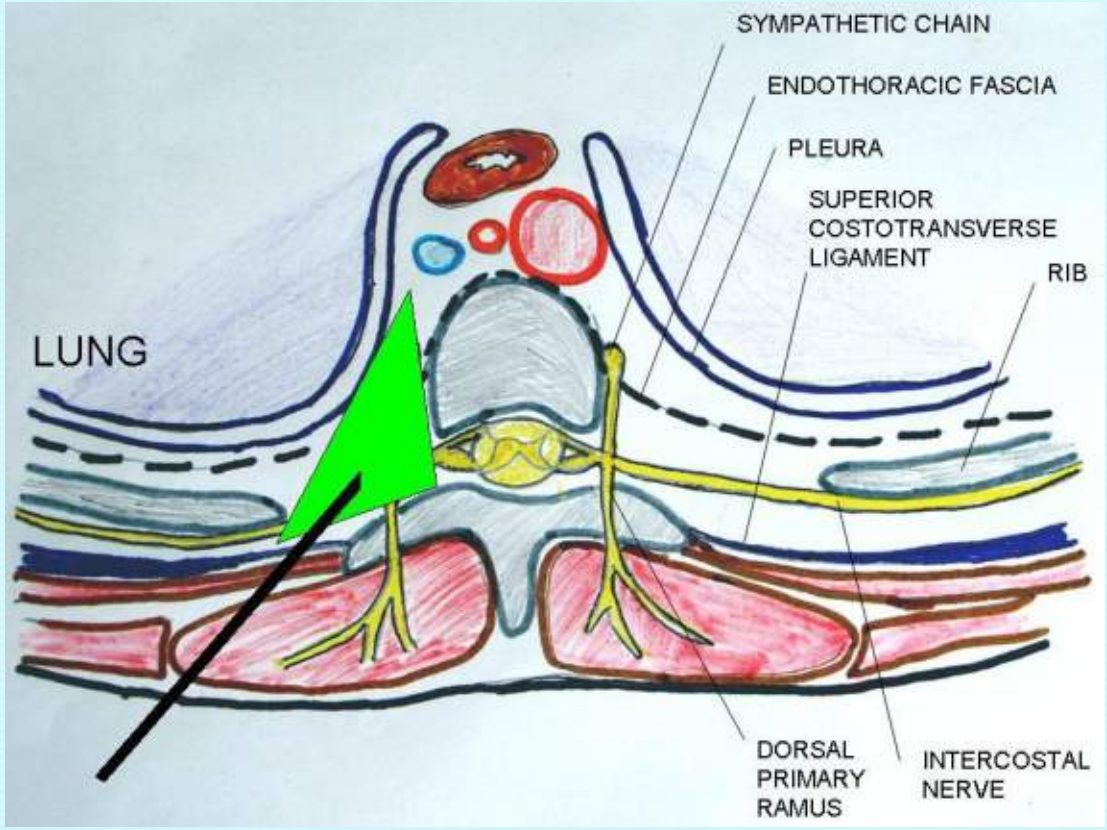


درست است که در بلوک پاراورتبرال اعصاب همان سطح تحت مورد هدف هستند ولی دارو به سطوح بالاتر و پایین تر انتشار می یابد پس پاسخ یک از مفهوم پاسخ سه متفاوت است.

هم سیمپاتتیک و هم سوماتیک بلاک می شود.

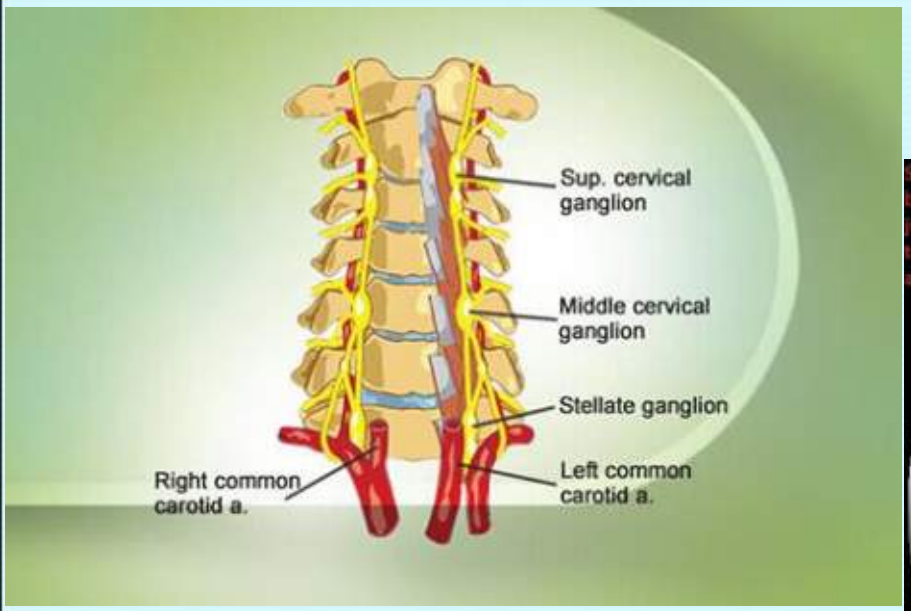


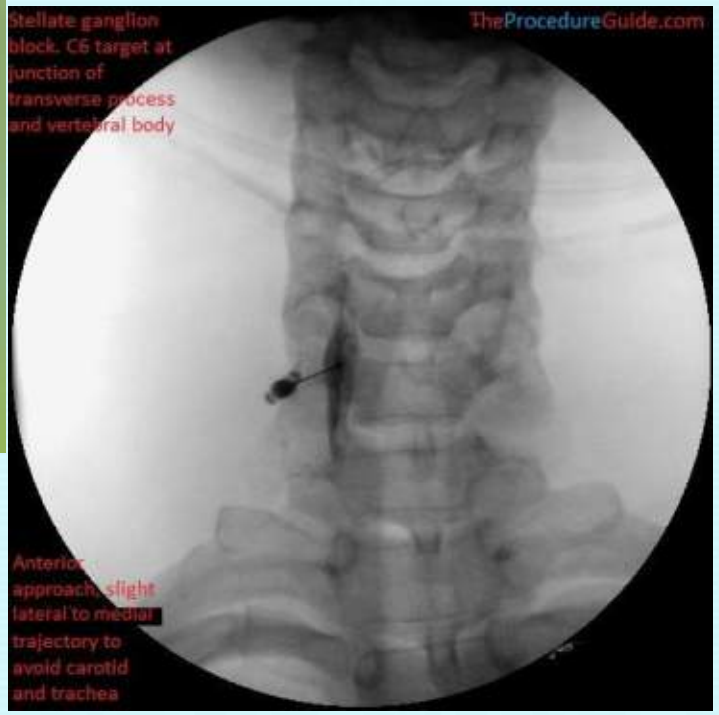


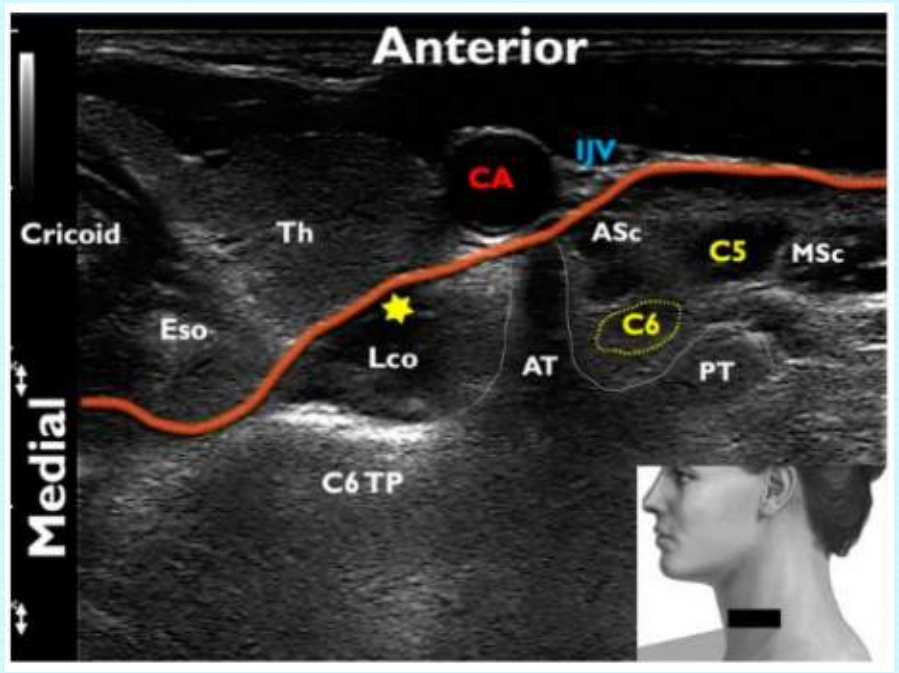


فرید ابوالحسن قره داغی، فلوشیپ درد

- *Post-mastectomy pain syndrome (PMPS)*: PMPS can be prevented by multimodal approaches using local anaesthetics with gabapentin and pregabalin and with antidepressants like amitriptyline, venlafaxine. Stellate ganglion block has been found to be useful in some patients to treat PMPS.



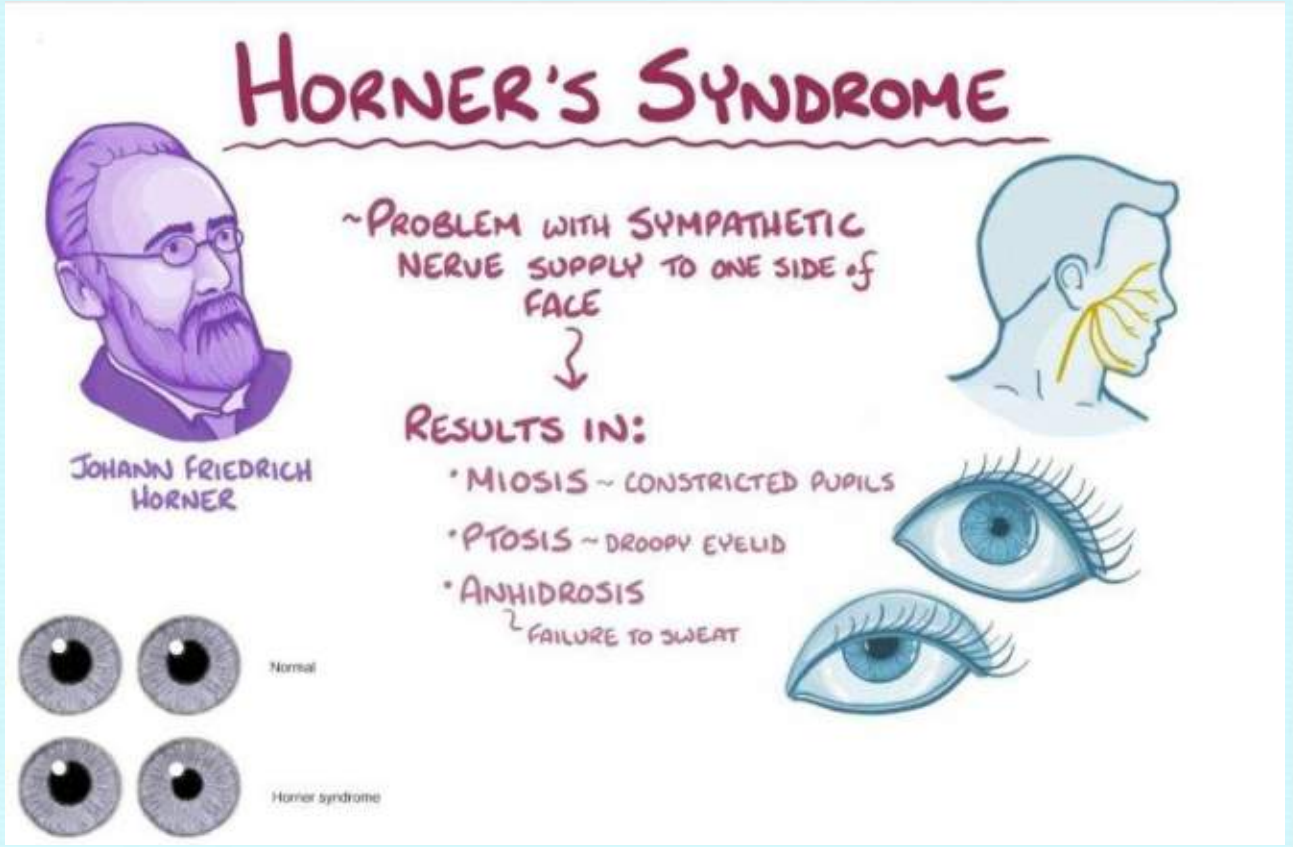




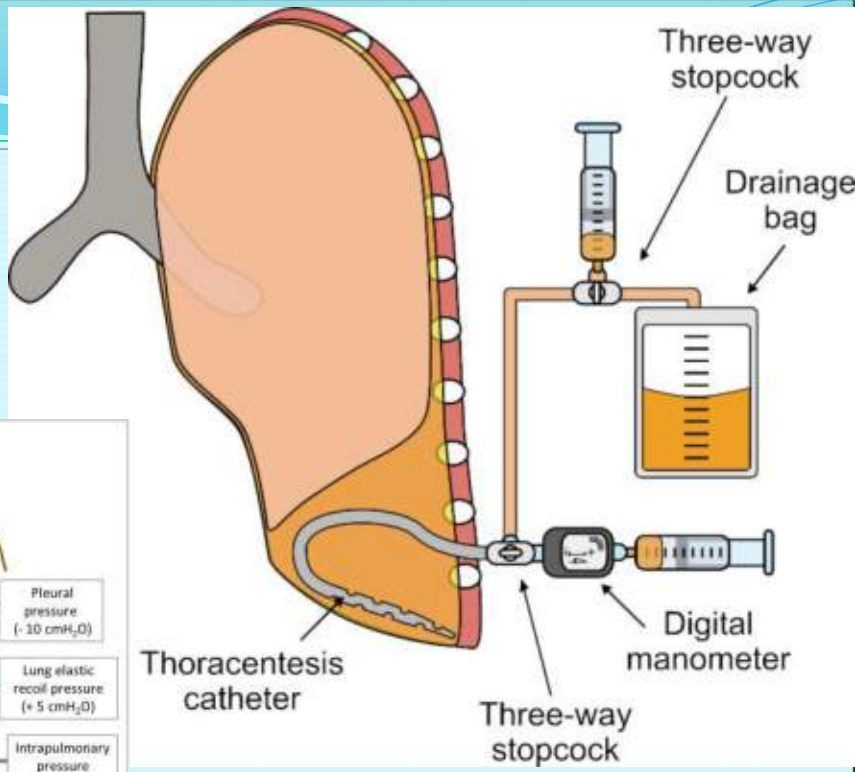
- Involvement of brachial plexus by tumour results in pain and Horner's syndrome, whereas sensory symptoms like paresthesia, numbness, dysesthesia and swelling and weakness of arm occur in radiation induced injury to brachial plexus.
- **Horner's syndrome**(oculosympathetic paresis), sympathetic trunk is damaged.
- (ipsilateral) miosis (a constricted pupil)
- Partial ptosis (a weak, droopy eyelid)
- Apparent anhydrosis (decreased sweating)
- With apparent enophthalmos (inset eyeball).
- The nerves of the sympathetic trunk arise

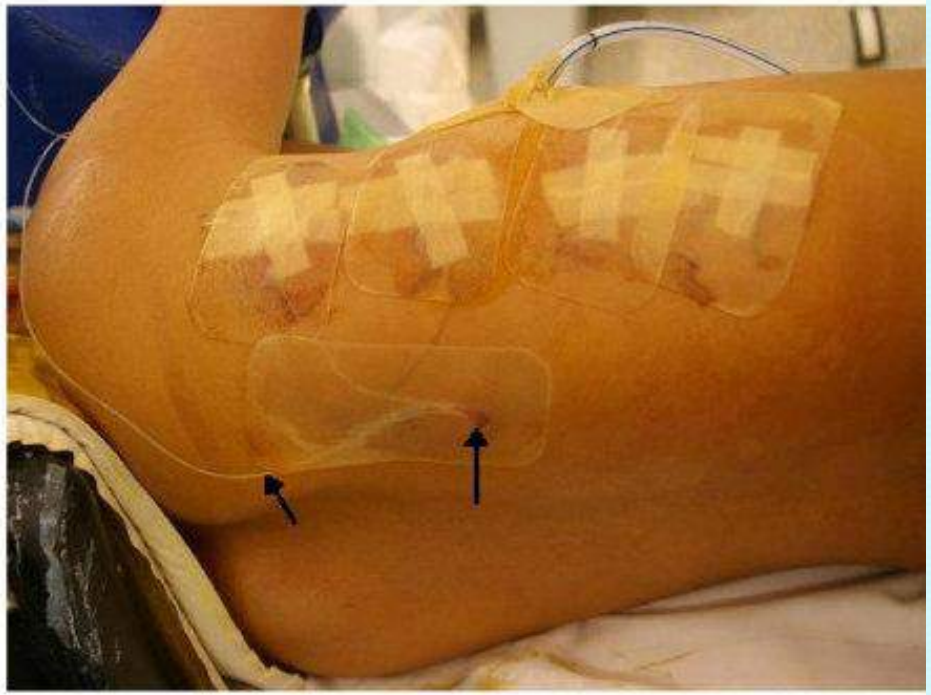
from the spinal cord in the chest,

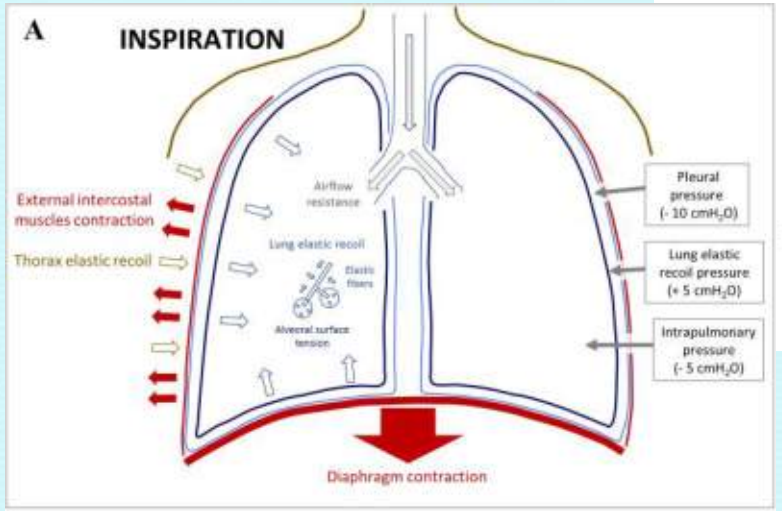
and from there ascend to the neck and face.

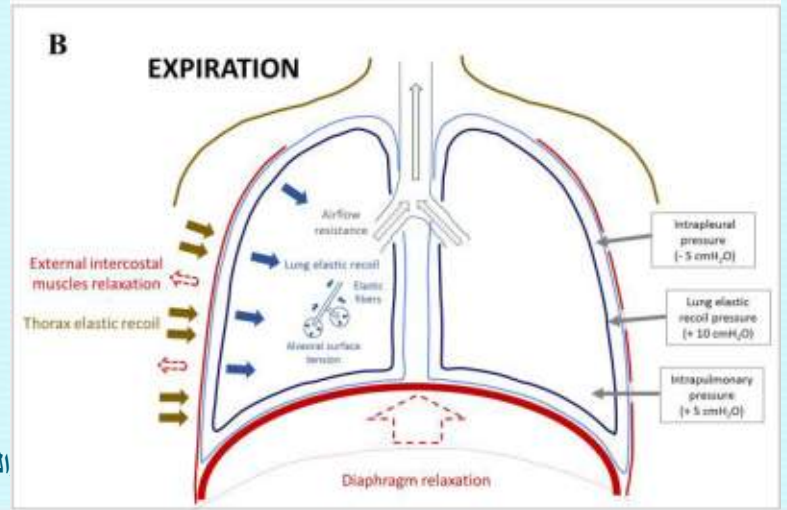


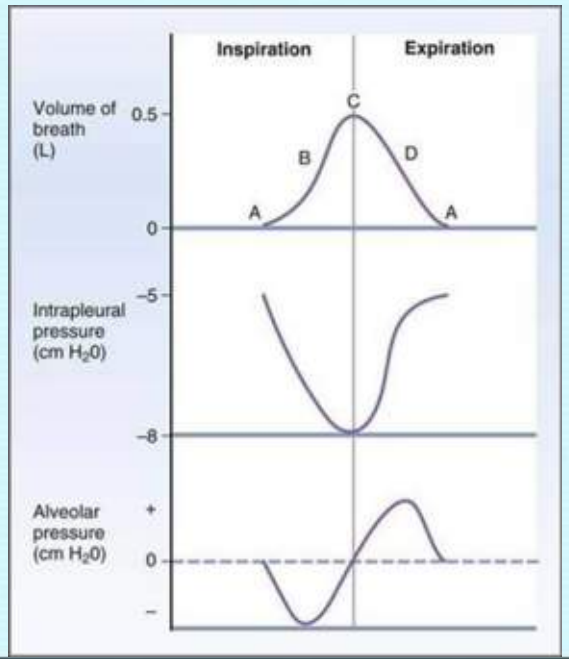
Intrpleural catheter



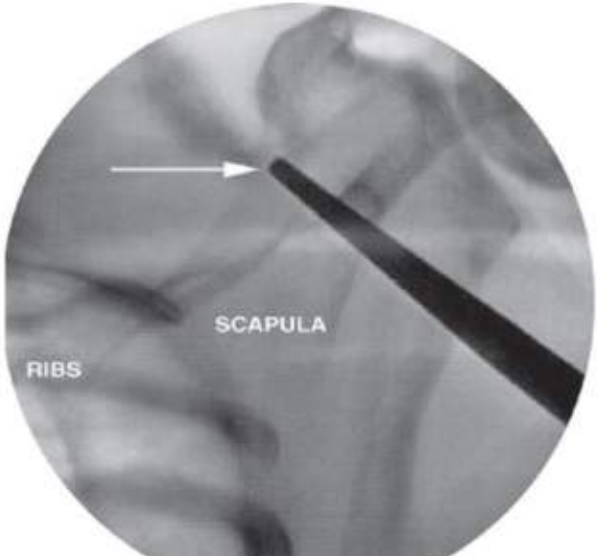


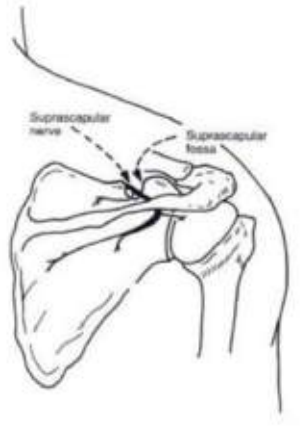






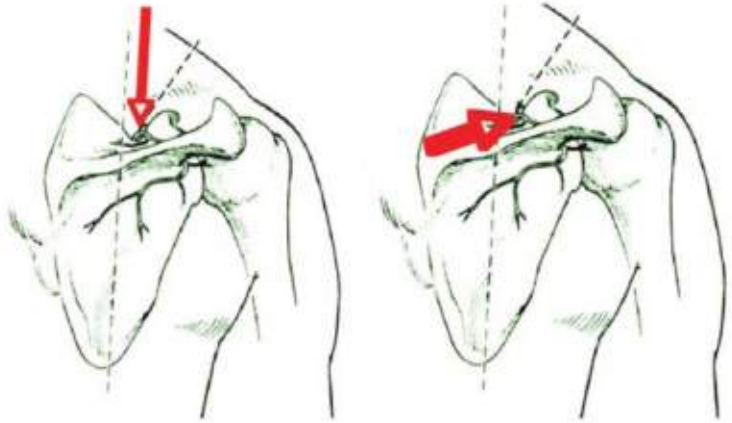
Suprascapular nerve blockade and RF



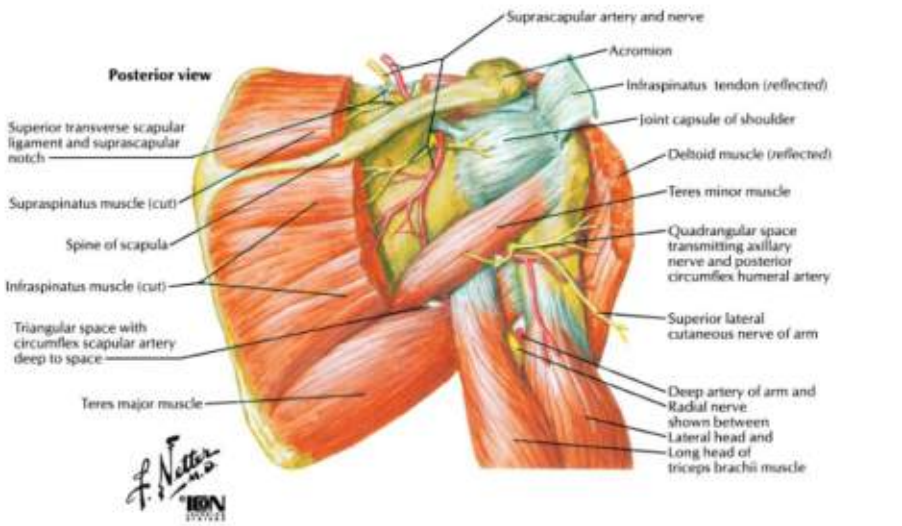


A. Path of suprascapular nerve in relation to scapula and humerus.

B. Positioning of patient and C-arm for suprascapular nerve block.



C. Identification of suprascapular nerve.



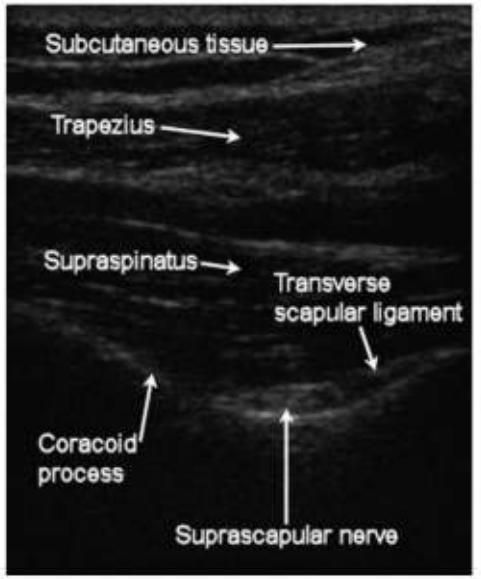
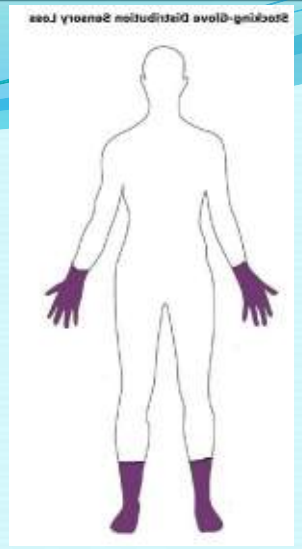


Fig 2. *Transverse view of suprascapular fossa and scapular notch with a SonoSite ultrasound system and a 6-13 MHz linear transducer.*

فرید ابوالحسن قره داغی، فلوشیپ درد

Managing pain from chemotherapy for breast cancer



- Nerve damage in the hands and feet in certain people. It usually affects fingers and toes(stocking-glove distribution pattern)
- This type of pain, called neuropathy
- We may initially recommend that that the patient use weaker analgesics.
- Other options for nerve and muscle pain include medications normally used for other conditions, including antidepressants, anticonvulsants, anti-anxiety drugs, and steroids. Some women have had success with acupuncture.
- Most of this pain improves after completion of chemotherapy, with time, but some numbness unfortunately can be chronic.

According to WHO, pharmacotherapy constitutes the main treatment for cancer pain

- The analgesics are used as per five principles:
- by mouth', 'by the clock', 'by the ladder', 'for the individual' and 'attention to detail'.

Agents That Have Been Used for Prevention of chemotherapy Induced Peripheral Neuropathy

Amifostine	Glutathione
Org2766	Pyridoxine
Leukemia inhibitor factor	Calcium-managesium solution
Lithium	IGF-1
Alpha-lipoic acid	Nimodipine
Folinic acid	Glutamate

Drug	Brand	Class
Sertraline	Zoloft	SSRI
Escitalopram	Lexapro	SSRI
Fluoxetine	Prozac	SSRI
Bupropion	Wellbutrin	NDRI
Paroxetine	Paxil	SSRI
Venlafaxine	Effexor	SNRI
Citalopram	Celexa	SSRI
Trazodone	Desyrel	SRI
Amitriptyline	Elavil	TCA
Duloxetine	Cymbalta	SNRI
Mirtazapine	Remeron	TeCA
Nortriptyline	Pamelor	TCA
Imipramine	Tofranil	TCA

TABLE 1. The authors' comparison of antidepressants for the treatment of neuropathic pain

ANTIDEPRESSANTS	EFFICACY	EVIDENCE -BASED SUPPORT	DOSE	SIDE EFFECT LOADING
Tertiary amine tricyclic antidepressants (amitriptyline, doxepin, imipramine)	Yes	+++	Low to Standard	+++
Venlafaxine	Yes	++	Standard	+
Duloxetine	Yes	++	Standard	+
Bupropion	Yes	+	Standard	+
Secondary amine tricyclic antidepressants (desipramine, nortriptyline)	Yes	++	Low to Standard	+++
Paroxetine, citalopram	Modest	+	Standard	+
Fluoxetine	No	--	Standard	+

+++ = High; ++ = Moderate; + = Low

Note: This summary reflects the authors' interpretation of the available data.

Drug	Dosage	Comments
Acetaminophen	10-15mg/kg PO , every4-6h Dose limit of 65 mg/kg/day or 4 g/day, whichever is less	Lacks gastrointestinal and hematologic side effects;lacks anti-inflammatory effects(may mask infection-associated fever)
Ibuprofen	5-10 mg/kgPO,every 6-8 h Dose limit of 40 mg/kg/day;max dose of 2400mg/day	Anti-inflammatory activity.Use with caution in patients with hepatic or renal impairment , compromised cardiac function or hypertension (may cause fluid retention , edema), history of GI bleeding or ulcers, may inhibit platelet aggregation
Naproxen	10-20mg/kg/dayPO,divided every 12 h Dose limite of 1 g/day	Anti-inflammatory activity. Use with caution and monitor closely in patients with impaired renal function. Avoid in patients with severe renal impairment
Diclofenac	1mg/kg PO, every 8-12h Dose limit of 50 mg/dose	Anti-inflammatory activity. Similar GI renal and hepatic precautions as noted above for ibuprofen and naproxen

Note : increasing the dose of nonopioids beyond the recommended therapeutic level produces a ceiling effect (i.e.,there is no additional analgesia but there are major increases in toxicity and side effects). PO,per os ; GL,gastrointestinal. From McGrath PA,BrownSC:Paediatric palliative medicine : pain control . In Doyle D,Hanks GWC,Chemy NI, Calman K(eds) : Oxford Textbook of palliative Medicine, 3rd ed . Oxford , Oxford University press,2004, p 781, with permission.

drug	equianalgesic	Starting dosage IV	IV:POratio	Starting dosage PO/Transdermal	Duration of action
Morphine	10 mg	Bolus dose = 0.05mg/kg 0.1mg/kg every2-4 h Continuous infusion=0.01-0.04mg/kg/h	1:3	0.15-0.3mg/kg/dose every 4 h	3-4h
Hydromorphone	1.5 mg	0.015-0.02mg/kg every 4 h	1:5	0.06mg/kg every 3-4 h	2-4h
Codeine	120 mg 5-10 mg	Not recommended		1mg/kg every 4 h (dose limit 1.5 mg/kg/dose)	3-4h
Oxycodone	75 mg	Not recommended		0.1-0.2 mg/kg every 3-4h	3-4h
Morphine [a]	gµ100	0.5-1 mg/kg every 3-4h	1:4	1-2mg/kg every 3-4h (dose limit 150mg)	1-3h
Fentanyl [b]		g/kg/h as continuous infusion µ1-2		g patchµ25	72h(patch)
Controlled-release morphine[cd]				0.6 mg/kg every 8 h or 0.9 mg/kg every 12h	
Controlled-release hydromorphone[d]				0.18 mg /kg every 12 h	
Controlled-release codeine[d]				3 mg/kg every 12h	
Controlled-release oxycodone[d]				0.3-0.6mg/kg every 12 h	
Methadone	10mg	0.1 mg/kg every 4-8 h	1:2	0.2mg/kg every 4-8 h	12-50h

Drug category	Drug , Dosage	indications	comments
antidepressants	Amitriptyline Initial dose 0.2-0.5mg/kgPO Titrate upward by 0.25mg/kg every 2-3 days Maintenance:0.2-3mg/kg Alternatives:nortriptyline,doxepin,imipramine	Neuropathic pain (i.e.,vincristine-induced, radiation plexopathy, tumor invasion, CRPS-1),insomnia	Usually improved sleep and pain relief within 3-5 days. Anticholinergic side effects are dose-limiting. Use with caution for children with increased risk for cardiac dysfunction
Anticonvulsants	Gabapentin Initial dose 5 mg/kg/day PO Titrate upward over 3-7 days dividedTID Maintenance:15-50mg/kg/day PO Cabamazepine Initial dose 10mg/kg/day PO divided OD or BID Maintenance :up to 20-30 mg/kg/day PO divided every 8 h . Increase dose gradually over 2-4 weeks Alternatives : clonazepam	Neuropathic pain , especially shooting , stabbing pain .	Monitor for hematologic, hepatic , and reactions. Side effects include gastrointestinal upset, ataxia, dizziness, disorientation , and somnolence
Sedative, hypnotics, anxiolystics	Diazpam,0.025-0.2 mg/kg/day PO every 6 h Lorazpam,0.05mg/kg/dose SL Midazolam,0.5mg/kg/dose PO administered 15-30minprior to procedure;0.05mg/kg/dose IV for sedation	Acute anxiety , muscle spasm; premedication for painful procedures	Sedative effect may limit opioid use . Other side effects include depression and dependence with prolonged use
Antihistamines	Hydroxyzine,0.5mg/kg PO every 6 h Diphenhydramine,0.5-1 mg/kg PO /IV every 6 h	Opioid-induced pruritus,anxiety , nausea	Sedative side effects may be helpful
Psychostimulants	Dextroamphetamine , Methylphenidate,0.1-0.2mg/kg BID Escalate to 0.3-0.5mg/kg as needed	Opioid-induced somnolence potentiation of opioid analgesia	Side effects include agitation, sleep disturbance , and anorexia. Administer second dose in the afternoon to avoid sleep disturbances
corticosteroids	Prednisone, prednisolone, and dexamethasone dosage depends on clinical situation Dexamethasone initial dose : 0.5mg/kg IV.Dose limit 10mg. Subsequent dose 0.3 mg/kg/day IV divided every 6 h	Headache from increased intracranial pressure, spinal, or nerve compression; widespread metastases	Side effects include edema, dyspeptic symptoms , and occasional gastrointestinal bleeding

CRPS-1, Complex regional pain syndrome type 1; PO,per os;IV , intravenous;SL,sublingual.
From McGrath PA,Brown SC : Paediatric palliative medicine : pain control. In Doyle D,Hanks GWC,ChemyNI,Calman K (eds):Oxford Textbook of Palliative medicine, 3rd ed. Oxford, Oxford University Press,2004, p 782, with permission.

- haloperidol, chlorpromazine,

Starting and Maintenance Dosing Regimens for Anticonvulsants

Phenytoin	**Loading 20 mg/kg .Maintain at 5-8 mg/kg, often 300 mg daily . BID or daily regimen orally . IV formulation infusion max 50 mg/kg.**
Fosphenytoin	**Loading 20 mg /kg. Up to 150 mg /min IV. Full loading by intramuscular route possible. Large volume IM tolerated well.**
Carbamazepine	**200 mg daily. Maintain 600-1200 mg daily, lower in elderly. TID regimen. Slow release forms (Tegretol XR, Carbatrol) given BID.**
Oxcarbazepine	**300mg BID. Maintain 1200 mg/day.Max 2400 mg/daily. BID regimen.**
Gabapentin	**300 mg daily. Maintain 900-3600 mg daily**
Pregabalin	**150 mg daily. Maintain 300-600 mg daily TID or BID regimen.**
Phenobarbital	**Loading 20 mg/kg divided in two . Start orally at 60-90 mg daily. Maintain 90-120mg daily.**
Levetiracetam	**500mg BID. Maintain 1000-3000 mg**
Topiramate	**25 mg daily. Maintain 200-400 mg/kg BID regimen. For migraine 50-100 mg typically.**
Valproic acid	**250 mg daily . Depakene TID .Dpakote BID. Depacon is IV formulation at 100 mg / ml , requires dilution , slow infusion a couple of times/day.**
Zonisamide	**100 mg once daily then BID with higher doses. Increase by 100 mg/wk. Maximum 400 mg daily .**
Lamotrigine	**50 mg daily (25 mg if taking valproic acid) increasing slowly over 4-6 wk to maintenance of 300-500 mg/day in a BID regimen.**
clonazepam	**0.5 mg TID . Maintain 2-6 mg daily .**
BID, twice daily; IM , intramuscular;IV , intravenous TID, three times a day .	

Potency of the Bisphosphonates for bone metastatic pain

Generic Name	Relative Potency	Route of Administration
Etidronic acid	1	PO, IV
Clodronic acid	10	PO, IV
Pamidronic acid	100	IV
Alendronic	1000	PO, IV
Ibandronic acid	10000	PO, IV
Zoledronic acid	100000	IV
IV ,intravenouly; PO, per os.		

Tramadol conti.inf=TE morphine

- Tramadol administered by continuous intravenous infusion may be as effective as thoracic epidural morphine

  Bloch et al . Anesth Analg 2002; 94:523–8

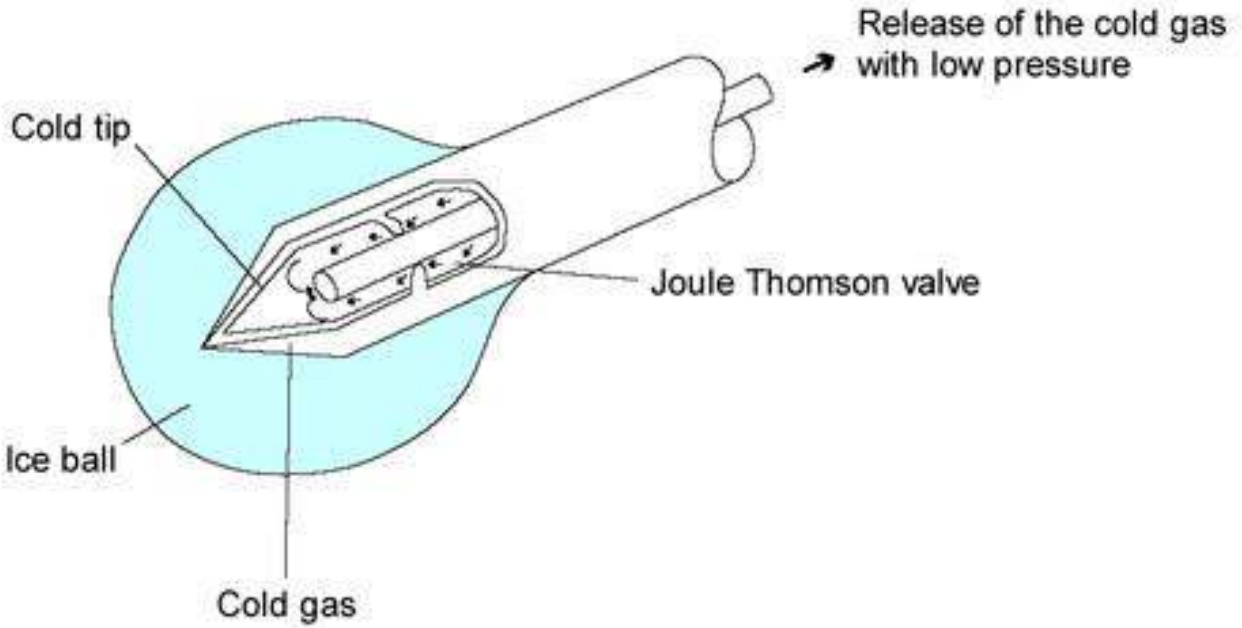
- **Satisfactory pain control was achieved after thoracotomy using either TEA or ICN+PCA. The ICN+PCA ≈ TEA.**

Cryoanalgesia

- Cryoanalgesia of intercostal nerves performed prior to wound closure produces intercostal blockade lasting several months. Despite the theoretical attractions, in one of the few controlled trials of the technique it did **not produce improved pain scores or respiratory function**. In addition, cryoanalgesia may lead to the development of intercostal neuralgia (disrupts the nerve structure and creates wallerian degeneration, but leaves the myelin sheath and endoneurium intact.).فُ لٰذ ً ضللّه

- **Cryoanalgesia be considered as a simple, inexpensive, long-term form of post-thoracotomy pain relief, which does not cause any long-term histological damage to intercostal nerves**
- **Moorjanni et al, Eur J Cardiothorac surg. 2001,20. 501-507**

Physiotherapy Cryoanalgesia & Cryomassage



The type B (golf) trolly has been designed totransport a type F gas cylinder.

براي چه بيماري ترانس درمال فنتانيل كاربرد دارد

Relatively constant pain+ infrequent breakthrough pain

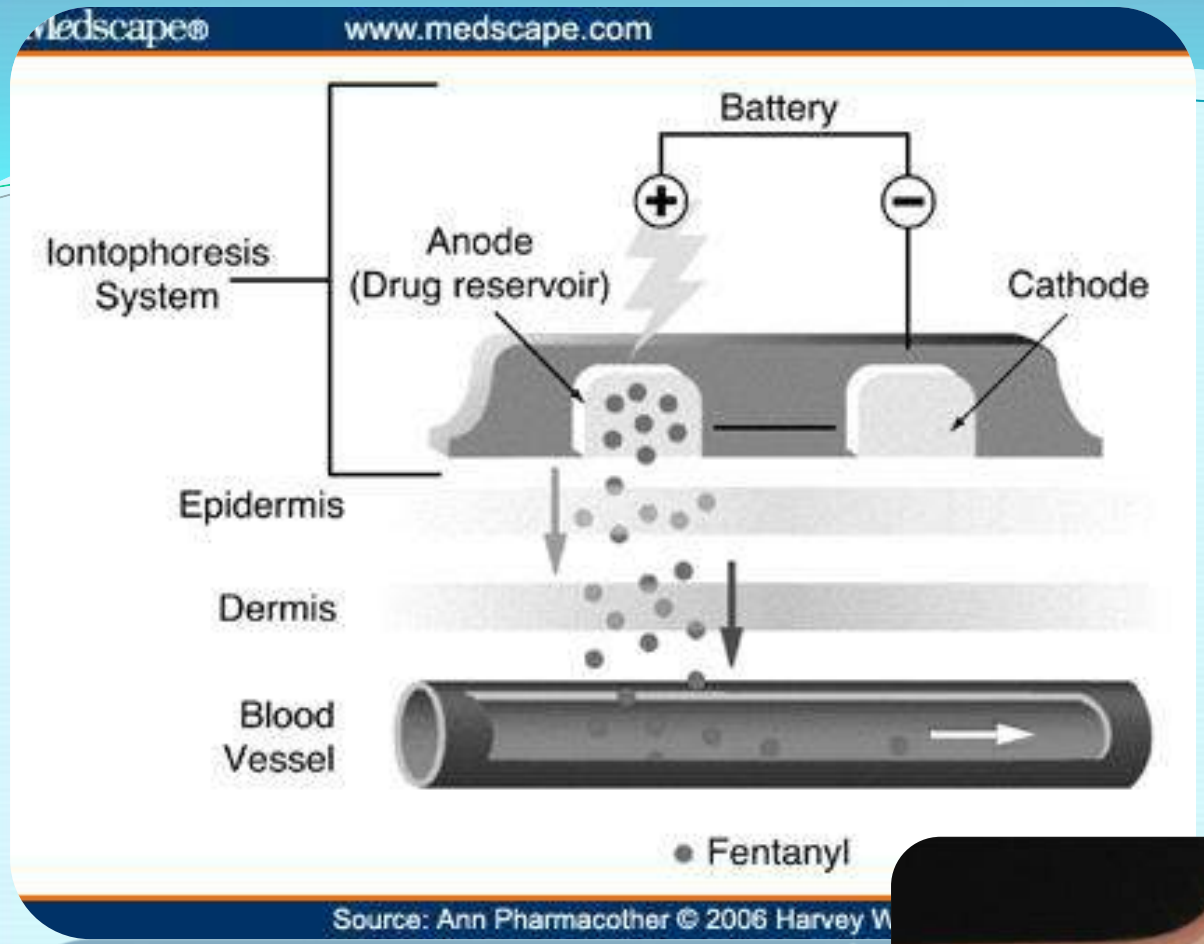
- Transdermal fentanyl (TDF) is used for managing patients with stable cancer pain who cannot take oral medications.
- Patches are available with a delivery rate of 25, 50, 75 and 100 µg/h, and need to be changed after every 72 h. The dose increase is usually 30-50 per cent, but sometimes 100 per cent (from 25 to 50 µg patch)

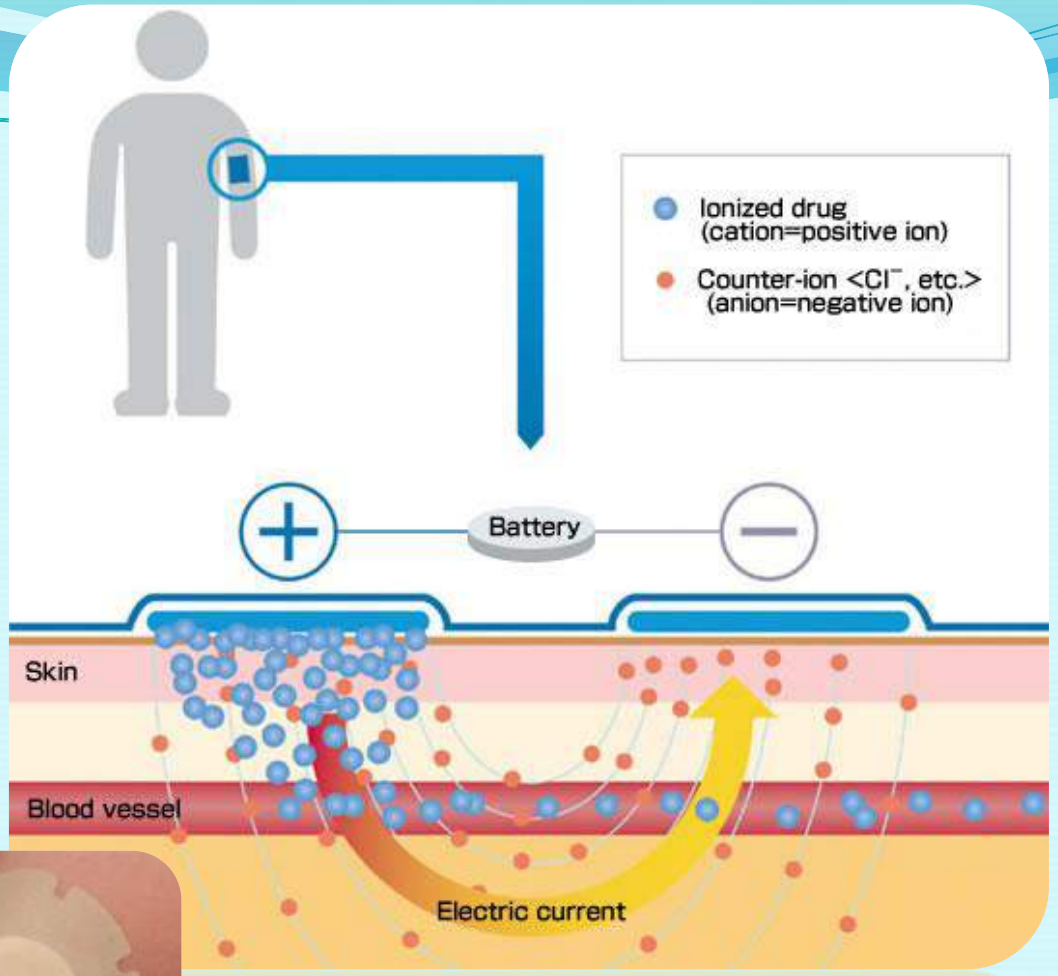
Key points

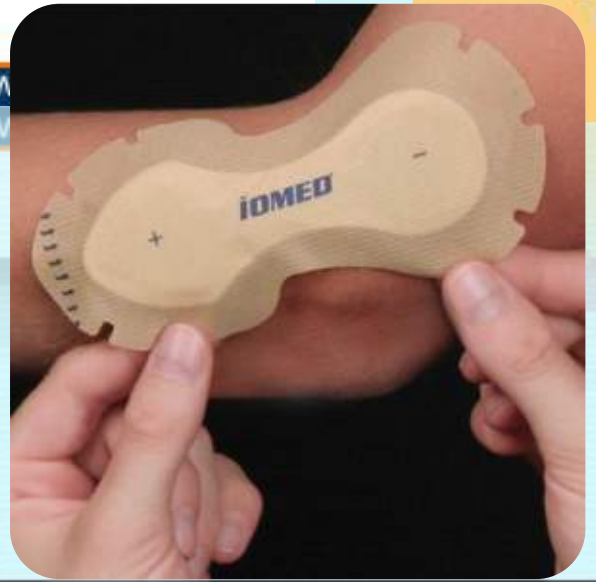
- “یاًن ًٍِی آینخ ٌقً اً ٍُهف أ ٌ
- “یاًن ۷۲ آ ًخا ٌ گ ًایق ٍ ٌّگ غ نضقگ
- غه ًٍّف ٌّی ‘ “أ ُظ ز“ ل آج چ Patch گ ًایگ
- ًقهع ف “ًأیض ل گیکقف غ ئ ًلگی غ نیئقگ ۱–۲ آ ًخا ٌ“تًحگ ً آ ٌ
- ًّلله ً ٌّ ۱۸ آ ًخا ٌ “ ٌ“ ل “ًالأ ًینذ ف رعح ٌ کققذ ز غه ی آگ
- غه غ ل خغید ۱۵–۲۱ یق ٌّ ً آ ٌ
- طیعیئگف ًّقاً ٌ ً ٌ ۵ ۴۰ آ ًٌُفط یاًگچگقگ ۱/۳ ٌّی ‘ ٍفیاًلد ًٌّذ إ غ ز گ لگ

IONTOPHORESIS

- **Iontophoresis** is a method of transdermal delivery of drugs in an **ionized** state using an electric current.
- **Morphine** has been administered using this route for postoperative analgesia.
- fentanyl by iontophoresis is being investigated more extensively than that of other opioids.
- Iontophoresis has the advantage of achieving a rapid steady state and the ability to vary delivery rate.
- application of anti-inflammatory medications.plantar fasciitis, bursitis, and some types of hyperhidrosis.







فرید ابوالحسن قره داغی، فلوشیپ درد

Clinical Pearls

PERIPHERAL OPIOIDS SUMMARY

- Tramadol 200 mg or buprenorphine 0.3 mg both enhance local anesthetic effect and prolong analgesia when used for peripheral nerve block.
- Morphine in doses up to 5 mg provides significant analgesia when injected intraarticularly but does require a pre-existing inflammatory site of action.
- Morphine 5 mg injected into the donor site during bone graft harvest may reduce acute and chronic bone graft site pain.

Studies Examining Buprenorphine as an Analgesic Adjuvant with Local Anesthetics

Author/Date	Patients/ Groups	Block Type	Dose	Local Anesthetic	Systemic Control	Results
Viel[22] 1989	20/2	Supraclavicular	3 mcg/kg	Bupivacaine 0.5% 40 mL	No	Prolonged analgesia compared to morphine group (35 vs 18.25 h). No difference in sensory block.
Bazin[23] 1997	89/4	Supraclavicular	3 mcg/kg	Bupivacaine 0.5% Lidocaine 1%	No	Prolonged analgesia compared to control group (20 vs 11.5 h)
Candido[21] 2001	40/2	Supraclavicular	0.3 mg	Mepivacaine 1% Tetracaine 0.2%	No	Prolonged analgesia compared to control group (17.4 vs 5.3 h)
Candido[20] 2002	60/3	Axillary	0.3 mg	Mepivacaine 1% Tetracaine 0.2%	Yes IM	The mean duration of postoperative analgesia was 22.3 h in axillary group vs 12.5 h in IM group, and 6.6 h in placebo group.

Clinical Pearls

- Buprenorphine (0.3 mg) enhances anesthesia and prolongs analgesia when added to local anesthetic for peripheral nerve block.

CHRONIC NON-SPINAL PAIN

There is little support for the use of opioids on peripheral nerves due to a lack of site of action.

Other pain syndrome secondary to breast cancer or related to medical/treatment conditions

- Craniofacial pain secondary to trigeminal neuralgia, posterior auricular neuralgia, glossopharyngeal neuralgia; chest wall pain with multiple conditions including post-thoracotomy neuromas, persistent pain after rib fractures, and post herpetic neuralgia in thoracic distribution; abdominal and pelvic pain secondary to ilioinguinal, iliohypogastric, genitofemoral, subgastric neuralgia; pudendal neuralgia; neuritis.

Other pain syndrome secondary to breast cancer or related to medical/treatment conditions

- low back pain and lower extremity pain secondary to lumbar facet joint pathology, pseudosciatica, pain involving intraspinous ligament or supragluteal nerve, sacroiliac joint pain, cluneal neuralgia, obturator neuritis, and various types of peripheral neuropathy; and upper extremity pain secondary to suprascapular neuritis and other conditions of peripheral neuritis.

Breakthrough Cancer Pain

Table 1. Identifying Breakthrough Pain

Characteristics of Breakthrough Pain
- Rapid onset
- Severe in intensity
- Self-limiting

Types of Breakthrough Pain
- Incident: Induced by activities/movement (coughing, walking, turning in bed)
- Spontaneous/idiopathic: Unpredictable, without identifiable cause
- End-of-dose failure: Associated with declining serum levels of around-the-clock pain medication

Ideal Treatment
- Quickly absorbed
- Rapid onset
- Low adverse events

Management of breakthrough cancer pain (BTcP)

- BTcP can be controlled by treating the underlying aetiology, optimising around the clock medications and using specific medications.
- In patients with well controlled baseline pain having BTcP episodes, increase in baseline opioid dose results in better pain relief.
- For BTcP episodes, about one-sixth (17%) of the daily dose of morphine can be used

Faster onset of action

- Effervescent morphine tablets provide faster analgesia as compared to IR oral morphine.
- Nasal morphine spray is rapidly absorbed through nasal mucosa and has plasma profile similar to slow iv administration of morphine. It provides a faster and convenient alternative than oral morphine for managing episodic pain
- Morphine eff & nasal sparay>> oral

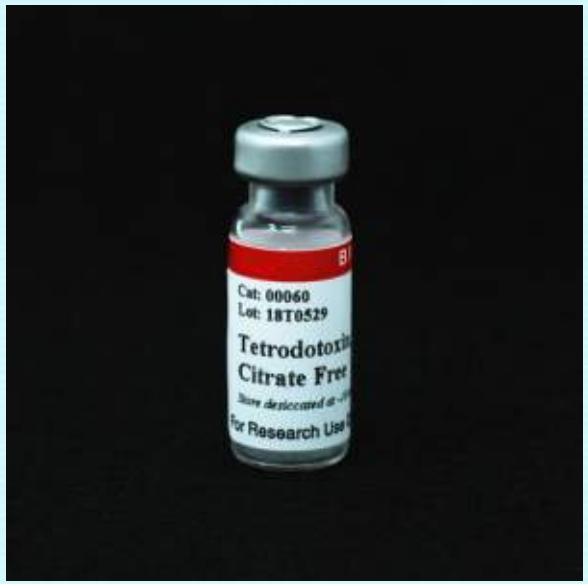
- Transmucosal administration of fentanyl provides rapid onset of action via non-invasive route.
- Oral transmucosal fentanyl citrate (OTFC) is a fentanyl-impregnated lozenge, available in six dosage strengths (200, 400, 600, 800, 1200 and 1600 µg).
- Absorption rate and bioavailability of OTFC is greater than oral absorption and serum fentanyl levels increase linearly with dose. Intranasal fentanyl spray (INFS) has faster onset of action (at 10 min), attaining peak effect at 12-15 min.
- It can be self administered, is acceptable to patients with reduced salivary flow and has greater preference than OTFC.

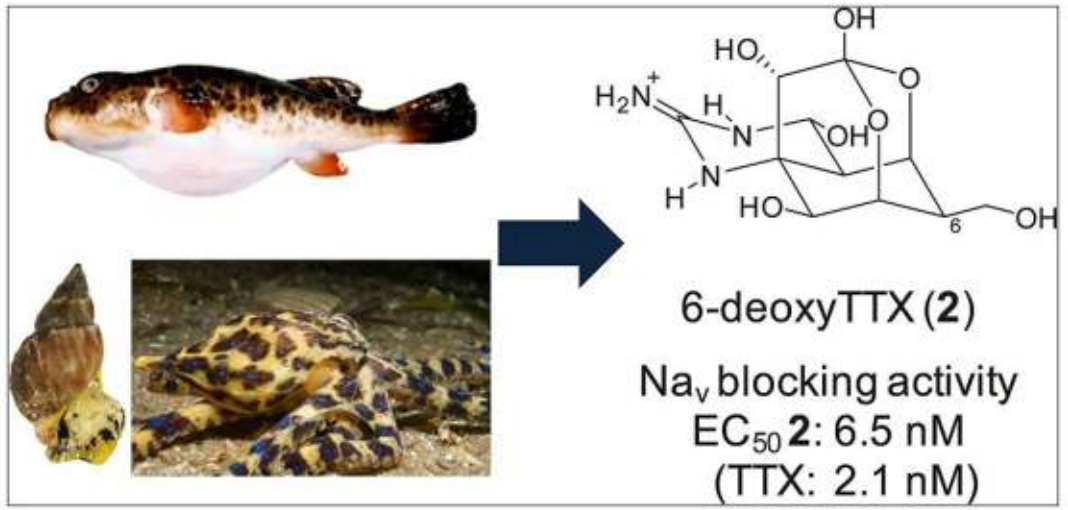
- Fentanyl buccal tablet (FBT) is an effervescent drug delivery system employed to augment the rate and extent of fentanyl absorption across the buccal mucosa. Its absolute bioavailability is greater than OTFC
- Fentanyl buccal tablet (FBT)>> OTFC

Novel therapies: Pharmacological therapies

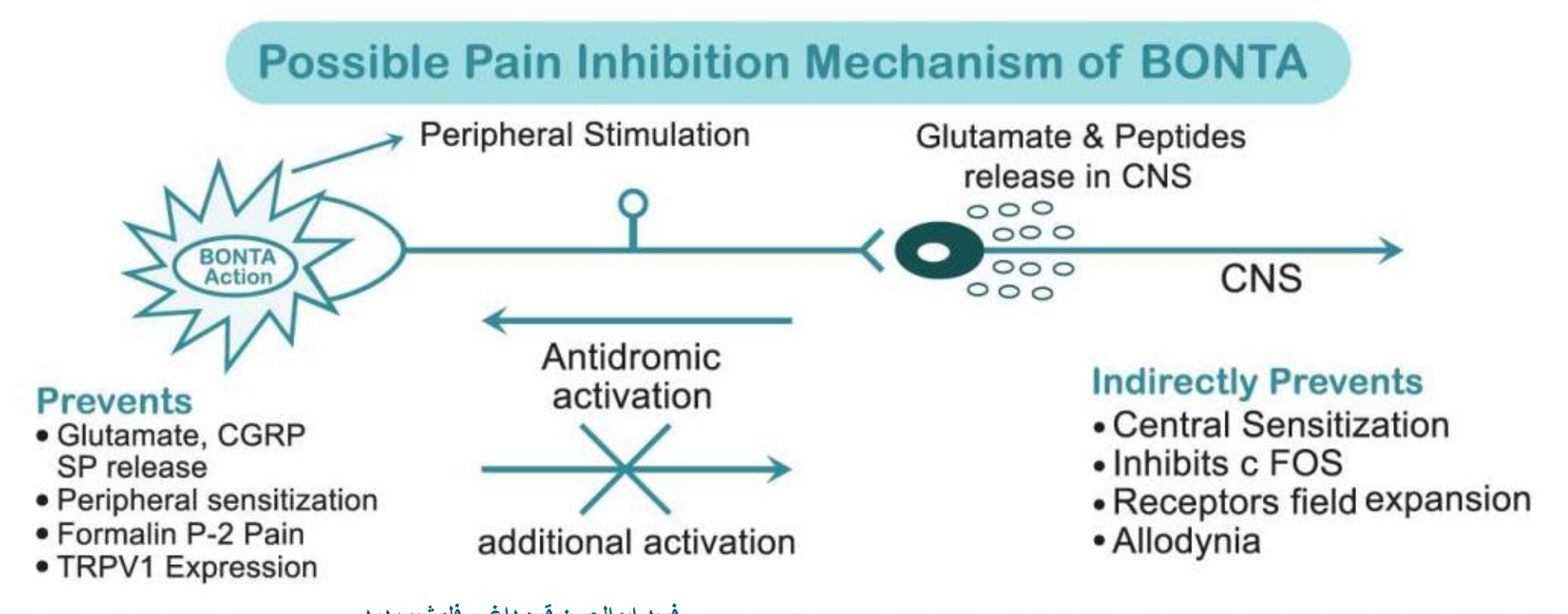
- CB2 agonist : Cannabinoid receptor 2 (CB2) agonist is a novel therapeutic target, which has proved efficacious against neuropathic pain.
- Low dose of delta-9-tetrahydrocannabinol (THC) produces mild analgesic effects on cancer patients, but higher dose results in side effects in the form of somnolence, dizziness, ataxia, and blurred vision.
- Johnson *et al*- found in a multicentric trial that tetrahydrocannabinol:cannabidiol (THC:CBD) extract is efficacious for pain relief in patients with advanced cancer pain refractory to opioids.
- A phase III clinical trial to determine effect of cannabinoid extract (Sativex) in reducing chemotherapy induced neuropathic pain is being conducted

- *(ii) Tetrodotoxin*: Upregulation of voltage gated sodium (Na^+) channels has been seen in metastatic cancers including breast cancer. Their expression is inhibited by selective Na^+ channel blocker - tetrodotoxin, which produces the analgesic effect by blocking action potential propagation or ectopic discharges. A recent trial suggests that tetrodotoxin may alleviate moderate to severe, treatment-resistant cancer pain even for prolonged periods following treatment, with acceptable toxicity(tetraodontide=puffer fish)





-) *Botulinum toxin*: Botulinum toxin has ability to suppress the release of neurotransmitters involved in transmission of pain impulses/nociception *i.e.* endothelin-1, substance P, and calcitonin gene related peptide (CGRP) and neuropeptide Y. It has been used to control post-mastectomy pain and has potential to reduce cancer induced bone pain.(transient **receptor** potential cation channel subfamily V member 1 (**TrpV1**), also known as the capsaicin **receptor** and the vanilloid **receptor** 1, ...)



- *(iv) Caffeine*: Caffeine is an antagonist of adenosine receptors-A[1], A[2A], A[2B]. It has shown beneficial effects when given as an adjuvant with NSAIDs and opioids. Clinical trials to establish the efficacy of caffeine as an adjuvant to opioids in reducing pain (*ClinicalTrials.gov* #NCT00879775)[67] and in alleviating post-operative pain after breast surgery are being carried out

- *(v) Soy* Some studies have shown analgesic effect of *isoflavones*: soy isoflavones in animal models. A clinical trial was being conducted to determine the outcome of soy isoflavones consumption as analgesic after surgery for breast carcinoma

- Isoflavones, phenolic compounds, are commonly found in legumes, especially in soybeans. Their structural similarity to 17-β-estradiol (E2), the main female sex hormone, allows them to induce estrogenic and antiestrogenic effects by binding to estrogen receptors, and their consumption has been associated with a decreased risk of hormone-related cancers. In addition, numerous epidemiological studies and related meta-analyses suggest that soy consumption may be associated with a lower incidence of certain diseases. However, there are some doubts about the potential effects on health, such as the effectiveness of cardiovascular risk reduction or breast cancer-promoting properties. The purpose of this review is to present the current knowledge on the potential effects of soy isoflavone consumption with regard to civilization diseases.

- N-methyl-D-aspartate (NMDA) receptor antagonists like ketamine and amantadine provide an alternative for management of opioid resistant cancer pain.
- When pain is not responding to opioids, oral ketamine can be used; only after improvement with a trial of low-dose intra venous ketamine.
- When pain is not responding to opioids, oral ketamine can be used; only after improvement with a trial of low-dose intra venous ketamine

با سپاس از همراهی شما