NEUROPATHIC CANCER PAIN MANAGEMENT

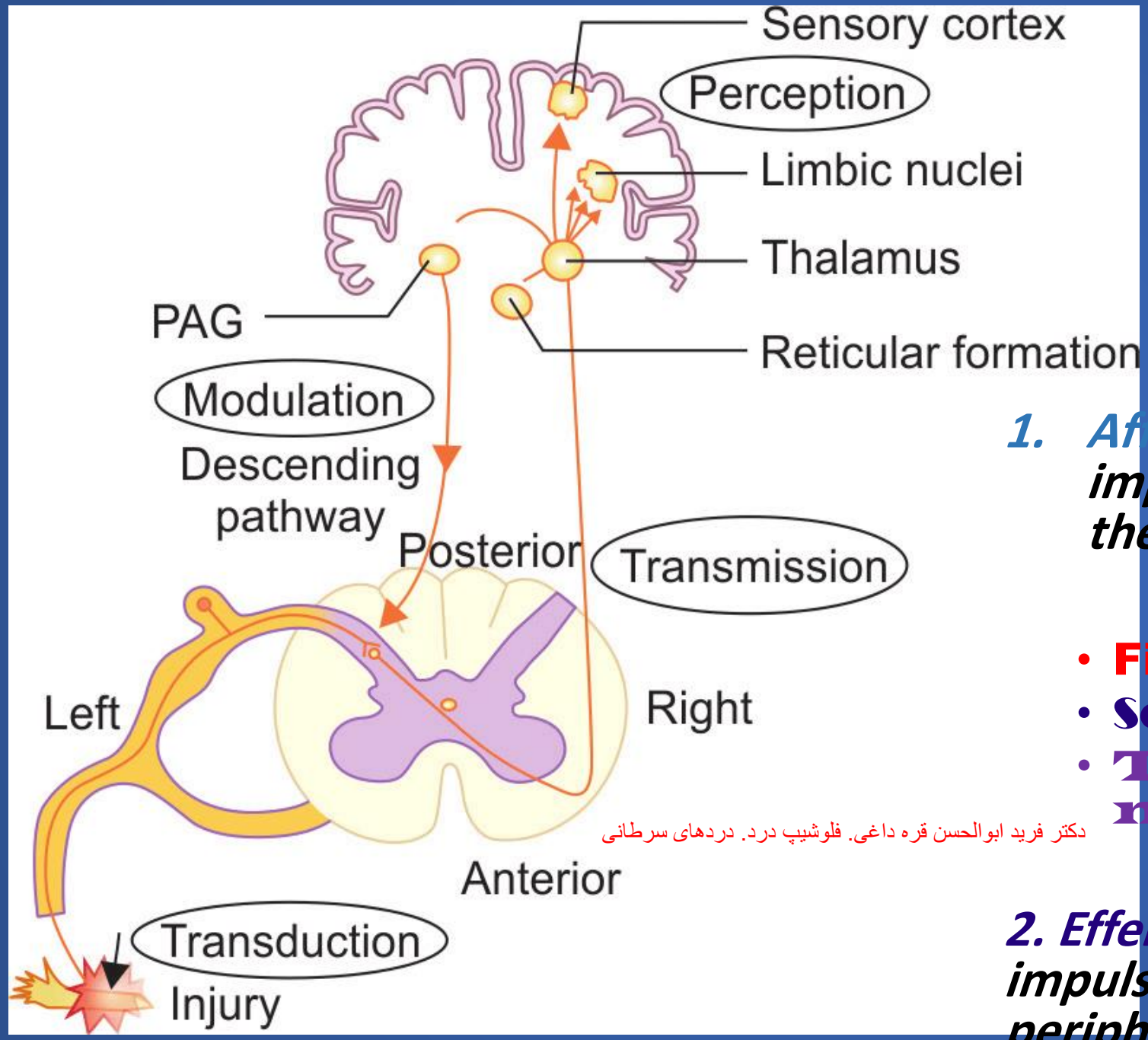
دکتر فرید ابوالحسن قره داغی

Varios Schemes for Classifying Cancer Pain

Etiologic classification	**Primarily caused by cancer** **Treatment of maligancy** **Debility** **Concurrent pathology**
Pathophysiologic classification We talk about this	**Nociceptive (somatic,visceral)** **Neuropathic** **Mixed pathophysiology** **Psychogenic**
Location of cancer pain syndromes	**Head and neck pain** **Chest wall syndromes** **Vertebral and radicular pain** **Abdominal or pelvic pain** **Extremity pain (e.g., brachial plexopathy or bony spread)**
Temporal classification	**Acute** **Breakthrough** **Chronic**
Serverity-based classificaton	**Mild** **Moderate** **Severe**

Clinical Characterisitics of the Pathophysiologic Classes of cancer Pain

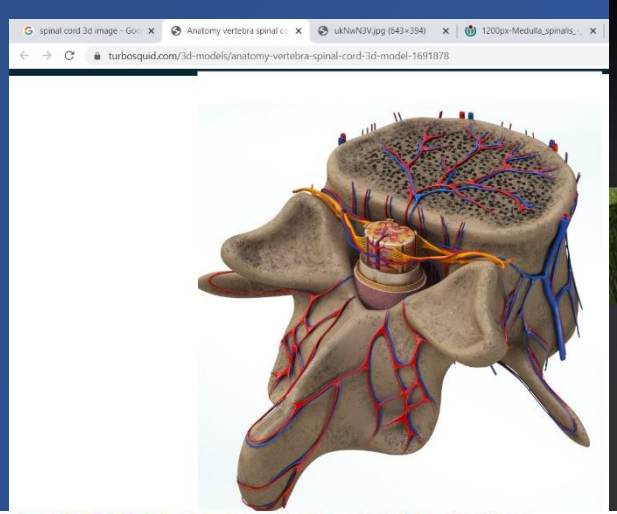
Nociceptive Pain **Somatic Pain** **Visceral Pain**	 **Character of somatic pain is aching, stabbing , throbbing pain is usually well localized** **Character of pain usually gnawing or cramping when due to obstruction of hollow viscus pain typically described as aching , sharp , throbbing when due to tumor involvement of organ capsule** **Usually diffuse and difficult to localize** **Visceral pain may be referred to somatic structures**
Neuropathic Pain Nerve Compression Deafferentation Nerve Injury Sympathetically Mediated	Character of pain often discribed as burning , pricking , electric-like Pain usually located in the area innervated by the compressed peripheral nerve. Plexus or nerve root Radiographic imaging may show the malignancy compressing the neuronal structure Character of pain similar to that of nerve compression may also be shooting or stabbing in nature Dysesthesia or allodynia may be present Often associated with loss of afferent sensory function in the painful region Superficial burning pain with allodynia , may also have deep aching component Associated symptoms include cutaneous vasodilation . Increased skin temperature, abnormal pattern of sweating , trophic changes and allodynia Hallmark is nondermatomal pattern of pain Confirmed with diagnostic sympathetic block دکتر فرید ابوالحسن قره داغی. فلوشیپ درد. دردهای سرطانی



1. ***Afferent (Ascending) – transmit impulses from the periphery to the brain***

- **First Order neuron**
- **Second Order neuron**
- **Third Order neuron**

2. ***Efferent (Descending) – transmit impulses from the brain to the periphery***



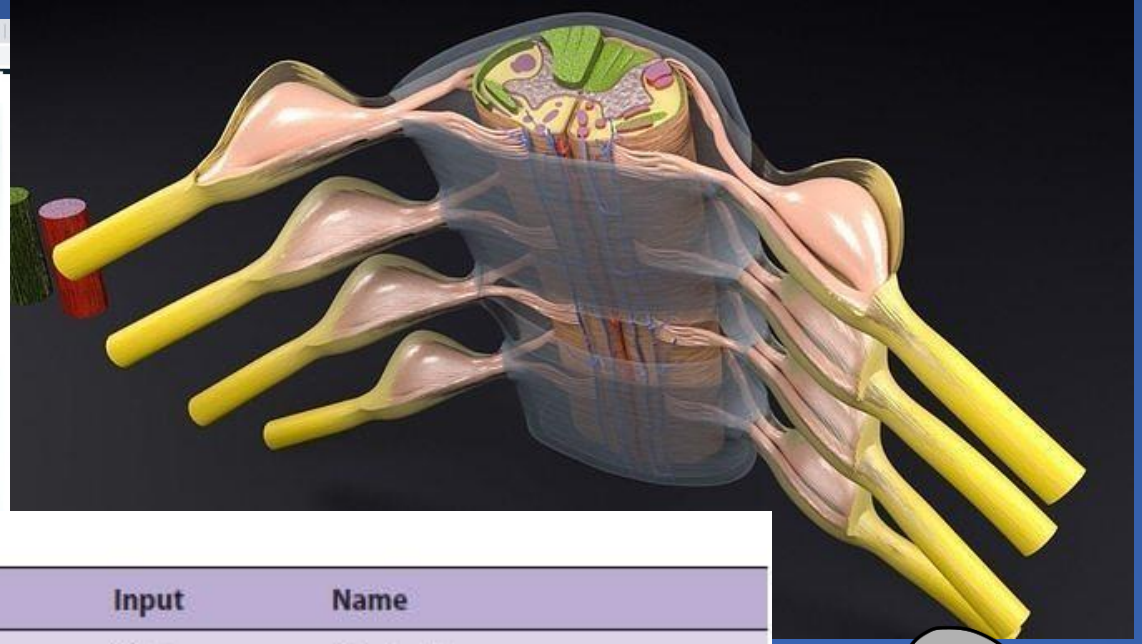
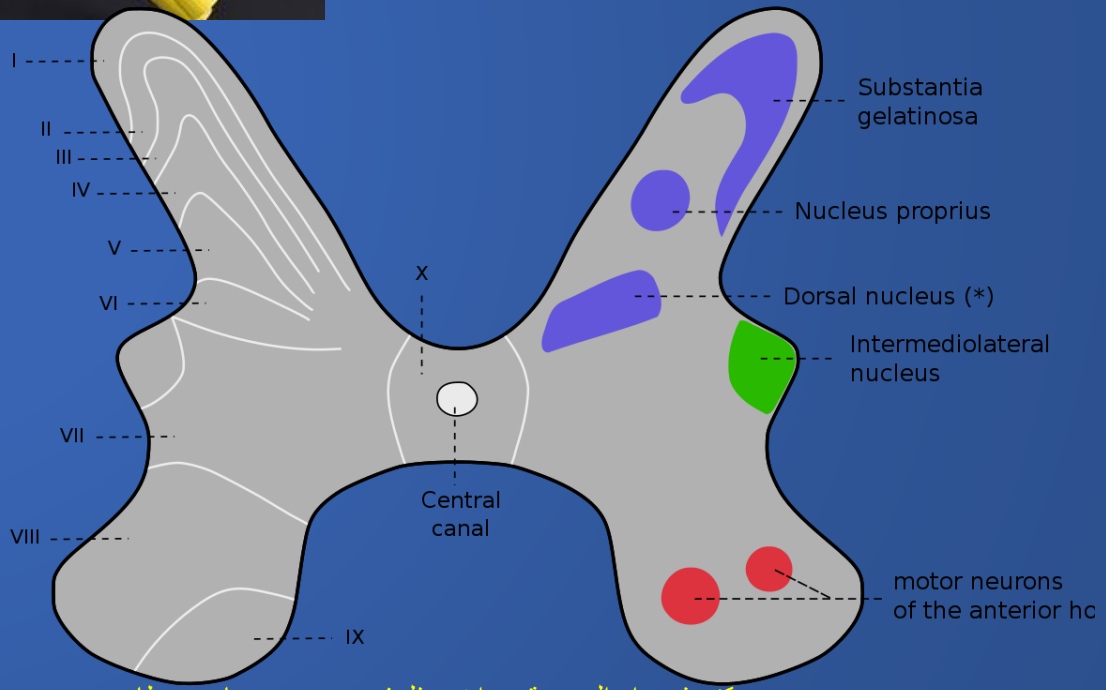


TABLE 47–3 Spinal cord lamina.

Lamina	Predominant Function	Input	Name
I	Somatic nociception thermoreception	Aδ, C	Marginal layer
II	Somatic nociception thermoreception	C, Aδ	Substantia gelatinosa
III	Somatic mechanoreception	Aβ, Aδ	Nucleus proprius
IV	Mechanoreception	Aβ, Aδ	Nucleus proprius
V	Visceral and somatic nociception and mechanoreception	Aβ, Aδ, (C)	Nucleus proprius WDR neurons[1]
VI	Mechanoreception	Aβ	Nucleus proprius
VII	Sympathetic		Intermediolateral column
VIII		Aβ	Motor horn
IX	Motor	Aβ	Motor horn
X		Aβ, (Aδ)	Central canal

[1]WDR, wide dynamic range.



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* Posterior thoracic nucleus or Column of Clarke

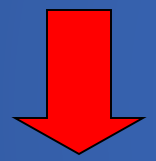
Neuroplastic Pain: pain by: changes within the nervous system.
Structural and functional changes can occur at **every level** of the nervous system.

Neuroplasticity:
ability of the nervous system to alter its structure and function.

Neuroplastic pain: Changes Occur at Multiple Levels of the Human Somatosensory System

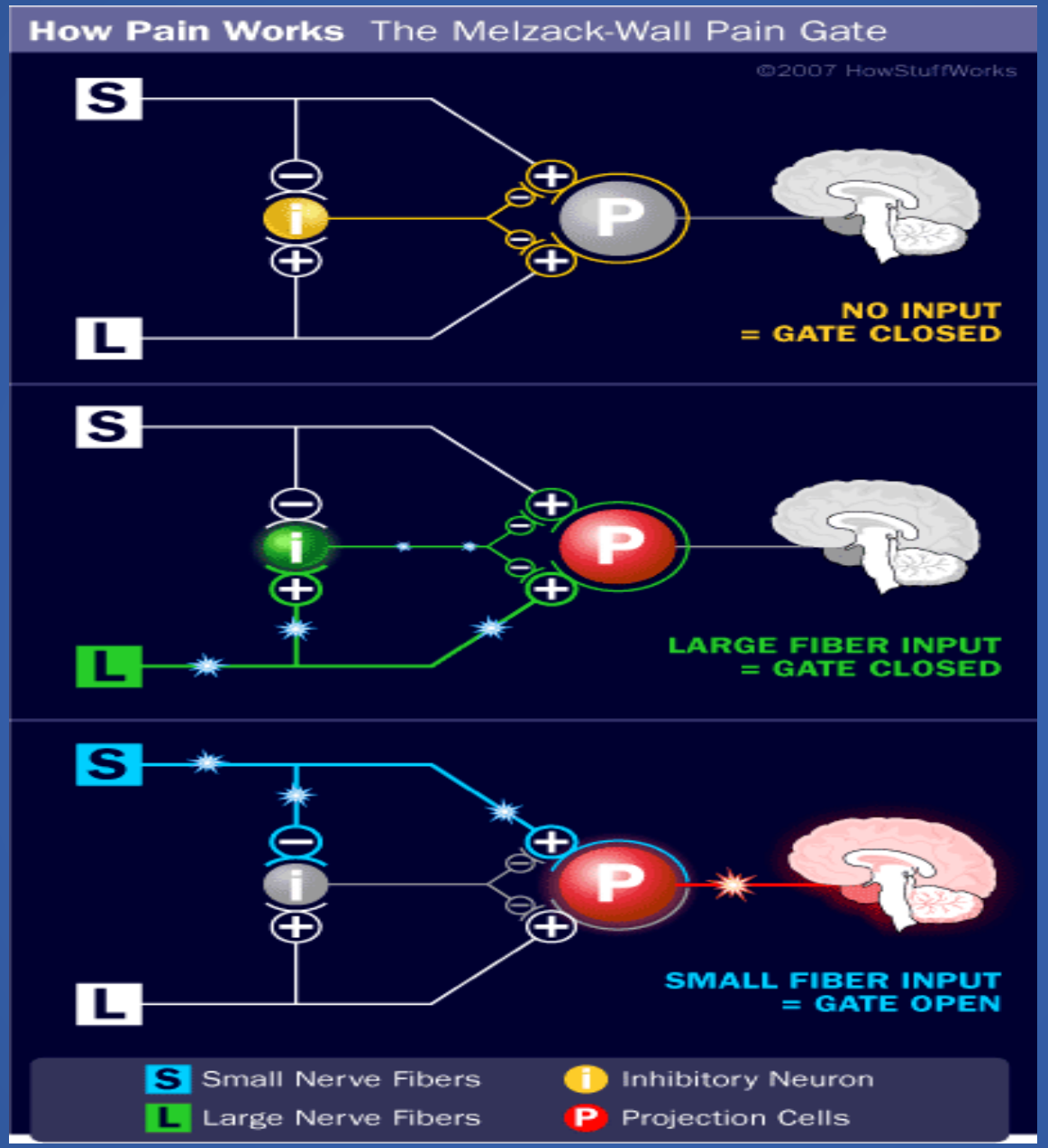
Neuronal Plasticity

- Nervous system changes in
  - ❖ **Neuronal structure**
  - ❖ **Connections between neurons**
  - ❖ **Quantity/properties of neurotransmitters, receptors, ion channels**
- ❖ **DECREASES BODY'S PAIN INHIBITORY SYSTEMS**



Increased Pain

- Injury, inflammation, and disease.
- Produces short-term and permanent changes.
- ↑hypersensitivity of inflammatory pain
  - Enables NS to modify its function according to different conditions


How Pain Works The Melzack-Wall Pain Gate
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S
L
i
P
NO INPUT
= GATE CLOSED
LARGE FIBER INPUT
= GATE CLOSED
SMALL FIBER INPUT
= GATE OPEN
S Small Nerve Fibers
L Large Nerve Fibers
i Inhibitory Neuron
P Projection Cells

Edmonton Staging System for Cancer Pain

A.Mechanism of pain
A1 . Visceral
A2 .Bone or soft tissue
A3.Neuropathic
A4 . Mixed
A5 . Unknown

B.Pain Characteristics
B1. Non in
B2.Incidental

C . Psychological Distress
C1.No major psychological distress
C2.Major psychological distress

D .Opiate Tolerance
D1.Increase of < 5 % of initial dose / day
D2 . Increase of > 5 % of initial dose / day

E. Pst history
E1.Negative history for alcoholism or drug addication
E2 .Positive history for alcoholism or drug addiction

Stage 1 : Good prognosis
A1,A2,B1,C1,D1,E1

Stage 2 : poor prognosis
A3(any B-C-D-E)
A4(any B-C-D-E)
A5(any B-C-D-E)

Scoring : (Results would indicate Stage1 or 2)

Cancer-Related Neuropathic Pain

Tumor invasion / compression of peripheral nerves
Radiculopathy
Obliteration of space by direct tumor growth
bony metastases
plexopathies by compression
brachial (lung cancer in superior sulcus syndrome “ pancoast tumor “)
Lumbosacral (cervical cancer , pelvic/retroperitoneal sarcomas)
Peripheral neuropathy
Chemotherapy (e.g.,cisplatin , vinca alkaloids) , :glove/stocking “ distribution
surgically induced (e.g.,postthoracotomy , postmastecotomy [rare in sentinal node lymphadenectomies] ,postnephrectomy , post-neck dissection , stump pain , postabdomino-perineal resection)
postradiotherapy syndromes
viscera (enteritis,cyctitis)
Plexitis (branchial , lumbosacral)
Myelopathy
postherpetic neuralgia in immunocompromised patients

1. Evaluate the child with pain

. Assess sensory characteristics of pain
. Conduct medical examination and appropriate diagnostic tests
. Evaluate probable involvement of nociceptive and neuropathic mechanisms
. Appraise situational factors contributing to child's pain

• 2 . Diagnose the primary and secondary causes

. Current nociceptive and neuropathic components
. Attenuating physical symptoms
. Relevance of key congnitive, behavioral , and emotional factors

3 . Select appropriate therapies Drug AND Nondrug

. Analgesics
. Adjunct analgesics
. Anesthetics

. Psychological
.Physical
. Behavioral

4 . Implement pain management plan

. Provide feedback on causes and contributing factors to parents (and child)
. Provide rationale for integrated treatment plan
. Measure child's pain regulary
. Evaluate effectiveness of treatment plan
. Revise plan as needed

Key Components of Evaluating a child's Pain

Sensory 	**Pain onset** **Location** **Intensity** **Quality** **Duration** **Spread to other sites (consistent with neurologic pattern)** **Radiation** **Temporal pattern** **Accompanying symptoms**
Medical/surgical appraisal	Investigations conducted Radiologic and laboratory results Consult results Analgesic and adjuvant medications(type ,dose,frequency , route , length of medication trial)
Clainical and situational factors	Roles of medical and associated healt professionals Documentation of pain Criteria for determining analgesic efficacy Congnitive factors (understanding, expectations , control) Behavioral factors (child, parents,staff) Emotional factors (child, parents)

Treatment for neuropathic Pain Syndromes

Oral and parenteral Analgesia **. Steroids** **. Opioids** **. Adjuvants (tricyclic antidepressants , antiepileptics)**
Transcutaneous Delivery Systems
Patient – controlled Analgesia
Neuraxial Analgesia

Tricyclic antidepressants (TCAs)
Antiepileptic drugs
Mild opioids
Strong opioids
Topical agents Capsaicin Lidocaine patch
Physical techniques
Behavioral techniques

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

TABLE 16-5 Routes of Administration and Bioavailability

Route of Administration	Bioavailability
Intravenous	100 % (all opioids)
Transdermal	90 % (fentanyl)
Subcutaneous	80 % (hydromorphone)
Transmucosal	30-60% (morphine – fentanyl)
Rectal	30-40% (morphine)
Oral	33 % (morphine) and 60-80% (oxycodone)

TABLE 22-1 Tricyclic Antidepressants

Generic Name	Trade Name	Generic Available?	Available Dosage Forms and Strengths
Tertiary Amines			
Amitriptyline	Elavil, enovil	Yes	Tablet: 10mg, 25 mg, 50 mg, 75 mg, 100mg, 150mg Injection : 10 mg/ml(10ml)
Clomipramine	Anafranil	Yes	Capsule: 25 mg, 50 mg, 75 mg
Doxepin	Adapin, sinequan	Yes(capsule,solution)	Capsule : 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg Cream: 5%, 30 g, 45g (contains benzyl alcohol) Solution: 10 mg/ml, 120ml
Imipramine	Tofranil-PM Tofranil	Yes (tablet)	Capsule (pamoate) : 75 mg, 100 mg, 125 mg, 150 mg Tablet: 10 mg, 25 mg, 50 mg
Secondary Amines		دکتر فرید ابوالحسن قره داغی. فلوشیپ درد. دردهای سرطانی	
Amoxapine	Asendin	Yes	Tablet: 25mg, 50 mg, 100 mg, 150 mg
Deisipramine	Norpramine	Yes	Tablet:10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150mg
Notriptyline	Aventyl, pamelor	Yes	Capsule : 10 mg, 25 mg, 50 mg, 75 mg Solution: 10 mg/5ml(473ml)
Protriptyline	Vivactil	No	Tablet: 5 mg, 10 mg
Trimipramine	Surmontil	no	Capsule : 25 mg, 50 mg, 100 mg
Modified from Lexi-comp :Lexi-Comp clinical reference library online . November 15,2033.			

TABLE 22-2 Dosing of Tricyclic Antidepressants a 14,38-41

Generic Name	Initial Dose(Ault)	Dose Range (Adult)	Initial Dose(Elderly)	Dose Range (Elderly[mg/day])	Comments
Amitriptyline	25mg QHS	25-100mg/day(pain) 50-300mg/day (depression)	10-25mg QHS	25-150 mg/day	Increase dose by 25 to 50 mg every week as tolerated Do not administer IV
Amoxapine	25mg BID to TID	50-30mg/day Maximum dose : 400mg (outpatient) 600mg (inpatient)	25mg QHS	50-150 mg/day	Increase dose by 25 mg every week as tolerated May be given as a single bedtime dose when<300 mg/day
Clomipramine	25 mg QD	25-250mg/day	25 mg QD	-	May increase to 100 mg/day during first 2 weeks
Desipramine	75 mg QD	150-200mg/day, but may require doses up to 300 mg	10-25 mg QD	75-100 mg/day, but may require doses up to 300 mg	Increase dose by 10- 25 mg every 3 days for inpatients and every week for outpatients
Doxepin	30-150mg QHS or in 2-3 divided doses	50-300mg/day	10-25mg QHS	10-75mg/day	Increase dose by 10-25 mg every 3 days for inpatients and every week for outpatients Single doses should not exceed 150 mg Topical: apply QID (at least 3-4 hr apart)
Imipramine	25 mg TID to QID	Maximum dose :300 mg/day	10-25mg QHS	50-150 mg/day	Increase dose by 10-25 mg every 3 days for inpatients and every week for outpatients May give total dose QHS
Nortriptyline	25 mg TID to QID	Maximum dose :150 mg/day	10-25mg QHS	75 mg QHS(average)	Increase dose by 10-25 mg every 3 days for inpatients and every week for outpatients One of the best tolerated TCAs in elderly patients
Protriptyline	15 mg TID to QID	15-60mg TID to QID	5-10 mg/day	15-20mg/day	Increase dose every 3-7 days by 5-10 mg
Trimipramine	50 mg QHS	Maximum dose: 200mg (outpatient) 300mg (inpatient)	25mg QHS	Maximum :100 mg/day	Increase dose by 25 mg every 3 days for inpatients and every week for outpatients

a Administer all TCAs with caution in patients with hepatic or renal dysfunction.
b Start at lower doses and adjust gradually on elderly.
BID, twice a day; QD, DAILY;qhs, at bedtime;QID, FOUR TIMES A DAY ; tid , three times a day.

TABLE 22-3 Receptor-Binding Properties of TCAs[14,38-42]

Reuptake Antagonism					
Generic Name	**Half-Life(hr)**	**Onset of Therapeutic Effect (days)a**	**Norepinephrine**	**serotonin**	**Important Metabolites/Comments**
					Potency/selectivity of TCA for inhibition of NE and 5-HT vary significantly
Amitriptyline	**9-25** **22-88 (metabolite)**	**7-21**	**2+**	**4+**	**Nortriptyline(active);** **10-Hydroxy-noritripyline,** **10-Hydroxy-amitriptyline,** **Demethylnortriptyline**
Amoxapine	**11-16 (parent)** **30 (metabolite)**	**7-14**	**3+**	**2+**	**7-OH-amoaxapine has significant dopamine receptor blocking activity similar to haloperidol** **8-Hydroxy-amoxapine (active)**
Clomipramine	**30-150**	**14**	**2+**	**3-5+**	**Desmethylclomipramine (active)**
Desipramine	**7-60**	**7-21**	**4+**	**1-2+**	
Doxepin	**6-8**	**14**	**1-2+**	**2+**	**Desmethyldoxepine (active)** **2-Hydroxyimipramine** **Desipramine** **2-Hydroxydesipramine**
Imipramine	**6-18**	**14**	**2-3+**	**3-4+**	**Desipramine (active)** **2-Hydroxynortriptyline**
Nortriptyline	**28-31**	**7-21**	**2-3+**	**2-3+**	**8-Hydroxyamoxapine;** **10-Hydroxynoriptyline** **Blocks cholinergic receptors**
Protriptyline	**54-92**	**14**	**3-4+**	**2+**	
Trimipramine	**20-26**	**7-21**	**1-2+**	**1-2+**	**2-Hydroxydesipramine**

Symbols :4+= high,3+=moderate, 2+= low, 1+= very low, 0= none
a Based on antidepressant literature.

TABLE 22-4 Tricyclic Antidepressants Inhibitory Potential on the Cytochrome P450Enzyme [14-16,38-41,43]

Generic Name	Receptors						
	CYP1A2	CYP2B6	CYP2C8/9	CYP2C19	CYP2D6	CYP2E1	CYP3A4
Amitriptyline	Substrate inhibitor	Substrate	Substrate inhibitor	Substrate inhibitor	Substrate inhibitor	inhibitor	Substrate
Amoxapine		Substrate			Substrate		
Clomipramine	Substrate			Substrate	Substrate inhibitor		Substrate
Desipramine	Substrate				Substrate inhibitor	inhibitor	
Doxepin	Substrate				Substrate		Substrate
Imipramine	Substrate inhibitor	Substrate		Substrate inhibitor	Substrate inhibitor	inhibitor	Substrate
Nortriptyline	Substrate			Substrate	Substrate inhibitor	inhibitor	Substrate
Protriptyline					Substrate		
Trimipramine				Substrate	Substrate		Substrate

Bolded text= enzyme appears to play a clinicallly significant role in drug's metabolism.
. Grapefruit juice may inhibit the metabolism of some TCAs and clinical toxicity may result.
. Avoid concurrent use of valerian, St . John's wort , SAMe,and kava kava with TCA.
.All TCAs are highly protein bound.
.↑plasma concentrations of TCA:Cimetidine, diltiazem,SSRIs , haloperidol, methylphenidate, oral contraceptives, phenothiazines, verapamil.
. ↓Plasma concentrations of TCA : Barbiturates, carbamazepine, phenytoin.
. TCA ↑Plasma concentrations of oral anticoagulants and hydantoins and ↓plasma concentrations of levodopa.
TCA,tricyclic antidepressant;SAMe , 5-Adenosylmethionine; SSRI, selective serotonin reuptake inhibitor.

TABLE 22-5 Adverse Effects of Tricyclic Antideprssants [14,31,33,38-42,44]

Generic Name	Anticholinergic Effects	Conduction Abnormalities	Orthostatic Hypotention	Tachycardia	Sedation	Seizures	sexual	Weight Gain
Amitriptyline	4+	3+	3+	3+	4+	3+	2+	4+
Amoxapine	3+	2+	2+	2+	2+	3+	0	2+
Clomipramine	3-4+	3+	2+	2+	3-4+	4+	4+	4+
Desipramine	1+	2+	2+	1+	1-2+	2+	1+	1+
Doxepin	2-3+	2+	2+	2+	3-4+	3+	2+	4+
Imipramine	2-3+	3+	4+	2+	2-3+	3+	2+	4+
Nortriptyline	2+	2+	1+	1+	2+	2+	1+	1+
Protriptyline	2-3+	3+	2+	1+	1+	2+	1+	0
Trimipramine	2-4+	3+	3+	2+	3-4+	3+	2+	4+

. Use these agents with caution in patients with a seizure history-may lower seizure threshold.
. Do not administer any TCA within 14 days of a monoamine oxidase inhibitor (MAOI)
. Use with caution in hyperthyroid patients or those receiving thyroid supplementation.
. All TCAs may cause SIADH and alterations in glucose control.
. Amoxapine may cause extrapyramidal side effects .
. Symbols : 4+=high , 3+= moderate , 2+=low, 1+= very low , 0=none, - = unknown.
SIADH,syndrome of inappropriate antidiurectic hormone; TCA, TRICYCLIC ANTIDEPRESSANT.

AED	Initial dose (mg/kg/day)	Maintenance dose	Daily dose	Presentation
Diazepam	2-5 years: 1.5 6-11 years: 0.9	Same Same	3 times	Solution: 5 mg/5 ml Tablets: 10 mg
Carbamazepine	5-10	15-20 mg/kg/day	2 or 3 times	Suspension: 100 mg/5 ml Tablets: 200 mg
Clobazam	0.25	1 mg/kg/day	Once or twice	Tablets: 10 mg
Clonazepam	0.01	0.1 mg/kg/day	2 or 3 times	Suspension: 0.1 mg/1ml Tablets: 2 mg
Phenytoin	4-5	4-8 mg/kg/day	2 or 3 times	Suspension: 37.5 mg/5 ml Tablets: 100 mg
Phenobarbital	5	Same	Once or twice	Tablets: 100 mg
Gabapentin	10-15	30-100 mg/kg/day	2 or 3 times	Capsules: 300 and 400 mg
Lamotrigine	0.5	2-10 mg/kg/day	Twice	Tablets: 25, 50, and 100 mg
Levetiracetam	10	40-60 mg/day	Twice	Solution: 100 mg/ml Tablets: 250, 500, and 1000 mg 500 mg extended release
Oxcarbazepine	5-10	20-30 mg/kg/day	Once or twice	Suspension: 300 mg/5 ml Tablets: 300 and 600 mg 150, 300, and 600 mg extended release
Pregabalin	3.5-5	15-20 mg/kg/day	Twice	Capsules: 75 and 150 mg
Topiramate	0.5-1.0	4-8 mg/kg/day	Twice	Tablets: 25, 50, and 100 mg
Valproic acid	10-15	15-30 mg/kg/day	2 or 3 times	Syrup: 250 mg/5 ml Sprinkle: 125 mg Capsules: 250 mg and 500 mg 250 mg and 500 mg extended release
Vigabatrin	40	80-100 mg/kg/day (150 mg/kg/per day for childhood spasms)	2 or 3 times	Tablets: 500 mg

TABLE 24-1 Analgesic Effects of Topical Lidocaine Patch and EMLA Cream

Pain Syndrome	Treatment	Design	NNT	Result	Reference
PHN	Lidocaine patch	RCDBX	35	↓Pain at 4,6,9,12 hr	Rowbotham , 1996
PHN	Lidocaine patch	RCDBX	32	↓Pain , median time to exit>14days Vs 3.8 days with vehicle	Galer , 1999
PHN	Lidocaine patch	RCDBX	96	↓All common neuropathic pain qualities	galer., 2002
PHN	Lidocaine patch	Open label	332	↓Pain and interference with quality of life	Katz , 2003
Neuropathic pain	Lidocaine patch	Open label	16	Moderate or better pain relief in 87%	Devers,2000
Neuropathic pain	Lidocaine patch	RCDBX	40	↓Pain over a period of 7 days (NNT=4.4)	Miere,2003
PHN	EMLA cream	Open label	12	↓ pain after 6 hr	Stow, 1989
PHN	EMLA cream	Open label	11	↓ paroxysmal pain and mechanical hyperalgesia with repeated application. No effect on ongoing pain	Attal, 1999
Neuropathic pain	EMLA cream	RCDB	45	Time to 1st analgesic request ↑ and analgesic consumption on d 2-5 ↓. At 3 mo , pain ↓	Fassoulaki , 2000

C , controlled;DB, double-blind; EMLA , eutectic mixture of local anesthetics;NNT,number needed to treat;PHN, postherpetic neuralgia; R, randomized; X, crossover.

TABLE 24-2 Analgesic Effects of Systemic Local Anesthetics

Pain Syndrome	Treatment	design	NNT	Result	Reference
Diab					
Diab					7
PHN					, 1991
Centr					92
Perip injur					6
Peripheral nerve injury	IV Lidocaine 2 mg/kg vs 5 mg/kg	RCDBX	25	↓ Pain with both doses + dose response	Galer, 1996
neuropathy : cancer treatment related	IV Lidocaine 5 mg/kg	RCDBX	10	NS	Ellemann , 1989
C P					
C P					
P					
P					
P					
f					
migraine	IV Lidocaine max2.7 mg/kg	RCDB	76	↓ Pain	Bell , 1996

TABLE 38-3 Surgical Invasine Therapies to Reduce Pain

Spinal opioids
Celiac ganglion block
Superior mesenteric ganglion block
Inferior mesenteric ganglion block
Hypogastruc or splanchnic nerve block
Midline myelotomy

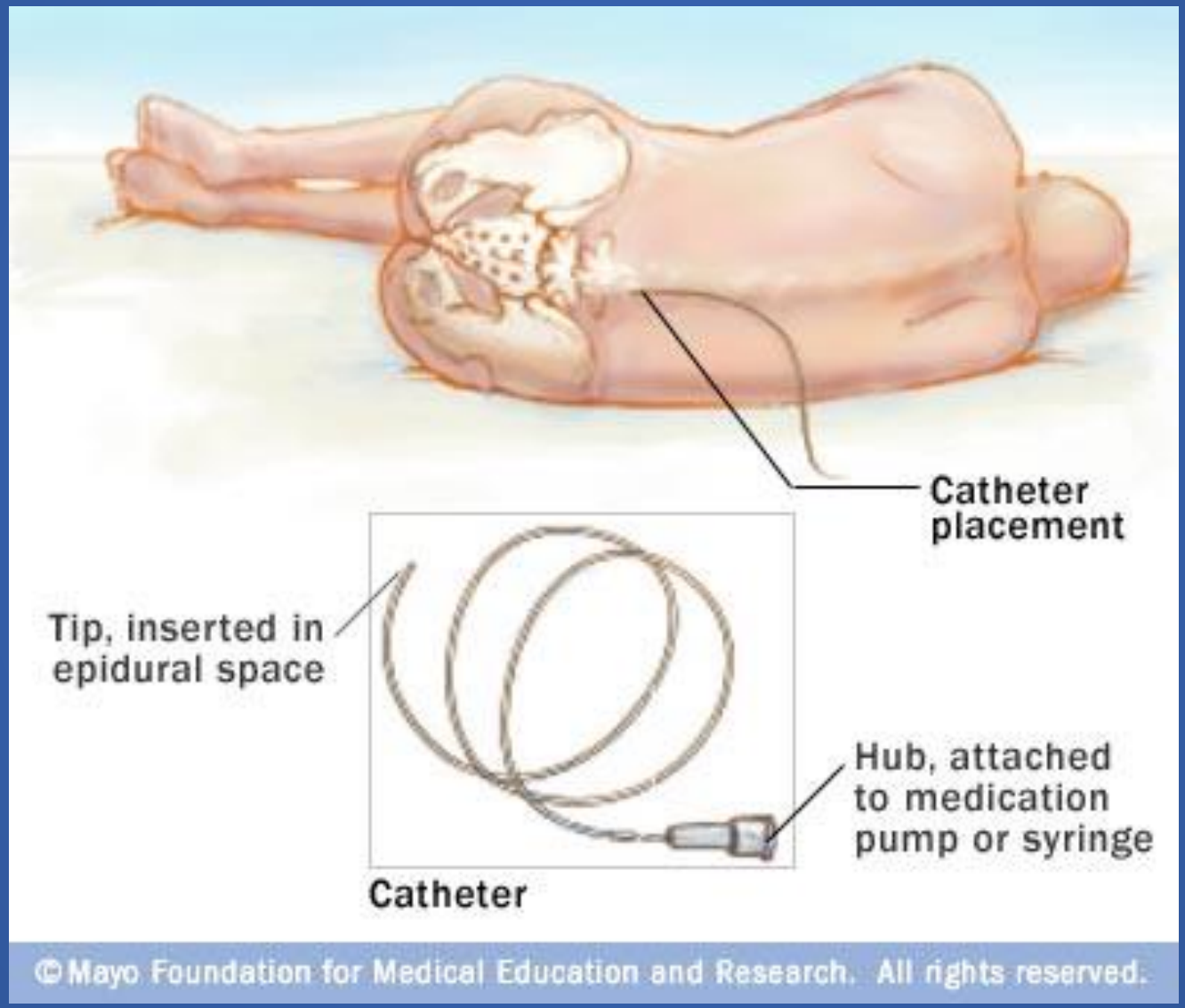
Medication	Initial Dose	Maximum Dose	Side Effects
Gabapentin (Neurontin)	5 mg/kg or 100-300 mg TID PO	70 mg/kg/d or 1200mg TID	Dizziness,ataxia,somnolence,fatigue
Amitriptyline (Elavil)	0.1 mg/kg or 12.5 mg once a day at bedtime PO	1 mg/kg/d	Dizziness, somnolence,dry mouth, cardiac dysrhythmias
PO,per os; TID , three times daily.			

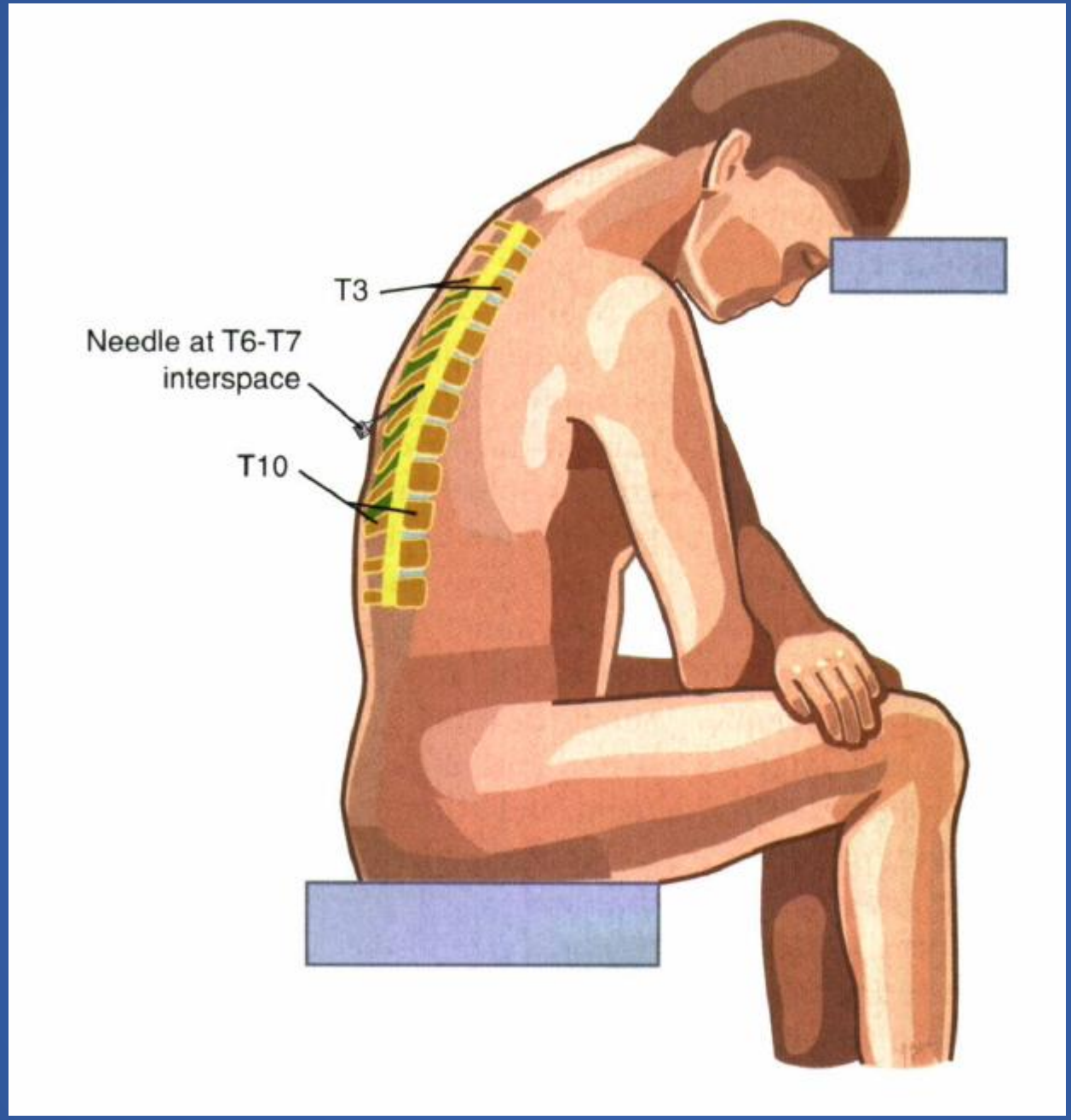
Adjuvant Analgsic Drugs

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 Universaity Press, 2004, p 782, with permission.

Epidural analgesia




T3
Needle at T6-T7
interspace
T10

Inetrcostal block


Physiotherapy Cryoanalgesia
&
Cryomassage
C - 502 T2


pin index yoke
for N2O cylinder
golf trolly
with plastic cover
The type B (golf) trolly has been designed totransport a type F gas cylinder.

Thank you so much for your attention