Updates in PM&R and Pain

Andrew Friedman MD
April 2026

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I have no conflicts to disclose.
I will talk about non-FDA approved use of medications

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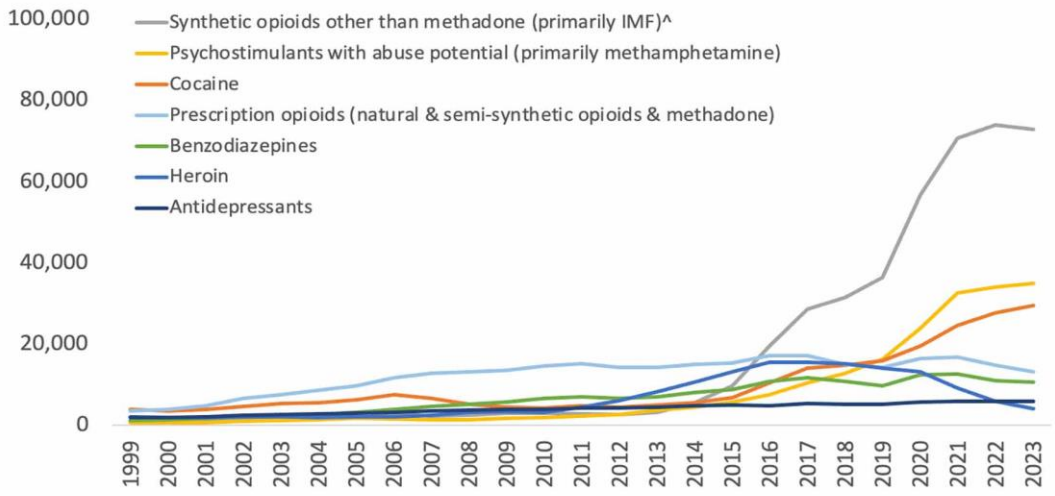
Drug Poisoning Deaths

Figure 2. U.S. Overdose Deaths*, Select Drugs or Drug Categories, 1999-2023



*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision. ^Illicitly manufactured fentanyl. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2023 on CDC WONDER Online Database, released 1/2025.

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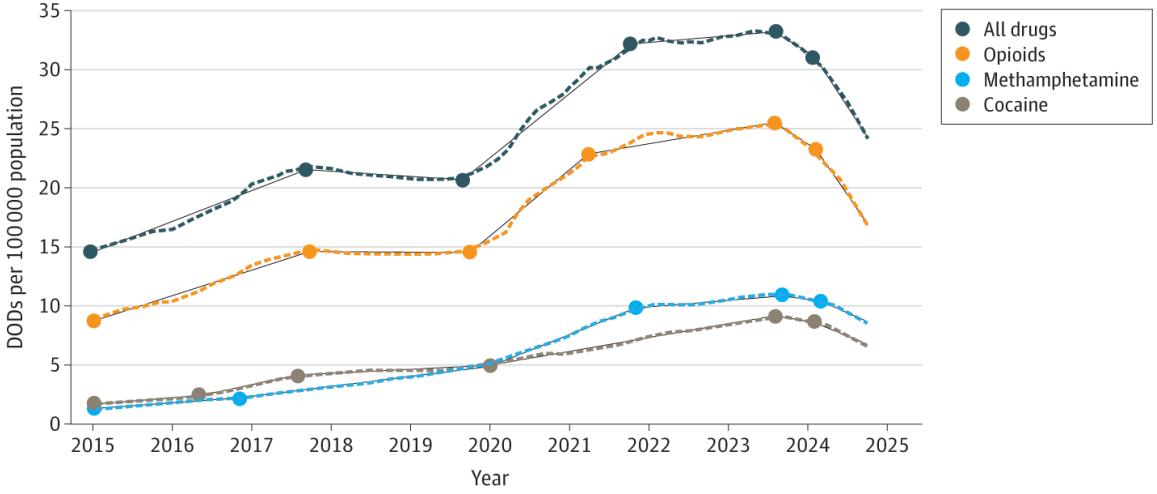
Recent positive trend



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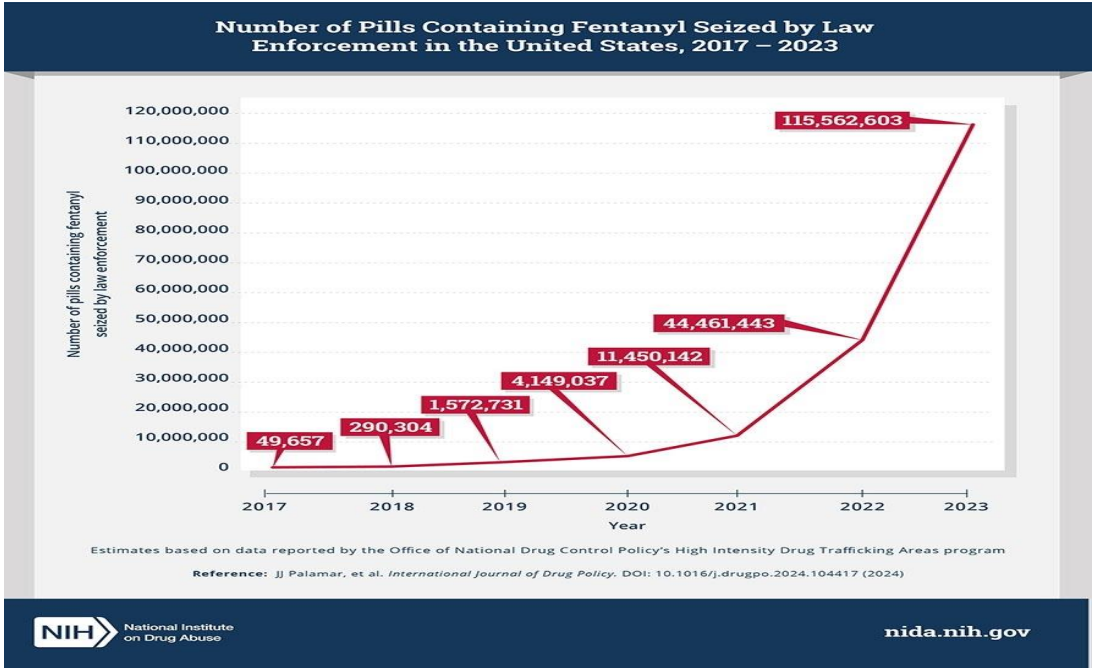

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Buprenorphine for Pain

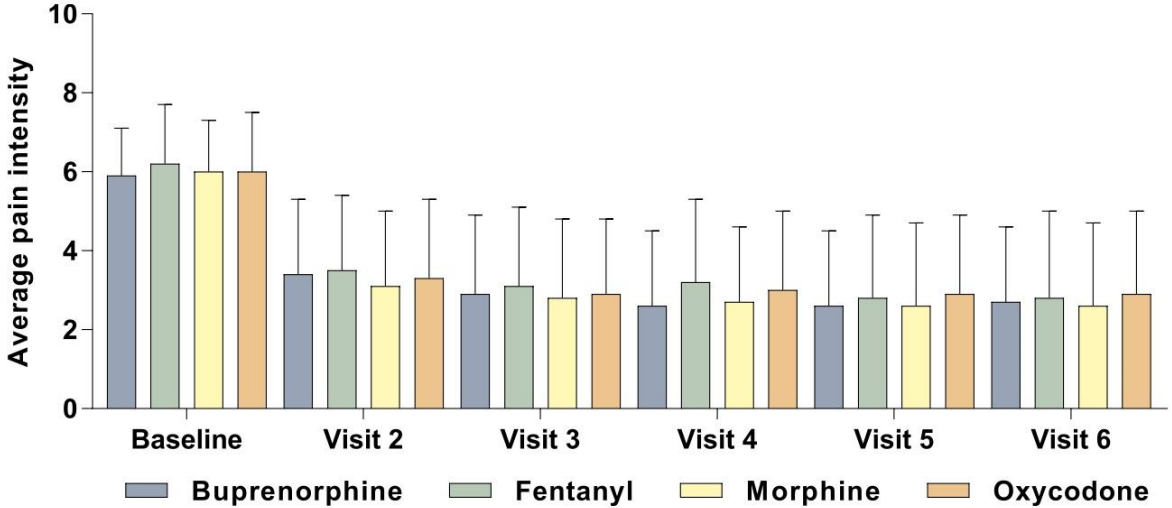

Figure 3 Efficacy of Transdermal Buprenorphine Compared With Conventional Opioids in Patients With Chronic Cancer Pain. Average pain intensity was measured on a numeric rating scale. Data are mean (SD). Data from Corli et al (2016).[45]

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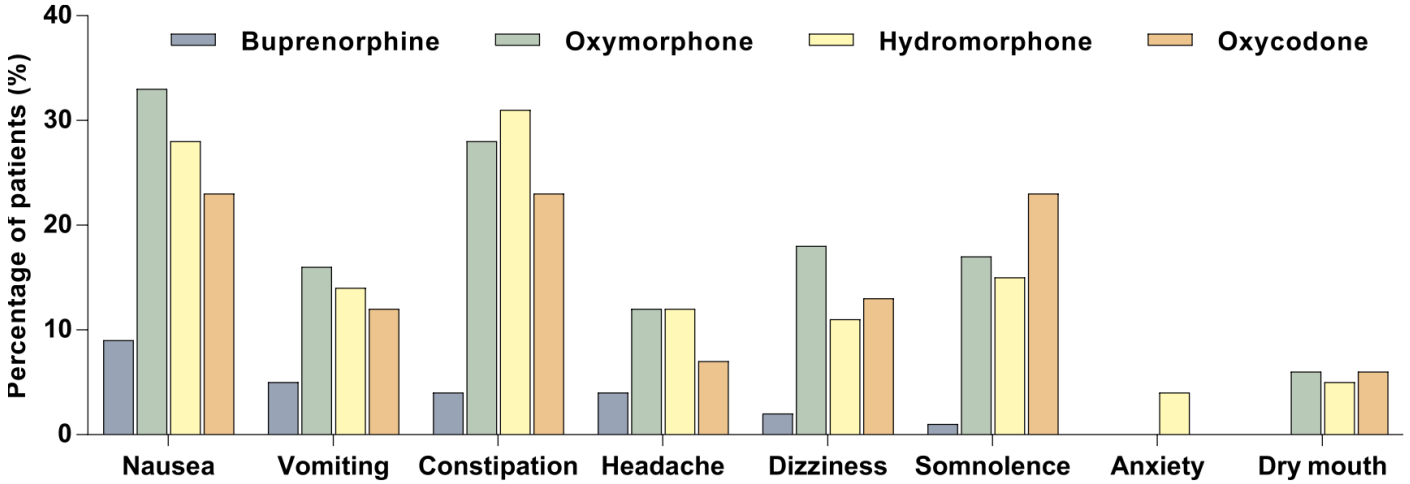

igure 7 Adverse Events Reported in Clinical Trials of Buprenorphine Buccal Film Compared With Conventional Opioids for Chronic Pain. The percentage of patients who eported adverse events in clinical trials for buprenorphine buccal film[21] compared with those reported for extended-release formulations of oxymorphone,[87] ydromorphone,[88] and oxycodone.[69]

lotes: Copyright ©2019. Dove Medical Press. Adapted from Pergolizzi JV, Jr., Raffa RB. Safety and efficacy of the unique opioid buprenorphine for the treatment of chronic ain. *J Pain Res*. 2019;12:3299–3317.[7]

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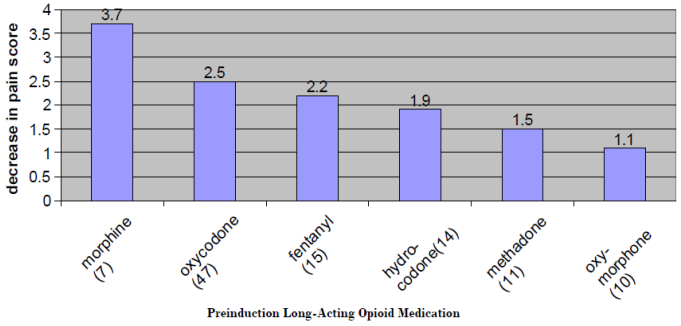
Patients on High Dose Opioids

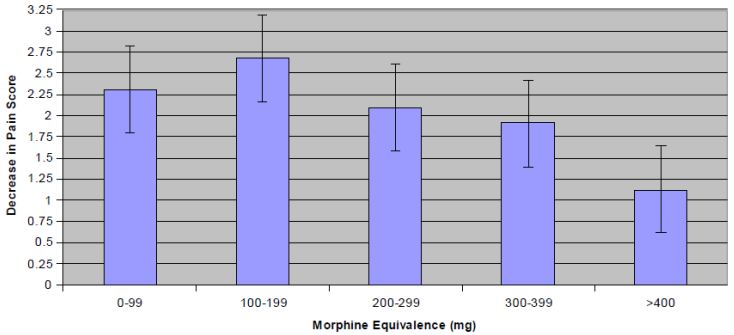
Daitch J et al. *Pain Physician*. 2012;15:ES59-ES66.

Patients: 104 patients from chronic pain clinic on full opioid agonists – high dose or ineffective use

- Pre-induction MED: 180mg (range 10-840)
- 45% converted from oxycodone, 14% from fentanyl, 13% from hydrocodone, 11% from methadone, 7% from morphine

Intervention: Suboxone starting 24hr after last dose of full agonist





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Have you heard of the new non-opioid pain medicine and is it an option for me?

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Suzetrigine/Journavx®

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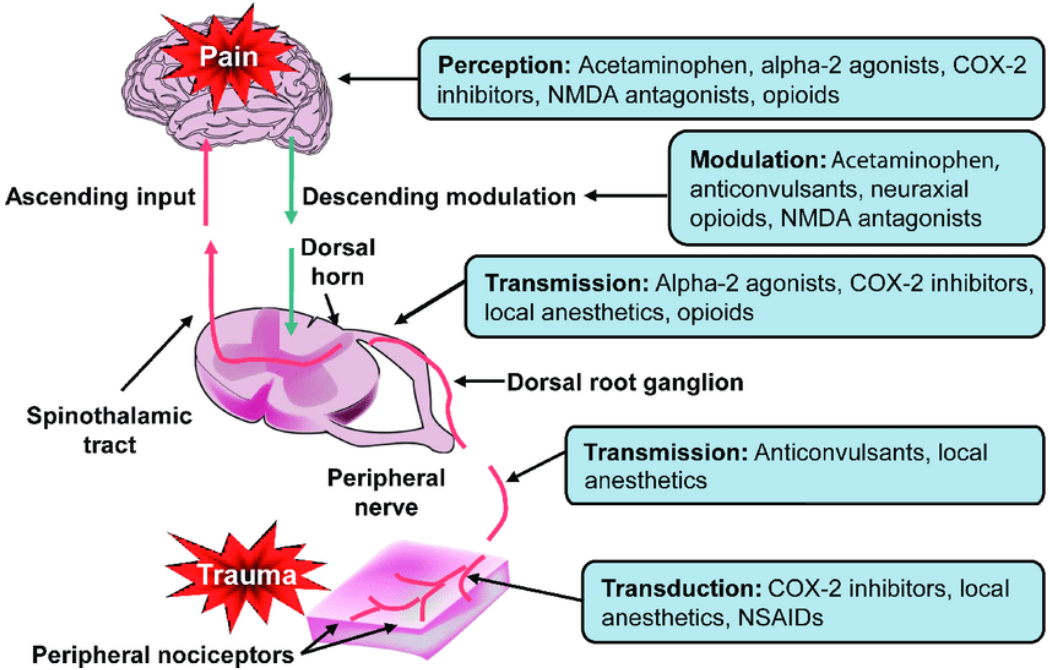
Analgesics site of action



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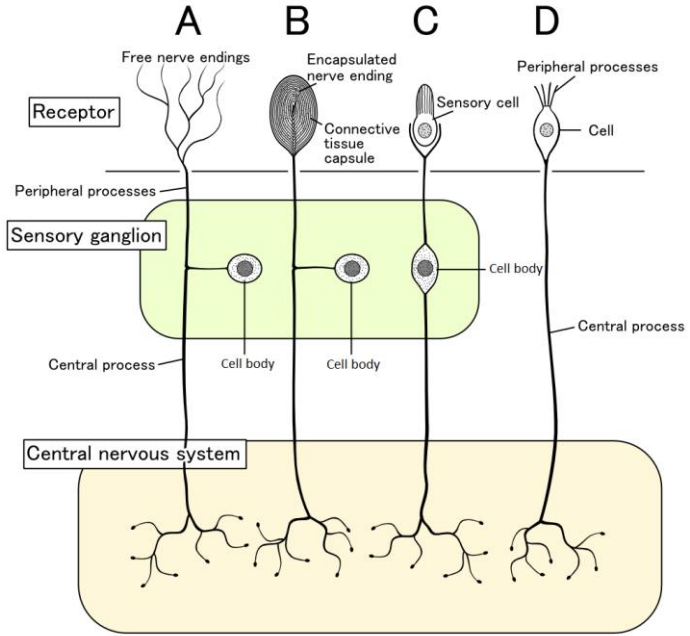
Types of Sensory Receptors



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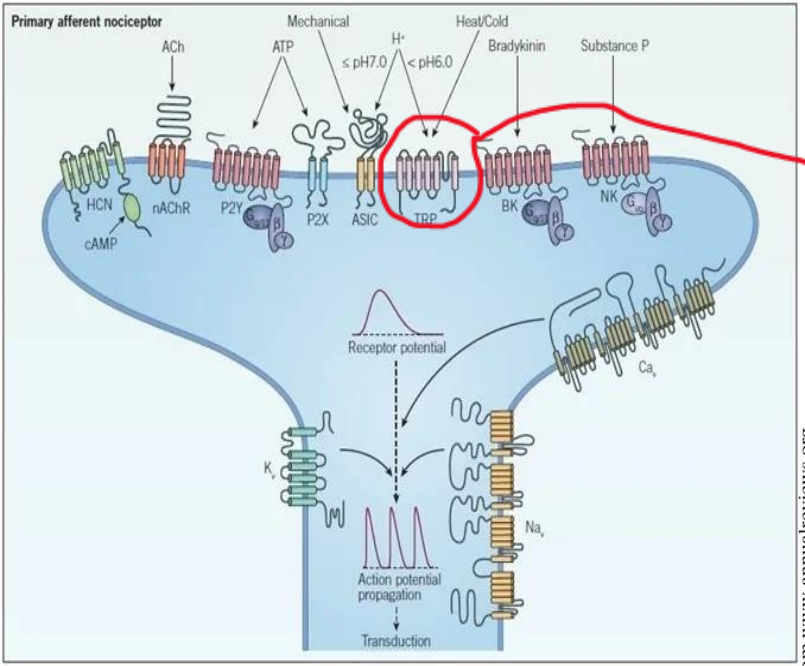

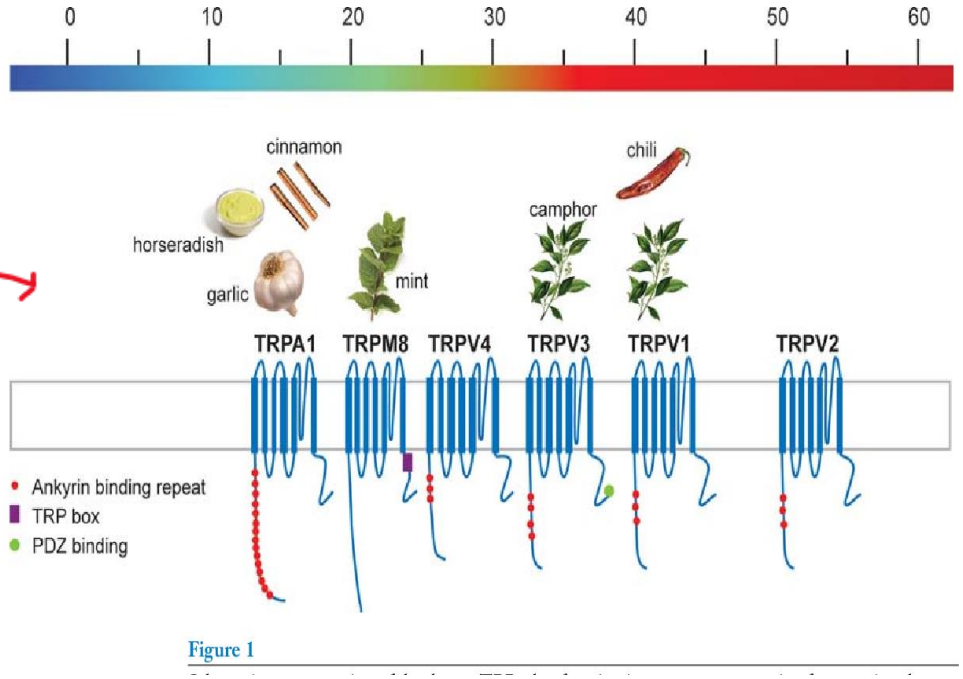

Figure 1

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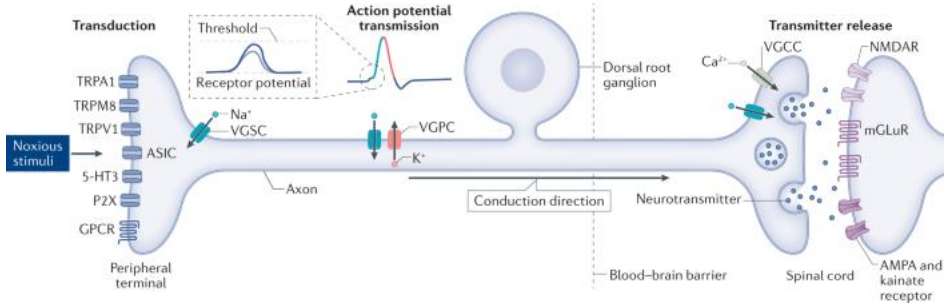

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Sodium Receptor Sub-types

species	channel isoform	Activation V50 (mV)	Fast inactivation (τ in ms at I_{peak})	50% block tetrodotoxin (nM)	tissue localization
Salpingoeca (choanoflagellate)[@]	Na_v2	-22	**50**	**>10,000**	none
Polyorchis (jellyfish)[#]	Na_v1	-20	1.9	**>10,000**	radially-symmetrical nerve ring
Loligo (squid)[$]	Na_v1	-20	0.8	1	nervous system
Drosophila (fly)[%]	Na_v1	-25	0.5	0.3	nervous system
human[&]	$Na_v1.1$	-20	0.7	10	brain and spinal cord, heart: ventricular myocytes (at transverse tubules)
human[&]	$Na_v1.2$	-24	0.8	11	brain and spinal cord, highest density in unmyelinated axons and in developing pre-myelinated axons
human[&]	$Na_v1.3$	-24	0.8	4	brain and spinal cord, expressed mostly in embryonic and neonatal stages of development
human[&]	$Na_v1.4$	-30	0.6	25	skeletal muscles (homologs also in fish electric organ)
human[&]	$Na_v1.5$	-26	1	**1,500**	heart: atria and ventricular myocytes (at intercalated disks)
human[&]	$Na_v1.6$	-29	1	1	brain and spinal cord: most abundantly expressed isoform in adult brain, somato-dendritic localization, nodes of Ranvier, DRG neurons
human[&]	$Na_v1.7$	-27	0.5	25	peripheral nervous system: pain neurons in DRG, trigeminal ganglion neurons, sympathetic neurons
human[&]	$Na_v1.8$	**-16**	**6**	**60,000**	peripheral nervous system: pain sensory neurons (C-fibers) in DRG neurons
human[&]	$Na_v1.9$	**-32**	**16**	**39,000**	peripheral nervous system: pain neurons in DRG, trigeminal ganglion neurons, intrinsic myenteric neurons
human[*]	Na_x	Na^+ ion-sensitive, non-voltage-gated Na channel with a gating threshold of ~150 mM for extracellular [Na+] *in vitro*. Identified in sensory circumventricular organs (eg. subfornical organ),			

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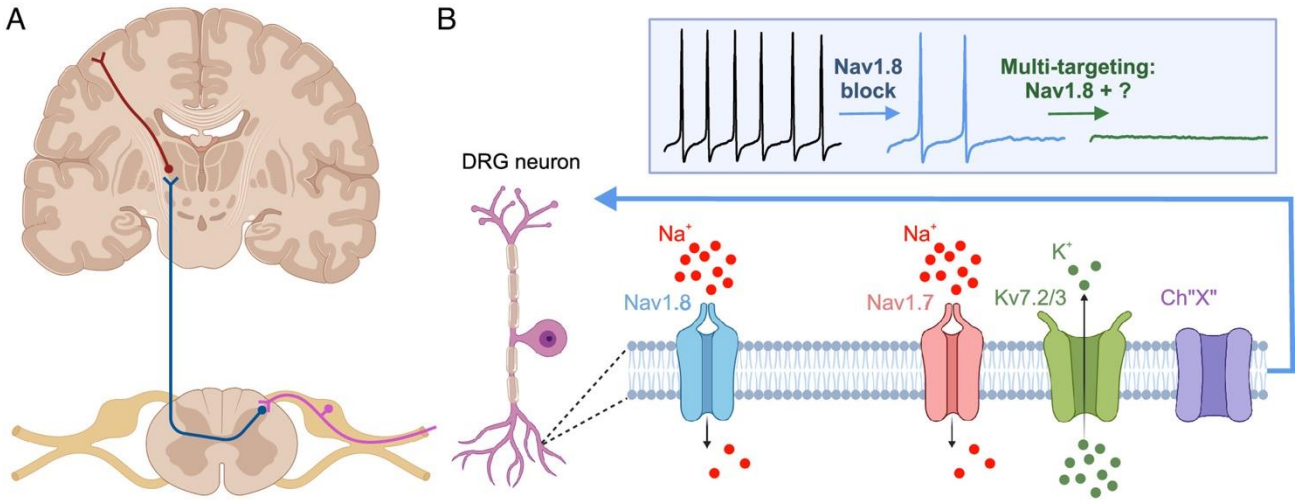
Sodium Channel Blockers

Local Anesthetics—Lidocaine, Bupivacaine etc

Antiepileptics—Phenytoin, Carbamazepine, Valproate, Topiramate, Lamotrigine

Antiarrythmics—Flecainide, Quinidine, Procainamide



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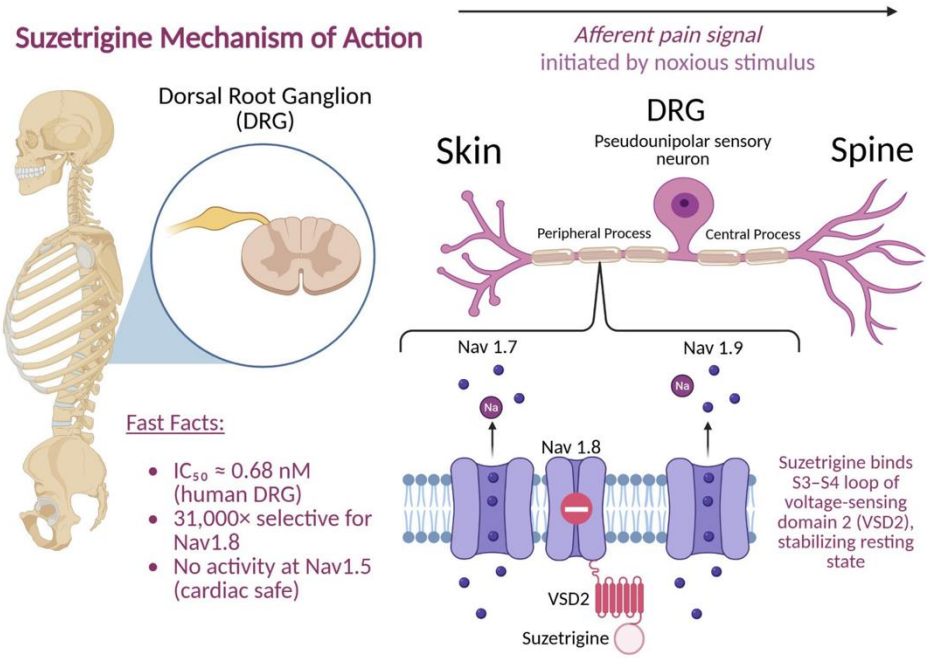
Suzetrigine



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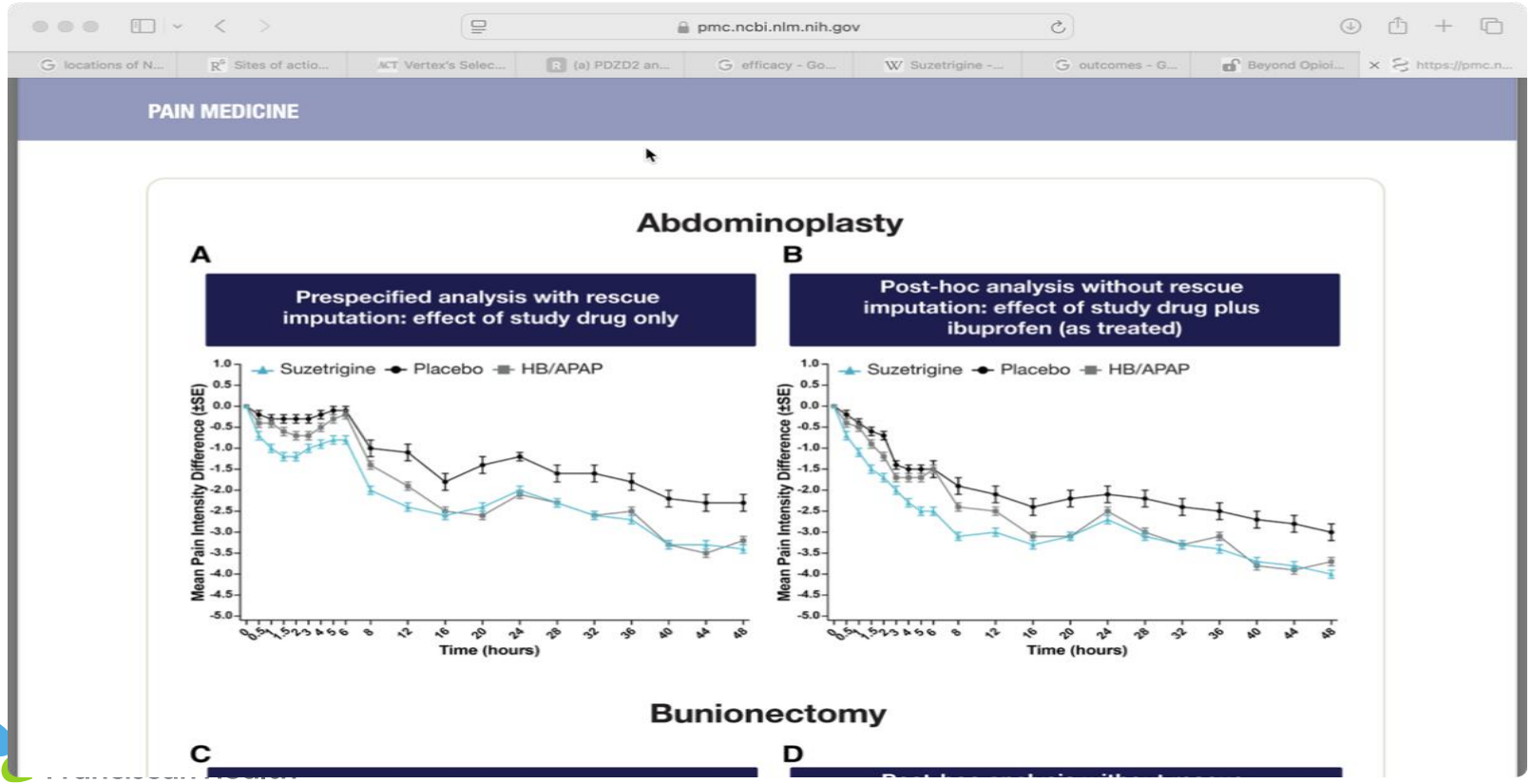
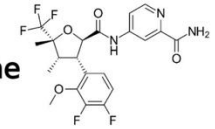
Suzetrigine vs Hydrocodone vs Placebo



Pharmacology of Suzetrigine

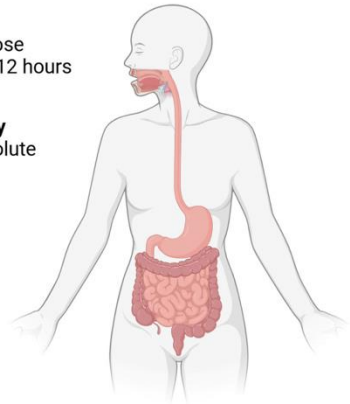


Dosing (Oral)
100 mg loading dose
then 50 mg every 12 hours

Oral Bioavailability
No published absolute value

Volume of Distribution
495 L

Elimination
~50% feces
~44% urine



CNS Safety
No signs of toxicity, dependence, or withdrawal

Cardiac Safety
No QTc prolongation or cardiovascular changes

Absorption
3.0 hr fasting
5.0 hr fed

Metabolism
CYP3A4→M6-SUZ

90% Steady State: 3 days
Half-life: 26.6 hours

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CYP3A4

Inhibitors*

--Erythromycin
--Clarithromycin
--Ritonavir
--Ketoconazole
--Verapamil

*Contraindicated

Inducers

--Rifampin
--Carbamazepine
--Phenytoin

Avoid grapefruit. Use alternatives to hormonal contraception during use

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Suzetrigine

Table 2: Adverse Reactions Reported in ≥1% of JOURNAVX-Treated Patients and Greater than Rate of Placebo in Two 48-hour Trials in Moderate to Severe Acute Pain (Trials 1 and 2, Pooled)			
Adverse Reactions (Preferred Term)	**Placebo (N = 438) n (%)**	**JOURNAVX (N = 874) n (%)**	**HB/APAP [a] (N = 879) n (%)**
Pruritus	7 (1.6)	18 (2.1)	30 (3.4)
Muscle spasms	2 (0.5)	11 (1.3)	6 (0.7)
Increased blood creatine phosphokinase	2 (0.5)	10 (1.1)	7 (0.8)
Rash	2 (0.5)	10 (1.1)	6 (0.7)

[a] Patients received 5 mg/325 mg of oral hydrocodone bitartrate/acetaminophen (HB/APAP) every 6 hours.

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Case Presentation

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Case # 1

45 y.o. man presents with right upper extremity weakness. Symptoms started 4 weeks ago when he awoke from sleep with severe shoulder and arm pain. Pain improved after a week but subsequently he noticed weakness in the right shoulder and arm and awakens at night with shortness of breath.

Examination reveals deltoid atrophy, winged right scapula and less than antigravity strength in the right shoulder abductors and elbow flexors.

What is the diagnosis?

Parsonage Turner Syndrome/Neuralgic Amyotrophy

--Middle age on presentation Average age 40

--Previously underrecognized. Incidence 3-100/100,000

--Male predominance 2.5:1

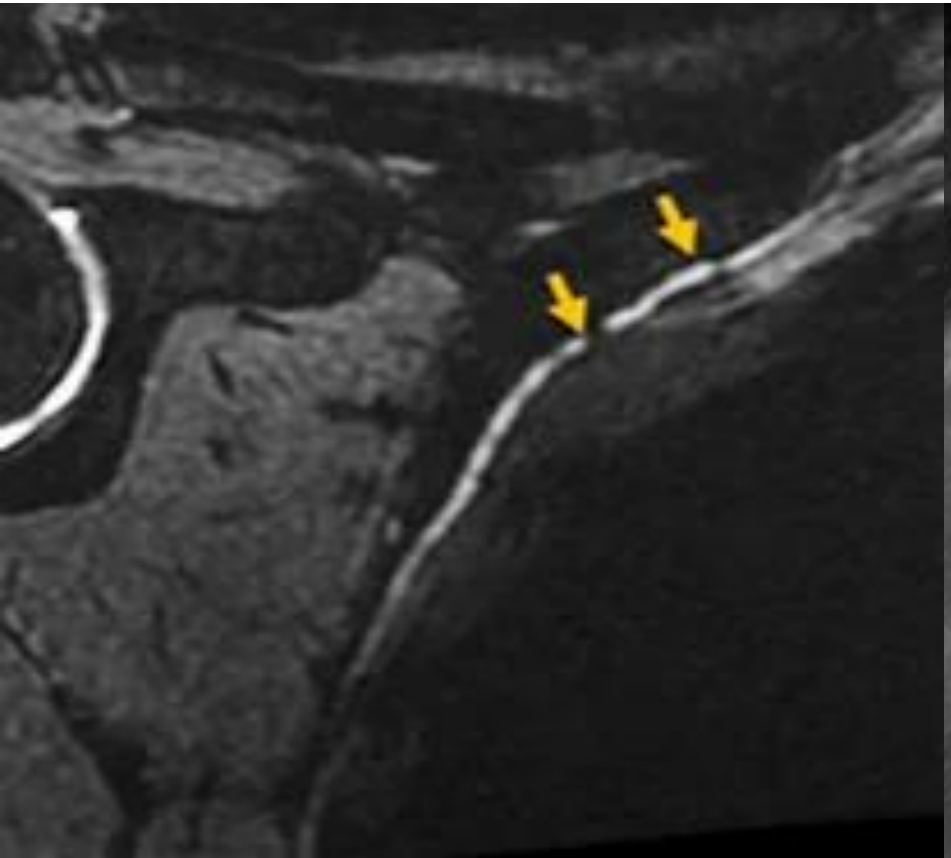
--Often preceded by upper extremity exercise, viral illness, surgery, childbirth

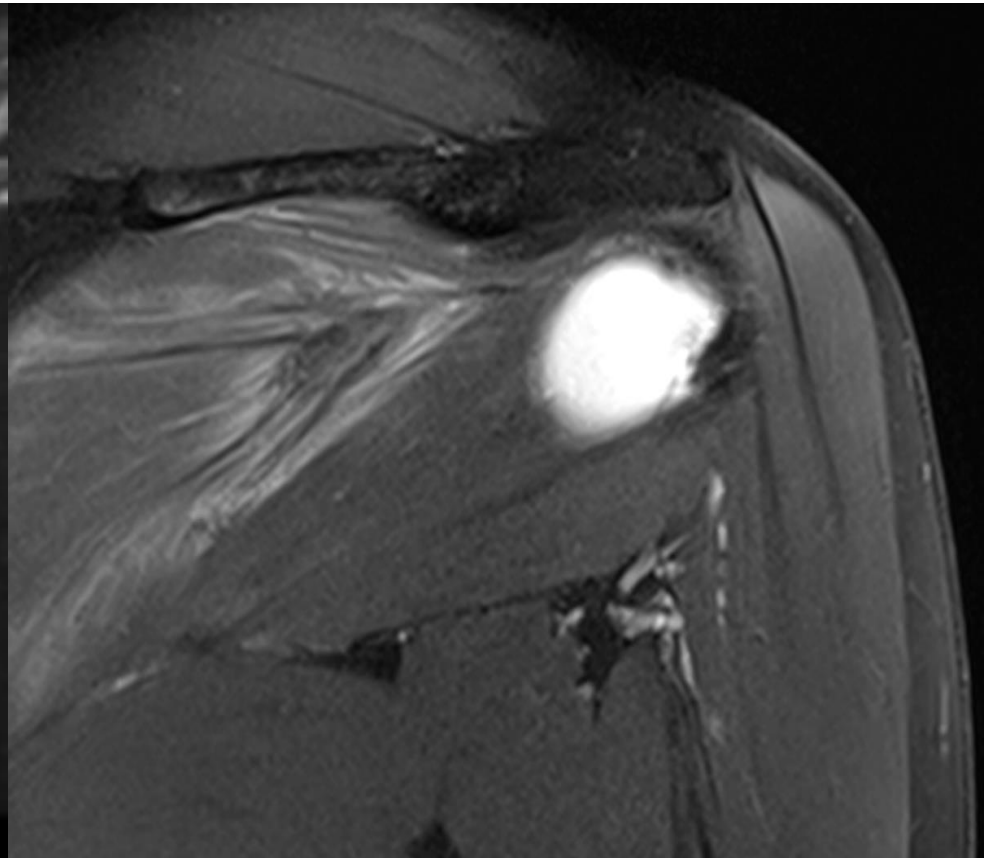
--Characterized by multifocal nerve involvement—especially upper brachial plexus--hourglass constrictions and nerve torsion

--Majority of patients (70%) recover near full nerve function over months

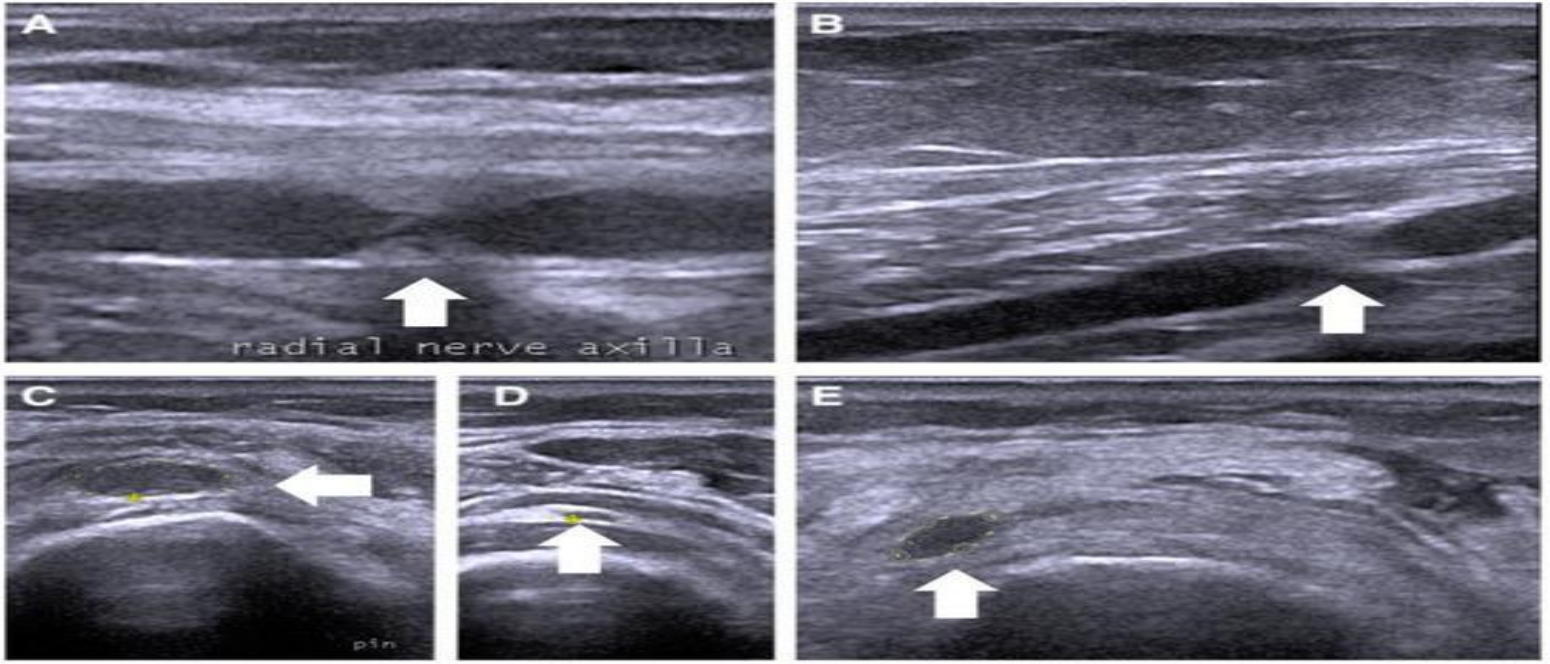
--Failure to improve or severe cases should be referred to tertiary neurology or specialized multidisciplinary nerve centers

MRI





Ultrasound



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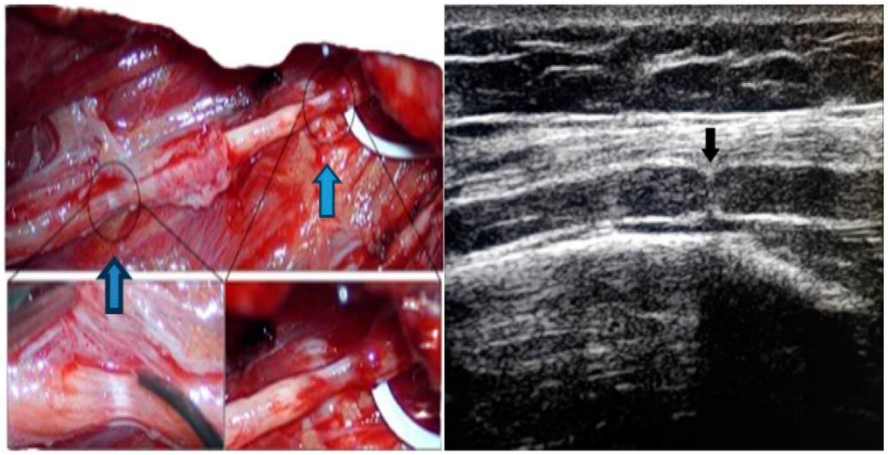
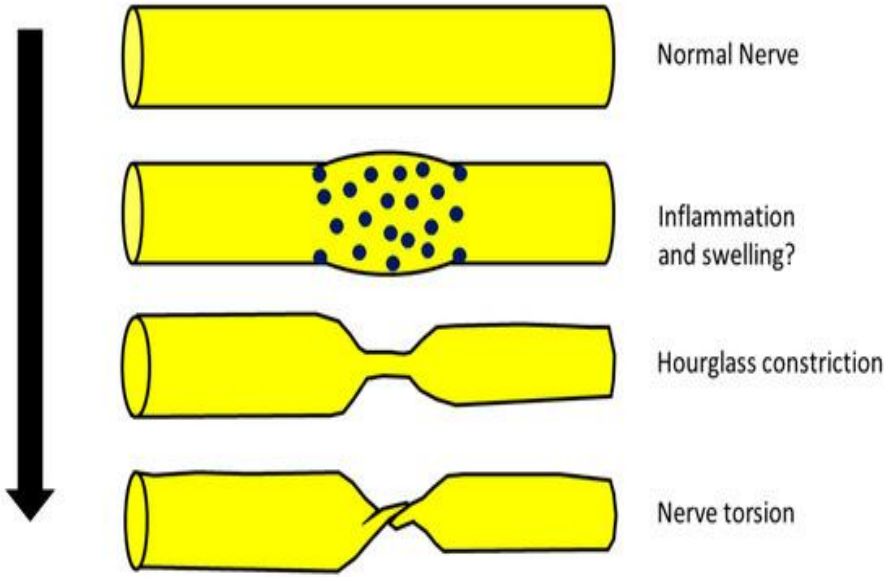
Glorioso, J. Clin. Med 2023



(a) (b)


Normal Nerve
Inflammation and swelling?
Hourglass constriction
Nerve torsion

EMG

Side	Muscle	Nerve	Root	Insertion Activity	Fibrillation Potential	Positive Sharp Waves	Amplitude	Duration	Polyphasic Potentials	Recruitment Ratio	Interference Pattern
Right	Infraspinatus	Suprascapular	C5-6	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml
Right	Flexor carpi radialis	Median	C8-T	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml
Right	**Biceps**	**Musculocutaneous**	**C5-6**	**Nml**	**Nml**	**1+***	**Nml**	**Nml**	**0**	**Nml**	**Nml**
Right	Trapezius	Spinal accessory	Cranial nerve XI, C3-4	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml
Right	Rhomboid Major	Dorsal scapular	C5	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml
Right	Supraspinatus	Suprascapular	C5-6	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml
Right	Latissimus dorsi	Thoracodorsal	C6-8	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml
Right	**Serratus anterior**	**Long thoracic**	**C5-7**	**Nml**	**Nml**	**2+***	**Nml**	**Nml**	**0**	**Reduced**	**Nml**
Right	1st Dorsal Interosseous	Ulnar	C8-T1	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml
Right	Triceps	Radial	C6-7-8	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml
Right	Deltoid	Axillary	C5-6	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml

Abbreviation: Nml, normal.

* Positive sharp waves (fibrillations) of the musculocutaneous and long thoracic nerves and reduced recruitment of the serratus anterior are denoted in bold.

DDX

--Cervical radiculopathy

--Shoulder pathology (RTC, Frozen shoulder)

--Brachial plexus pathology

--Vasculitic neuropathy

--Motor neuron disease

Side	Muscle	Nerve	Root	Insertion Activity	Fibrillation Potential	Positive Sharp Waves	Amplitude	Duration	Polyphasic Potentials	Recruitment Ratio	Interference Pattern
Right	Infraspinatus	Suprascapular	C5-6	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml
Right	Flexor carpi radialis	Median	C6-7	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml
Right	**Biceps**	**Musculocutaneous**	**C5-6**	**Nml**	**Nml**	**1+***	**Nml**	**Nml**	**0**	**Nml**	**Nml**
Right	Trapezius	Spinal accessory	Cranial nerve XI, C3-4	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml
Right	Rhomboid Major	Dorsal scapular	C5	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml
Right	Supraspinatus	Suprascapular	C5-6	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml
Right	Latissimus dorsi	Thoracodorsal	C6-8	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml
Right	**Serratus anterior**	**Long thoracic**	**C5-7**	**Nml**	**Nml**	**2+***	**Nml**	**Nml**	**0**	**Reduced**	**Nml**
Right	1st Dorsal interosseous	Ulnar	C8-T1	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml
Right	Triceps	Radial	C6-7-8	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml
Right	Deltoid	Axillary	C5-6	Nml	Nml	Nml	Nml	Nml	0	Nml	Nml

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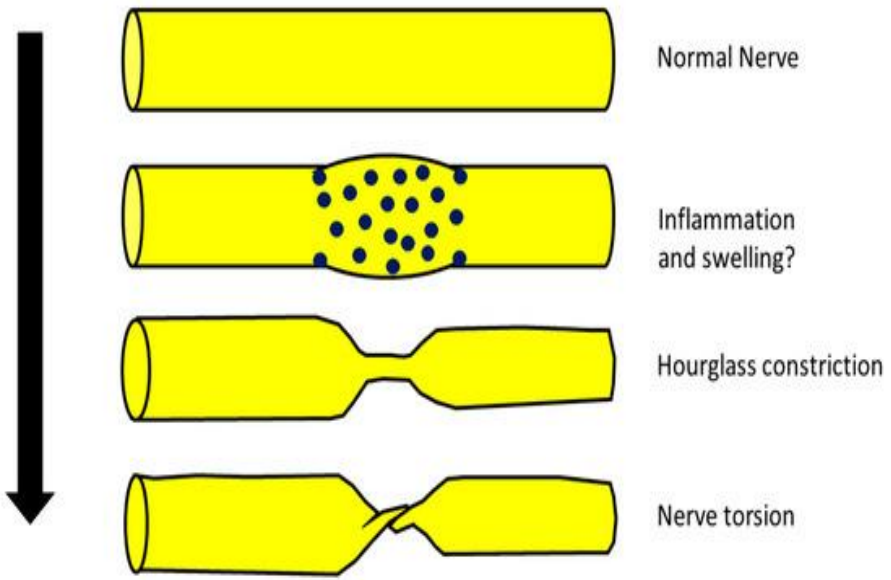
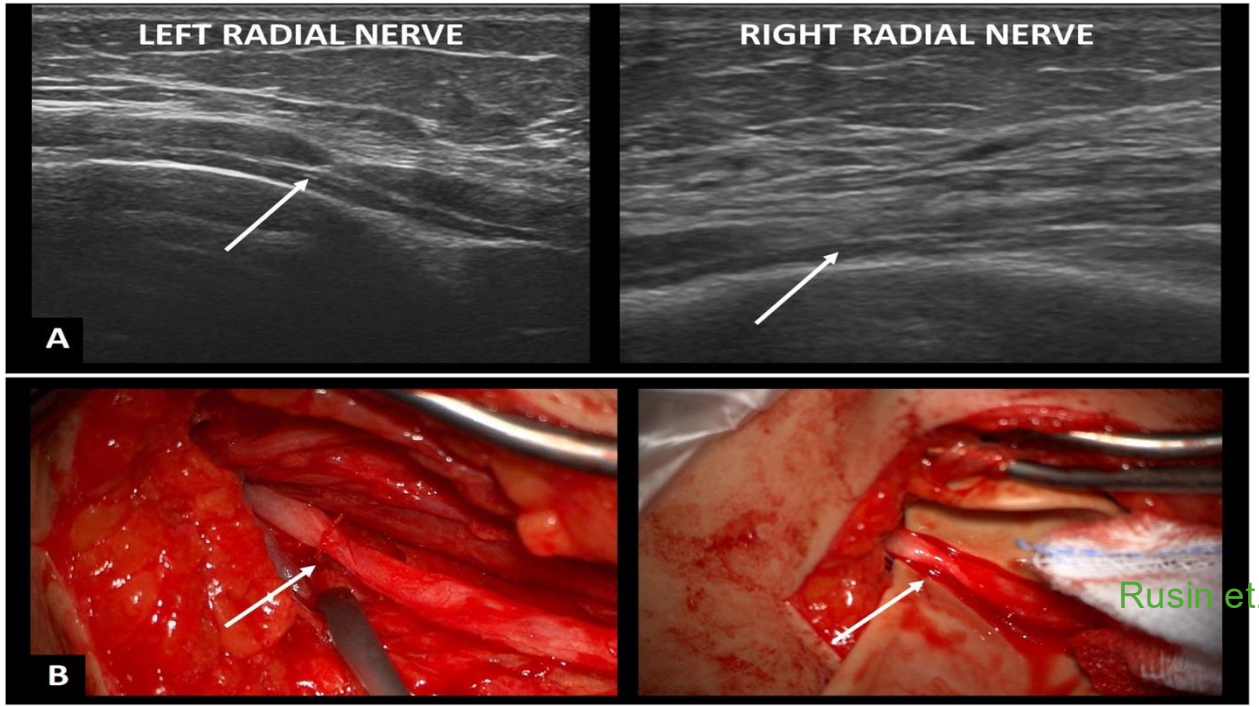


Hereditary Neuralgic Amyotrophy



Rusin et. Al Neurologia 2023

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HNA

--Average age of onset 20

--Diaphragmatic involvement suggestive

--Recurrence rate 75%

--Often involves nerves less typical in NA including lower extremities, lower plexus

--phenotype may include narrow set eyes, skin folds on skin of neck or scalp, cleft palate

--Associated with mutation of SEPT9 gene

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Case #2

49 y.o. man with history of IDDM and hypercholesterolemia on atorvastatin x 2 years presents with 2 months of diffuse muscle weakness and pain. CPK 16,000.

Statins were stopped without clinical improvement. Follow up 2 weeks later: CPK 20,000. CRP=20 Patient unable to walk.

What is the diagnosis?

Statin-induced necrotizing myopathy

AKA Imune Mediated Necrotizing Myopathy

--diagnosis: anti-HMGCOa Reductase AB

--Very elevated CPK

--Muscle pain and weakness

--Does not improve after d/c statin

--Treatment is immunosuppression, steroid, IVIG, ritixumab. Long-term treatment is often required

Table 1: Necrotising Autoimmune Myopathy	
Clinical presentation	Subacute proximal muscle weakness Additional symptoms: dysphagia, dyspnoea, myalgia Markedly elevated creatine kinase
Biopsy findings	Myocyte necrosis and regeneration Minimal or absent inflammatory cell infiltrate MHC-I immunostaining
Associations	Anti-HMGCR antibody (with statin exposure or statin naïve) Anti-SRP antibody Malignancy Connective tissue disease
Treatment	Prednisolone Steroid-sparing agents (methotrexate, azathioprine, mycophenolate) IVIG Rituximab
Poor prognostic features	Statin naïve anti-HMGCR positive Anti-SRP positive Possibly MHC-II and MAC immunostaining on biopsy

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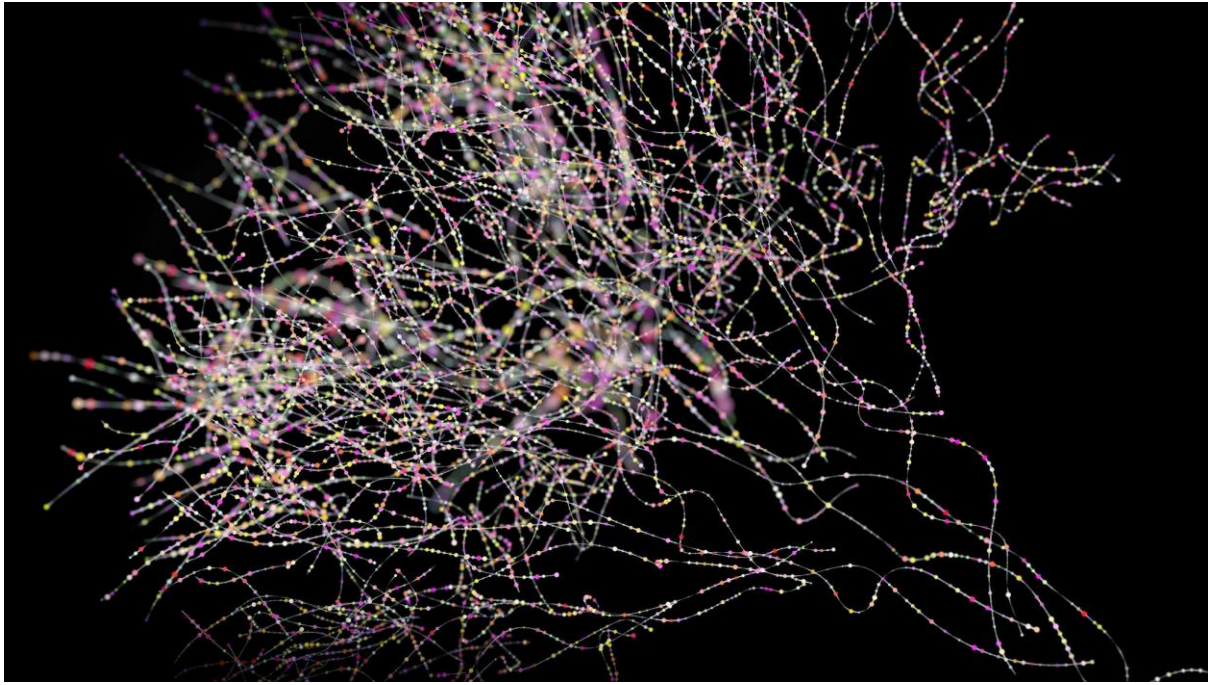
Thank you!



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