HEADACHE IN CLINICAL CASES

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GOAL

INCORPORATE BEST AVAILABLE TREATMENT PROTOCOLS IN THE MANAGEMENT OF PEOPLE LIVING WITH HEADACHE

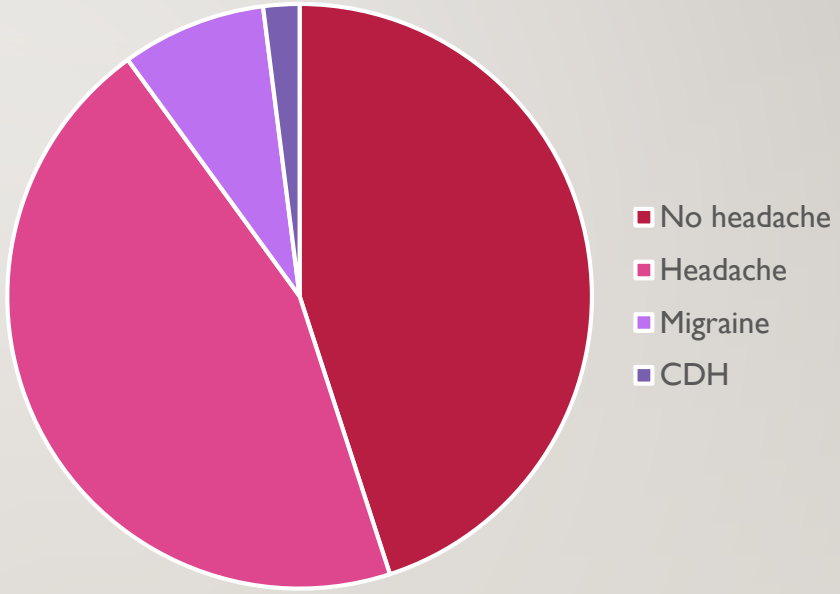
Nina Riggins, MD, PhD

3 BY THE END OF THIS SESSION, PARTICIPANTS WILL BE ABLE TO:

- List patient-centered ways to optimize evidence-based Headache treatment plans.
- Apply an understanding of migraine pathophysiology to the effective management of the patients with Migraine.
- Describe advancements in preventive and acute management of primary headaches.
- Formulate future directions of research in the field of migraine and other headache disorders.

Pediatric Epidemiology

- Headache ~ 54.5%
  - 59.2% of girls
  - 49.3% of boys
- Migraine ~ 9.1%
  - 10.5% of girls
  - 7.6% of boys
- Chronic Daily Headache ~1.7%-3.5%



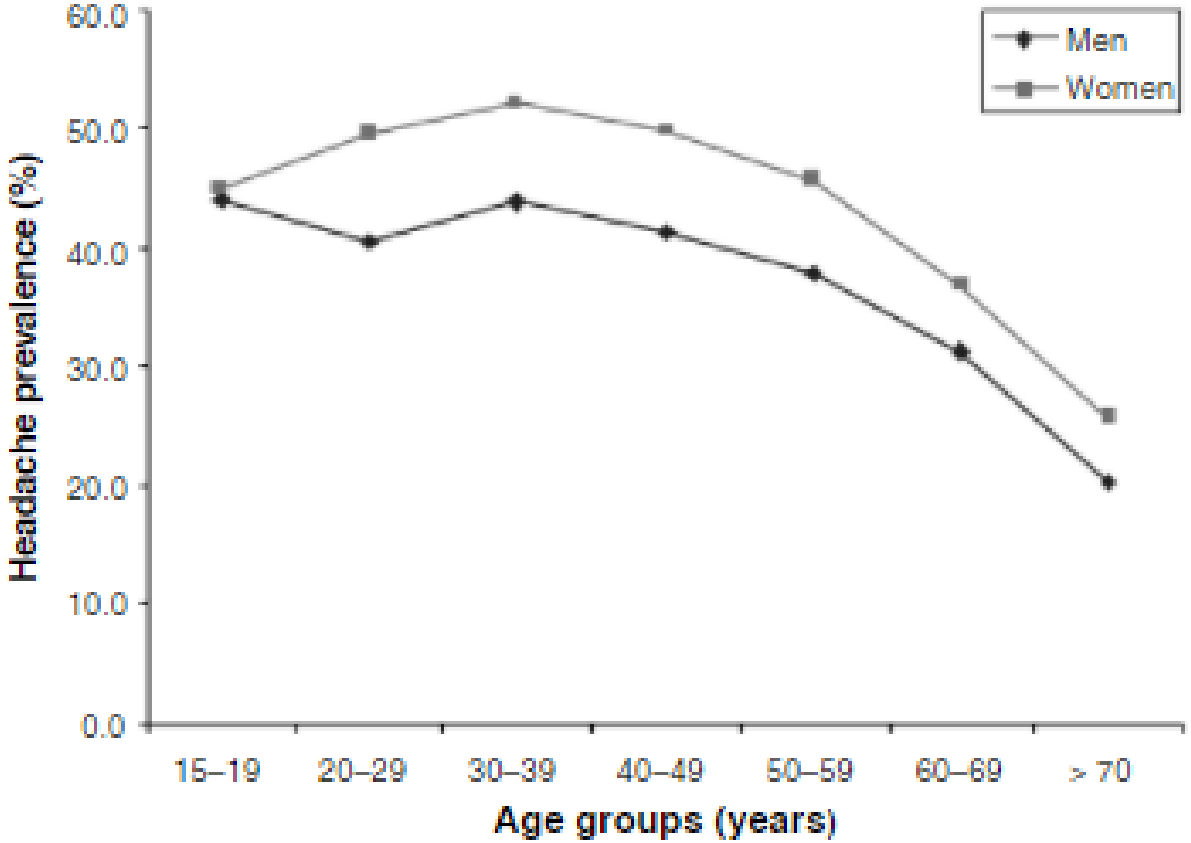
Wober-Bingol, 2013

Adult Epidemiology

- Migraine
  - 12% of Americans
    - Chronic Migraine: 2% of Americans
  - Over 36 million individuals
  - 1 in 4 households
  - In adults, more common in women (18%) than men (6%)

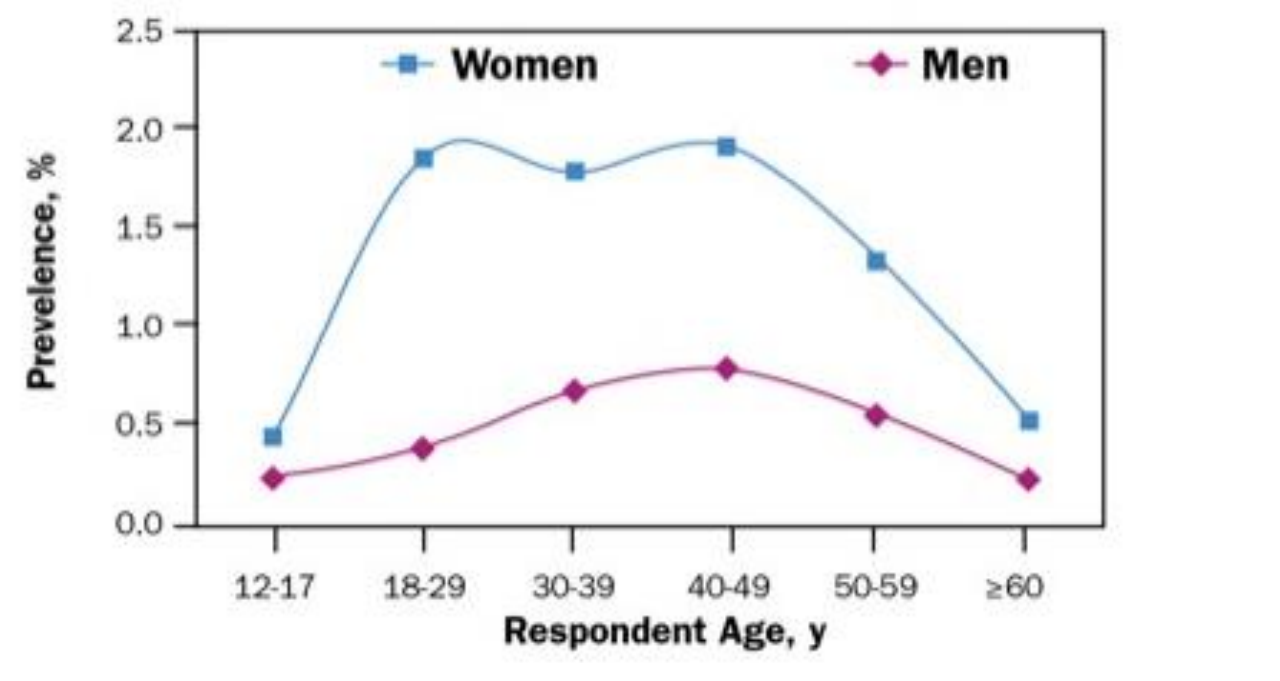
Lipton, 2001; Robbins & Lipton, 2010; GBD, 2010

- Headache lifetime prevalence: 46%
- Peaks in 30s-40s, then declines



Stovner, Lars Jacob, et al. "Epidemiology of headache in Europe." *European journal of neurology* 13.4 (2006): 333-345.

Prevalence across the lifespan



Lipton, 2001

ICHD-3: THE INTERNATIONAL CLASSIFICATION OF HEADACHE DISORDERS 3RD EDITION

- ICHD-3 is published as the first issue of *Cephalalgia* in 2018, exactly 30 years after the first edition of the *International Classification of Headache Disorders*, ICHD-I as we now call it

ICHD -3 THE INTERNATIONAL CLASSIFICATION OF HEADACHE DISORDERS 3RD EDITION

- Part 1- Primary Headaches (Migraine, Cluster)
- Part 2- Secondary Headache due to another disorder (attributed to cranial or cervical vascular disorder, to infection, to substance or its withdrawal)
- Part 3- Neuropathies and facial pains (Example – trigeminal neuralgia attributed to multiple sclerosis, post-herpetic trigeminal neuralgia)
- Part 4 – Appendix – is for research, future studies

ICHD-3
PART ONE: THE PRIMARY HEADACHES

- 1. Migraine
- 2. Tension-type headache
- 3. Trigeminal autonomic cephalalgias
- 4. Other primary headache disorders

MIGRAINE: WITH AURA (~30%) AND WITHOUT AURA (~70 %)

Attacks last 4-72 hours (Kids: 2-72 hours)	Headache has 2 of 4 features:	Headache is accompanied by either:
	• Unilateral location • Pulsating quality • Moderate to severe pain • Aggravates/prevents physical activity	• Nausea and/or vomiting • Photophobia and phonophobia

HEMIPLEGIC MIGRAINE FAMILIAL AND SPORADIC

- 1. CACNA1A
- 2. ATP1A2
- 3. SCN1A
- 4. Sporadic hemiplegic migraine

DIFFERENTIAL DIAGNOSIS – HEMIPLEGIC MIGRAINE – TIA/STROKE, SEIZURE ETC.

SYNDROME OF TRANSIENT HEADACHE AND NEUROLOGICAL DEFICITS WITH CEREBROSPINAL FLUID LYMPHOCYTOSIS (HANDL)

TENSION-TYPE HEADACHE DIAGNOSIS

At least 10 episodes of headache occurring on <1 day per month on average	Lasting 30 minutes-7days	Characteristics (at least 2)	Both of the following
		• Bilateral • Pressing/tightening quality • Mild-moderate intensity • Not aggravated by routine physical activity	• No nausea/vomiting • Not more than one of sensitivity to light and sound

CASE

30 y of age female is in the medical office with chief complaint of headache.

SYMPTOMS

- Intensive Headache on one side of the head
- Pulsating
- Sensitivity to light and sound
- Nausea and sensitivity to movement with headache attacks
- One Headache attack lasts for about 8 hours
- Not at night
- She has most intensive headache at about 2 pm

HISTORY OF HEADACHE

Onset -13 y of age

Migraine onset at menarche (about 33 %)

60-70 % of migraine attacks associated with menses

Maturitas. 2020;142:24-30.
Semin Thromb Hemost. 2011;37:77-86

HEADACHE DIARY

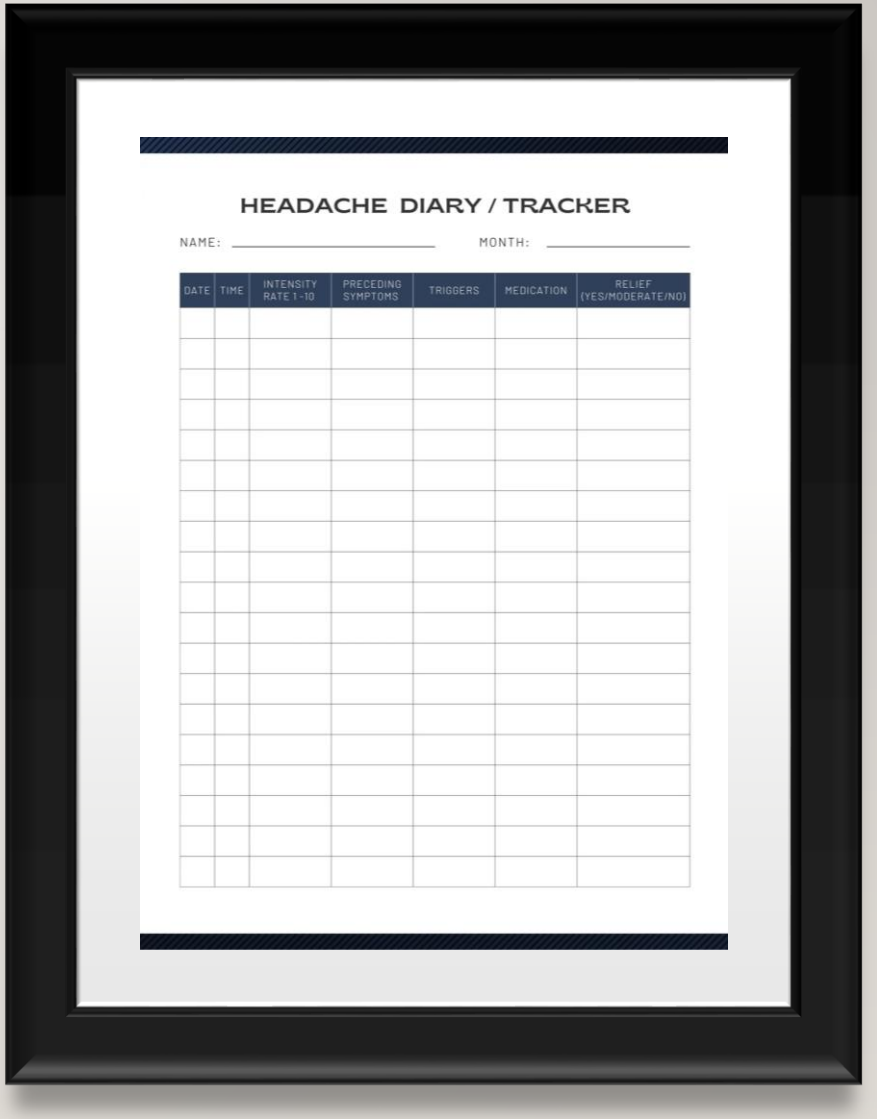
- Multicentre European and Latin American study

- Jensen R et al multicentre European and Latin American study. Cephalalgia. 2011 Nov;31(15):1549-60. doi: 10.1177/0333102411424212. Epub 2011 Oct 21. PMID: 22019575.

HEADACHE DIARY

- 626 patients from nine countries and 16 centres
- 2 groups: Headache Diary and No Headache Diary
- The Headache Diary prior to new patient visit were complete in 97.5% of cases
- Headache diary group: info complete for diagnosis in 97.7% of cases
- No Headache diary group: clinical interview alone - in only 86.8% of cases ($p < 0.001$).
- Headache diary was very well accepted by both patients and medical care providers.

HEADACHE FREQUENCY INCREASED GRADUALLY DURING LAST 3 MONTHS FROM 5 DAYS A MONTH TO 14 DAYS A MONTH



TRIGGERS

- Changes in sleep
- Hunger
- Dehydration
- Menstrual cycle
- Weather changes
- Alcohol
- Stress

WHAT MAKES IT BETTER

- Laying down in the dark room
- Hydration

PAST MEDICAL HISTORY

- Kidney Stones
- Obesity
- Covid 19 – in 2020

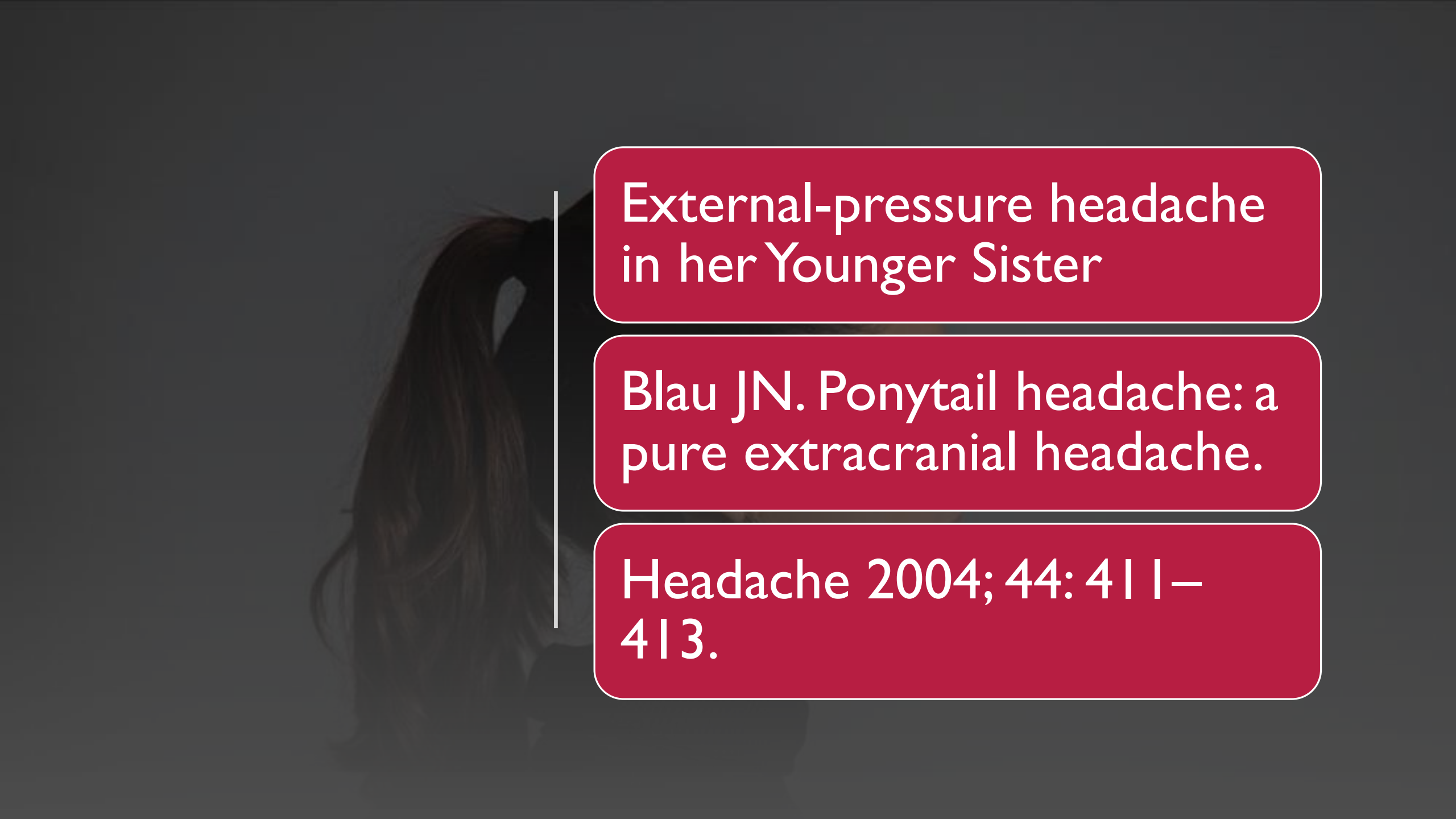
HEADACHE AMONG PATIENTS WITH COVID-19

- Headache among patients with Covid 19 in hospitals – may be a marker of host processes which enhance Covid 19 survival
- ~10 % inpatients report headache ~ twice as likely to survive (with Covid -19)

- Gallardo, VJ, Shapiro, RE, Caronna, E, Pozo-Rosich, P. The relationship of headache as a symptom to COVID-19 survival: A systematic review and meta-analysis of survival of 43,169 inpatients with COVID-19. *Headache*. 2022; 00: 1- 10. doi: 10.1111/head.14376

FAMILY HISTORY

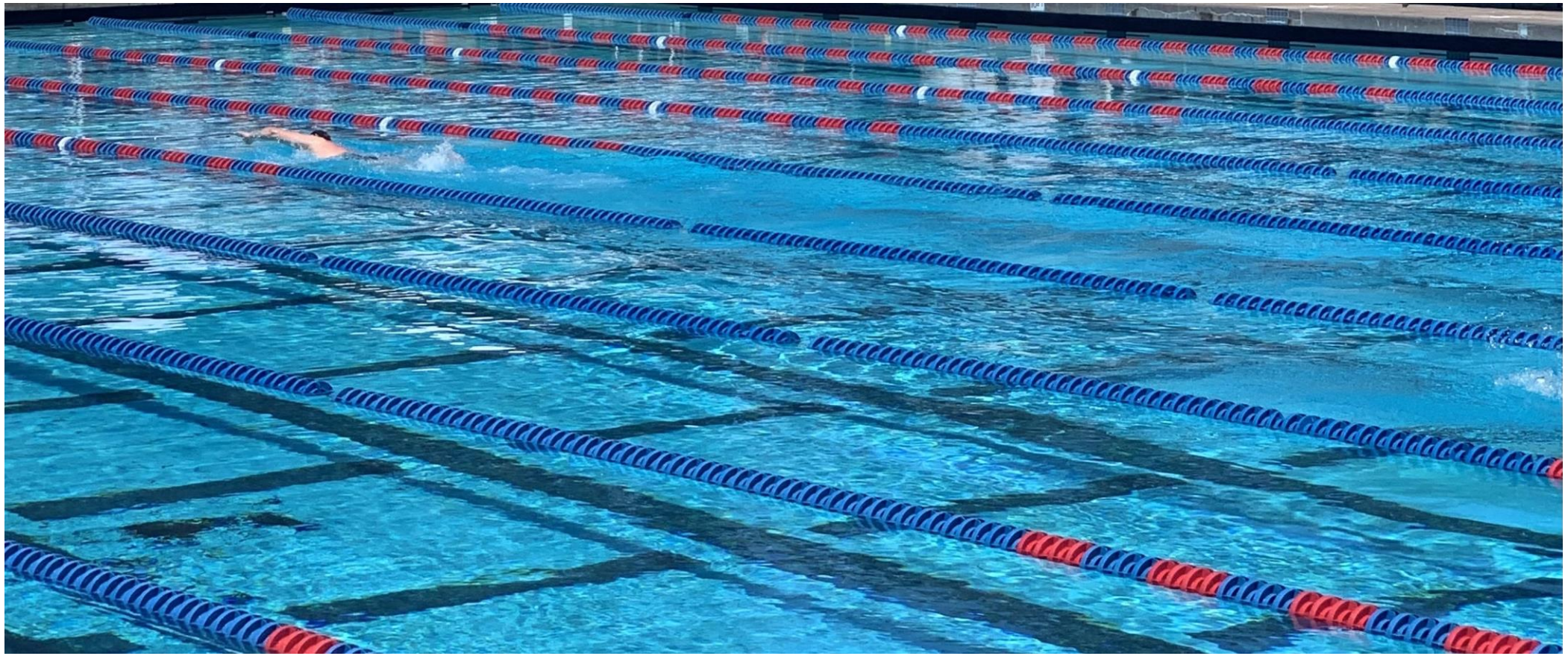
- Mother and Older Sister have Migraine



External-pressure headache in her Younger Sister

Blau JN. Ponytail headache: a pure extracranial headache.

Headache 2004; 44: 411–413.



INFANT COLIC, OR EXCESSIVE CRYING

- Cross-sectional online survey study of biological parents
- 1,715 surveys
- Maternal migraine was associated with increased odds of infant colic - OR 1.7 (1.3-2.4)
- Gelfand, A.A et al. Headache: The Journal of Head and Face Pain, 59: 988-1001. https://doi.org/10.1111/head.13575

MIGRAINE GENES

Genome-wide analysis of 102,084 migraine cases identifies 123 risk loci and subtype-specific risk alleles

More to learn!

Nature genetics
https://doi.org/10.1038/s41588-021-00990-0

HAROLD G. WOLFF LECTURE AWARD FOR THE BEST PAPER, AHS 2022

- Complexity of neuronal pathways changes with disease – including migraine
- NTG model: previously showed decreased neuronal complexity in the trigeminal nucleus caudalis (TNC) and periaqueductal gray (PAG).
- In contrast, found increased neuronal complexity in the thalamus
- Restoration of this neuronal complexity corresponds with anti-migraine effects of known and experimental pharmacotherapies

- Bertels Z, Mangutov E, Conway C, Siegersma K, Asif S, Shah P, Huck N, Tawfik VL, Pradhan AA. Migraine and peripheral pain models show differential alterations in neuronal complexity. Headache. 2022 Jul;62(7):780-791. doi: 10.1111/head.14352. Epub 2022 Jul 13. PMID: 35676889.

SOCIAL HISTORY

- She is a school nurse
- One glass of wine a week
- No tobacco
- Married with 2 kids

(5 and 7 y of age)

ASKING ABOUT MARIJUANA USE (SOCIAL HISTORY)

- **Cardiovascular Pharmacology of Cannabinoids is complex**

The most common chemicals in cannabis:

- THC (tetrahydrocannabinolic acid), the component of the plant that induces a "high"

THC also appears to stimulate the sympathetic nervous system, which is responsible for the "fight or flight" response

- CBD (cannabidiol)

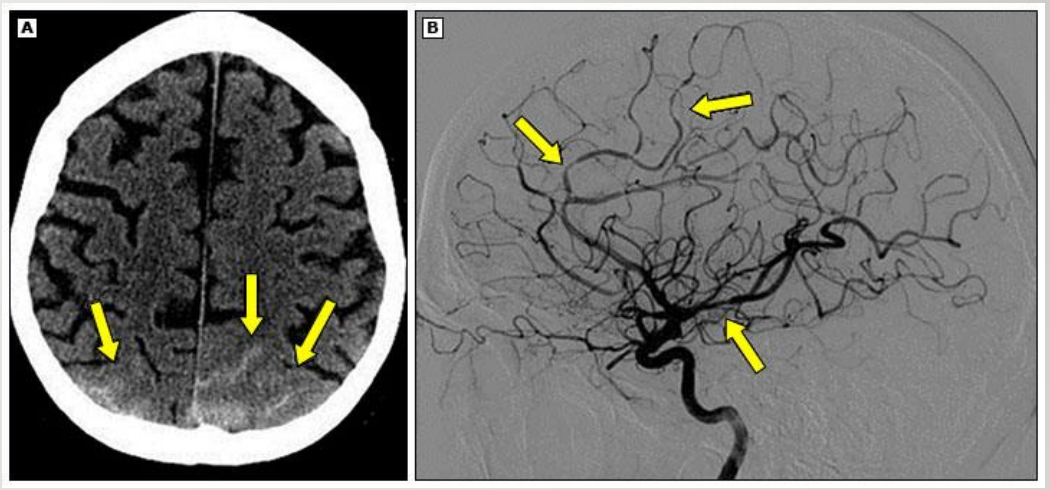
does not produce a "high" or intoxication

associations with reduced heart rate, lower blood pressure, increased vasodilation

❑ American Heart Association Scientific Statement, Aug 2020

REVERSABLE CEREBRAL VASOCONSTRICTION SYNDROME

- with chronic use of cannabis and toxicity ->cyclical hyperemesis
- compulsive bathing in hot water
- autonomic symptoms of sweating, flushing, thirst, abdominal pain, and alterations in body temperature



Uhegwu N, Bashir A, Hussain M, Dababneh H, Misthal S, Cohen-Gadol A. Marijuana induced Reversible Cerebral Vasoconstriction Syndrome. J Vasc Interv Neurol. 2015 Feb;8(1):36-8. PMID: 25825630; PMCID: PMC4367805.

SOCIAL HISTORY

- No use of Marijuana in this patient

EXAM AND TESTS

- Neurologic exam
- Imaging
- Lab work
- ECG

MIGRAINE: WITH AURA (~30%) AND WITHOUT AURA (~70 %)

- Attacks last 4-72 hours (Kids: 2-72 hours)
- Headache has 2 of 4 features:
  - Unilateral location
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- Headache is accompanied by either:
  - Nausea and/or vomiting
  - Photophobia and phonophobia

HOME MEDICATIONS

- Amitriptyline 75 mg → palpitations and weight gain
- Intrauterine device
- Naproxen for "as needed" headache on 3 days a week
- Semaglutide Once a week injectable to assist her long-term weight management → increase in headache frequency

SEMAGLUTIDE

- Glucagon-like peptide-1 (GLP-1) receptor agonists
- Class of antidiabetic medications
- Weight loss in patients with or without type 2 diabetes
- Augmenting insulin secretion
- Vasodilatory actions are being studied

- Singh G et al. J Investig Med. 2022 Jan;70(1):5-13. doi: 10.1136/jim-2021-001952. Epub 2021 Oct 27. PMID: 34706925; PMCID: PMC8717485.

SEEDS FOR SUCCESS

mnemonic

- Sleep
- Exercise
- Eat
- Diary
- Stress

- Robblee J, Starling AJ. SEEDS for success: Lifestyle management in migraine. Cleve Clin J Med. 2019

ONABOTULINUMTOXINA

- Patient is asking if she should have OnabotulinumtoxinA

- Possibly reduction of pre-existing inflammation -> reduction in abundance of immune cells in the calvarial periosteum
- OnabotulinumtoxinA – for chronic migraine

- Lisa Gfrerer, Wenjie Xu, William Austen, Jr, Sait Ashina, Agustin Melo-Carrillo, Maria Serena Longhi, Aubrey Manack Adams, Timothy Houle, Mitchell F Brin, Rami Burstein, OnabotulinumtoxinA alters inflammatory gene expression and immune cells in chronic headache patients, *Brain*, Volume 145, Issue 7, July 2022, Pages 2436–2449, https://doi.org/10.1093/brain/awab461

ARE THERE MEDICATIONS WHICH CAN HELP HEADACHE AND WEIGHT LOSS?

- Topiramate -→ Side effects include kidney stones
- Atogepant

- Once-daily atogepant was associated with modest (-1.57%) but clinically relevant weight loss compared with placebo or standard care

ATOGEPANT

“Does The Migraine Treatment Atogepant Make You Lose Weight? “

- MigraineAgain
- NeurologyLive
- New ad hoc data presented at the American Headache Society (AHS) Annual Scientific Meeting on June 11, 2022, in Denver (David W. Dodick et al)
- More weight loss on 60 mg Daily dose

GEPANTS

- Calcitonin gene-related peptide receptor antagonists
- "Acute targets might also function as preventive targets"

- Ferrari MD, Goadsby PJ, Burstein R, Kurth T, Ayata C, Charles A, Ashina M, van den Maagdenberg AMJM, Dodick DW. Migraine. Nat Rev Dis Primers. 2022 Jan 13;8(1):2. doi: 10.1038/s41572-021-00328-4. PMID: 35027572

ATOGEPANT

- Small-molecule, calcitonin gene-related peptide (CGRP) receptor antagonist
- Approved in the USA by FDA for the preventive treatment of episodic migraine in adults

AT THE FOLLOW UP VISIT IN 3 MONTHS

- Discontinued Amitriptyline and medication for weight loss
- On Atogepant
- Naproxen 440 mg once a week for "as needed" Headache
- Keeping headache diary
- Started exercise program and achieving her goals for weight loss
- Headache is improving in frequency and intensity

MIGRAINE

1 in 4 households affected by Headache in US

Billion people live with Migraine worldwide

We are working on solutions together!

Lancet Neurol. 2018;17:954-976; *Neurology*. 2007;68:343-9; *Curr Pain Headache Rep*. 2013;17:341

DIAGNOSTIC CRITERIA FOR CLUSTER HEADACHE

- A At least five attacks fulfilling criteria B-D
- B Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15-180 minutes (when untreated)
- C Either or both of the following:
  - 1 at least one of the following symptoms or signs, ipsilateral to the headache:
    - – conjunctival injection and/or lacrimation
    - – nasal congestion and/or rhinorrhoea
    - – eyelid oedema
    - – forehead and facial sweating
    - – miosis and/or ptosis
  - 2 a sense of restlessness or agitation
- D Occurring with a frequency between one every other day and 8 per day
- E Not better accounted for by another ICHD-3 diagnosis.

CHRONIC CLUSTER HEADACHE

- Cluster headache attacks occurring for one year or longer without remission, or with remission periods lasting less than 3 months.

EPISODIC CLUSTER HEADACHE

- Cluster headache attacks occurring in periods lasting from 7 days to one year, separated by pain-free periods lasting at least 3 months.

- **Comment:**
- Cluster periods usually last between 2 weeks and 3 months.

CASE

- 47 y old right-handed man with one-sided headache which re-started 5 weeks ago

CASE

- Similar headache episodes :
- 2 years ago, and 4 years ago for about 1 month
- In the past: Headache went away when he took course of Verapamil and had some injection on the back of his head in pain management clinic.
- 2 months ago, he changed his Verapamil to ER

CASE

- Time of Headache attacks:
- In about 1 hour after he goes to sleep
- During the day “at about noon “

CASE

- **Triggers**

- Alcohol is the strongest trigger, he can not drink any alcohol when he is in “cycle” of his headache
- Stress
- Changes in his sleep “too little”, “too much”

CASE CONTINUED

- Attacks of headache is very stereotypical
- Pain is around right eye
- He has ptosis, lacrimation and nasal congestion on the right side with attacks, His right eye is red, he feels restless, agitated during attacks
- Rapid onset of attacks
- They last 45-60 min (up to 90 min)

CLUSTER HEADACHE

- Cluster headache is a stereotypic, primary headache disorder that is marked by repeated short-lasting attacks of severe, unilateral head pain and associated autonomic symptoms. Cluster headache is probably due to an abnormality in the circadian hypothalamic generator with subsequent trigeminovascular activation.

Periodicity -

Result of dysfunctional Hypothalamus

Cluster Headache

DW Dodick, TD Rozen, PJ Goadsby, ...

First Published November 1, 2000 Research Article Find in PubMed

https://doi.org/10.1046/j.1468-2982.2000.00118.x

CASE/CONTINUED FAMILY HISTORY

- Headache in Mother, he believes it is Migraine and she treats it with Sumatriptan few days a month

CLUSTER HEADACHE: WHAT ROLE DOES FAMILY HISTORY PLAY

- Systematic review of 40 articles.
- Publications from 1985 to 2016, were obtained from PubMed, Embase, and Cochrane Library. A total of 22 large cohort studies, 1 twin-based study, and 17 case reports or small case series were included in the analysis.

- **Reference:**
Waung MW, Taylor A, Qualmann KJ, Burish MJ. Family history of cluster headache: a systematic review [Published online April 20, 2020]. *JAMA Neurol*. doi:10.1001/jamaneurol.2020.0682

"CLUSTER HEADACHE IS AN INHERITED DISORDER IN A SUBSET OF FAMILIES AND IS ASSOCIATED WITH MULTIPLE HEREDITARY PATTERNS,"

"There is an unexpectedly high preponderance of women and girls with familial cluster headache; genetic subanalyses limited to female participants are necessary to further explore this observation, because these data are otherwise masked by the higher numbers of male participants with cluster headache,"

Reference:
Waung MW, Taylor A, Qualmann KJ, Burish MJ. Family history of cluster headache: a systematic review [Published online April 20, 2020]. *JAMA Neurol*. doi:10.1001/jamaneurol.2020.0682

PAST MEDICAL HISTORY

- HTN – he is on Verapamil ER 40 mg BID daily
- Hypothyroidism – he is on Levothyroxine 25 mcg daily
- Seasonal allergy – he is on Flonase nasal spray daily

HOME MEDICATIONS

- Verapamil ER 40 mg BID
- Levothyroxine 25 mcg Daily
- Sumatriptan 6 mg SC injections – PRN headache, stops headache within 10 min – prescribed by primary care doctor , used daily during last week
- Past medical trials
- Steroids did not help his headache in the past – had 2 courses of prednisone PO

REVIEW OF SYSTEMS

- He has no asthma, no chest pains, no history of GI ulcers
- He reports that he has insomnia and feels anxious due to stress at his work

SOCIAL HISTORY

- No history of smoking, used marijuana back in college
- Alcohol – not now, but before cycle of headache, he used to drink glass of wine 2 days a week
- He works for IT company and reports that he works long hours, it is stressful

TESTS

- Imaging – MRI/A brain and MRA neck are normal
- Pituitary view on MRI brain – normal

ECG – HR 72, sinus rhythm with PR interval NL

Lab work – he had pituitary function tests, CBC, CMP, ESR with his PCP office and has low TSH with NL free T3 and T4

TESTS

"Neuroimaging should be considered in all patients with CCH, especially those with an atypical presentation or evolution. Response to acute treatment does not exclude a secondary form of cluster headache. There may be shared pathophysiological mechanisms of primary and secondary cluster headache"

- Annelien De Pue,
- Bart Lutin &
- Koen Paemeleire
- *The Journal of Headache and Pain* **volume 17**, Article number: 23 (2016)

SECONDARY HEADACHES MIMIC CLUSTER:

- ◆ Acute-angle glaucoma
- ◆ Impacted molar tooth
- ◆ Maxillary sinusitis
- ◆ Tolosa-Hunt syndrome
- ◆ Temporal arteritis
- Causes of Symptomatic Cluster Headache
- ◆ Neoplastic
- ◇ Pituitary tumors
- ◇ Meningioma
- ◇ Glioblastoma

Continuum, July 2018
Burish M. Cluster Headache and Other Trigeminal Autonomic Cephalalgias. 24(4):1137-1156.

VASCULAR AND OTHER SECONDARY HEADACHES MIMICKING CLUSTER HEADACHE

- ◇ Carotid or vertebral artery dissection
- ◇ Cerebral arteriovenous malformations
- ◇ Stroke (in setting of moyamoya disease)
- ◇ Subclavian steal syndrome
- ◆ Infectious
- ◇ Sinusitis
- Continuum, July 2018 Burish M. Cluster Headache and Other Trigeminal Autonomic Cephalalgias. 24(4):1137-1156.

ACUTE TREATMENT CLUSTER HEADACHE

- Oxygen –100% via a nonrebreather
- mask at a rate of 12 L/min to 15 L/min for at least 20 minutes
- Sumatriptan, other triptans
- DHE
- Lidocaine Spray In the past, now – SPG blocks
- nVNS

TRIPTANS

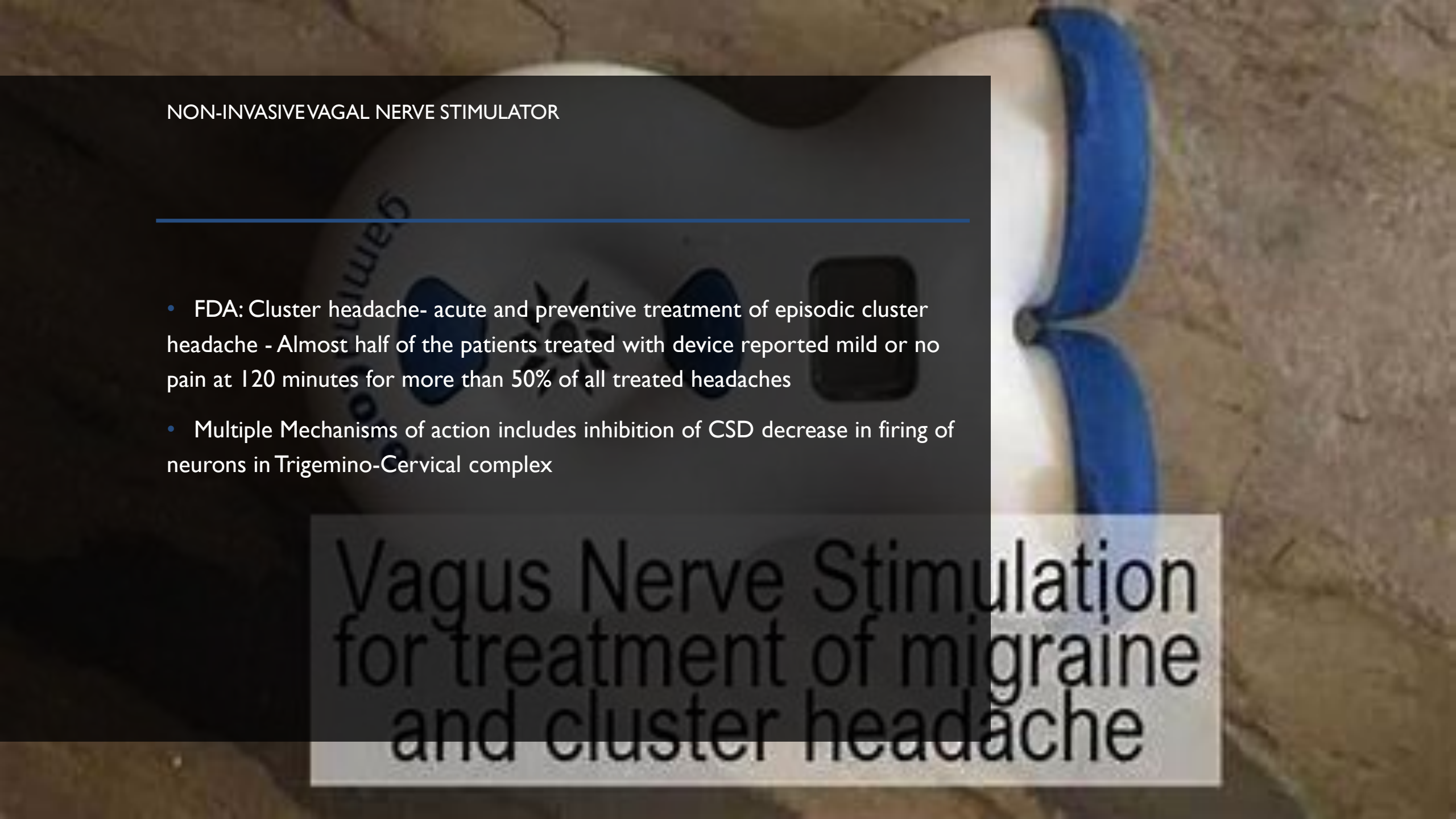
- Many of our Headache patients still describe discovery of triptans as event that transformed their life (triptans were first introduced for medical use in 1990s)
- Triptans bind to brain serotonin receptors 5-HT1B /5-HT1D and amplify effects of serotonin, which helps in acute treatment of migraine, cluster. These receptors also present in blood vessels.
- Triptans constrict blood vessels.
- We don't recommend them for patients who are at risk for stroke or have cardiac risk factors.

PREVENTION

- Prednisone - risk of osteonecrosis of the hip, Limit use!
- Li
- Verapamil
- Occipital nerve blocks, SPG blocks
- Galcanezumab
- Melatonin
- Neuroleptics
- Some weaker evidence for Topiramate and Baclofen

NON-INVASIVE VAGAL NERVE STIMULATOR

- FDA: Cluster headache- acute and preventive treatment of episodic cluster headache - Almost half of the patients treated with device reported mild or no pain at 120 minutes for more than 50% of all treated headaches
- Multiple Mechanisms of action includes inhibition of CSD decrease in firing of neurons in Trigemino-Cervical complex



CGRP MODULATION IN MIGRAINE, CLUSTER

- CGRP is protein which levels are elevated in people with migraine and cluster (and higher during attacks)
- Onabotulinum toxin and triptans block CGRP release
- Knowledge about CGRP allows targeted therapy

Goadsby PJ, et al. Ann Neurol 1988

Edvinson L, et al. J Auton Nerv Syst, 1998

GALCANEZUMAB IN CHRONIC CLUSTER HEADCAHE

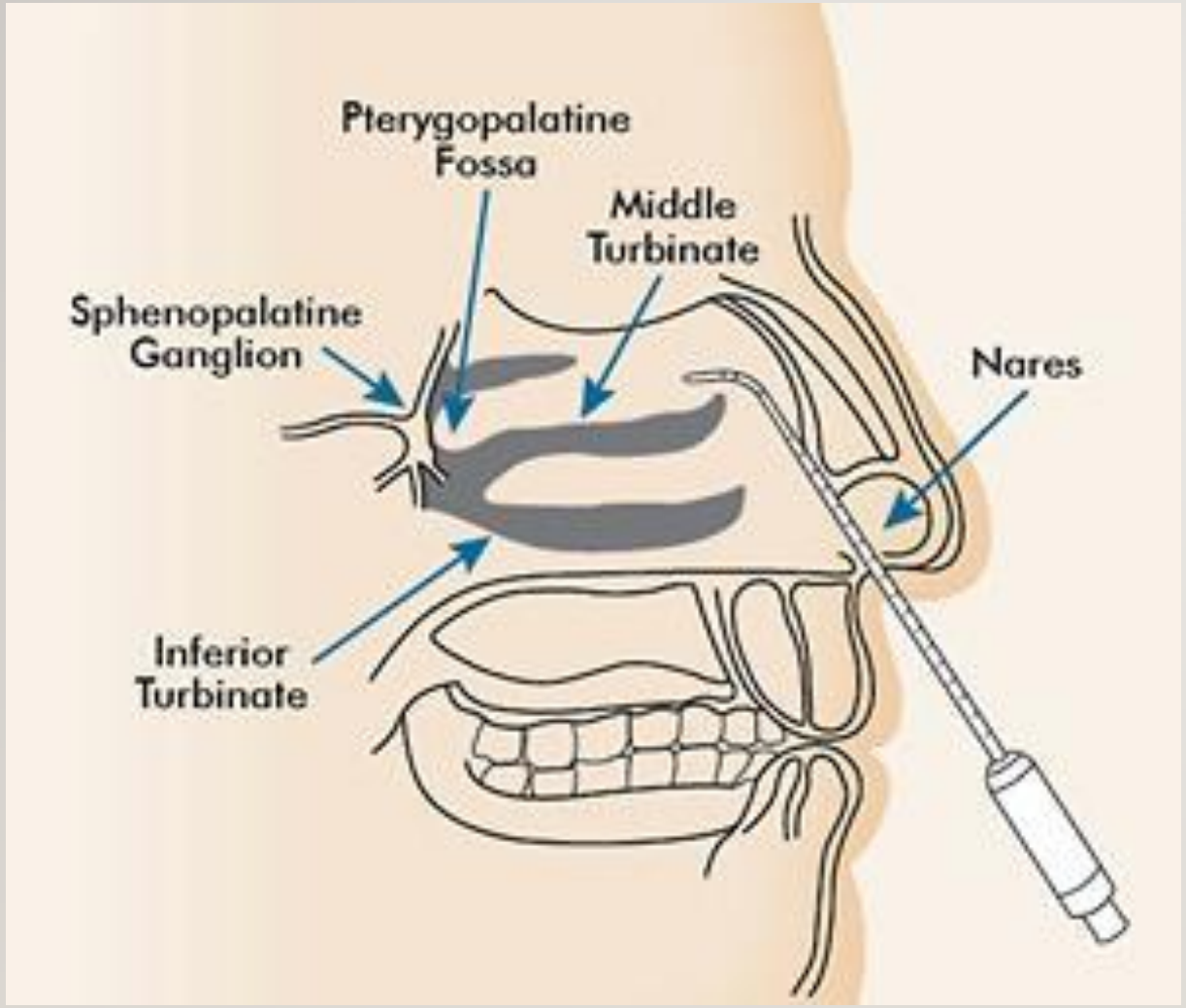
THE PRIMARY ENDPOINT WAS NOT MET; MEAN CHANGE IN WEEKLY ATTACK FREQUENCY WAS -4.6 PLACEBO VERSUS -5.4 GALCANEZUMAB (*P* = 0.334)

- Dodick DW, Goadsby PJ, Lucas C, Jensen R, Bardos JN, Martinez JM, Zhou C, Aurora SK, Yang JY, Conley RR, Oakes T. Phase 3 randomized, placebo-controlled study of galcanezumab in patients with chronic cluster headache: Results from 3-month double-blind treatment. Cephalalgia. 2020 Aug;40(9):935-948. doi: 10.1177/0333102420905321. Epub 2020 Feb 12. PMID: 32050782; PMCID: PMC7787002.

EPISODIC CLUSTER GALCANEZUMAB

- The mean reduction in the weekly frequency across weeks 1 through 3 was 8.7 attacks in the galcanezumab group, as compared with 5.2 in the placebo group (P = 0.04).
- The percentage of patients who had a reduction of at least 50% in headache frequency at week 3 was 71% in the galcanezumab group and 53% in the placebo group.
- There were no substantial between-group differences in the incidence of adverse events

- Goadsby PJ, Dodick DW, Leone M, Bardos JN, Oakes TM, Millen BA, Zhou C, Dowsett SA, Aurora SK, Ahn AH, Yang JY, Conley RR, Martinez JM. Trial of Galcanezumab in Prevention of Episodic Cluster Headache. N Engl J Med. 2019 Jul 11;381(2):132-141. doi: 10.1056/NEJMoa1813440. PMID: 31291515.



PROCEDURES

- SPG blocks – Lidocaine
- Occipital nerve blocks – with steroids

LIDOCAINE NASAL SPRAY WAS BACK DURING PANDEMIC

- Bobker SM, Ehrlich A., Recchioni C., Levin M., Riggins N**.** “Retrospective Chart Review: The Feasibility of a Self-Administered Nasal Spray Targeting the Sphenopalatine Ganglion (SPG) in Treatment of Chronic Migraine., J Anaesth Anesth Drug (2022).

CASE

- Verapamil regular release – 80 mg TID
- Oxygen high flow PRN headache (uses for attacks at home, usually night time)
- Sumatriptan 6 mg SC – PRN cluster attack
- Galcanezumab 300 mg SC once a month
- Melatonin 12 mg qhs
- Behavioral therapy to address insomnia and anxiety
- nVNS for cluster headache

CLUSTER CYCLE STOPPED AFTER SECOND SC INJECTION OF GALCANEZUMAB 300 MG

WHAT WOULD BE NEXT STEP IF CYCLE DID NOT STOP

BACKGROUND AMERICAN MIGRAINE FOUNDATION WEBSITE "DHE: AN OLD DOG WITH NEW TRICKS…MAYBE?"

- In 1918, ergotamine was isolated from ergot, and later in 1926 ergotamine was introduced as a treatment for migraine.
- In 1938, Graham and Wolff proposed that the major action of ergotamine was constriction of the blood vessels of the brain. In 1945, ergotamine was modified in the laboratory and introduced as dihydroergotamine or DHE.
- DHE is a more potent form of ergotamine with several different properties from the original.

- By Paul G. Mathew, MD, FAHS
  Brigham & Women's Hospital/Harvard Medical School
  Department of Neurology
  John R. Graham Headache Center
  Boston, MA, F.M. Cutrer, MD, Mayo Clinic, Department of Neurology
  Rochester, MN, Aug 18,2015

BACKGROUND: DHE

- Anti-headache efficacy is thought to be due to agonist activity at 5-HT1B/1D/1F receptors. (Serotonin receptors)
- Triptans also agonists 5HT1B/1D
- Ditans 1F receptors (Lasmiditan is FDA approved for acute treatment of migraine)
- DHE also has agonist activity at 5-HT1A/2A and dopamine D2 receptors

IV DHE

- Dr Raskin – 3 days IV DHE
- 5 days: current

- Neurology. 2011 Nov 15;77(20):1827-32. doi: 10.1212/WNL.0b013e3182377dbb. Epub 2011 Nov 2.
- **Intravenous dihydroergotamine for inpatient management of refractory primary headaches.**
- Nagy AJ[1], Gandhi S, Bhola R, Goadsby PJ.

CURRENT TREATMENT PROTOCOL

- DHE
- 11.25 mg dose – over 5 days

CLUSTER HEADACHE PATIENTS EXPERIENCE INTERICTAL SYMPTOMS IN ADDITION TO PAIN

- Authors Heiko Pohl, MD, Andreas R. Gantenbein, MD, Peter S. Sandor, MD, and Jean Schoenen, MD, PhD based the study on the 2007 EUROLIGHT questionnaire, a survey of over 1,100 Cluster Headache
- **Results of the EUROLIGHT Cluster Headache Project, an Internet-Based, Cross-Sectional Study of People With Cluster Headache**
- First published:25 November 2019
- https://doi.org/10.1111/head.13711

"AS CUMULATIVE BURDEN MIGHT BE IRREVERSIBLE, PREVENTION STRATEGIES NEED TO BE DEVELOPED". HEADACHE JOURNAL 11/2019

- When asked to think about the last headache-free day**, more than half the CH patients reported having not felt symptom-free.**
- Two-thirds responded having been worried or anxious about their next attack, and about half of them reported having avoided "something" to prevent further headache attacks.
- Worrying about future attacks and avoiding potential triggers occurred independently from attack frequency and disease duration.
- Interictal burden contributes to the total burden of CH

CASE SERIES – ERENUMAB FOR CLUSTER HEADACHE , HEADACHE JOURNAL

Erenumab Efficacy on Comorbid Cluster Headache in Patients With Migraine: A Real-World Case Series

•Marcello Silvestro MD
•Alessandro Tessitore PhD
•Fabrizio Scotto di Clemente MD
•Gioacchino Tedeschi MD
•Antonio Russo PhD

•Headache: The Journal of Head and Face Pain
•First Published: 2 May 2020

- cases of 5 patients Improvements of both intensity and frequency of CH attacks occurred only after at least 3 months of treatment, with monthly erenumab 140 mg, suggesting that longer treatment and higher doses are needed in CH in comparison to migraine.
- can be taken into account in designing future trials.

CASE – PRIMARY HEADACHE

- 76 Y old lady presents with new onset headache since 4 mo ago, BL, no CAS, on about 28 days a month, causing wakening from sleep in 3 hours after she goes to bed, lasts for 2 hours after she is awake

- What is the treatment?

HYPNIC HEADACHE SYNDROME; "ALARM CLOCK" HEADACHE.

- **Diagnostic criteria: ICHD3**
- A Recurrent headache attacks fulfilling criteria B-E
- B Developing only during sleep, and causing wakening
- C Occurring on ≥10 days/month for >3 months
- D Lasting from 15 minutes up to 4 hours after waking
- E No cranial autonomic symptoms or restlessness
- F Not better accounted for by another ICHD-3 diagnosis

HYPNIC HEADACHE ICHD 3

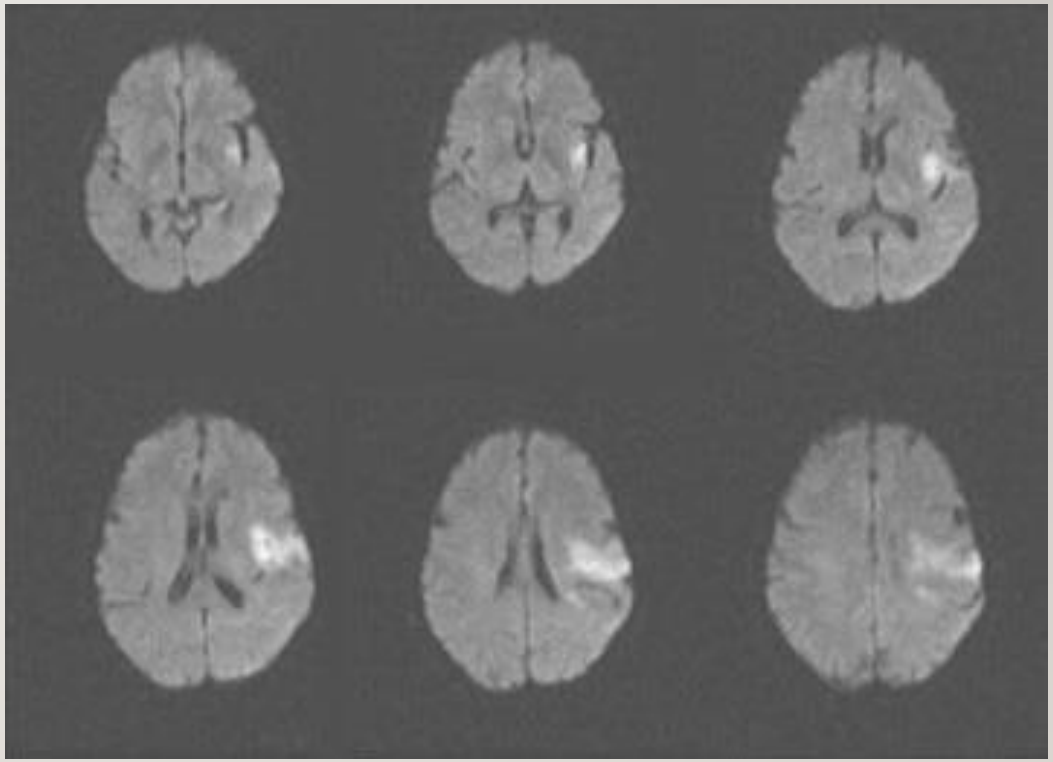
- *Hypnic headache* usually begins after age 50 years, but may occur in younger people.
- The pain is usually mild to moderate, but severe pain is reported by one fifth of patients. Pain is bilateral in about two-thirds of cases. Attacks usually last from 15 to 180 minutes, but longer durations have been described.
- Most cases are persistent, with daily or near daily headaches, but an episodic subtype (on <15 days/month) may occur.

HYPNIC HEADACHE ICHD 3

- Onset of *Hypnic headache* is not related to sleep stage. A recent MRI study showed grey matter volume reduction in the hypothalamus in patients with *Hypnic headache*.
- Lithium, caffeine, melatonin and indomethacin have been effective treatments in several reported cases.

- PART 2 SECONDARY Headache

CHANGE: NEW ACUTE



HEADACHE IN ED

- Short-term stroke risk after emergency department treat-and-release headache visit - Liberman - Headache: The Journal of Head and Face Pain - Wiley Online Library
- Approximately 1 in 700 patients discharged to home from the ED with a headache diagnosis had a stroke in the following month. Stroke risk was three to four times higher after an ED visit for headache compared to renal colic or back pain.

https://headachejournal.onlinelibrary.wiley.com/doi/abs/10.1111/head.14387

SECONDARY HEADACHES

Head or neck trauma

Crania or cervical vascular disorder

Non-vascular intracranial disorder

Substance or its withdrawal

- Substance
- Medication Overuse Headache
- Withdrawal: Caffeine, opioid, estrogen

Infection

Disorder of homeostasis

Disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial/cervical structure

Psychiatric disorder

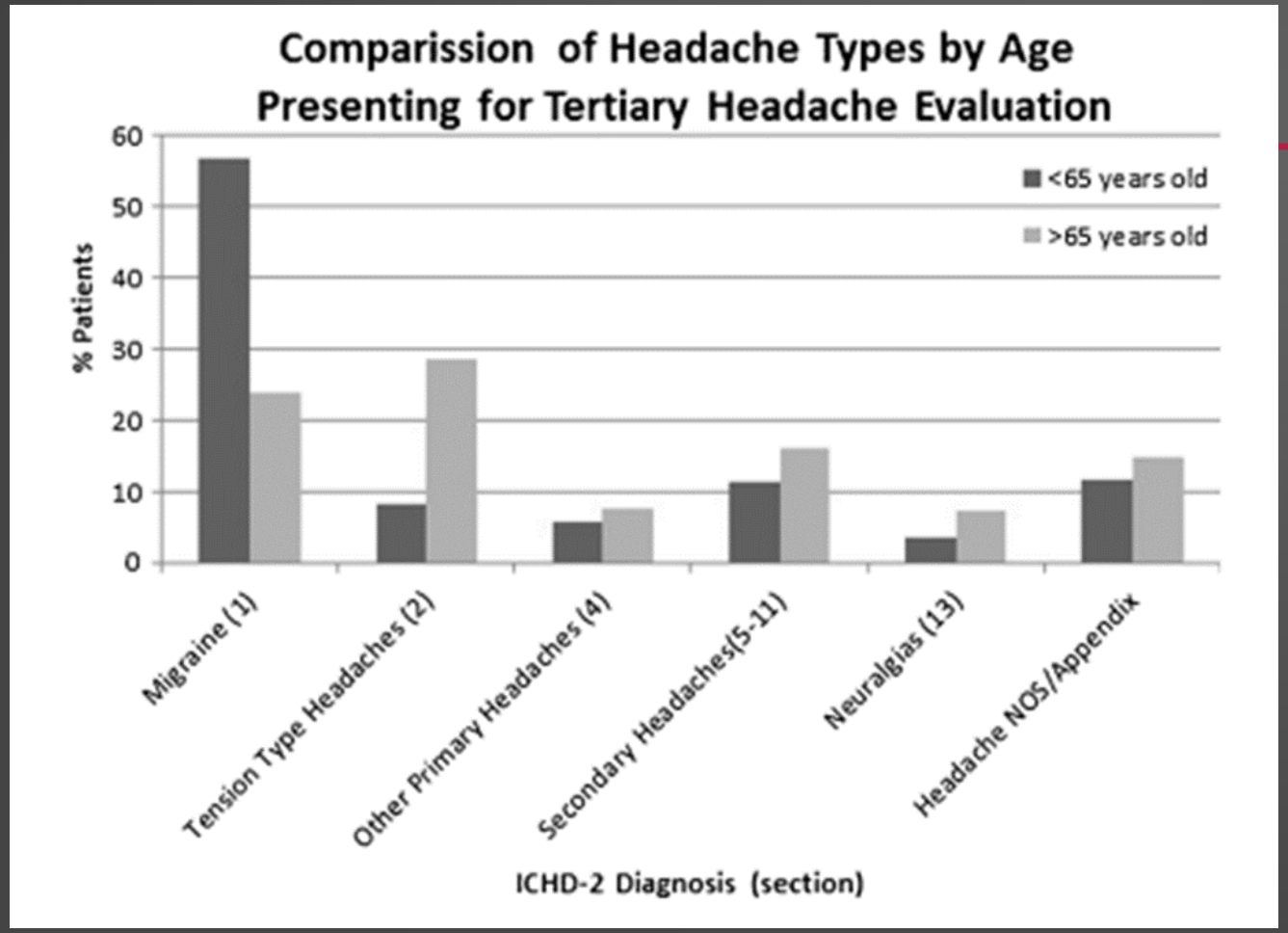
ICHD-3b


Corporate needs you to find the differences
between this picture and this picture.
They're the same picture.

SNOOP4

TABLE. THE SNOOP MNEMONIC FOR SECONDARY HEADACHE DISORDER RED FLAGS

Mnemonic	History features	Physical examination features
Systemic	History of malignancy, immunosuppression, or HIV or complaints of fever, chills, night sweats, myalgias, weight loss, or jaw claudication	Abnormal systemic examination, including blood pressure and temperature
Neurologic	Focal or global neurologic symptoms, including change in behavior or personality, diplopia, transient visual obscurations, pulsatile tinnitus, motor weakness, sensory loss, or ataxia	Abnormal neurologic examination
Onset, sudden	Headache reaches peak intensity in less than 1 minute (thunderclap)	
Onset age <5 or >65	New-onset headache before age 5 years New-onset headache after age 65	
Pattern change	Progressive headache (evolution to daily headache) or change in headache characteristics	
	Precipitated by Valsalva maneuver	
	Postural aggravation	
Papilledema	n/a	Papilledema
Pregnancy	New-onset headache during pregnancy Change in headache during pregnancy	
Phenotype of rare headache	Trigeminal autonomic cephalalgia; hypnic; exercise-, cough-, or sex-induced	



BRAVO, THOMAS P. "HEADACHES OF THE ELDERLY." *CURRENT NEUROLOGY AND NEUROSCIENCE REPORTS* 15.6 (2015): 30.

CASE

- 40 y of age male with Blood pressure 180/110 referred to the Headache Center because he has a new onset of Headache, which according to referring clinician causes increase in Blood pressure. They believe this is hemiplegic migraine because he has left hemiparesis. Headache reached intensity in less than 1 min so they think patient would benefit from Botox injections

TABLE. THE SNOOP MNEMONIC FOR SECONDARY HEADACHE DISORDER RED FLAGS

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Phenotype of rare headache	Trigeminal autonomic cephalalgia; hypnic; exercise-, cough-, or sex-induced	

CASE

- Patient is 35 years old man who has chronic Migraine
- Patient takes Sumatriptan for headache daily "to function"

MEDICATION OVERUSE HEADACHE

REGULAR INTAKE OF ONE OR MORE TRIPTANS,1 IN ANY FORMULATION, ON 10 DAYS/MONTH FOR >3 MONTHS

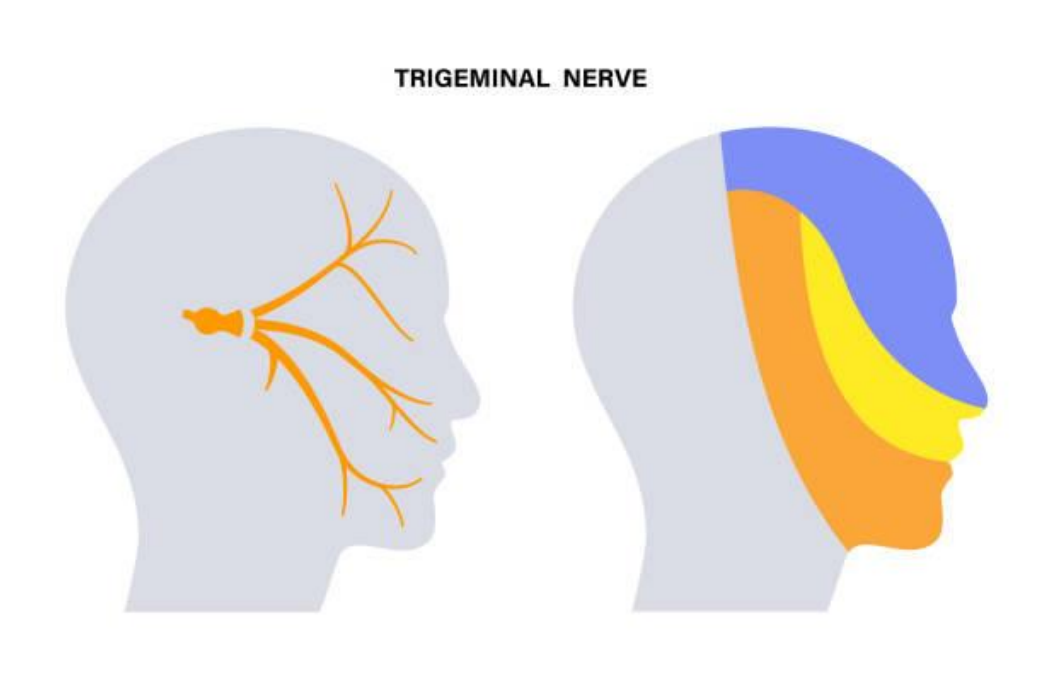
HEADACHE CLASSIFICATION COMMITTEE OF THE INTERNATIONAL HEADACHE SOCIETY (IHS) THE INTERNATIONAL CLASSIFICATION OF HEADACHE DISORDERS, 3RD EDITION. CEPHALALGIA. 2018;38(1):1-211.

RENAL DIALYSIS HEADACHE

Headache with no specific characteristics occurring during and caused by hemodialysis. It resolves spontaneously within 72 hours after the hemodialysis
session has ended.

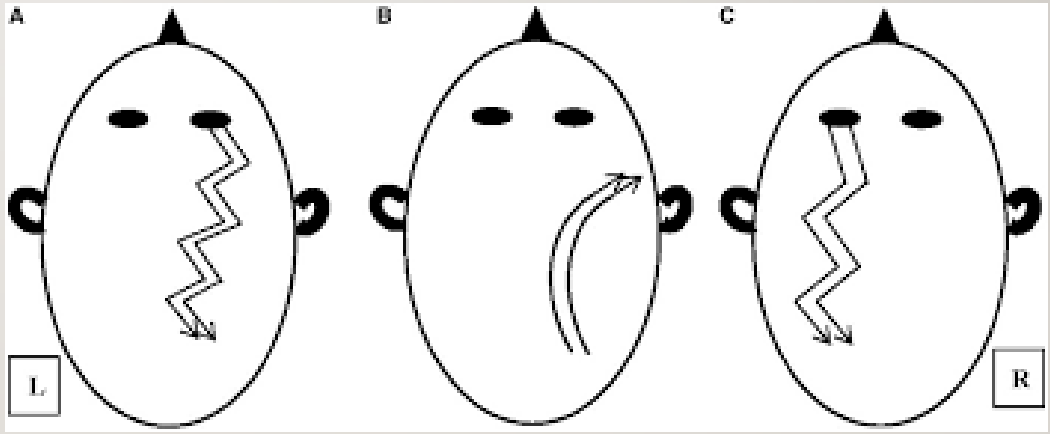
PART 3

- Neuropathies and facial pains



PART 4 – APPENDIX

- Epicrania Fugax



THANK YOU!!

QUESTIONS?