Hi, my name is Natalia Murinova MD, Director of the Headache Clinic.

Today’s talk is about integrative approach to headache and includes headache diagnosis, headache comorbidities and headache management.

I am the Director of Neurology Headache Clinic at the University of Washington in Seattle.


“Why such a long wait to be seen?”

- Headaches are very common—28 million women, and 10 million men.
- 1 in 4 households have a migraineur.
- In total, there are only about 500 UCNS-headache certified specialists in USA.
- Most physicians and neurologist are not headache trained.

State Breakdown of UCNS-Certified Headache Specialists

Overview

• Making sure patient is getting safe and effective therapy

• The International Classification of Headache Disorders 3rd edition

• Treatment options
  – Modifying therapies for success
  – New treatments

Headache Diagnosis

Through precision questioning, we can quickly identify the headache type as well as significant comorbidities and develop a treatment plan.

New Headache?

Headache Diagnosis Through precision questioning, we can quickly identify the headache type as well as significant comorbidities and develop a treatment plan.

Emergent Red Flags (address immediately)

• “First and worst”
• Thunderclap onset (worst)
• Fever and meningismus
• Papilledema with focal signs
• Altered mental status
• Acute glaucoma
• Age over 50

Headache 2.1 million ED per year

0.22% 0.76%

Pathological Diagnosis
11% – 4,620

Pathological Diagnosis
5.5% – 16,170

Diagnosis?

Diagnosis?
**Headache Diagnosis UW**

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**Cluster headaches and other trigeminal autonomic cephalgias (TAC) (ICD10:G44.001-G44.099)**

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**Benign intracranial hypertension (ICD10:G93.2)**

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**Acute post-traumatic headache (ICD10:G44.311-G44.319)**

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**Cerebral aneurysm, nonruptured (ICD10:I67.1)**

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Dissection of carotid artery (ICD10:I77.71)

Acute angle-closure glaucoma (ICD10:H40.211-H40.219)

Primary thunderclap

UW Medicine

Meningitis, unspecified (ICD10:G03.9)
Bacterial meningitis (ICD10:G00.0-G00.9)

Herpesviral meningitis (ICD10:B00.3)

Cerebrospinal fluid leak (ICD10:G96.0)

Intracranial hypotension following ventricular shunting (ICD10:G97.2)

Headache Diagnosis

Correct Diagnosis

- >150 diagnosis

- Focus on the most common disabling headaches, episodic and chronic migraine, tension type, cluster using International Headache Society Criteria
The International Classification of Headache Disorders 3rd edition (2018)

- “document is not intended to be learned by hear”.
- “Even members of the Classification Committee are unable to remember all of it.”
- It is a document that should be consulted time and time again. In this way you will soon get to know the diagnostic criteria for 1.1 Migraine without aura, 1.2 Migraine with aura, the major types of 2. Tension-type headache, 3.1 Cluster headache and a few others.
- In clinical practice you do not need the classification for the obvious case of migraine or tension-type headache, but it is useful when the diagnosis is uncertain.

https://ichd-3.org/

International Headache Society Criteria (ICHD-3) Migraine

- A. At least five attacks criteria B-D
- B. Headache attacks lasting 4-72 hours
- (untreated or unsuccessfully treated)
- C. Headache has at least two of the following four characteristics:
  1. unilateral location
  2. pulsating (throbbing)
  3. moderate or severe pain intensity
  4. aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs)
- D. During headache at least one of the following:
  1. nausea and/or vomiting
  2. photophobia and phonophobia
- E. Not better accounted for by another ICHD-3 diagnosis.

https://www.ichd-3.org/

Migraine, Simplified

- A. 5+ attacks
- B. >4 hours (when untreated)
- C. at least two of:
  - unilateral
  - pulsating
  - moderate or severe
  - can’t function (eg, walking or climbing stairs)
- D. at least one of:
  1. nausea and/or vomiting
  2. light and sound sensitivity

https://www.ichd-3.org/

Migraine, Even More Simplified

https://www.ichd-3.org/

Keep Headache Diary

Start tracking your headaches today!

Track Headache Days and Medication Use

Important for diagnosis

Migraine With Aura

https://www.ichd-3.org/
**Migraine With Aura**

- **Visual Aura Rating Scale (VARS) for migraine aura diagnosis**
  - duration 5-60 min: 3 points
  - develops over 5+ min: 2 points
  - scotoma: 2 points
  - zig-zag lines: 2 points
  - unilateral: 1 point
- Maximum score is 10 points


**Migraine Aura – at least 2 episodes in lifetime--reversible**

- Recurrent attacks, lasting minutes, of unilateral fully-reversible visual, sensory or other central nervous system symptoms
- A. At least two attacks fulfilling criteria B and C
- B. One or more of the following fully reversible aura symptoms:
  - 1. visual
  - 2. sensory
  - 3. speech and/or language
- C. At least two of the following four characteristics:
  - 1. at least one aura symptom spreads gradually over ≥5 min, and/or two or more symptoms occur in succession
  - 2. each individual aura symptom lasts 5-60 min
  - 3. at least one aura symptom is unilateral
  - 4. the aura is accompanied, or followed within 60 min, by headache

https://www.ichd-3.org/

**Headache Pearl**

**Visual Snow**


“Ongoing aura for days” with normal brain imaging

**How to ask about Headache Frequency**

- “What is the total number of any headache days you have per month?”
- **What is the number of headache-free days?**
  - Total up the headache days and headache-free days, the next question is
- “What about the rest of the days?”
  - This helps catch headaches in patients who experience more than one type of headache and are under-reporting their symptoms.

**Number 15**
Do you ever have 15 days of any Headache Days per month?

Chronic Migraine (CM)

- CM is missed in majority of new patients seen in the Headache Clinic at our institution.
- CM is often confounded by Medication-overuse headache (MOH). MOH needs to be addressed for optimal treatment success of any headache disorder but especially chronic migraine.

Chronic Migraine - 15+ Days per Month of Migraine +

- Headache occurring on 15 or more days per month for more than three months, which, on at least 8 days per month, has the features of migraine headache.

Diagnostic:

A. Headache occurring on ≥15 days per month for >3 months, which, on at least 8 days per month, has the features of migraine headache.
B. Occurring in a patient who has had at least five attacks fulfilling criteria B for 1.1 Migraine without aura and/or criteria B and C for 1.2 Migraine with aura.
C. On ≥8 days per month for >3 months, fulfilling any of the following:
   1. criteria C
   2. criteria B and C
   3. believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative.
D. NO other better explanation

Trigeminal and Cervical Nerves – Trigeminocervical Complex

Neck pain in migraine

Medications Overuse Headache ≥10 Days Total Use per Month

Pathophysiology

Habituation
Neurotransmitters
Insulin Resistance
CGRP
Homeostasis
ANS

CGRP = Calcitonin Gene-Related Peptide
Ketogenic Diet in Migraine

Representative recordings of visual evoked potentials in a migraine patient recorded before (left panel) and after a 1-month (right panel) ketogenic diet.


CGRP

Diet-induced obesity alters dural CGRP release and potentiates TRPA1-mediated trigeminovascular responses.

Balázs Marics et al.

Neurotransmitters that Modulate Pain Perception

Anti-pain system
Serotonin
Endorphins
Norepinephrine


Pro-pain
System
Nociceptin
CGRP
Substance P

Pathophysiology

CGRP
Homeostasis
ANS

Pathophysiology

Habituation
Neurotransmitters
Insulin Resistance
CGRP
Homeostasis
ANS

Medications Overuse Headache
≥10 Days Total Use per Month
Medication Overuse Story is even More Complex


Sugar and Pathophysiology

Habituation
Neurotransmitters
CGRP = Calcitonin Gene-Related Peptide
a. No response to habituation; high CGRP
b. Response to habituation; low CGRP

CGRP, Homeostasis, ANS

3 Triptans in One Week and Stress Later → MOH Model


Medication Overuse Headache

Medication and Central Sensitization

Following summation priming to model MOH, rats were hyper-responsive to environmental stress, demonstrating delayed cephalic and extracephalic allodynia and increased levels of CGRP in jugular blood, consistent with commonly observed clinical outcomes during migraine.
Neurotransmitters that Modulate Pain Perception

- Anti-pain system: Serotonin, Endorphins, Norepinephrine
- Pro-pain system: CGRP, Substance P

Be aware of the following cumulative headache triggers
- Typical triggers for headaches are cumulative and include:
  - Certain foods
  - Weather or environmental changes
  - Stress, anxiety, depression
  - Hunger, thirst
  - Hormonal cycles
  - Sleep deprivation or sleep pattern change

= headache

Additive triggers depend

Risk Factors for Migraine Progression

- Frequency of migraine attacks
- Obesity
- Acute medication overuse
- Caffeine overuse
- Stressful life events
- Depression
- Sleep disorders
- Traumatic brain injury

Initial Steps in Evaluation Using Precision Questions

- How long has this headache been a problem? (less than 3 months → acute)
- How many total headache days of any headaches do you have per month? (15)
- What is the duration of headache on average without medications? (>4 h)
- How do you treat your headaches now? (acute treatment 10 days per month)
- What treatments were tried?

Headache Treatment

- Treatment outcomes are optimized by using most effective treatments for the specific headache conditions, and developing a multimodal, comprehensive treatment plan for the patient that considers their diagnosis, other health issues, preferences and lifestyle.
- The newest headache treatments using neuromodulation and antibodies are also discussed, along with how to use them most effectively.

Targeting CGRP pathway in migraine

- Calcitonin gene-related peptide (CGRP) is a neuropeptide that is released from peripheral and central nerve endings in the trigeminal system during migraine attacks.
**CGRP receptor antagonists**

- Act at multiple sites to block action of CGRP
- Blockade of CGRP receptor does not cause significant vasoconstriction
- CGRP inhibition studied for both prevention and acute migraine treatment

**AntiCGRP antibody treatments**

Indications for Initiating Treatment With Monoclonal Antibodies to Calcitonin Gene-Related Peptide or its Receptor

- Prescribed by a licensed medical provider who is authorized to practice and performing within the scope of practice
- Patient at least 12 years of age
- Diagnosis of CH 1 or episodic migraine with or without aura (International Headache Society criteria) and both of the following:
  - Response to treatment (due to side effects) or inadequate response to ≥2 of the following:
    - Triptans
    - Nebulized sulmatoilate/Hemisulmatoilate
    - Beta-blocker: metoprolol, propranolol, timolol, esmolol, nadolol
    - Triptan: amitriptyline, sumatriptan, sumatriptan
    - Sumatriptan in combination with propranolol or almotriptan, haloperidol
    - Oral and/or IV treatments (established efficacy or probable effectiveness) according to AHS guidelines
  - At least moderate disability (NASG 1, 11-15/20)

**Medications can Cause Rebound Headache ≥10 days per Month**

- External Trigeminal Nerve Stimulation device (e-TNS)
  - Photo: Natalia Murinova MD

- Vagal Nerve Stimulation
  - Photo: Courtesy of Dr. Natalia Murinova. GammaCore Vagal Nerve stimulation approved by FDA for migraine treatment.
Naproxen gel caps 220 to 660 mg

Photo Courtesy of Dr. Natalia Murinova

Naproxen approved for acute migraine treatment

Breaking Cycle Of Medication Use

When patients who have frequent, disabling migraines take medications to relieve their symptoms, they run the risk that the attacks will increase in frequency to daily or near-daily as a rebound effect comes into play. This pattern, called medication overuse headache, is more likely to happen with butalbital and opioids than with migraine-specific drugs, as partial responses lead to recurrence, repeat dosing, and, eventually, overuse. Breaking the cycle involves weaning the patient from the overused medications, setting up a preventive regimen, and setting strict limits on the use of medications to relieve acute symptoms.


Preventive Medications

Trial of Amitriptyline, Topiramate, and Placebo for Pediatric Migraine

There were no significant between-group differences in the primary outcome, which occurred in 52% of the patients in the amitriptyline group, 55% of those in the topiramate group, and 61% of those in the placebo group.

There were also no significant between-group differences in headache-related disability, headache days, or the percentage of patients who completed the 24-week treatment period.

Patients who received amitriptyline or topiramate had higher rates of several adverse events than those receiving placebo, including fatigue (30% vs. 14%) and dry mouth (25% vs. 12%) in the amitriptyline group and paresthesia (31% vs 8%) and weight loss (8% vs. 0%) in the topiramate group.

Three patients in the amitriptyline group had serious adverse events of altered mood, and one patient in the topiramate group had a suicide attempt.

For Headache, Exercise=Medicine
Multimodal Approach for Headache Management

We recommend multimodal approach for headache management.

• What we tell our patients:
• “Your participation in your care is immensely important and we are excited about the work you have done so far to improve your overall health and headache symptoms”.

Modifiable Factors in Headache Management

Supplements

Neuromodulation External Trigeminal Nerve Stimulation

Supplements

Treatment- Address Med Overuse, and Non-pharmacology
Neuromodulation Vagal Nerve Stimulation

Photo Courtesy of Dr. Natalia Murinova. GammaCore Vagal Nerve stimulation approved by FDA for migraine treatment.

AntiCGRP antibody treatments

GammaCore Vagal Nerve stimulation approved by FDA for migraine treatment.

Migraine Prevention Medicines

Beta-blockers


Anti Epileptics—Topiramate for Migraine Prevention

- Topiramate “super model drug”


Amitriptyline Nortriptyline
Serotonin Norepinephrine Reuptake Inhibitors (SNRI)
- Help brain hold onto both serotonin and norepinephrine
- FDA approved for chronic pain
- Side effects: weight loss, sleep disturbance
- Duloxetine (Cymbalta)
- Venlafaxine (Effexor)

Duloxetine (Cymbalta)
SNRI serotonin-norepinephrine reuptake inhibitor

Magnesium up to 400 mg three times a day
- Helps with constipation

B vitamins

Feverfew tea

SAMe 200 to 1600 mg a day
Melatonin

- Melatonin significantly reduced headache frequency compared to placebo (p=0.009), but not to amitriptyline (p=0.19).

Peres, Mario, and Andre Gonçalves. "Double-Blind, Placebo Controlled, Randomized Clinical Trial Comparing Melatonin 3 mg, Amitriptyline 25 mg and Placebo for Migraine Prevention (S40. 005)." Neurology (2013).

Acupuncture for Migraine

Effective for Migraine Prophylaxis

Biofeedback for Migraine

Effective for Migraine Prophylaxis, needs to be practiced

Dietary Modifications

- Ketogenic diets directly modify brain function
- Restrictive diets may avoid triggers in processed foods
- Changing the diet changes the microbiome

Group Therapy for Headache

CBT and ACT are safe and effective, require time commitment

Physical Exercise for Headache

Migraine patients may fear exercise but it is helpful
Dopamine Release Drops During Migraine


Sleep disorders and Headaches

- Of the 864 patients, 548 (63.5%) endorsed sleep problems.

Submitted for Poster IHC 2017 data UW 2017

Glymphatic system

*Neurochemical Research*

December 2015, Volume 40, Issue 12, pp 2383–2399

The Glymphatic System: A Beginner’s Guide

The glymphatic system - a macroscopic waste clearance system - utilizes a unique system of perivascular tunnels. Formed by astroglial cells, to promote efficient elimination of soluble proteins and metabolites from CNS

Glymphatic System

Thank You Very Much

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