



Addressing the Unique Needs of Women with Migraine

Peter Goadsby, MD, PhD, DSc

Kathleen Mullin, MD

WOMEN'S HEALTH:
Beyond the Annual Visit

Learning Objectives

- Identify the signs and symptoms of migraine needed to make an accurate and timely diagnosis
- Discuss the safety and efficacy data for current therapeutic options for migraine prevention and acute treatment
- Describe treatment strategies for women diagnosed with migraine at different stages of life

Women with Migraine

Diagnosis

Professor Peter J. Goadsby



UCLA

KING'S
College
LONDON

Disclosure in ICJME + ACCME format 2019-2021

Dr Goadsby reports

- Grants and personal fees from

- Amgen (erenumab)
- Eli-Lilly (galcanezumab/lasmiditan)
- Celgene

- Other

- Consulting; Gerson Lerhman, Guidepoint
- Trigemina Inc (stock options; no fees)
- MedicoLegal work
- Publishing: Up-to-Date, Massachusetts Medical Society, Oxford University Press, Wolters Kluwer

- Patents

* Magnetic stimulation for headache pending licensed to eNeura (Aruen) without fee

- ACCME: I have no spousal/partner conflicts, nor relationships with companies that market, distribute, or resell health care goods or services consumed by, or used on, patients unless otherwise explicitly stated.

- Personal fees from

- Aeon Biopharma
- Allergan (onabotulinum toxin type A/ubrogepant/atogepant)
- Biohaven (rimegepant, zavegepant)
- Clexio
- Dr Reddys
- Electrocore LLC (nVNS)
- eNeura Inc (Aruen; sTMS)
- Epalex
- GlaxoSmithKline
- Impel Neuropharma (dihydroergotamine)
- Lundbeck/Alder Biopharmaceuticals (eptinezumab)
- Novartis (erenumab)
- Praxis
- Pfizer
- Sanofi
- Santara Therapeutics
- Satsuma
- Teva Pharmaceuticals (fremanezumab)

wellcome trust

NIHR | National Institute
for Health Research

MRC

Medical
Research
Council

International Classification of Headache Disorders-3

I-Primary

1. Migraine
2. Tension-type headache
3. Trigeminal autonomic cephalalgias
 - 3.1 Cluster headache
 - 3.2 Paroxysmal hemicrania
 - 3.3 SUNCT/SUNA
 - 3.4 Hemicrania continua
4. Other Primary Headaches
 - 4.1 Cough headache
 - 4.2 Exercise Headache
 - 4.3 Sexual activity headache
 - 4.4 Thunderclap headache
 - 4.5 Cold stimulus: external/ingestion
 - 4.6 External pressure: compression/traction
 - 4.7 Stabbing Headache
 - 4.8 Nummular headache
 - 4.9 Hypnic headache
 - 4.10 New Daily Persistent Headache

II-Secondary

5. Trauma or injury to the head
6. Cranial or cervical vascular
7. Intracranial non-vascular
8. Substances
9. Infection
10. Homoeostasis
11. Disorder head, neck, eyes...
12. Psychiatric

III-Cranial neuropathies/facial pain

13. Cranial neuralgias/facial pain
 - 13.1.1 trigeminal neuralgia
 - 13.1.2 trigeminal neuropathy
 - 13.2 Glossopharyngeal neuralgia
 - 13.3 Nervus intermedius neuralgia
 - 13.4 Occipital neuralgia
 - 13.5 Neck-tongue syndrome
 - 13.8 Tolosa-Hunt
 - 13.9 Paratrigeminal oculosympathetic (Raeder's)
 - 13.11 Burning Mouth Syndrome

Case

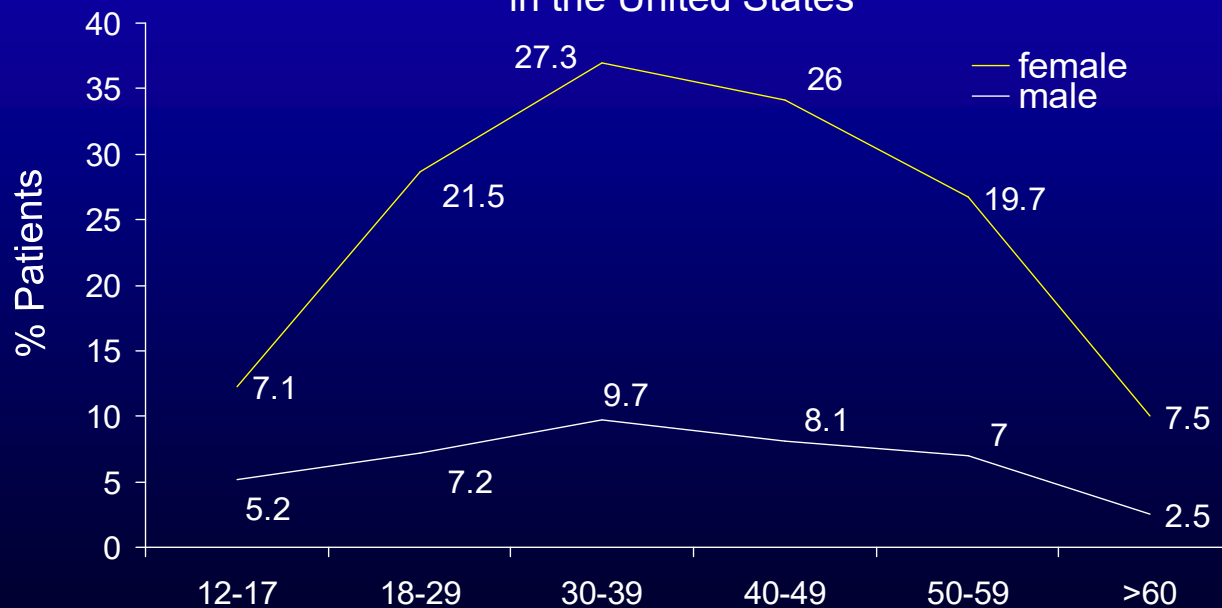
Demographics	Female, 38 years
Background	Headache from age 12; more troublesome over the last 7 years
Presenting problem	Headache on 22 days a month with 10 severe days

Migraine

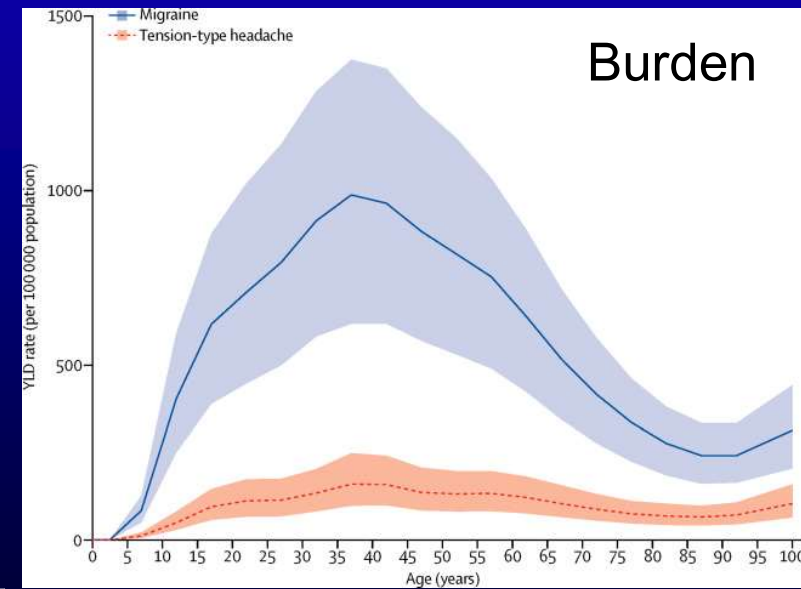
Epidemiology & Burden

- Lifetime cumulative incidence: 43% females/18% males
(Stewart WF, et al. *Cephalalgia*. 2008;28(11):1170-1178.)

Age-Specific One-Year Prevalence
in the United States



Lipton RB, et al. *Headache*. 2001;41(7):646-657.

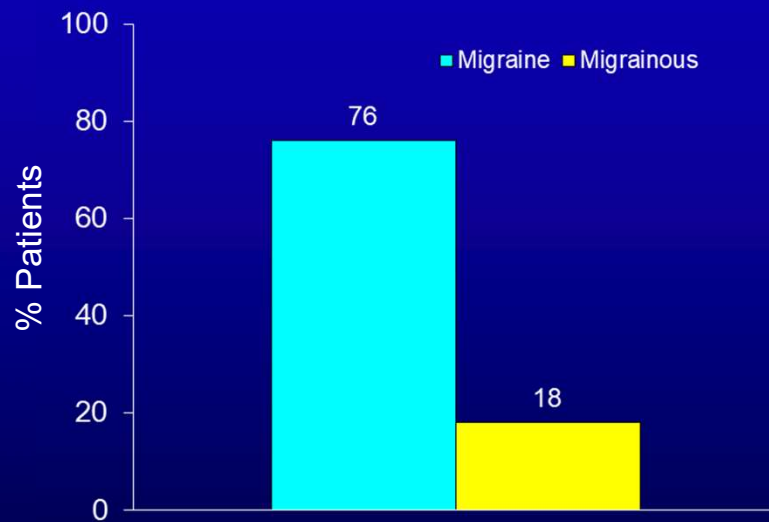


GBD 2016 Headache Collaborators.
Lancet Neurol. 2018;17(11):954-976.

Headache

The Burden

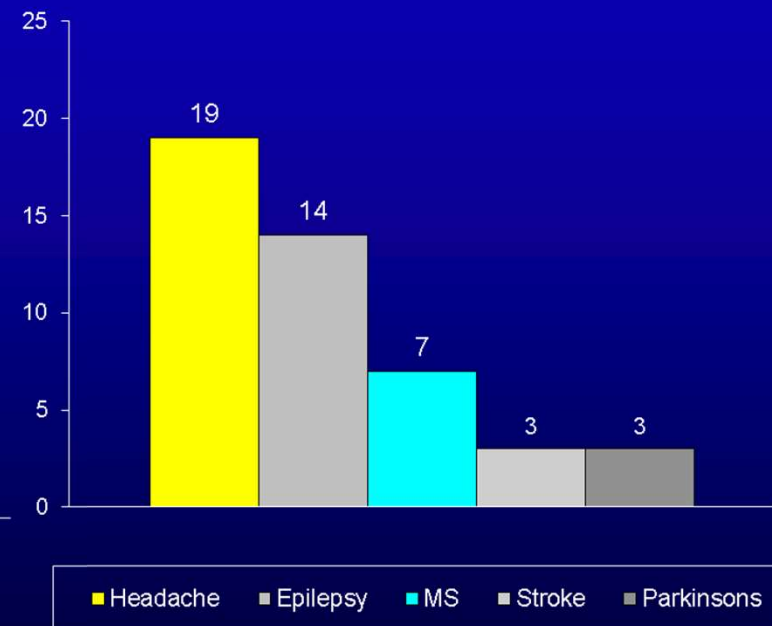
General Practice¹



Landmark Study

- Prospective, open-label study
- Patients tracked for 3 months or 6 attacks
- Assigned *IHS* diagnoses by experts

Neurology OPD²



1. Stone J, et al. *Clin Neurol Neurosurg*. 2010;112(9):747-751.
2. Tepper SJ, et al. *Headache*. 2004;44(9):856-864.

Case

Severe days	Phenotype
Canonical	Pain: Unilateral throbbing, severe Pain: Movement worse Associated: Nausea/photophobia/phonophobia
Added	Allodynia: Cranial Vertigo: None Aura: None
Cranial autonomic symptoms	Bilateral tearing Bilateral periorbital edema
Premonitory-like	Neck discomfort, concentration impairment, yawning, tiredness, mood change
Postdrome	Weary/tired for 1 day

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ICHD-3¹

- ✓ At least 5 attacks fulfilling criteria B–D
- ✓ Headache attacks lasting 2/4–72 hours (when untreated or unsuccessfully treated)
- ✓ Headache has at least 2 of the following 4 characteristics:
 1. Unilateral location
 2. Pulsating quality
 3. Moderate or severe pain intensity
 4. Aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs)
- ✓ During headache at least 1 of the following:
 1. Nausea and/or vomiting
 2. Photophobia and phonophobia
- ✓ Not better accounted for by another ICHD-3 diagnosis

1. *Cephalalgia*. 2018;38(1):1-211.

Case

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Migraine

Attacks

- ✓ Throbbing
- ✓ Movement worse
- Associations
 - Nausea
 - Photophobia
 - Phonophobia
- Aura

Individuals

- Family history
- Triggers
 - Sleep: missing/excess
 - Eating: including alcohol
 - Weather
 - Hormonal
 - Stress- *relaxation*

Tension-type Headache

- x Non-throbbing
- x *No effect of movement*
- x Associations
 - No nausea
 - No photophobia
 - No phonophobia
- ? aura

Case

Medical history	Hypercholesterolemia
Family history	Mother had headache with menstrual periods
Personal history	No smoking/alcohol Three children Owns small business
O/E	81 kg Cranial nerves/limbs: unremarkable MRI brain: normal

Attacks

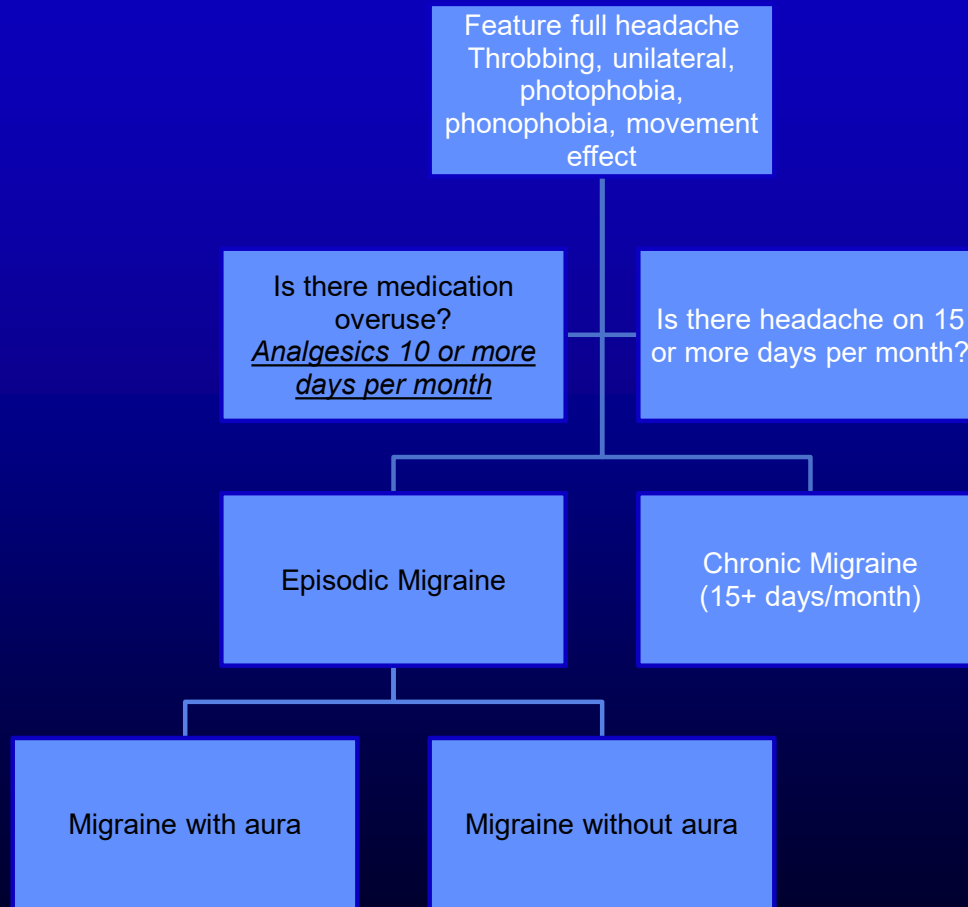
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 - Stress – *relaxation*

Migraine

Clinical Approach



Migraine

Attacks¹

- **Premonitory (prodromal)**
 - Neck discomfort
 - Higher centre
 - Cognitive impairment/**Mood**
 - Homeostatic
 - Yawning/sleep
 - Polyuria/polydipsia
 - **Food cravings**
 - **Cranial autonomic symptoms (74%)³**
- **Canonical (“IHS symptoms”)**
 - Pain
 - Moderate/Severe
 - Unilateral
 - Pulsating
 - Worse with movement
 - Nausea/vomiting
 - Sensory sensitivity
 - photophobia
 - phonophobia
 - *osmophobia*
 - *allodynia (70%)*
 - *vertigo (40%)⁴*
- **Postdrome**
 - Tired/weary
 - Concentration impairment
- **Aura**

Disorder²

- **Repeated attacks**
 - < 15 days/month: Episodic
 - **≥ 15 days/month**: Chronic
- **Family history**
- **Triggers (biology)**
 - Sleep: missing/excess
 - Food: skipping meals
 - Chemical: alcohol or nitroglycerin
 - Weather
 - Sensory: light, smells
 - Hormonal
 - *Stress- relaxation*

Misdiagnosis

- Cranial Autonomic symptoms
 - Lacrimation
 - Conjunctival injection
 - Nasal symptoms
 - Aural fullness
 - “Sinusitis”
- Food cravings
 - Sweet/savory
 - Food triggers
- Mood change
 - Depression
- **≥ 15 days per month**
 - Tension-type headache

1. *After ICHD-3 Cephalalgia* 2018;38:1-211.
2. *Goadsby et al., Physiol Rev* 2017;97:553-622.
3. *Karsan et al., Neurology* 2021;96:1662.
4. *Vandenbussche et al., Cephalalgia* 2019;39(1S):90.



New Migraine Treatment Options

Kathleen Mullin, MD

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WOMEN'S HEALTH:
Beyond the Annual Visit

Disclosure Information

- **Speaking/Consulting Fees:** Amgen, Biohaven, Impel NeuroPharma, Lilly, Teva, Vorso Corp

Previous Standard of Care

Prevention

- Antidepressants
 - Nortriptyline, amitriptyline, venlafaxine
- Blood Pressure Medications
 - Propranolol, nadolol, timolol, metoprolol, verapamil, candesartan, lisinopril
- Seizure Medications
 - Divalproex, topiramate, gabapentin
- Other
 - Memantine, methylergonovine, onabotulinumtoxinA

Acute

- Triptans
 - Sumatriptan, rizatriptan, naratriptan, eletriptan, zolmitriptan, frovatriptan, almotriptan
- Non-Steroidal Anti-Inflammatories
 - Naproxen, nabumetone, ibuprofen, diclofenac
- Muscle Relaxers
 - Cyclobenzaprine, baclofen, tizanidine
- Ergot Derivative
 - Dihydroergotamine nasal

Problems with Old Standard of Care

Prevention

- Not disease-specific
- Titration to optimal dose took too long
- Poorly tolerated
- Issues with compliance

Acute

- Inefficacy/recurrence
- Tolerability
- Medication overuse
- Contraindications

New Acute Medications

Ditans 5HT1F serotonin receptor agonist	Gepants CGRP small molecule receptor antagonists
<p>Reyvow (lasmiditan) – approved 10/19 by FDA</p> <ul style="list-style-type: none">• 50-200 mg (50, 100 mg pills) as needed (only one dose in 24 hours)• Driving restriction	<p>Ubrelvy (ubrogepant) – approved 12/19 by FDA</p> <ul style="list-style-type: none">• 50-100mg (50, 100 mg pills) as needed (2nd dose option up to 200 mg in 24 hours) <p>Nurtec (rimegepant) – approved 1/20 by FDA</p> <ul style="list-style-type: none">• 75 mg ODT as needed once in 24 hours

New Preventive Medications

CGRP Monoclonal Antibodies	Gepants
<p>Emgality (galcanezumab) Ajovy (fremanezumab) Aimovig (erenumab) Vyepti (eptinezumab) IV</p>	<p>Nurtec (rimegepant) – FDA 5/21</p> <ul style="list-style-type: none">• 75 mg ODT every other day <p>Qulipta (atogepant) – FDA 9/21</p> <ul style="list-style-type: none">• 10, 30, or 60 mg once a day
<p>Migraine-specific Convenient Well tolerated No interactions with SSRIs, OCPs, etc.</p>	<p>Migraine-specific No needles Flexibility with Nurtec Short half-life Well tolerated</p>

Devices



- Cefaly Device (e-TNS)



- GammaCore (nVNS)



- Nerivio (PNS)