Migraines

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Disclosures

- No financial disclosures
- Some medications noted may be off-label.

Migraine: Objectives

- Epidemiology
- Definitions
- Triggers
- Symptoms
- Diagnosis/Work-up
- Treatment
- Other Considerations

"My Migraine," a self-portrait by Lynda Robinson. Pastel, 55cm by 35cm

Migraine: Epidemiology

- Global Burden of Disease Study 2010 - Third most prevalent disorder in the world
- The most common neurological disorder
- Third highest cause of disability in males/females under 50
- 38 million people in the US (12% of the population)
- 3x more common in women; 30% of women over lifetime
- 1/4 households in America has a member with migraine

Migraine: Costs

- $6,575/per patient
- $20 million/year in US (direct medical expenses and lost productivity)
- Outpt - $3.2 billion
- ER visit - $700 million; $775.09 (subq/IM injection)
- Inpt hospitalization - $375 million; $7317.07 (CT)

American Migraine Foundation 2019

Cephalalgia. 2011 Nov;31(15):1570-5. doi: 10.1177/0333102411425960. Epub 2011 Oct 19.

Migraine: Definitions

- Episodic
- Chronic
  - >15 days/month
  - 2% pop
  - 1/5 with occupational disability

Javier Sotomayor

Migraine without aura	Migraine with aura
>/= 5 attacks fulfilling criteria B-D	>/= 2 attacks fulfilling criteria B and C
B. Untx'd or unsuccessfully tx HA attacks lasting 4-72 hours	B. 1+ fully reversible aura symptoms: visual, sensory, speech/language, motor, brainstem, retinal
C. HA has at least 2 of the following: Unilateral, pulsating quality, mod-severe pain intensity, aggravation by or causing avoidance of routine physical activity	C. At least 2 of the following 4: At least 1 aura sx spreads gradually over >/= 5 min; 2+ aura sx's occur in succession, each individual aura sx lasts 5-60 min; at least one aura sx is unilateral; at least 1 aura sx is positive; the aura is accompanied or followed within 60 min by HA
D. During HA, at least 1 of the following: N/V/photophobia and photophobia	D. Not better accounted for by another ICHD-3 dx
Not better accounted for by another ICHD-3 dx	

International Classification of HA Disorders

Seminars in Neurology. Vol 38, Dec 2018. Greer, David M (Ed).pp609

Migraine: Triggers

- Diet (Cured meats, MSG, Artificial sweeteners, Frozen foods, Food dyes, Alcohol, Caffeine)
- Sleep
- Dehydration
- **Weather
- Bright light
- Strong odors
- Hormonal Fluctuations
- Physical/Mental Stress

Migraines: Hormones

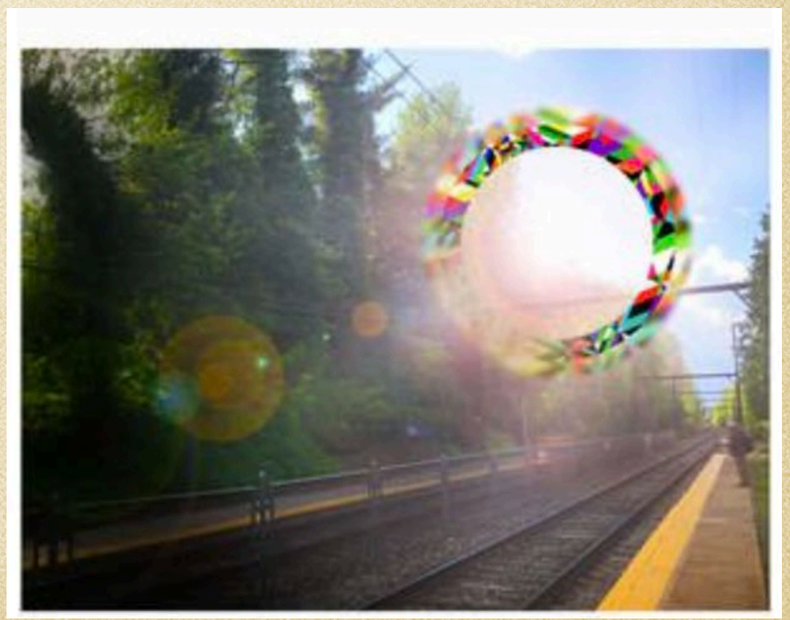
- In days prior to onset of menses, decline in serum levels of both estrogen and progesterone - the drop in estrogen levels leads to menstrual migraine
- Stability of estrogen during pregnancy (higher) and menopause (lower) leads to a reduction in migraine for a majority of women

Migraine: Clinical Symptoms

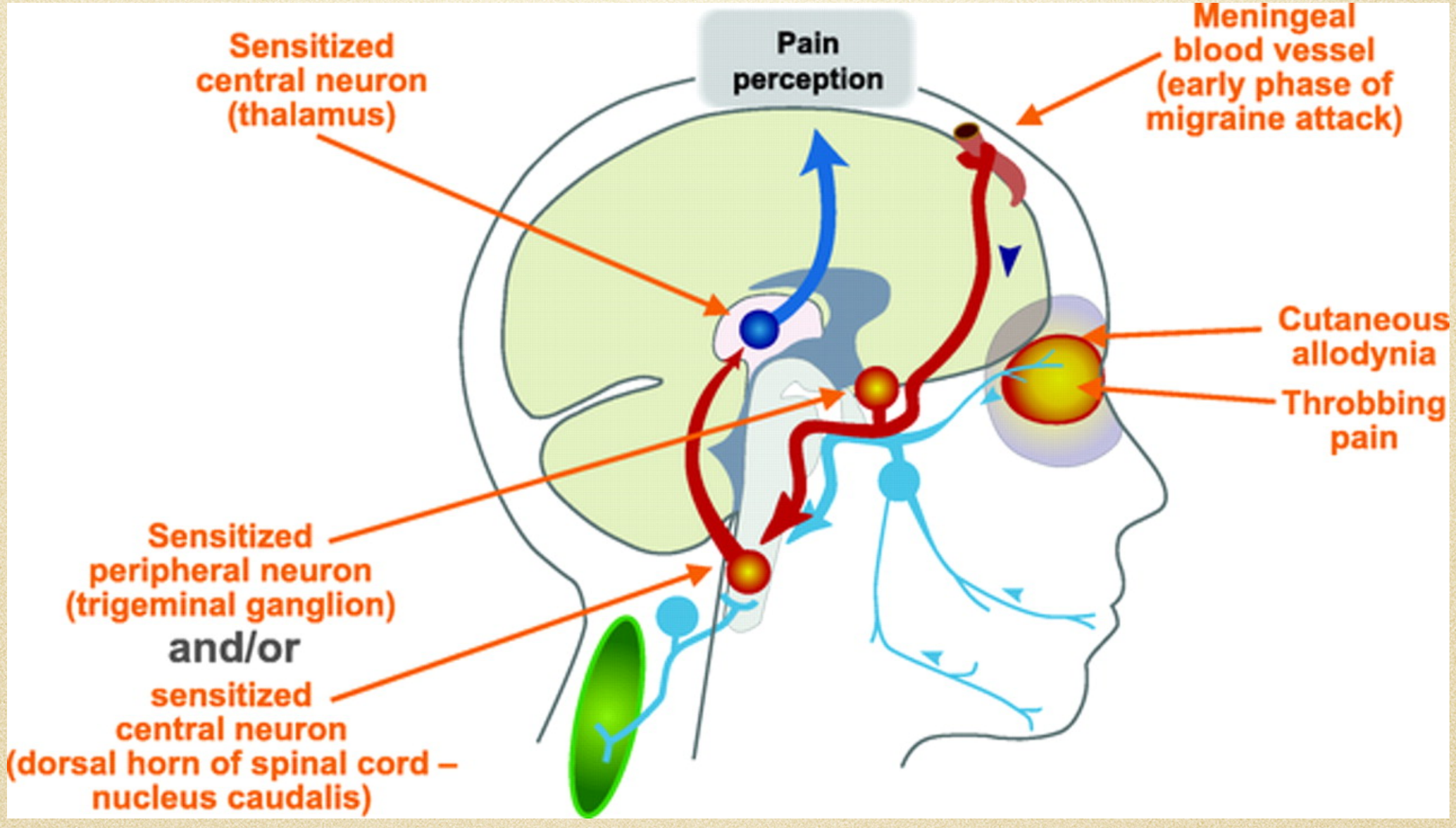
- Prodrome - hours-days prior - fatigue, anorexia, food cravings, mood changes, restlessness
- Post-drome - fatigue, elated/depressed mood - may last 48 hours post
- Aura - 30% of migraines during lifetime
- Unilateral, throbbing, gradual intensity, aggravated by routine activity
- Pain intensity is mild to debilitating, lasting hours to days
- Muscle tenderness of head/neck is common

Migraine: Aura

- Usually visual phenomena (90%) - begin/evolve over 5-20 minutes
- Visual, sensory, motor, language
- Cortical spreading depression



Migraine: Pathology



"Spectrum of illness; Understanding biological patterns and relationships in chronic migraine." Neurology. Aurora, Sheena. Feb 2, 2009.

Diagnosis… Consider Secondary Causes

- S…systemic symptoms
- N…neurologic symptoms
- O…onset (sudden)
- O…onset after age 50
- P4…pattern change, precipitated by Valsalva, postural aggravation, papilledema

Dodick D. Semin Neurol. 2010; 30: 74-81

Migraine: Diagnosis

- 80% of “sinus” HA pts meet IHS migraine criteria for migraine
  - HA is a minor criteria of sinusitis (Major: purulence of nasal cavity, facial pain, congestion; nasal obstruction/blockage/discharge, fever, hyposmia/anosmia)
- 85% of “tension” HA pts meet IHS criteria for migraine

Schreiber CP et al. *Arch Intern Med*. 2004;164(16):1769-1772.
Kaniecki R et al. *CMRO*. 2006;22(8):1535-1544.

Migraine: Co-Morbidities

- Gastroparesis - can delay tablet absorption
- Depression/Anxiety - 25%/50% more likely respectively
- Fibromyalgia

"Spectrum of illness; Understanding biological patterns and relationships in chronic migraine." Neurology. Aurora, Sheena. Feb 2, 2009.

2019 ACR Appropriateness Criteria

Variant 4: **New headache. Classic migraine or tension-type primary headache. Normal neurologic examination. Initial imaging.**

Procedure	Appropriateness Category	Relative Radiation Level
Arteriography cervicocerebral	Usually Not Appropriate	☢☢☢
CT head with IV contrast	Usually Not Appropriate	☢☢☢
CT head without and with IV contrast	Usually Not Appropriate	☢☢☢
CT head without IV contrast	Usually Not Appropriate	☢☢☢
CTV head with IV contrast	Usually Not Appropriate	☢☢☢
CTA head with IV contrast	Usually Not Appropriate	☢☢☢
MRV head without and with IV contrast	Usually Not Appropriate	O
MRV head without IV contrast	Usually Not Appropriate	O
MRA head without and with IV contrast	Usually Not Appropriate	O
MRA head without IV contrast	Usually Not Appropriate	O
MRI head without and with IV contrast	Usually Not Appropriate	O
MRI head without IV contrast	Usually Not Appropriate	O

https://acsearch.acr.org/docs/69482/narrative/

2019 ACR Appropriateness Criteria

Variant 3: **New or progressively worsening headache with one or more of the following 'red flags': subacute head trauma, related activity or event (sexual activity, exertion, position), neurological deficit, known or suspected cancer, immunosuppressed or immunocompromised state, currently pregnant, or 50 years of age or older. Initial imaging.**

Procedure	Appropriateness Category	Relative Radiation Level
CT head without IV contrast	Usually Appropriate	☢☢☢
MRI head without and with IV contrast	Usually Appropriate	O
MRI head without IV contrast	Usually Appropriate	O
CT head with IV contrast	Usually Not Appropriate	☢☢☢
CTA head with IV contrast	Usually Not Appropriate	☢☢☢
MRA head without IV contrast	Usually Not Appropriate	O
CT head without and with IV contrast	Usually Not Appropriate	☢☢☢
Arteriography cervicocerebral	Usually Not Appropriate	☢☢☢
MRA head without and with IV contrast	Usually Not Appropriate	O

https://acsearch.acr.org/docs/69482/narrative/

2019 ACR Appropriateness Criteria

Variant 6: **Chronic headache. No new features. No neurologic deficit. Initial imaging.**

Procedure	Appropriateness Category	Relative Radiation Level
CT head without IV contrast	Usually Not Appropriate	☢☢☢
MRI head without and with IV contrast	Usually Not Appropriate	O
MRI head without IV contrast	Usually Not Appropriate	O
Arteriography cervicocerebral	Usually Not Appropriate	☢☢☢
CT head with IV contrast	Usually Not Appropriate	☢☢☢
CT head without and with IV contrast	Usually Not Appropriate	☢☢☢
CTV head with IV contrast	Usually Not Appropriate	☢☢☢
CTA head with IV contrast	Usually Not Appropriate	☢☢☢
MRV head without and with IV contrast	Usually Not Appropriate	O
MRV head without IV contrast	Usually Not Appropriate	O
MRA head without and with IV contrast	Usually Not Appropriate	O
MRA head without IV contrast	Usually Not Appropriate	O

https://acsearch.acr.org/docs/69482/narrative/

2019 ACR Appropriateness Criteria

Variant 7: **Chronic headache. New features or increasing frequency. Initial Imaging.**

Procedure	Appropriateness Category	Relative Radiation Level
MRI head without and with IV contrast	Usually Appropriate	O
MRI head without IV contrast	Usually Appropriate	O
CT head without IV contrast	May Be Appropriate	☢☢☢
CT head without and with IV contrast	May Be Appropriate	☢☢☢
CT head with IV contrast	Usually Not Appropriate	☢☢☢
MRA head without IV contrast	Usually Not Appropriate	O
Arteriography cervicocerebral	Usually Not Appropriate	☢☢☢
CTA head with IV contrast	Usually Not Appropriate	☢☢☢
CTV head with IV contrast	Usually Not Appropriate	☢☢☢
MRA head without and with IV contrast	Usually Not Appropriate	O

https://acsearch.acr.org/docs/69482/narrative/

ABIM Choosing Wisely

- Don't perform neuroimaging in pts with stable headache that meet criteria for migraines
- Don't perform CT imaging for HA when MRI is available except in emergency settings
- Don't recommend surgical deactivation of migraine trigger points outside of a clinical trial
- Don't prescribe opioid or butalbital-containing medications as first-line tx for recurrent HA disorders
- Don't recommend prolonged or frequent use of OTC pain medications for headache

http://www.choosingwisely.org/wp-content/uploads/2015/02/AHS-Choosing-Wisely-List.pdf

Red Flags

- First/worst
- Change from previous pattern
- Abnormal neuro exam
- Onset >age 50
- New onset in an immunocompromised patient (HIV/CA)
- Accompanied by fever
- Concomitant epilepsy
- New daily, persistent HA
- Escalation of HA frequency/intensity IN ABSENCE of medication overuse HA

Migraine: Episodic Treatment

- Non-specific analgesics:
  - Acetaminophen, Ibuprofen, Naproxen, Diclofenac (Level A - Am Headache Society)
  - Ketorolac (Level B - Am Headache Society)

Migraine: Episodic Treatment

- Migraine-specific analgesics:
  - Triptans (Level A - Am Headache Society)
  - Ergots (Level A - Am Headache Society)

Migraine: Episodic Treatment

- Adjunctive treatment for associated symptoms
  - Metoclopramide (Level B - Am HA Society)
  - Prochlorperazine (Level B - Am HA Society)

Priya Rama

Medication Overuse Headache

- Associated Meds: triptans, meds containing caffeine (Excedrin) (>10 days per month), butalbital (Fioricet) (>5 days per month), and opioids (>8 days per month)
- Careful with blame!
- Expectations - 4-8 weeks to improve AFTER the weaning process

Bigal ME, Lipton RB. Overuse of acute migraine medications and migraine chronification. Curr Pain Headache Rep. 2009 Aug;13(4):301-7.

Medication Overuse Headache

- Cease the offending drug use
- Initiate prophylaxis medication
- Consider corticosteroid burst/taper (Prednisone 60mg over 6-8 days)/ DHE
- Consider Phenobarbital 30mg/day in place of 100mg/day butalbital with gradual taper over weeks-month

Migraine: Prevention

- Onabutulinumtoxin A (Botox - Allergan) - FDA approved for chronic migraine
  - Clinical practice guideline: Do not offer for episodic migraine

Migraine: Episodic Prevention in Adults

Neurology®

April 24, 2012; 78 (17) SPECIAL ARTICLES

Evidence-based guideline update: Pharmacologic treatment for episodic migraine prevention in adults

Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society

S.D. Silberstein, S. Holland, F. Freitag, D.W. Dodick, C. Argoff, E. Ashman

First published April 23, 2012, DOI: https://doi.org/10.1212/WNL.0b013e3182535d20

- ARBs:
  - Candesartan - possibly effective (Level C)
- ACE-I:
  - Lisinopril - possibly effective (Level C)
- Alpha Agonists:
  - Clonidine and guanfacine - possibly effective (Level C)

Migraine: Episodic Prevention in Adults

- Antidepressants:
  - Amitriptyline and Venlafaxine - probably effective - Level B
  - Clomipramine - probably ineffective - Level B
  - Fluoxetine, Fluvoxamine, protriptyline - conflicting/inadequate evidence - Level U

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Migraine: Episodic Prevention in Adults

- AEDs:
  - Divalproex sodium, sodium valproate, topiramate - effective - Level A
  - Lamotrigine - ineffective - Level A
  - Carbamazepine - possibly effective - Level C
  - Oxcarbazepine - possibly ineffective - Level C
  - Gabapentin - conflicting/inadequate evidence - Level U

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Migraine: Episodic Prevention in Adults

- Beta-blockers:
  - Metoprolol, propranolol, timolol - effective - Level A
  - Atenolol, nadolol - probably effective - Level B
  - Nebivolol, pindolol - possibly effective - Level C
  - Acebutolol - possibly ineffective - Level C
  - Bisoprolol - conflicting/inadequate evidence - Level U
- CCBs:
  - Nicardipine, nifedipine, nimodipine, verapamil - evidence conflicting/inadequate - Level U

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Episodic Migraine Treatment in Adults

- Frovatriptan - effective; offer for short-term menstrually associated migraine - Level A
- Naratriptan/Zolmitriptan - probably effective for MAM - Level B

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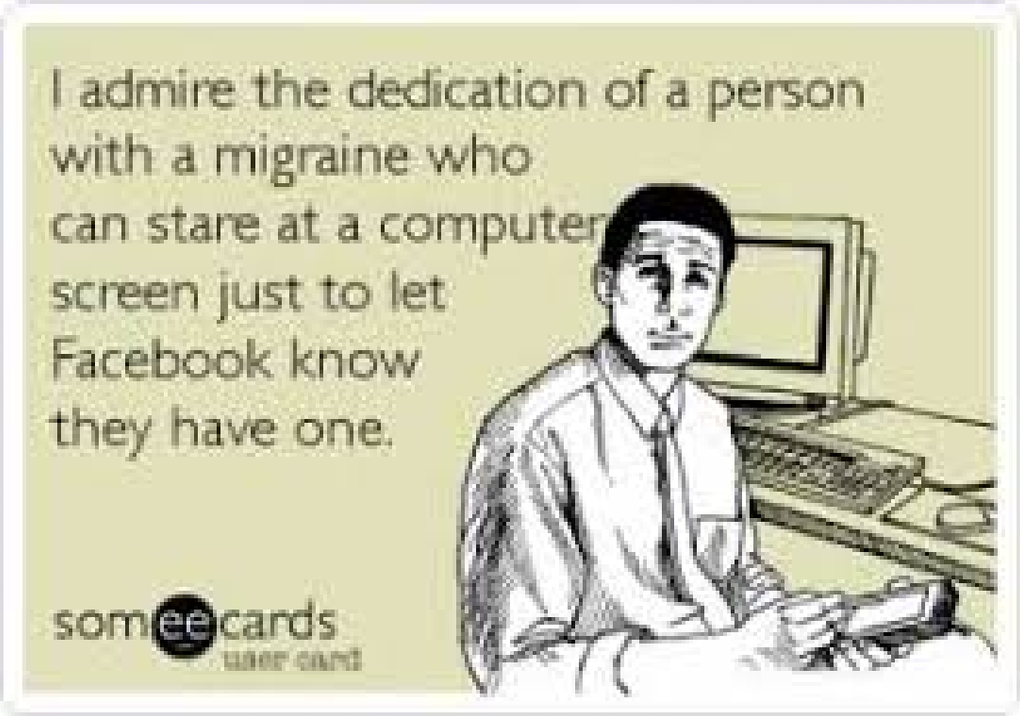
Nonpharmacologic Treatment

- Reduce exposure to common triggers (sleep, alcohol, hunger, dehydration…)
- Stress Management - relaxation training - guided imagery/meditation, cognitive behavioral training, biofeedback
- Acupuncture - conflicting evidence; not generally recommended but not contraindicated
- OMT - particularly directed at cervical pain; can be used both for acute and preventative treatment

AAN: Nonpharmacologic Treatment

- Established efficacy - Butterbur - 75mg BID - RETIRED
- Probably effective
  - Magnesium
  - Feverfew - 6.25mg TID
  - Riboflavin
  - Coenzyme Q10 - 100mg TID



CGRP Inhibitors

- Monoclonal antibodies to the calcitonin gene receptor peptide/receptor (CGRP is released from trigeminal nerves during migraine with vasodilatation/inflammation.)
  - First class of medications specifically designed for migraine prevention; May 2018
  - Monthly/Quarterly injectables
  - Efficacy occurs early in treatment
  - Constipation; Injection site reactions
  - Long-half life; No reversal agent
- Gepants - smaller molecules that cross BBB; expected abortive/preventative

Migraine Treatment: Other Considerations

- Noninvasive neuromodulation
  - Supraorbital transcutaneous stimulation (Cefaly)
  - Transcutaneous occipital nerve stimulation - with a TENS device
  - Transcranial magnetic stimulation (SpringTMS)
  - Noninvasive vagal nerve stimulation
  - Direct current stimulation

AAN Clinical Practice Guideline: Pharmacological Tx of Migraine HA in Children/Adolescents

- Acute Tx:
  - Ibuprofen is effective and should be considered in children (Level A)
  - Sumatriptan NS is effective and should be considered in adolescents (Level A)
  - Acetaminophen is probably effective and should be considered for children (Level B)
  - No data for the use of oral triptans in children/adolescents (Level U)
  - Inadequate data to make a judgment on the efficacy of subq sumatriptan (Level U)

AAN Clinical Practice Guideline: Pharmacological Tx of Migraine HA in Children/Adolescents

- Preventative Tx:
  - Flunarizine probably effective/can be considered but not available in the US (Level B)
  - Pizotifen and nimodipine and clonidine did not show efficacy and are not recommended (Level B)
  - Cyproheptadine, amitriptyline, divalproex sodium, levetiracetam, topiramate - insufficient evidence to make any recommendations - Level U
  - Conflicting evidence for propranolol and trazodone - Level U

AAN: Opportunities for Improvement

- Overutilization of neuroimaging
  - Recurrent HA without red flags
  - HA with typical patterns of migraine/tension
  - Medication overuse/rebound HA
- Underuse of preventative therapies
  - 38% would benefit; 13% utilize
  - Decrease occurrence by 50-80% and reduce severity/duration
  - Consider in 4+/per month or 8+ days/month

1. Estemalik E, Tepper S. Preventive treatment in migraine and the new US guidelines. Neuropsychiatr Dis Treat 2013;9:709–720.

AAN: Opportunities for Improvement

- Inappropriate acute treatment
  - Barbiturates/Opioids
  - Triptan and ergots are the guideline-recommended acute treatments
- Under-treatment of comorbidities
  - Consider other medical, neurologic, psychiatric disorders


THE END IS NEAR
THIS WILL NEVER END
YOUR OPTIMISM DISGUSTS ME.