Migraine Headache Part 1:
Prevalence, Pathophys, Symptoms, Triggers

Beth A. Martin, RPh; PhD, TTS, FAPhA

Professor of Pharmacy (CHS)
UW School of Pharmacy
1022 Rennebohm Hall
beth.martin@wisc.edu

Potential Conflict of Interest Disclosure Statement

My spouse works for Amgen, Inc

I do not receive any direct remuneration or funding from Amgen, Inc

Objectives

Discuss the prevalence of migraine and its debilitating effects.

Explain current thinking regarding the pathophysiology of migraine.

Characterize the symptoms, diagnosis & classification of migraine.

Identify common migraine triggers and aggravating factors.

Discuss the safe and effective use of pharmacologic and non-pharmacologic therapies for alleviating migraine attacks.

Compare and contrast pharmacologic treatment therapies (e.g. route of administration, onset of action, time to relief).

Discuss therapeutic strategies for migraine prevention.

Choose an appropriate therapeutic regimen based on an individual migraine patient's history and needs.

Migraine Is Associated With Other Medical Disorders

Neurologic

- Epilepsy
- Stroke in women under 45

Medical disorders

- Raynaud's syndrome
- Asthma

Psychiatric

- Depression
- Anxiety disorders
- Panic disorder
- Manic-depression bipolar disorder

Buse DC, et al. Poster P61. Presented at: the American Headache Society (AHS) 61st Annual Scientific Meeting; July 11-14, 2019; Philadelphia, PA

Migraine Prevalence and Burden

13% >10%

30% Aura

6% vs 18%

Peak ages: 25-55 yo

$8924 > cost for migraineurs

40% of Episodic Migraines would benefit from Prevention

1. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. *Lancet*. 2018;392:1789-1858. 2. Lipton RB, et al. *Neurology*. 2007;68:343-349. 3. Bonafede M, et al. *Headache*. 2018;58:700-714.

Many Regions of the Brain Are Involved in Migraine Pathophysiology[1]

A wide range of factors and mechanisms are involved in migraine[1]

The clinical features of a migraine vary based on genetic, anatomical, and environmental factors[1]

Thalamus[1,3]

Sensitization and alteration of thalamo-cortical circuits

Sensory sensitivity and allodynia

Target for neuromodulation

Hypothalamus[1,4]

Activation in premonitory phase

Premonitory symptoms

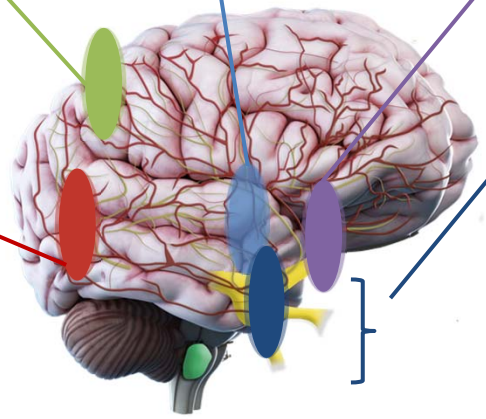
Target for hypothalamic peptides and modulators

Cortex[1,2]

Cortical spreading depolarization, altered connectivity

Migraine aura and cognitive symptoms

Target for neuromodulation



Trigeminocervical Complex[1,5]

Pain transmission or sensitization

Headache and neck pain

Target for medications and neuromodulation

Meningeal nerves and vessels[5]

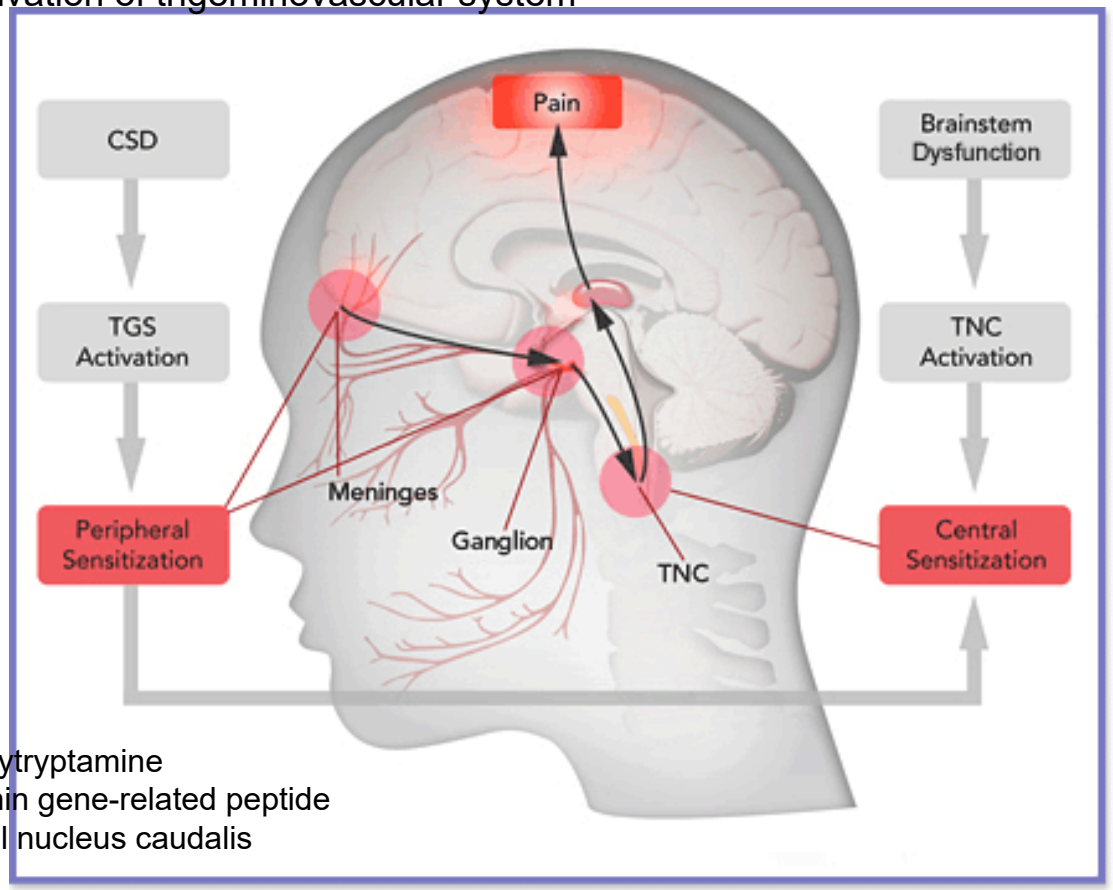
Headache pain

1. Charles A. *Lancet Neurol.* 2018;17:174-182. 2. Tedeschi G, et al. *Cephalalgia.* 2016;36:139-147.
3. Noseda R, et al. Nat Neurosci. 2010;13:239-245. 4. Maniyar FH, et al. *Brain.* 2014;137:232-241.
5. Russo AF. *Annu Rev Pharmacol Toxicol.* 2015;55:533-552.

Cortical spreading depression (CSD) responsible for aura & activation of trigeminovascular system

5-HT, CGRP & other vasoactive neuropeptides released

Vasodilation, inflammation and pain perception



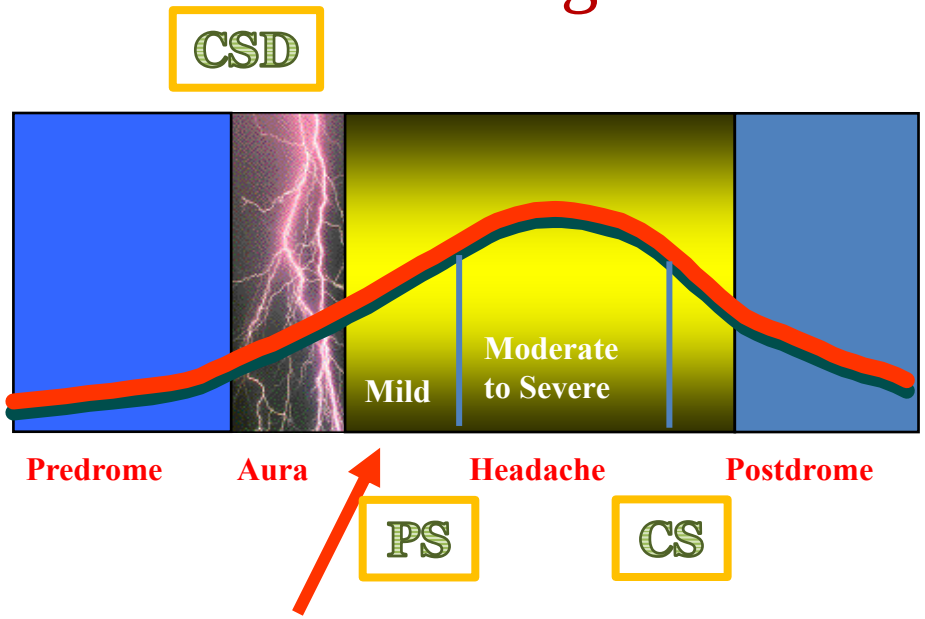
5HT: 5-hydroxytryptamine
CGRP calcitonin gene-related peptide
TNC trigeminal nucleus caudalis

Dysmodulation theory poses migraine w/o aura associated with abnormal neuronal excitability and response to sensory stimuli

http://www.cgrpinmigraine.com/cgrpmig/cgrpinmigraine/hcp/pathophysiology/sensitization_perpetuation.jsp?WT.svl=2

https://www.youtube.com/watch?v=tA-KvkH-0GY

The Phases of a Migraine Attack



Cortical Spreading Depression
Peripheral Sensitization
Central Sensitization

I.C.H.D.-3 Criteria

At least five attacks fulfilling these criteria:

Migraine Without Aura

- 4 to 72 hours
- Pain (2 of 4)
  - **I**ntensity mod to severe
  - **U**nilateral
  - Pulsatile or **T**hrobbing
  - Aggravated w/ (or c/Avoidance of) **A**ctivity
- In addition (1 of 2)
  - **N**ausea &/or vomiting
  - **S**ensitivity to light & sound
- No evidence of organic disease

Tension-Type (TTH)

- 30 minutes to 7 days
- Pain (2 of 4)
  - Bilateral
  - Pressing/tightening
  - Mild to Moderate
  - Not aggravated by activity
- In addition
  - No nausea
  - Photo or phonophobia (or neither)

75% of migraine patients reported neck pain with their attack

ICHD, International Classification of Headache Disorders; IHS, International Headache Society. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. *Cephalalgia*. 2018;38:1-211.

A-U-S-T-I-N

Mnemonic for diagnosing **Migraine Without Aura:**

- **A**ctivity aggravates the headache
- **U**nilateral location
- **S**ensitivity to light and/or sound
- **T**hrobbing
- **I**ntensity moderate/severe
- **N**ausea/vomiting

Soul Bossa Nova – Quincy Jones

Migraine Can Be Further Categorized Into Several Diagnostic Subtypes[1,2]

Migraine diagnosis:[1]

HD frequency

Patients can receive a diagnosis of episodic (< 15 HD/month) or chronic migraine (≥ 15 HD/month)[1,2]

Presence or absence of aura

Patients can receive a diagnosis of migraine with aura or migraine without aura[1] Aura is associated with increased cardiovascular risk (IR = 7.9)[3]

Based on acute medication overuse

Patients with ≥ 15 HD/month and with > 3 months of regular overuse of acute medication can receive a diagnosis of medication overuse headache[1]

HD, headache days.

1. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition. *Cephalalgia*. 2018;38:1-211.2. Buse DC, et al. *Headache*. 2012;52:1456-1470. 3. AAN 2013 Abstract 1892

Headache History

About one-third of individuals with migraine reported experiencing headache on ≥ 4 days/month

- **age at onset***
- frequency
- location
- **time from onset to peak intensity***
- **Pain scale*** (0-3 or 0-10)
- **Aggravating*** and relieving factors
- duration
- **associated symptoms***
- previous medications
- triggers

- Do the headaches interfere with activities?
  - miss work or school
  - work at a slowed pace
  - cancel social activities
- Is the pattern stable?
- menstrual association
- family history
- How effective is current treatment?

***RED FLAGS for Secondary HA**

Rule out a secondary headache

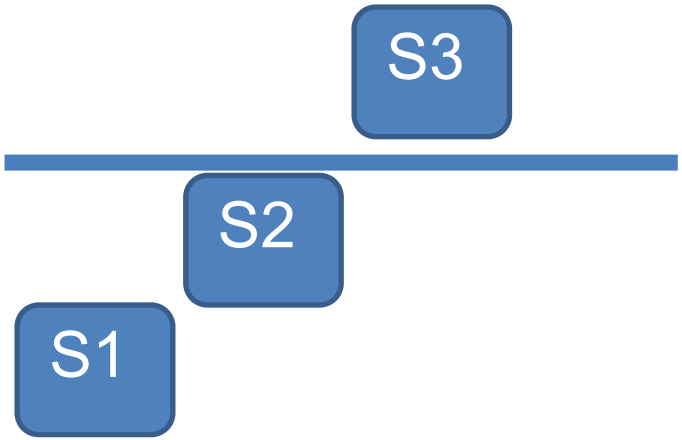
Investigate SNOOP symptoms

- **S** — **Systemic** symptoms (eg, fever, rash, stiffness, muscle aches, fatigue, weight loss) or known disease (eg, influenza, HIV, Lyme disease, sinusitis)
- **N** — **Neurologic** symptoms or signs (eg, confusion, weakness, vision changes, speech difficulty)
- **O** — **Onset** that is sudden (thunderclap headache)
- **O** — **Onset** at older age (>40 years)
- **P** — **Pattern** change (change in headache type/key features, headache progression, shortening or loss of headache-free periods)

(Source: Reference 1)

Ref 1. Dodick DW. Diagnosing headache: clinical clues and clinical rules. *Adv Stud Med.* 2003;3(2):87-92.

Clinically, migraine is a loss of central inhibition and ability to accommodate various stressors



Triggers and Aggravating Factors

Fasting

- Skipping meals/eating specific foods/caffeine intake

Medication

- Analgesic overuse

Circadian Rhythms

- Changes in sleep/wake cycles

Environment

- Weather
- Lighting
- Fragrances/odors

Hormones

- PMS, oral contraceptives, pregnancy, menopause, menses

Stress/Overexertion

What would you do?

- 25-year-old woman, administrative assistant
- In OTC aisle looking for a headache medicine
- Describes as moderate intensity

A. Recommend ibuprofen or naproxen

B. Recommend Excedrin

C. Tell her to see her doctor

D. Assess her headaches

Objective Migraine Disability Assessment: The MIDAS Questionnaire

1. On how many days in the last 3 months did you miss work or school because of your headaches? ☐☐
2. How many days in the last 3 months was your productivity at work or school reduced by half or more because of your headaches? ☐☐
3. On how many days in the last 3 months did you not do household work because of your headaches? ☐☐
4. How many days in the last 3 months was your productivity in household work reduced by half or more because of your headaches? ☐☐
5. On how many days in the last 3 months did you miss family, social or leisure activities because of your headaches? ☐☐

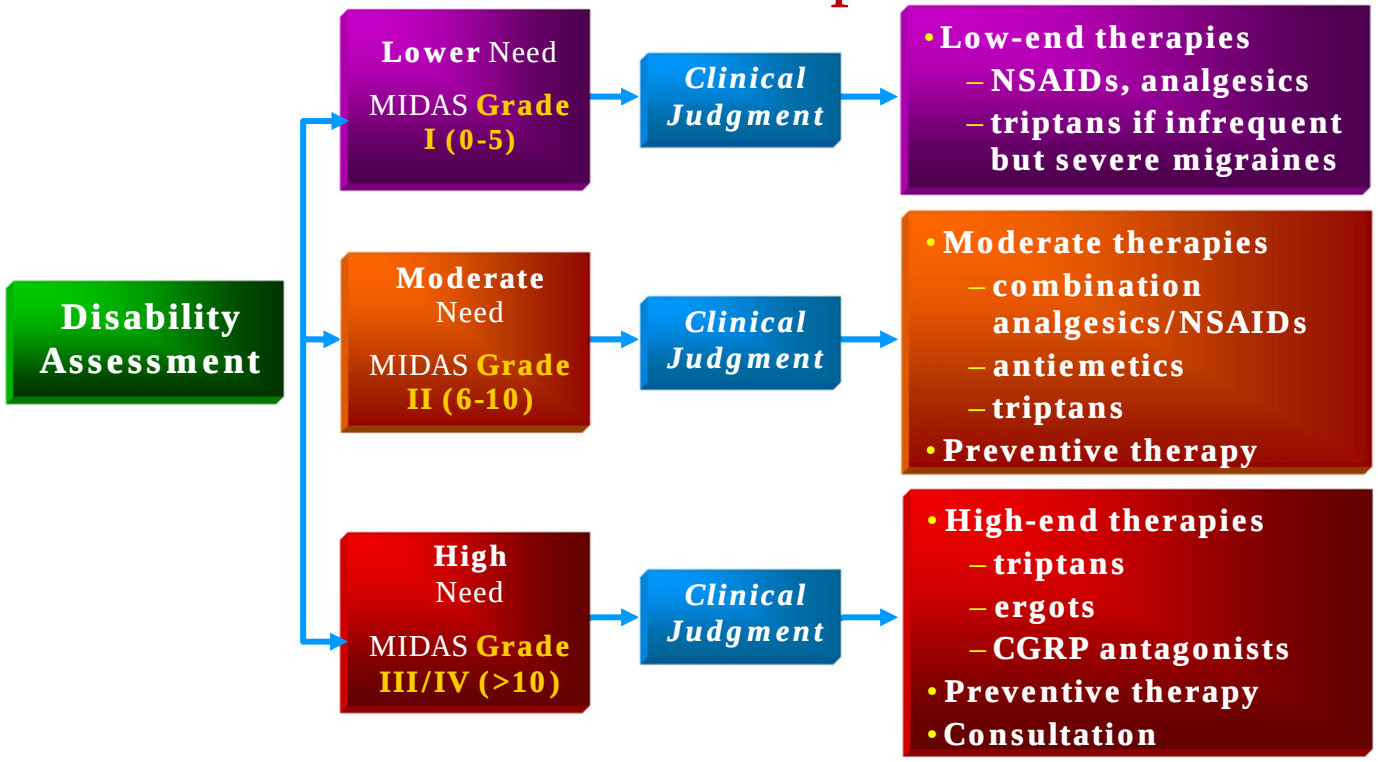
TOTAL ☐☐ days

A. On how many days in the last 3 months did you have a headache? ☐☐

B. On a scale of 0-10, on average how painful were these headaches? (0=no pain, 10=pain as bad as it can be) ☐

Once you have filled in the questionnaire, add up the number of days from questions 1-5 (ignore A and B). If your total is above 6, we suggest that you make an appointment to see your doctor.

Stratified Care Provides Tailored Treatment Options



Based on a MIDAS score of 7, what treatment options would you consider?

A. Low end (NSAIDs, analgesics, combos)

B. Moderate (combos, triptans)

C. High end (triptans, ergots, opioids, CGRPs)

D. Not sure

Four Main Points:

1. Migraine is 3x more common in women than men and affects adults during their peak years of productivity.
2. Describe the pathophysiology of migraine, phases of a headache, and optimal treatment time.
3. Classify a migraine patient based on a thorough history, reported migraine symptoms (AUSTIN), and disability (MIDAS).
4. Apply a stratified care approach to treatment.