Migraine: 101

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Faculty Disclosures

Company	Service provided by Faculty	Compensation Received	Years
Supernus Pharmaceuticals	Speaker's Bureau (Trokendi XR) APP Advisory Board	Honoraria Travel	2017-2019
Eli Lilly and Company	Speaker's Bureau (Emgality, Reyvow)	Honoraria Travel	2018-Present
Allergan/Abbvie	Speaker's Bureau (Ubrelvy, Qulipta)	Honoraria Travel	2020-Present
Biohaven Pharmaceuticals	Speaker's Bureau (Nurtec) APP Advisory Board	Honoraria	2020-Present
Lundbeck	Speaker's Bureau (Vyepti)	Honoraria	2021

Why is migraine important?

Over 31 million Americans live with migraine.

1 out of every 4 households in the U. S. have a person with migraine.

Identified as the 2nd most common cause of years lived with disability worldwide

Roughly half of those with migraine receive an accurate diagnosis.

Interferes with work productivity and educational goals, contributes to absenteeism and impairs family and social relationships.

Genetics and Headache

Migraine is the most common genetic neurological condition in the world.

Over 40 genes identified so far that encode for primary headache syndromes

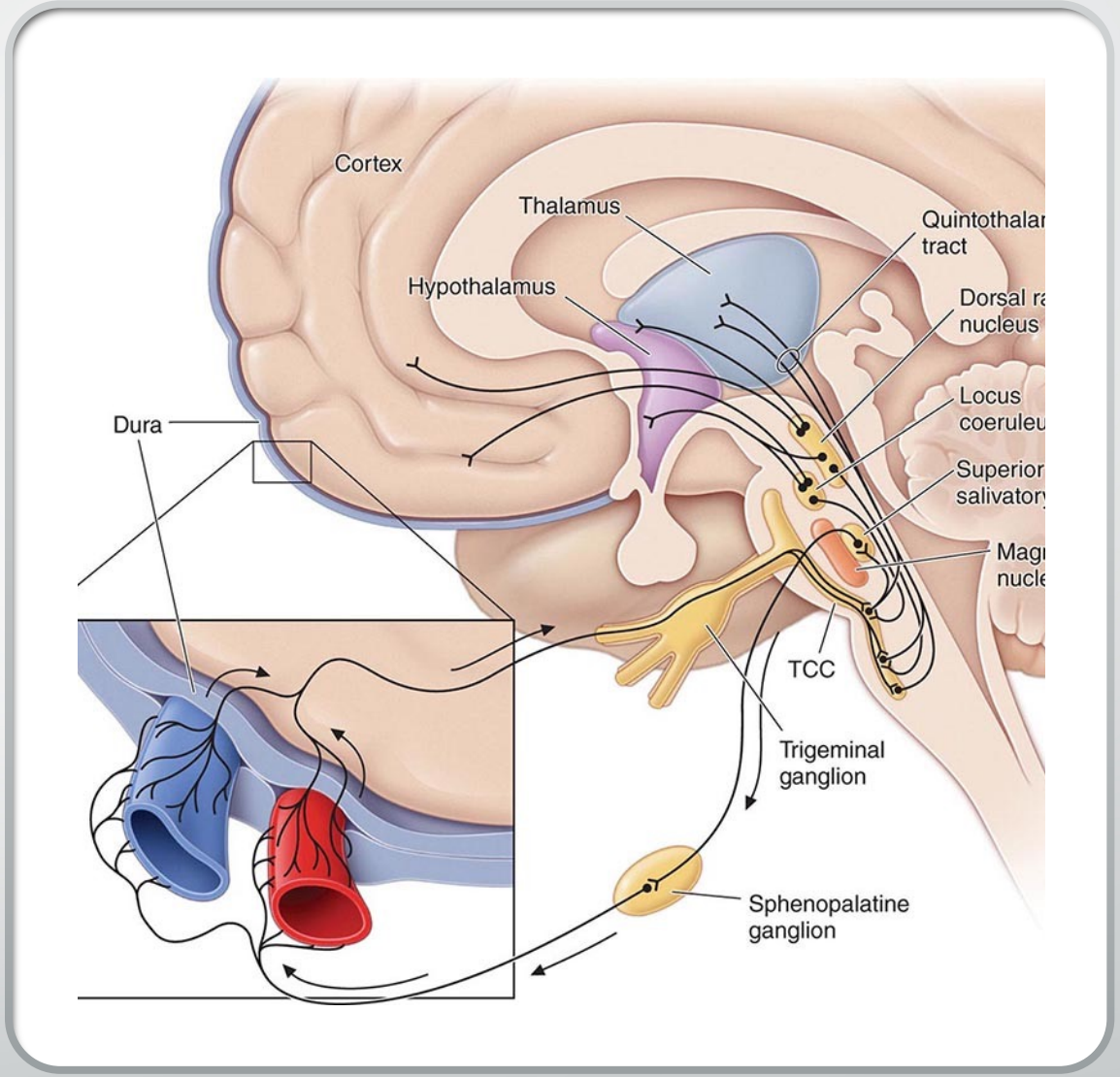
Every person has a unique genetic “threshold” for developing headache and predisposition for a specific headache phenotype

Migraine Pathophysiology

- Sensory nerve fibers arise from the trigeminal ganglion and trigeminal nucleus caudalis (TNC)

- Activated by mechanical thermal or chemical stimuli via release of "inflammatory soup" (bradykinin, PGE2, serotonin, histamine, others)

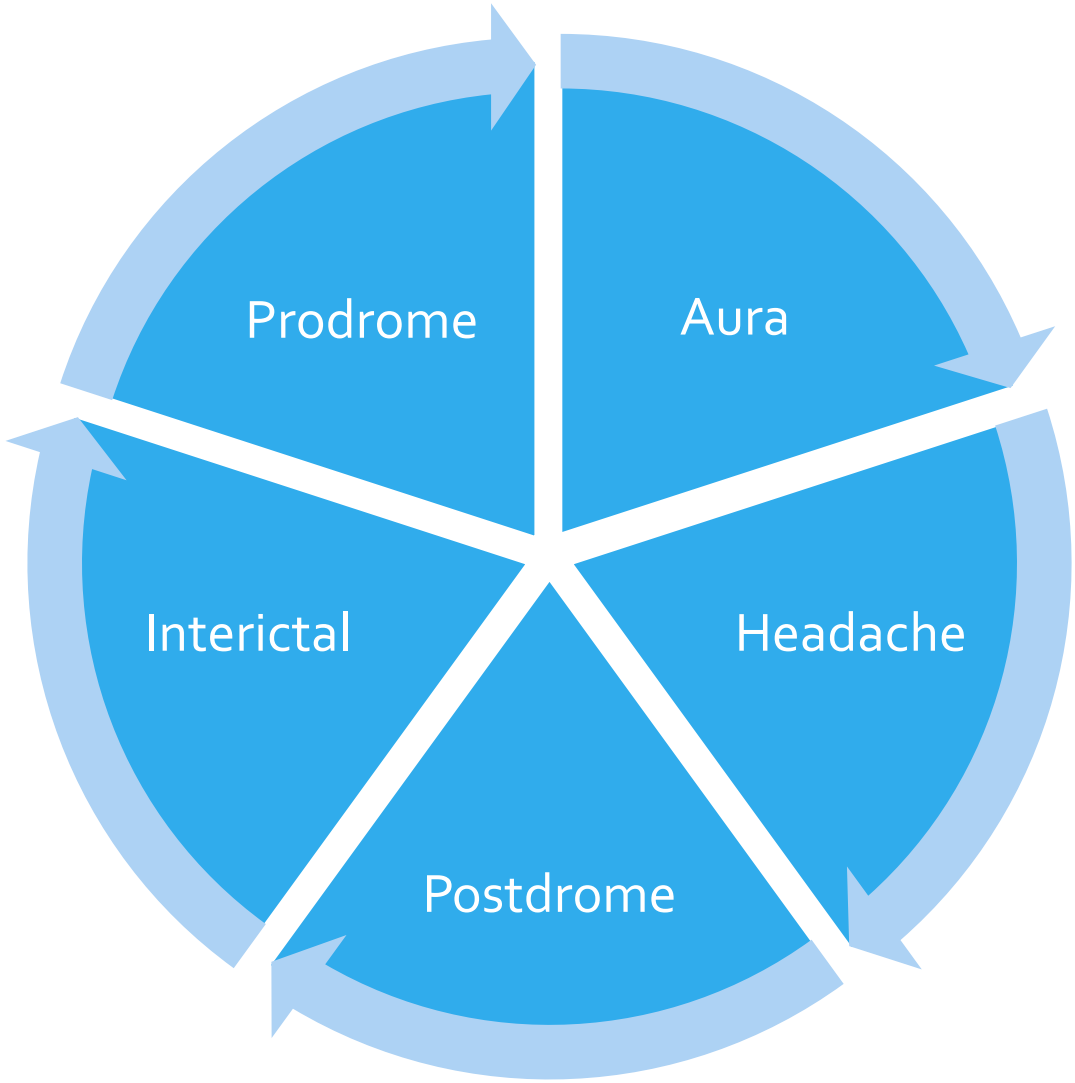
- Causes release of neuropeptides (CGRP, substance P, neurokinin A, others)and sensitization of meningeal pain receptors.



Calcitonin Gene Related Peptide (CGRP)

- CGRP has been the focus of research for over 20 years
  - Plays key role in migraine pathophysiology through arterial vasodilation, neurogenic inflammation and activation of meningeal nociceptors.
  - Enhances synaptic transmission through glutamatergic signaling and contributes to peripheral and central sensitization.
- CGRP targeted therapies have changed the landscape of migraine treatment since their initial FDA approval in 2018.
- Many older medications used off label for migraine treatment affect CGRP levels indirectly by blocking other chemicals that lead to CGRP release.

Stages of Migraine



Migraine Prodrome

- 70% of patients experience premonitory symptoms hours to days before headache onset.

Psychiatric	Neurologic	General
Anxiety Depression Euphoria Irritability Restlessness Mental slowness Hyperactivity Fatigue Drowsiness	Photophoiba Phonophobia Difficulty concentrating Hyperosmia	Neck stiffness Cold feeling Yawning Sluggishness Increased thirst Increased urination Nausea Anorexia Diarrhea Constipation Fluid retention Food cravings

Migraine Postdrome

- Defined as the time between headache resolution and feeling completely back to normal
- “Migraine Hangover”
- Often lasting 6-24 hours.
- Symptoms include fatigue, head pain, cognitive difficulty, GI symptoms, mood change and weakness.

Interictal Phase

- Time in between migraine attacks
- Functional MRI studies suggest widespread altered brain function between attacks
  - Results in hyperresponsivity and lack of habituation.
  - Some patients subsequently report continued sensory hypersensitivities, cognitive dysfunction, dizziness, imbalance or GI symptoms during interictal phase.

Migraine Diagnostic Criteria

- Characterized by 5 or more headache attacks, each lasting **4-72** hours
- With at least **2** of the following:
  - Unilateral location
  - Pulsating quality
  - Moderate to severe pain intensity
  - Aggravation by and/or causing avoidance of routine daily activity
- And at least **1** of the following:
  - Nausea and/or vomiting
  - Photophobia and phonophobia

ID Migraine®:
3 Item Migraine Screener

Do you feel nauseated or sick to your stomach with your **headache**?

Did your **headache** limit you from working, studying, or doing what you needed to do for any day in the previous 3 months?

Does light bother you more than when you don't have **headaches**?

"Any patient presenting to your clinic c/o headache that interferes with activities should be assumed to be migraine until proven otherwise."

--Dr. Brad Torphy, MD– Medical Director, Chicago Headache Institute

Migraine Diagnostic Considerations

Up to 1/3 of patients have migraine aura

IHS criteria do not require GI symptoms

Vomiting occurs in <1/3 patients

41% of migraine patients report bilateral pain

50% of the time pain in non-pulsating

Migraine Aura

Approximately 33% of patients experience migraine aura.

Focal neurological phenomena preceding or accompanying attacks caused by cortical spreading depression.

Most symptoms develop over 5-20 minutes, lasting less than 60 minutes.

Characterized by visual, sensory, motor, language or brainstem disturbances.

Migraine Aura Diagnostic Criteria

A. At least 2 attacks fulfilling criteria B-C

B. One or more of the following fully reversible aura symptoms: visual, sensory, speech/language, motor, brainstem or retinal symptoms

   1. At least 2 of the following characteristics: At least one aura symptom spreads gradually over 5 min or more and/or 2 or more symptoms occur in succession.
   2. Each single aura symptom lasts 5-60 min.
   3. At least one aura symptom is unilateral
   4. Aura is accompanied or followed by headache, possible lag phase lasts maximum of 60 min.

C. Not better accounted for by another diagnosis.

Sinus Headache

RHINOSINUSITIS AS A CAUSE OF HEADACHE IS RARE!

OBTAIN ADDITONAL HISTORY!

CONSIDER ADDING MIGRAINE SPECIFIC TREATMENT OPTION

Withholding Migraine Treatment

There are many contributing factors to migraine, but patient needs to have the right genetic makeup to present with typical migraine headache despite this.

Withholding migraine treatment due to the belief that there is a contributing factor driving the migraine is wrong and unethical.

Preferred approach is to treat the migraine while performing diagnostic workup or treating contributing issues concurrently.

Acute Migraine Treatment Strategies

Step care across attacks—using acute treatment for several attacks, escalating to another type of treatment if this is not effective.

Step care within attacks—escalating therapy within a single attack if the initial treatment is ineffective

Stratified care—Using different medications for 1st line treatment based on specific headache characteristics or environmental factors

Acute Migraine Treatment

Analgesics and anti-inflammatories (PO, IM, IV)

- Naproxen, diclofenac, ibuprofen, ketorolac, ASA, acetaminophen, caffeine, combo tx

Triptans

- Sumatriptan (PO, IV, SQ, NS), naratriptan, rizatriptan (PO, ODT), eletriptan, zolmitriptan (PO, NS), almotriptan, frovatriptan

Ergots

- DHE (IV, SQ), Migranal nasal spray, cafergot

Dopamine modulators (PO, IM, IV)

- Prochlorperazine, chlorpromazine, metoclopramide

Gepants

- Rimegepant, ubrogepant

Ditans

- lasmiditan

Analgesics and anti-inflammatories

- Naproxen, diclofenac, ibuprofen, ketorolac, ASA, acetaminophen, caffeine
- Variety of administration options (tabs, caps, rectal, topical, oral liquid, IM, IV)
- OTC options often utilized by patients independently due to easy access.
- Ensure proper dosing, patients often use doses too low or too high.
- Limit to no more than 2-3 times weekly to avoid rebound headaches.

Ergotamine

- DHE (IV, SQ), Migranal nasal spray, cafergot

Triptans

- Standard of care for acute migraine treatment since 1990s
- Sumatriptan (PO, IV, SQ, NS), naratriptan, rizatriptan (PO, ODT), eletriptan, zolmitriptan (PO, NS), almotriptan, frovatriptan
- Serotonin 5HT-1B &1D receptor agonists
- Contraindicated in patients with CV risk due to vasoconstriction.
- Use with other serotonergic medications NOT a contraindication
  - Rare--0 to 4 cases per 10,000 patient years
  - Expert consensus states benefits clearly outweigh risks

ED/Urgent Care

- IV fluids (usually NS)
- IV medications
  - Sumatriptan
  - DHE
  - Ketorolac
  - Depakote (if effective oral Depakote taper at home can be helpful)
  - Magnesium
  - Lidocaine
  - Dopamine antagonists (give with diphenhydramine for prevention of dystonic reaction)
    - Prochlorperazine
    - Metoclopramide
    - Chlorthalidone
    - Haloperidol
- Dexamethasone IV given once migraine resolves can help prevent migraine recurrence

Narcotics and barbiturates

Narcotic medications and butalbital-containing products widely used for headache tx in the past

Associated with significantly higher rates of rebound or medication overuse headache

Associated with dependency, addiction and withdrawal

Risk of overdose

Migraine Prevention

Medications taken at regular intervals to reduce migraine frequency

Antidepressants

- Tricyclic antidepressants (amitriptyline, nortriptyline)
- SNRIs (venlafaxine, duloxetine)

Antihypertensives

- Beta blockers (propranolol, metoprolol, atenolol, carvedilol)
- Calcium channel blockers (verapamil)

Anticonvulsants

- Topiramate, Depakote, lamotrigine, gabapentin

Botox

- 31 superficial IM injections around head, neck and shoulders
- Administered every 12 weeks (about 3 months)

Gepants

- Rimegepant (Nurtec)
- Atogepant (Qulipta)

CGRP Monoclonal antibodies

- Erenumab (Aimovig)
- Galcanezumab (Emgality)
- Ajovy
- Eptinizumab (Vyepti)

Non-Pharmacological Therapies

- Physical therapy
- Neuromodulation/neurostimulation
- Acupuncture
- Biofeedback/neurofeedback
- Chiropractic/osteopathic manipulation
- Massage therapy
- Cognitive-behavior therapy (CBT)/pain psychology
- Lifestyle Modification

Triggers/Contributing Factors

- Stress
- Sleep disturbance
- Diet
- Mood changes or uncontrolled mood issues
- Sensory cues (bright lights, strong smells or sounds, etc)
- Weather change
- Altitude change
- Hormone change
- Metabolic change
- Medical or psychiatric illness
- Medications

Migraine Hygiene

Follow consistent sleep schedule and obtain 6-8 hr sleep nightly

Consume 60-100 oz water daily (non-caffeinated flavorings or electrolyte containing drinks okay).

Consume snack or meal every 3-4 hr while awake.

Develop regular exercise program based on personal abilities, resources and limitations.

Limit caffeine intake to no more than 400 mg daily and intake shouldn't fluctuate significantly day to day.

Manage stress and psychiatric conditions , consider utilizing relaxation exercises, meditation or yoga

Migraine Diet

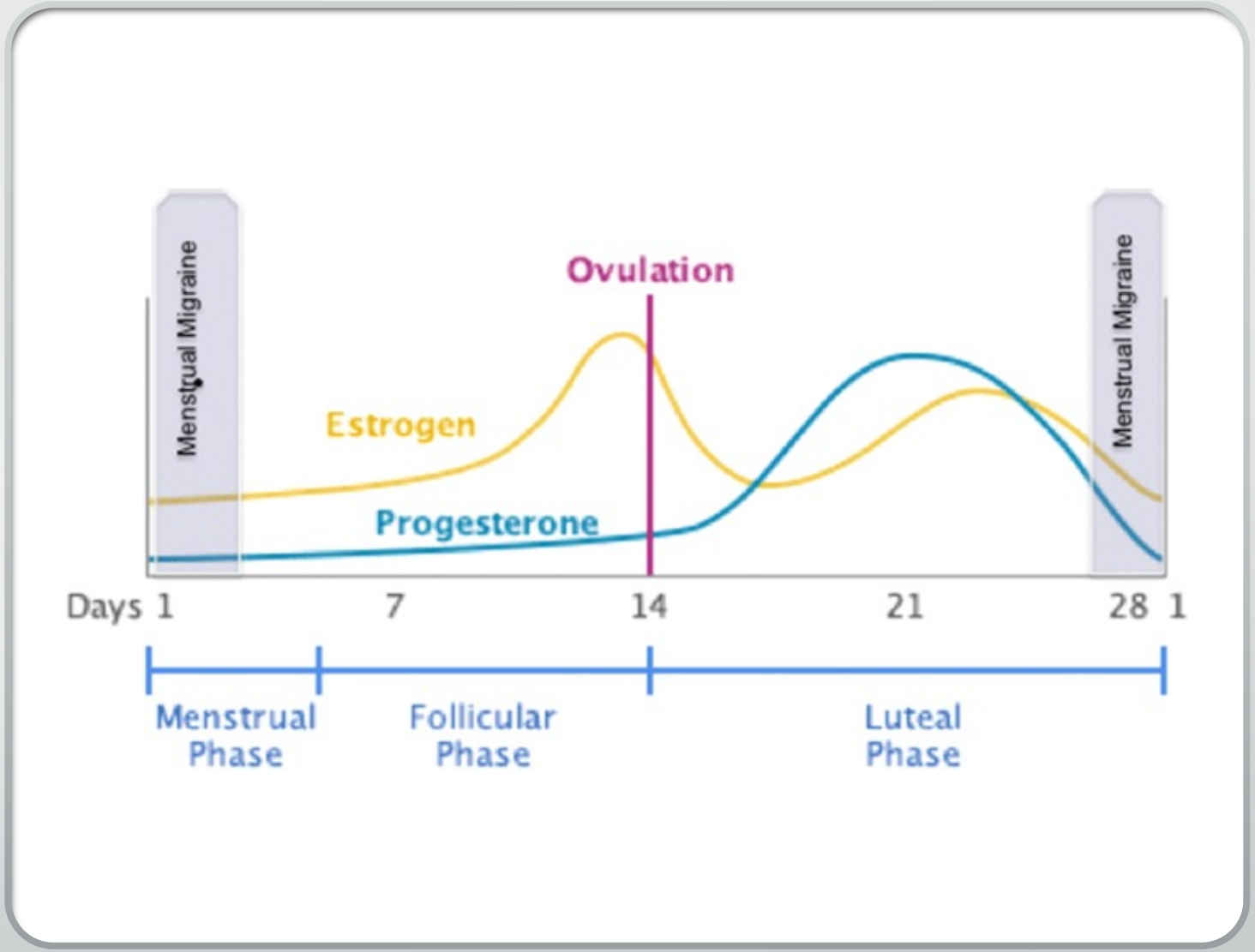
- Avoid caffeine
- Avoid wine and beer
- Avoid sugary foods and artificial sweeteners
- Avoid soda
- Avoid soy or soy lethicin
- Avoid MSG (monosodium glutamate, spice, natural flavor, mono or diglycerides, diguanylate, inositol)
- Avoid aged cheeses (ok—ricotta, cram cottage, Kraft singles, Velveeta, fresh mozzarella, cheese curds)
- Avoid processed meats (deli/lunch meats, cured, smoked, aged, hotdogs, ham, salami, pepperoni)
- Avoid beef (ok--buffalo, lamb, kosher beef)
- Avoid yeast and cut down on bread
- Avoid nuts and nut butters

Nutraceutical and Herbal Therapies

- Magnesium
- Riboflavin (B2)
- CoQ10
- Methylated folate
- Butterbur
- Feverfew

Menstrual Migraine

- Occurs with rapid drop in estrogen in late luteal phase and early follicular phase when estrogen and progesterone are lowest (day -2 to +3)



Menstrual Migraine Prevention

Hormonal Stabilization

- Depo Provera
- IUD
- Birth Control implants
- Oral contraception can be difficult in this population!

Mini Prevention

- NSAIDs
- Naratriptan or frovatriptan
- gepants

Oral Birth Control and Migraine

- Previous reports of increased stroke risk in women using combined hormonal contraception (CHC) based on studies from 1960s and 1970s with use of high-dose estrogen (≥30 mg daily)
- No increased stroke risk with very low dose combined hormonal contraception (CHC) containing 20-25 µg ethinyl estradiol (EE).
- Continuous ultra low-dose formulations (10-15 µg EE) may even reduce aura frequency, thereby potentially decreasing stroke risk.
- Extended dosing and/or estrogen step-down options helpful for prevention of menstrual related migraine

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Thank You!!

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