MIGRAINE

Oklahoma Academy of Physician Assistants
42nd Annual Conference
September 21, 2016

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Under Accreditation Council for Continuing Medical Education guidelines disclosure must be made regarding relevant financial relationships with commercial interests within the last 12 months.

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I have no relevant financial relationships or affiliations with commercial interests to disclose.
MIGRAINE

LEARNING OBJECTIVES

- Relate a practical definition of migraine
- Describe why several medical conditions manifested by transient symptoms with or without headache are actually due to migraine
- Describe the three main goals of migraine therapy
DIFFERENTIAL DIAGNOSIS: PRIMARY VS. SECONDARY HEADACHES

PRIMARY HEADACHES
- Bothersome but not life-threatening conditions
- Headaches are usually:
  - Intermittent
  - Similar to past headaches
- Scans & tests NOT necessary
- Examples:
  - Migraine
  - “Tension-type”
  - Trigeminal autonomic cephalalgias

SECONDARY HEADACHES
- Worrisome, potentially life-threatening conditions
- Headaches are usually:
  - Constant
  - Different from past headaches
- Scans & tests ARE necessary
- Examples:
  - Mass lesion (e.g., brain tumor)
  - Pseudotumor cerebri
  - Temporal arteritis
  - Meningitis
  - Subarachnoid hemorrhage
HEADACHE = HEAD PAIN
WHAT CAUSES HEAD PAIN?

- The brain, brainstem, and spinal cord are surrounded by a sack called the **meninges**

- The meninges are lined with pain nerves
  - Trigeminal nerve
  - Cervical nerve roots
  - Thoracic nerve roots

- Pain nerves in the meninges are turned on when the meninges are **stretched** or **irritated**
WHEN TO WORRY ABOUT A 2º HEADACHE & OBTAIN IMAGING OR OTHER TESTS

- 2º (secondary) headaches are due to underlying disease, e.g., tumor, hemorrhage, meningitis, temporal arteritis, CSF leak

- **Best indicators:**
  - First, worst, persistent, or different headache
  - Abnormal neurologic exam

- **Other potential indicators:**
  - Onset after Valsalva maneuver or head trauma
  - New onset after age 50
  - Exacerbation with head position
  - Lack of migraine-associated features

**Patients with indicators above should undergo appropriate testing:**

1. **CT**—C(−) for trauma or acute blood
2. **MRI**—C(−) for subacute blood; C(+) for tumor/abscess
3. Blood work—CRP & ESR for temporal arteritis; CBC for anemia
4. Lumbar puncture—for meningitis (or SAH if CT negative)

*CSF = cerebrospinal fluid; CT: computed tomography C(−): without contrast C(+) : with contrast MRI: magnetic resonance imaging CBC: complete blood count SAH: subarachnoid hemorrhage*

*If history consistent with migraine & neurologic exam is normal, brain scans & other tests are NOT necessary.*
DIFFERENTIAL DIAGNOSIS: PRIMARY HEADACHES

- Migraine
- Tension-type headache
- Trigeminal autonomic cephalalgias (TACs)

Many believe tension-type headaches are a form of migraine headache without aura

“Given abundant similarities between epidemiology, clinical features, & treatment response patterns of migraine & tension-type headache, it’s reasonable to believe they share common pathophysiology.” Cady et al. Headache 2002;42:204-216

“The diagnostic difficulty most often encountered among primary headache disorders is to discriminate between tension-type headache and mild migraine without aura.” Cephalalgia 2013;33(9):629-808 (ICHD-3 Criteria)

There is a genetic link between migraine, episodic tension-type headache, and irritable bowel syndrome. D. Uluduz. Presented at the 68th Annual Meeting of the American Academy of Neurology, April 2016
# PRIMARY HEADACHES: TRIGEMINAL AUTONOMIC CEPHALALGIAS

<table>
<thead>
<tr>
<th>TYPE OF TAC</th>
<th>KEY FEATURES</th>
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| Cluster     | • More common in **men** (3-6x) / mean age at onset 31 (27-37)  
• Symptoms occur in “clusters” (seasonal & diurnal)  
• Duration 60 min, frequency 1-3/day  
• Severe unilateral orbital pain  
• Agitation/restlessness common (90%), N/V, sensory phobias  
• Abortive Rx – **oxygen** (7-10 L/min x 15-20 min) or triptans  
• Prophylactic Rx – verapamil or lithium |
| Paroxysmal hemicrania | • More common in **women** (3x)  
• Duration 15 min, frequency ≥ 5/day  
• Prophylactic Rx – **indomethacin** |
| Hemicrania continua | • More common in **women** (2x)  
• Duration min to days, frequency variable  
• Prophylactic Rx – **indomethacin** |
| SUNCT\(^1\)/SUNA\(^2\)  
Short-acting unilateral neuralgiform headache attacks w/ (1) conjunctival injection & tearing or (2) cranial autonomic Sxs | • More common in **men** (3x)  
• Duration 5 sec to 5 min, frequency 1/day to 30/hour  
• Prophylactic Rx – **lamotrigine** |

All TACs have cranial dysautonomia which may include lacrimation, conjunctival injection, nasal congestion, rhinorrhea, ptosis, eyelid edema.

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OU Neurology
MIGRAINE DOES NOT = BAD HEADACHE
HEADACHE IS THE TIP OF THE MIGRAINE ICEBERG

“Headache is never the sole symptom of migraine, nor indeed is it a necessary feature of migraine attacks.”
Oliver Sacks, Migraine, Revised & Expanded, 1992

*light, noise, motion, smell, & temperature intolerance
HEADACHE VS. MIGRAINE: SYMPTOM VS. SYNDROME

- Headache
  - Pain in the head

- Migraine
  - A syndrome of episodic brain dysfunction with systemic manifestations (that may include headache)

Migraine is by far the most common cause of recurrent, episodic headache without sequelae, but... migraine with NO headache is also very common.
MIGRAINE IS VERY SIMILAR TO EPILEPSY
THE PARALLELS BETWEEN SEIZURES & MIGRAINE ATTACKS

- **Seizure**
  - Episode of abnormal electrical activity in the brain
  - $\uparrow$ activity (seizure) followed by $\downarrow$ activity (postictal state)

- **Epilepsy**
  - Condition in which a person has a predisposition to seizures

- **Migraine attack**
  - Episode of abnormal chemical activity in the brain
  - $\uparrow$ activity (cortical spreading excitation) followed by $\downarrow$ activity (cortical spreading depression)

- **Migraine**
  - Condition in which a person has a predisposition to migraine attacks

Like many other neurologic conditions, it is likely that epilepsy & migraine are channelopathies, i.e., due to dysfunction of neuronal ion channels with resultant hyperexcitable neurons.

Think of a migraine attack as a slow-motion seizure.

i.e.: id est (that is)
MIGRAINE EPIDEMIOLOGY: STUDIES ARE MISLEADING

- Two major studies suggesting 18% of women & 6% of men have migraine were misleading & greatly underestimated prevalence of the migraine “condition”
  - Used very restricted definition of migraine:
    - At least one severe headache in last 12 months
    - Unilateral or pulsatile pain
    - Either (1) nausea/vomiting or phonophobia/photophobia or (2) visual or sensory aura before the headache

- Thus, these studies excluded many migraine types and determined prevalence of a subset of migraine attacks within the last year, not the overall prevalence of the migraine condition

Stewart WF et al. JAMA. 1992;267;64-69
Lipton RB et al. Headache. 2001;41:646-657
MIGRAINE EPIDEMIOLOGY: THE TRUTH

- Migraine epidemiology studies should include:
  - Sinus headaches (all experts agree are migraines)
  - Tension/regular headaches (many experts feel are migraines)
  - Migraine with aura other than visual or sensory, e.g., vertigo (all experts agree these exist)
  - Nonheadache migraines, e.g., migraine aura without headache, abdominal migraine (all experts agree these exist)
  - Symptoms since birth (once a migraineur, always a migraineur)

- Actually, 75-90% of people have the condition migraine

**NOTE:** There is **no genetic basis for a gender difference** in migraine (women admit to symptoms more readily than men & have more attacks than men due to estrogen changes, but do NOT have the migraine gene more often than men)

e.g.: exempli gratia (for example)
MIGRAINE: WHAT IT IS
PRACTICAL DEFINITION & DESCRIPTION

Genetic condition in which a person has a predisposition to suffering recurrent transient episodes (attacks) of brain dysfunction with systemic manifestations that may include:

- headache/neck pain – from mild to severe, variable location
- focal neurologic symptoms – mimics stroke/TIA, Meniere
- GI symptoms (upper or lower) – equals IBS, mimics gallstones
- chest pain – mimics heart attack, equals atypical noncardiac CP
- autonomic dysfunction – BP, pulse, sinus congestion, epistaxis, red ear, Horner, etc.

“triggered” by hormonal or environmental changes or other medical conditions; each episode consists of:

4 possible phases (prodrome, aura, pain, postdrome).
MIGRAINE TRIGGERS: EXTERNAL & INTERNAL CHANGES

- Environmental changes
  - Barometric pressure (weather, altitude), motion
  - Scents, smoke, fumes

- Hormonal changes
  - Stress (esp. stress “letdown”), exercise, thyroid, testosterone
  - Estrogen > progesterone—menarche, pregnancy, hormonal contraceptives, menopause, ovulation/menstruation

- Sleep changes
  - Deficiency or excess, change in shift

- Diet changes
  - Hunger, dehydration
  - Alcohol (all types, but esp. red wine)
  - Artificial foods (nitrates, MSG, sulfites, aspartame, sucralose, etc.)

- Other physiologic changes / medical conditions
  - Head trauma, fever, increased intracranial pressure
  - Cerebral blood flow changes (AVM, endarterectomy/angioplasty, ischemia—paradoxical embolism via PFO)

Triggers can be additive, i.e., having multiple triggers at one time makes a migraine attack more likely than having one trigger alone.

PFO: patent foramen ovale
# Migraine Phases: Prodrome/Premonitory*

|-------------|---------|---------|-------------|

- Mood changes
  - Irritability, depression, euphoria/hyperactivity
- Difficulty concentrating
- Stiff neck
- Fatigue, malaise, yawning
- Autonomic/GI symptoms
  - Constipation, diarrhea, urinary frequency
- Anorexia or food cravings
  - Esp. foods that increase serum serotonin and/or magnesium, e.g., chocolate, bananas, nuts, peanut butter, sweets, fatty foods

*May begin hours to days before attack, persist through all 4 phases—likely related to serotonin, magnesium, hypothalamic changes.*
MIGRAINE PHASES:
AURA (1 of 3)

- **Transient neurologic symptoms**
  - Due to cortical spreading excitation/depression (with secondary local hyperemia/oligemia)
  - Symptoms referable to location of transient chemical changes in cerebral cortex

- **Pattern of symptoms**
  - Recurrent & stereotypical (previous similar spells)
  - Gradual onset
  - Traveling (1 part of body to another) over minutes to hours
  - Progressive (1 type of symptom to another)
  - Duration minutes to hours

*Chemical chain reaction in the brain leads to focal symptoms that change—in location & type—during an attack*
MIGRAINE PHASES: AURA (2 of 3)

- **Types of focal neurologic symptoms**
  - Visual—Usually positive (scintillation) followed by negative (scotoma)
    - Shimmering, scintillating, flashing lights
    - Spots, dots, bubbles, lines (zigzag, wavy, heat off pavement)
    - Any color, but often silver, gray, or clear
    - Usually associated w/ motion, e.g., moving, vibrating, coalescing
  - Sensory—Usually positive (tingling) followed by negative (numbness)
  - Motor—Hemiparesis (= “hemiplegic migraine”)
  - Cognitive—Aphasia, confusion, amnesia, olfactory hallucinations
  - Brainstem/temporal lobe—
    - Vertigo, ataxia, diplopia, tinnitus, dysarthria, ↓ consciousness
  - Autonomic nervous system – see next slide for dysautonomia sx's
MIGRAINE PHASES: AURA (3 of 3)

- **Autonomic nervous system symptoms (transient dysautonomia due to insula/brainstem dysfunction)**
  - GI symptoms – Nausea/vomiting, anorexia, dyspepsia, abdominal cramping, flatulence, diarrhea, constipation
  - Cranial dysautonomia – Horner syndrome, sinus congestion/epistaxis, facial/scalp flushing (e.g., red ear)
  - Temperature changes – Hypothermia, mild fever
  - Cardiovascular changes – Hypertension, hypotension, syncope, palpitations, arrhythmias

Migraine causes headache & transient hypertension, but hypertension does not cause headache
MIGRAINE AURA & BRAIN ANATOMY

Auras tend to “progress” and “travel”—visual aura most common, but many other auras possible depending on location of chemical changes.

Different parts of the brain have different functions. The chemical chain reaction of migraine typically starts at the back of the brain in the occipital lobe (vision area) and may move forward to involve other brain areas.

The brain’s chemical chain reaction during a migraine attack results in symptoms that:

- **progress** from one type to another (for example, from visual to tingling to abdominal) and/or
- **travel** from one part of the body to another (for example, from face to arm to leg).
MIGRAINE PHASES:
PAIN

Headache characteristics—No specific pattern
- Location variable
  - Unilateral, bilateral
  - Anterior (frontal, periorbital, etc.), posterior (occipital, neck)
  - Diffuse, focal (e.g., nummular = coin-shaped)
- Throbbing, pulsating, pounding, pressure, squeezing, dull, aching
- Severe, moderate, mild, absent
- Onset usually gradual; duration hours, days, weeks

Associated symptoms
- Sensory phobias – photo, phono, kinesio, thermo, osmo
- Allodynia – pain due to light touch, breeze, hair moving, etc.
- “Lightheadedness” – vibratory or buzzing paresthesia in head
- Chest pain – usually after headache, often w/ chest allodynia

Trigeminal nerve (CN5) & cervical nerve root sensitization in the meninges results in headache, sensory phobias, neuropathic symptoms
MIGRAINE PHASES: POSTDROME

- Fatigue, malaise
- Difficulty concentrating
- Mood changes
- Muscle aches
- Scalp tenderness
- Scalp, limb, or chest allodynia
- Food cravings or anorexia

The migraine hangover
MIGRAINE PATHOPHYSIOLOGY
A JIGSAW PUZZLE WITH MISSING PIECES

Trigger ➔ Hypothalamic dysfunction & hyperexcitable cortex (esp. occiput)

“Cortical spreading depression”
(excitation/depression w/ hyperemia/oligemia, esp. occiput)

Spreading depression in insula &/or brainstem serotonergic & noradrenergic dysfunction

CN V/cervical root sensitization with pain receptor stimulation & release of neuropeptides (e.g., CGRP)

➡️ Prodrome

➡️ Aura

➡️ Dysautonomia

➡️ Head & neck pain
(+ sensory phobias & cranial arterial changes, e.g., sinus congestion)

Platelet & serum serotonin levels decrease during attacks of migraine, tension headache, IBS, & PMS. Cerebral serotonin & magnesium decrease during a migraine attack.
ANOTHER VIEW OF THE MIGRAINE ICEBERG

Migraine patients often see multiple physicians for multiple symptoms...

...and when tests are normal, the physicians often assume the patient has a psychiatric condition.

HEADACHE

Gastrointestinal
- Nausea
- Vomiting
- Abdominal pain
- Flatulence
- Diarrhea
- Constipation
- GE reflux
- Infant colic

Ear, Nose, & Throat
- Sinus congestion
- Sinus drainage
- Epistaxis
- Flushed face
- Red ear
- Vertigo
- Motion sickness

Cardiology
- Hypertension
- Hypotension
- Arrhythmia
- Palpitations
- Syncope
- Chest pain

Neurology
- Visual scotomata
- Migratory tingling
- Allodynia
- Aphasia
- Hemiplegia
- Amnesia
- Confusion
- Diplopia
- Horner syndrome

Ob-Gyn
- PMS
- Morning sickness
- Postpartum headache
- Perimenopausal spells

Primary Care
- Malaise
- Yawning
- Food cravings
- Poor concentration
- Sensory phobias
- Photophobia
- Phonophobia
- Kinesiophobia
- Osmophobia
- Thermophobia

OU Neurology
THE BLIND MEN & THE ELEPHANT
Ancient Indian Parable Retold by American Poet John Godfrey Saxe (1800s)

It’s a snake!
It’s a rope!
It’s a spear!
It’s a fan!
It’s a wall!
It’s a tree!

Very old story from India of 6 blind men who come upon an elephant. Each man feels a different part of the elephant & comes to a different conclusion regarding what he is feeling. None realize they are actually feeling an elephant.
DOCTORS WITH BLINDERS & MIGRAINE
An Unfortunate Modern-Day Medical Story

Like the ancient Indian story, each specialist sees a different symptom of migraine & comes to a different conclusion regarding what the patient has. None of the specialists realize the patient actually has migraine.

These 6 are not the only possible false diagnoses. See next slide...
CONDITIONS LIKELY DUE TO (OR RELATED TO) MIGRAINE

- Tension-type headache
- Neck pain w/ headache
- Sinus headache
- Recurrent sinus congestion
- Recurrent vertigo/Meniere
- Recurrent epistaxis
- Red ear syndrome
- Motion sickness
- Regular/ordinary headache
- Irritable bowel syndrome
- Functional dyspepsia
- Infantile colic
- Chronic pelvic pain
- Premenstrual syndrome
- Panic attacks
- Atypical noncardiac chest pain
- Transient HTN w/ headache
- Transient global amnesia
- Episodic confusion
- POTS (postural orthostatic tachycardia syndrome)
- Syncope of unknown cause
- Postconcussion headache
- Hangover
- Frequent “strokes” or “TIAs” w/ normal MRI brain

These conditions cause temporary symptoms that are said to be of unknown cause, but which may be explained by migraine

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WHAT TESTS ARE ABNORMAL DURING A MIGRAINE ATTACK?

- Usually none
- During migraine attacks:
  - Brain scans are normal*
  - Heart evaluations are normal
  - Abdominal X rays, CT scans, & scopes are normal
- However, during migraine attacks:
  - Blood pressure may be high or low
  - Gallbladder & intestines may move more slowly than usual

*Though there may be chronic changes on MRI brain (see next slide)

If your patient keeps having spells of headache, belly ache, chest pain, visual symptoms, tingling, etc. and all the tests are normal—think migraine
MRI BRAIN & MIGRAINE WITH AURA:
CHRONIC CHANGES OF NO IMPORTANCE

- White spots on T2 & FLAIR brain MRI scans called “UBOs” are common in migraine with aura
  - Located at gray-white junction (just underneath the cortex)
  - Small & round with “fuzzy” borders
  - Often mistaken for multiple sclerosis or strokes
  - Not concerning clinically

"Unidentified Bright Objects" (UBOs) of migraine seen on FLAIR MRI

Kruit MC et al. JAMA 2004;291:427
Symptoms that seemed vague and psychiatric are clearly due to migraine when seen through the proper lenses.

- Diagnosis without migraine understanding—things don’t make sense, therefore patient is “crazy”
- Diagnosis with migraine understanding—a pattern emerges
NOT DIAGNOSING MIGRAINE LEADS TO WASTED DOLLARS & LIVES

- Imaging studies (CT, MRI, endoscopy, colonoscopy, etc.)
- Medications
  - Antibiotics (bacterial resistance)
  - Decongestants (chronic nasal congestion, HTN, chronic symptoms)
  - Anxiolytics, antidepressants (social consequences of false diagnosis)
  - Antithrombotic agents (hemorrhage)
  - Narcotics (chronic symptoms, drug-seeking behavior caused by docs)
- Surgeries
  - Gallbladder / colon
  - Uterus / ovaries
  - Sinuses / ear
- Disability, retirement, divorce
- Iatrogenic functional overlay (psychiatric symptoms superimposed on “organic” symptoms)

HTN: hypertension
MIGRAINE THERAPY: TWO KINDS

Prophylactic and Abortive Agents

- Prophylactic agents (preventers)
  - If a patient takes certain medications every day, s/he is likely to have less frequent and less severe migraines

- Abortive agents (stoppers)
  - If a patient takes certain medications as soon as possible at the start of a migraine attack, s/he may either stop the attack or make it less severe
MIGRAINE THERAPY: 3 MAIN GOALS

1. Aim to decrease frequency & severity of ALL migraine symptoms—not just headache

2. Use prophylactic agent(s) for more than just migraine – “kill 2 birds with 1 stone”
   - Choose prophylactic agent(s) that treat coexisting conditions pertinent to the patient

3. Avoid medication-overuse syndrome
   - Limit use of all combined abortive agents to ≤ 2 d/wk (except prescription naproxen)
   - Use prophylactic therapy to enable patient to use abortive therapy ≤ 2 d/wk
MEDICATION-OVERUSE SYNDROME

Most common cause of constant migraine symptoms

Also called “analgesic rebound” or “analgesic withdrawal”

Caused by:

- Analgesic*, triptan, decongestant, or muscle relaxant use > 2 days/week (*except for prescription naproxen)
- Any use of ondansetron, PPI, or dipyridamole

Relationship to migraine:

- More common in migraineurs
- Results in modification of 5-HT1 (migraine serotonin) brain receptors ...reversible after ≥ 4 wks w/o offending agent(s)
- Changes migraine symptoms from intermittent to chronic (incl. headache, GI, chest pain, tingling, vertigo, etc.)
- Renders all migraine therapies ineffective

Treatment: Avoid all possible offending agents x ≥ 4 weeks; begin prophylactic agent; consider oral naproxen and/or IV abortive agents

PPI: proton-pump inhibitor
MIGRAINE THERAPY: WHEN TO START PROPHYLACTIC AGENT

- If migraine symptoms ≥ 2 d/wk or
- If migraine symptoms are especially debilitating when they occur (interfere with activities of daily living) despite abortive therapy

Establishing migraine frequency:
- In most cases, general estimate by patient is sufficient
- In patients with great difficulty recalling frequency, advise use of migraine calendar or diary
MIGRAINE THERAPY:
WHEN TO STOP PROPHYLACTIC AGENT

You might consider discontinuing migraine prevention therapy if both:

- Migraine frequency considered “rare” and
- Medication not needed for coexisting condition (e.g., hypertension or depression)

Note, however, that sometimes a migraine prevention medication is not as effective after stopping and restarting it
MIGRAINE PROPHYLACTIC THERAPY: 5 GENERAL PRINCIPLES

1. All migraine prophylactic agents also treat other conditions ...always try to “kill 2 birds with 1 stone”
2. Different patients respond differently to different drugs ...even within the same class
3. Migraine patients are often very sensitive to side effects ...start low and go slow
4. Determining efficacy requires patience & time – often 2-6 months ...each change in dose takes 4 wks to work
5. Some patients eventually require multiple agents ...continue partially effective agents & add new ones
MIGRAINE PROPHYLACTIC THERAPY: CATEGORIES

Most migraine prevention medications come from one of three categories:

- **Blood pressure medicines**
- **Seizure medicines**
- **Depression medicines (antidepressants)**

A person may respond to a drug in a certain category even after not responding to another drug in the same category.

Only one NSAID (nonsteroidal inflammatory drug) is effective for migraine prevention: prescription naproxen (not over-the-counter naproxen sodium/Aleve/Anaprox).

Over-the-counter **magnesium oxide, melatonin, and riboflavin (vitamin B2)** may prevent migraine.
MIGRAINE PROPHYLACTIC THERAPY: TOP CHOICES BY MECHANISM

There is no “class effect” — a patient may respond well to a drug after not responding to a different drug in the same category.

- **Antiepileptic drugs**
  - topiramate
  - divalproex
  - gabapentin (less effective)

- **Antihypertensive agents**
  - candesartan
  - lisinopril
  - nadolol
  - propranolol
  - verapamil

- **Serotonin-norepinephrine reuptake inhibitor (SNRI)**
  - venlafaxine ER

- **Tricyclic antidepressants**
  - nortriptyline
  - amitriptyline
  - doxepin

- **NSAID**
  - naproxen

- **Antihistamine**
  - cyproheptadine

- **Over the counter**
  - magnesium oxide
  - vitamin B2 (riboflavin)
  - melatonin
  - +/- feverfew, butterbur, coQ10

SNRI: serotonin norepinephrine reuptake inhibitor
NSAID: nonsteroidal anti-inflammatory drug
ER: extended release
MIGRAINE PROPHYLACTIC THERAPY: SIDE EFFECTS

Side effects that may influence agent choice

All antihypertensives ➔ hypotension
Beta blockers ➔ depression, sedation, asthma?
Tricyclic antidepressants ➔ weight gain, sedation, constipation
Divalproex ➔ weight gain, hair loss, polycystic ovaries
Topiramate ➔ weight loss, abnl cognition, nephrolithiasis
Naproxen ➔ ulcers, renal disease
Magnesium ➔ loose stools
Verapamil ➔ constipation, peripheral edema

When choosing an agent, address coexisting conditions, e.g., hypertension, depression, anxiety, patient weight, seizures, osteoarthritis, insomnia, stool consistency
MIGRAINE PROPHYLACTIC THERAPY: TOP CHOICES BY AGE & IN PREGNANCY

- **Children & Young Adults**
  - topiramate
  - nortriptyline/amitriptyline
  - nadolol/propranolol
  - cyproheptadine

- **Older Adults**
  - candesartan/lisinopril
  - nortriptyline/amitriptyline
  - divalproex
  - venlafaxine

- **All Ages—primary or adjunct**
  - naproxen ➔ use around time of predictable triggers & for other pain
  - magnesium oxide ➔ also treats constipation
  - melatonin ➔ also treats insomnia

- **Pregnancy**
  - magnesium oxide (class B)
  - cyproheptadine (class B)
  - nadolol/propranolol (class C)
  (propranolol better for lactation)
MIGRAINE ABORTIVE THERAPY: GENERAL PRINCIPLES

- **KEY:** Take migraine abortive therapy early, but not often
  - Triptan efficacy 2/3 when HA mild, 1/3 when HA moderate
  - Limit use to ≤ 2 d/wk to avoid medication-overuse headaches

- Triptans—migraine-specific serotonin agonists—are most effective (bind to subsets of serotonin 1 receptor—1D & 1B)
  - But triptans may cause vasospasm; safety uncertain if:
    - Migraine associated w/ aphasia, hemiplegia, or vertigo
    - Vascular disease or risk factors (including hypercoagulability)
    - Patient < 12 or > 65 years of age

- Analgesics may also be effective

- Narcotics are generally NOT indicated—limit use to:
  - Pregnant women—only use acetaminophen (B) or narcotics (C)
  - Elderly & patients with vascular disease

HA: headache
MIGRAINE ABORTIVE THERAPY: SEROTONIN (5-HT) AGONISTS

TRIPTANS
Selective 5-HT$_{1D/1B}$ agonists

Fast onset/Short half-life
- eletriptan (Relpax)
- rizatriptan (Maxalt & Maxalt MLT)
- zolmitriptan (Zomig & Zomig ZMT)
- almotriptan (Axert)
- sumatriptan (Imitrex PO, PN, SC)

Slow onset/Long half-life
- frovatriptan (Frova)
- naratriptan (Amerge)

ERGOTS
Nonselective 5-HT$_{1D}$ agonists
- Cafergot (PO, PR)
- DHE (dihydroergotamine)
  - DHE-45 IV, IM
  - Migranal PN

TRIPTAN + NSAID
- sumatriptan/naproxen sodium (Treximet)

In most cases, start with the highest recommended triptan dose, e.g., sumatriptan 100 mg, eletriaptan 40 mg, rizatriptan 10 mg.
Take as early as possible at onset; may repeat x 1 after 2 h; do not exceed 2 tabs / 24 h; do not exceed 2 d / week.

PO: per os (by mouth)   PN: per nares (by nose)   SC: subcutaneously
PR: per rectum   IV: intravenously   IM: intramuscularly
MIGRAINE ABORTIVE THERAPY: NON-NARCOTIC ANALGESICS

While all these agents can be effective when used as early as possible at migraine onset, they all cause medication-overuse syndrome if used > 2 days per week

- **Nonspecific single-agent analgesics**
  - Aspirin, acetaminophen (Tylenol), ibuprofen or other NSAIDs

- **Nonspecific combination analgesics**
  - Excedrin Migraine (acetaminophen, aspirin, caffeine)
  - Excedrin Tension (acetaminophen, caffeine)
  - BC Powder (acetaminophen, aspirin, caffeine)
  - Goody’s Headache Powder (aspirin, salicylamide, caffeine)
  - Midrin, Amidrine, Duradrin, Epidrin (acetaminophen, dichloralphenazone, isomethoptyene)
  - Fiorinal (aspirin, butalbital, caffeine)
  - Fioricet, Esgic (acetaminophen, butalbital, caffeine)
MIGRAINE ABORTIVE THERAPY: PARENTERAL AGENTS IN HOSPITAL/ED

- Normal saline – 1 L IV bolus
- Magnesium sulfate – 1 g IV
- Valproic acid (Depacon) – 500 mg IV
- Metoclopramide (Reglan) – 10 mg IV
- Prochlorperazine (Compazine) – 10 mg IV
- Chlorpromazine (Thorazine) – 25 mg IV
- Dihydroergotamine (DHE) – 0.5-1.0 mg IV or IM

These agents may be repeated q8h PRN.

RARELY need analgesics. ALMOST NEVER need narcotics.

High-dose steroids are also effective, but rarely necessary.

In pregnant women, may use IV NS &/or IV metoclopramide (class B).

Avoid reflexively giving acetaminophen, NSAIDs, narcotics!
CHRONIC MIGRAINE THERAPY: BOTULINUM TOXIN TYPE A

- Indication – *chronic migraine* only
  - Headache ≥ 15 days/month x ≥ 3 months
  - Migraine features ≥ 8 days/month
  - No response to 3 prophylactic agents
  - Treatment for medication overuse given

- Dose – 155 units IM divided in 31 sites *q 12 wk*

- Mechanism of action is unclear

- Not a first-line therapy
  - Like all migraine therapies, effective for some, but not all patients
CLINICAL PEARL:
BELIEVE SYMPTOMS, NOT CAUSE

- **Always** believe your patient’s symptoms
- **Never** believe your patient’s explanations (rationalizations) for the cause of symptoms without thinking it through yourself

Your patient is the WHAT expert.
You are the WHY expert.
CLINICAL PEARL:
TRANSIENT HYPERTENSION SPELLS

- Any patient who can sense when his or her blood pressure is elevated is having migraine attacks
- Prescribe migraine abortive therapy (e.g., ibuprofen, Excedrin Migraine, triptan)
- Do NOT prescribe PRN blood pressure medication (NO clonidine!)
- Use a daily blood pressure medication for migraine prevention (e.g., candesartan, nadolol)
MIGRAINE
LEARNING OBJECTIVES

- Relate a practical definition of migraine
- Describe why several medical conditions manifested by transient symptoms with or without headache are actually due to migraine
- Describe the three main goals of migraine therapy
THE END