Primary Care Internal Medicine 2015

Updates in Headache: Assessment and Treatment

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Disclosure of Financial Relationships

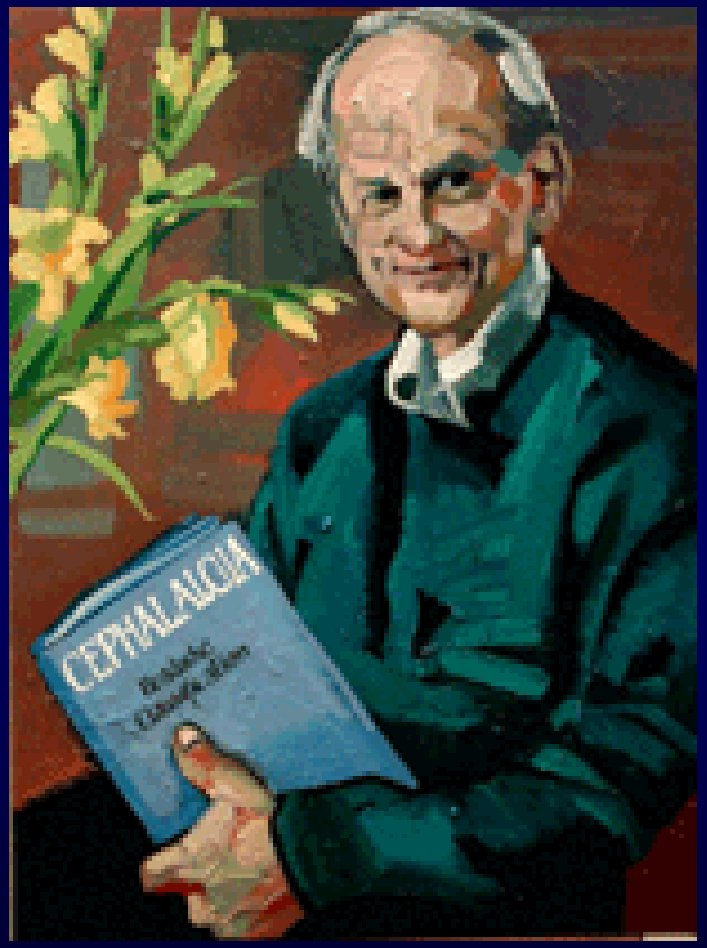
- No disclosures

Questions

- How are headaches diagnosed?
- What are the typical treatment strategies for the most common forms of headache?
- What are the warning signs for secondary headache and when is workup required?
- How to manage challenging headaches?

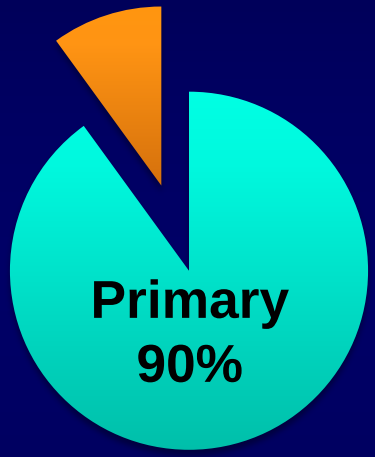
Headache Classification

- International Classification of Headache Disorders
- Third edition (beta) just released
- Find it at: www.ihs-classification.org/en



Headache Classification and Diagnosis

- **Primary Headaches**
  - Migraine
  - Tension-type
  - Cluster headache
- **Secondary Headaches**
  - Tumor
  - Meningitis
  - Giant cell arteritis



What's this headache?

- A 23 year old woman in for a routine visit mentions that she gets short, severe unilateral head pain when she eats ice cream or has a cold drink. The pain is sharp and lasts about 2 minutes. No associated symptoms. She wonders if this is something serious.

Cold stimulus headache

- AKA “brain freeze” or “ice cream headache”. More common in people prone to migraine
- Wikipedia: “The phenomenon is common enough to have been the subject of research published in the *British Medical Journal* and *Scientific American*.”
- Cause unclear but theories abound!
- Treatment: common sense! (Don’t gulp cold drinks)

What's this headache?

- 48 year old man with migraine that is well managed with eletriptan for individual attacks and propranolol 80 mg LA once daily for prevention
- In for routine visit, he mentions that his migraine is under control but he's having a new kind of headache: short, sharp 2-4 second jabs of sharp pain in the area of his migraines. Can occur up to 30 or 60 times a day.

Primary Stabbing Headache

- AKA ice-pick pains, jabs and jolts
- Transient, localized stabs of pain in the head
  - a single stab or a series of stabs
  - Exclusively or predominantly felt in the distribution of the first division of the trigeminal nerve
  - Last for seconds and recur irregularly once to many times daily
- If occasional, no treatment necessary. If troublesome, try indomethacin 25 mg po tid. This is one of the “indomethacin-responsive” headaches.

What's this headache?

- 68 year old woman presents accompanied by her husband
- Remote history of migraine – no problems since menopause
- For last 3 months experiences severe, sudden onset of excruciating 10/10 head pain with orgasm. Lasts about an hour then gradually goes away. Workup negative.

A scenario to take seriously

- Think aneurysm, posterior fossa lesions, etc
- If workup negative, it's "headache associated with sexual activity"
  - Preorgasmic and orgasmic
- Treatment is indomethacin and/or propranolol 1 hour prior to sexual activity

Frese A, Eikermann A, Frese K, et al. Headache associated with sexual activity: demography, clinical features, and comorbidity. Neurology 2003; 61:796.

Pascual J, Iglesias F, Oterino A, et al. Cough, exertional, and sexual headaches: an analysis of 72 benign and symptomatic cases. Neurology 1996; 46:1520.

ICHD Part I: Primary headaches

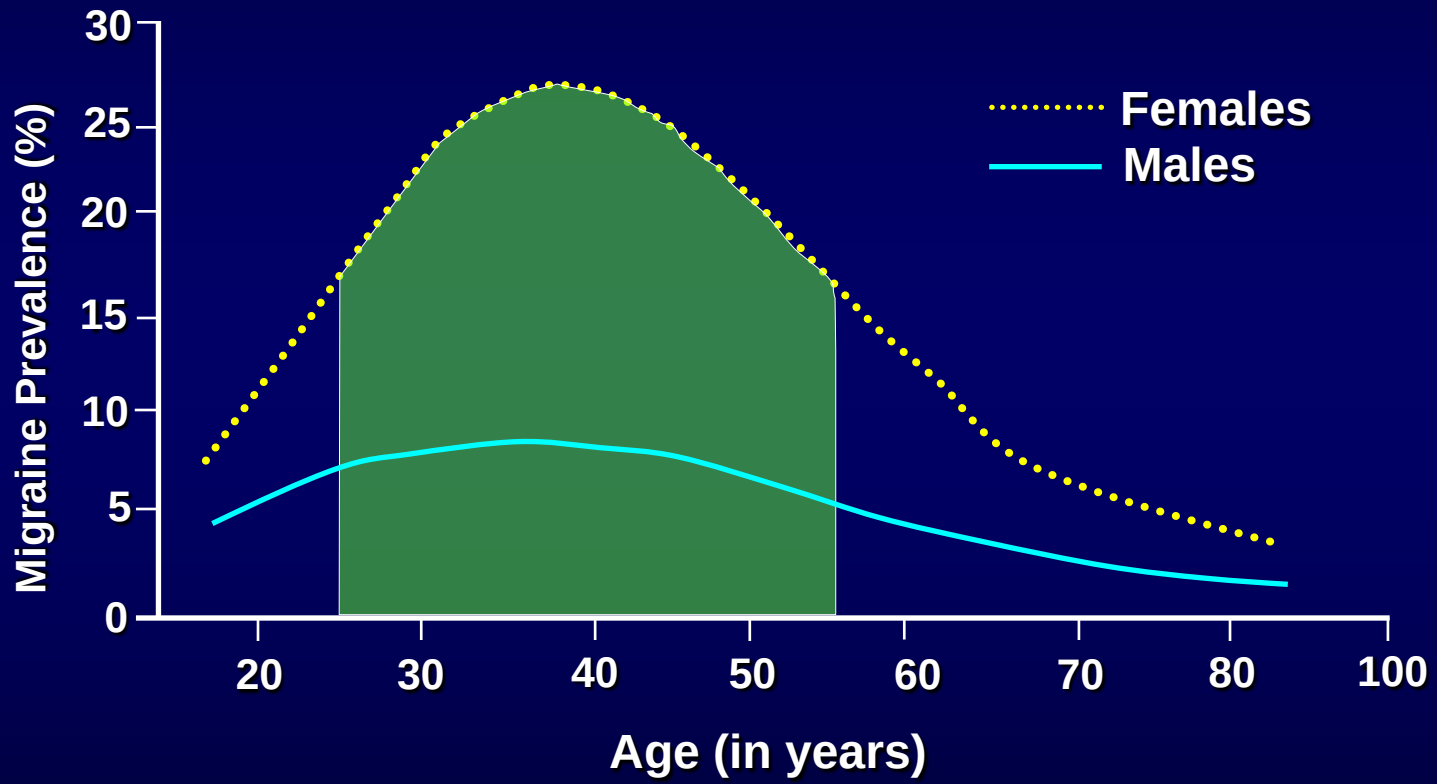
1 Migraine

2 Tension-type headache

3 Cluster headache and trigeminal autonomic cephalgias (TACs)

4 Other primary headaches

Prevalence of Migraine
Age & Sex



- Peak prevalence at age 40 years
- Greatest impact on ages 25 to 55 years

ICHD Diagnostic Criteria For Migraine Without Aura

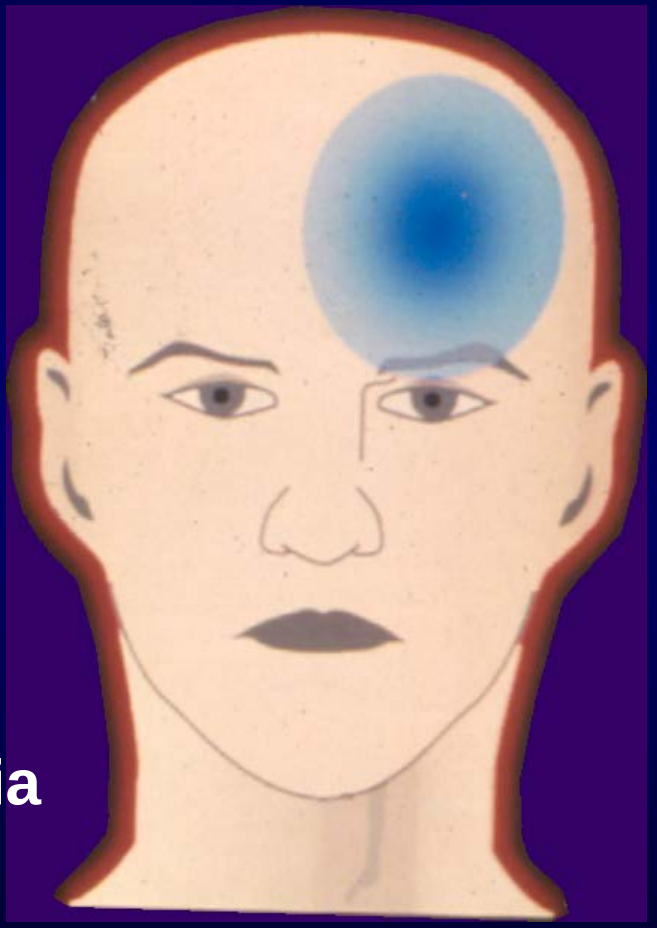
A. Lasting 4 to 72 hours

B. Two of the following
   - Unilateral location
   - Pulsating quality
   - Moderate or severe intensity
   - Aggravation by or causes avoidance of routine physical activity

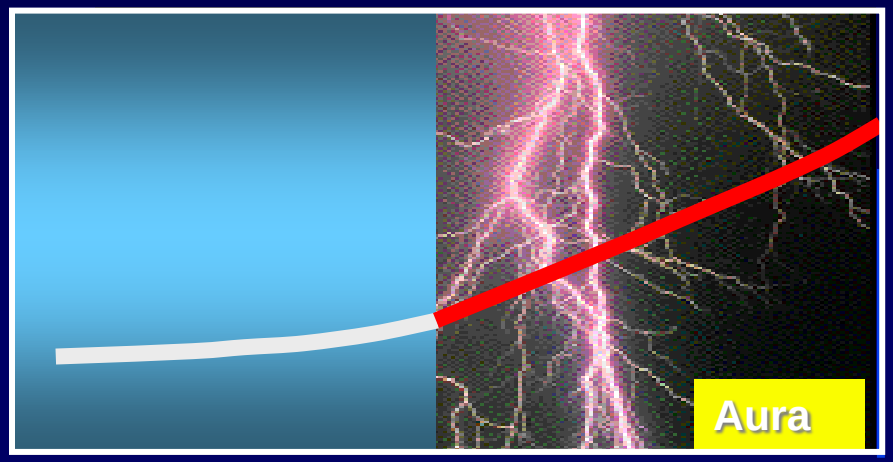
C. At least one of the following:
   - Nausea and/or vomiting
   - Photophobia and phonophobia

D. At least five attacks fulfilling the three bullet points above

E. No evidence of organic disease



Aura



- Focal neurologic event(s)…visual, sensory, motor
- Usually precedes headache…but not always
- Positive, negative, spreading and reversible

Visual Aura Rating Scale

Table 4 Visual Aura Rating Scale (VARS)

Visual symptom characteristic	Risk score
Duration 5–60 mins	3
Develops gradually ≥ 5 mins	2
Scotoma	2
Zig-zag line (fortificaiton)	2
Unilateral (homonymous)	1
Maximum VARS score	10
Migraine with aura diagnosis	≥5

Eriksen et al. The Visual Aura Rating Scale for Migraine Aura Diagnosis. Cephalalgia 2005;10:801-810.

ICHD Diagnostic Criteria For Tension-Type Headache

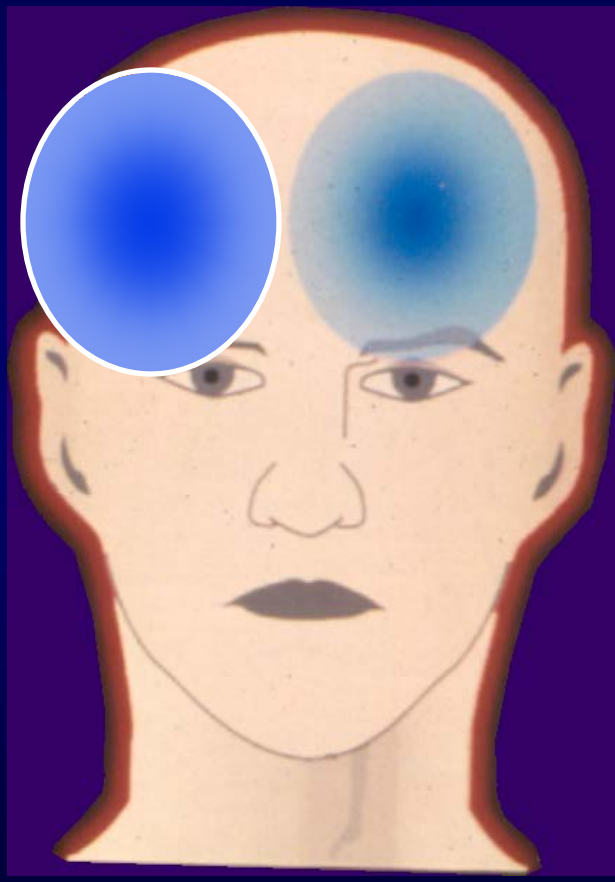
A. Lasting 30 minutes to 7 days

- Steady, pressing quality
- Bilateral location
- Mild to moderate intensity
- No aggravation by routine physical activity

C. No associated symptoms (mild nausea allowed)

D. At least five attacks fulfilling the three bullet points above

E. No evidence of organic disease



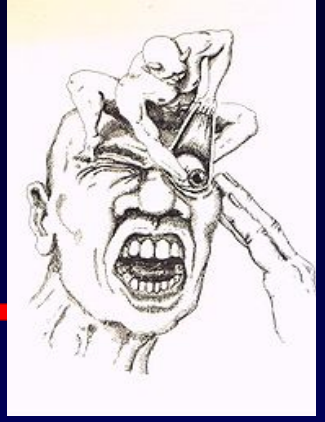
Differentiating Migraine from Tension Type Headache

- 41% of migraine patients had bilateral pain
- 50% of the time, pain was nonthrobbing
- Stress is a common trigger for migraine
- Neck pain may be present in both disorders
- Probable migraine vs tension-type headache

Lipton et al. *Headache.* 2001;41:646-657.

Pryse-Phillips et al. *Can Med Assoc J.* 1997;156(9):1273-1287.

An unhappy young man



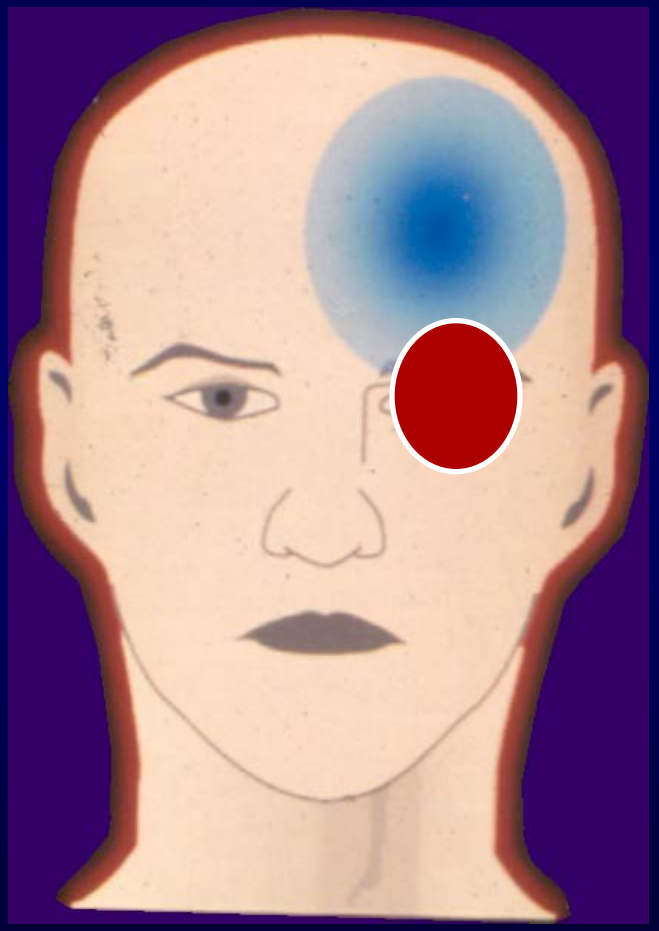
- 29 year old man with no prior personal or family history of headache began to have intermittent head pain 2 weeks ago
- Now having 2 headaches a day; one at 4 PM, the other 2 hours after he goes to bed
- Behind his right eye. Sharp, 10/10, no nausea, vomiting or other symptoms except his right eye waters. Lasts 30 minutes.

ICHD Diagnostic Criteria For Cluster Headache

A. Lasting 15 minutes to 3 hours
   - Steady, pressing quality
   - Strictly unilateral
   - Severe intensity

B. Associated ipsilateral autonomic signs/symptoms
   - Rhinorrhea, conjunctival injection
   - Meiosis, ptosis
   - Restless or agitation

C. No evidence of organic disease



Other facts about cluster headache

- Episodic and chronic forms
- Circadian, circannual rhythms
- Attacks often triggered by alcohol
- Misdiagnosis very common
  - Initial diagnosis often “dental-related”

Van Vliet et al. Jnl Neurol Neurosurg Psych 2003;74:1123-1125

In the clinic

- A 28 year old woman consults you with recurrent, disabling, throbbing headaches occurring intermittently for 8 years.
- Headaches occur with menstrual periods, last 48 hours, are associated with vomiting and photo and phonophobia.
- Benign past medical history
- Her neurologic examination is normal

Question: Can she take estrogen-containing contraceptives?

- No contraindication to exogenous estrogen in women who have migraine without aura AND are 35 or younger
- Exogenous estrogens contraindicated in women who have migraine with aura – at any age – and all women with migraine over 35.

Migraine and cardiovascular disease: systematic review and meta-analysis Markus Schürks, Pamela M Rist, Marcelo E Bigal, Julie E Buring, Richard B Lipton, Tobias Kurth
BMJ 2009;339:doi:10.1136/bmj.b3914 (Published 27 October 2009)

Testing

- Question:

What testing is necessary?

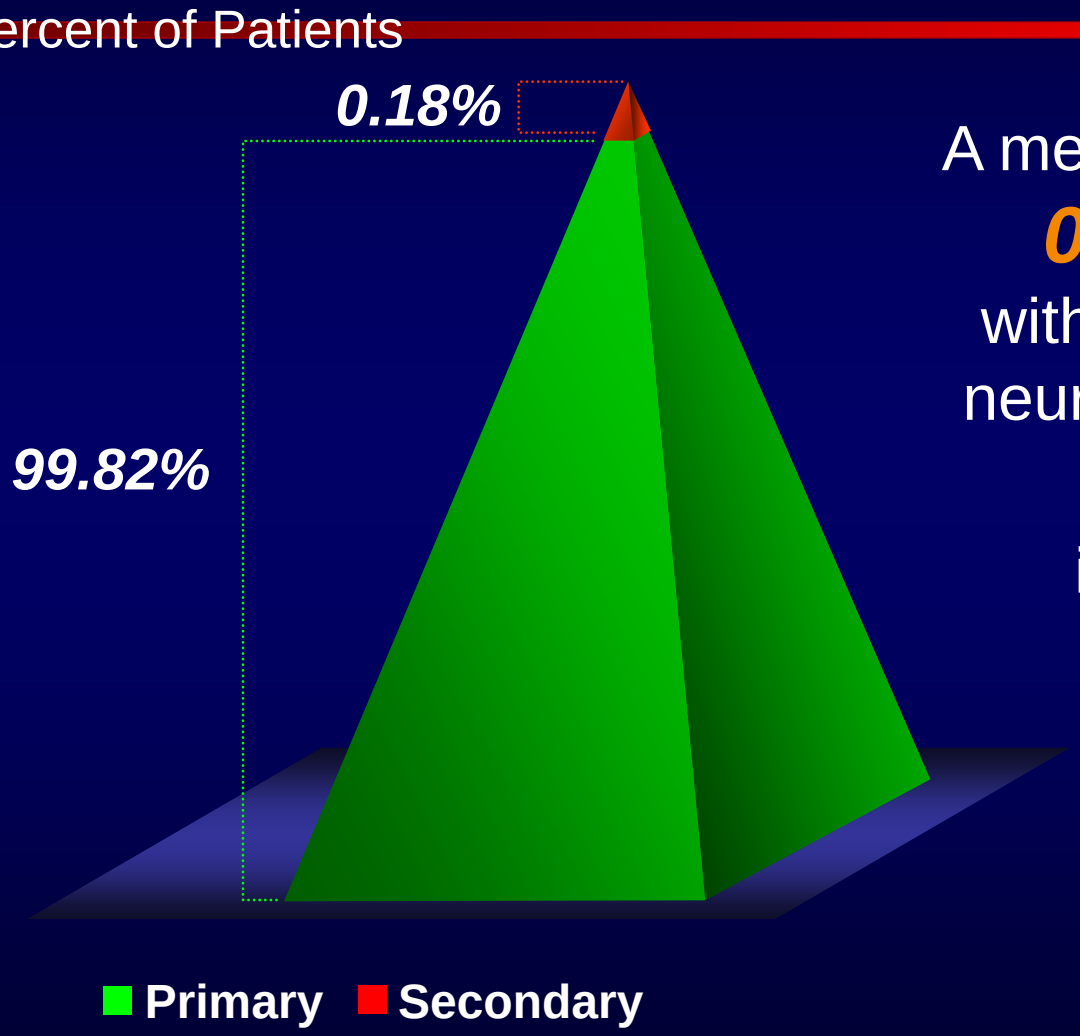
Testing

- Answer:

  Probably none

  American Academy of Neurology
  Position Statement: If a patient meets criteria for the diagnosis of migraine and has a normal neurologic examination, imaging is not recommended

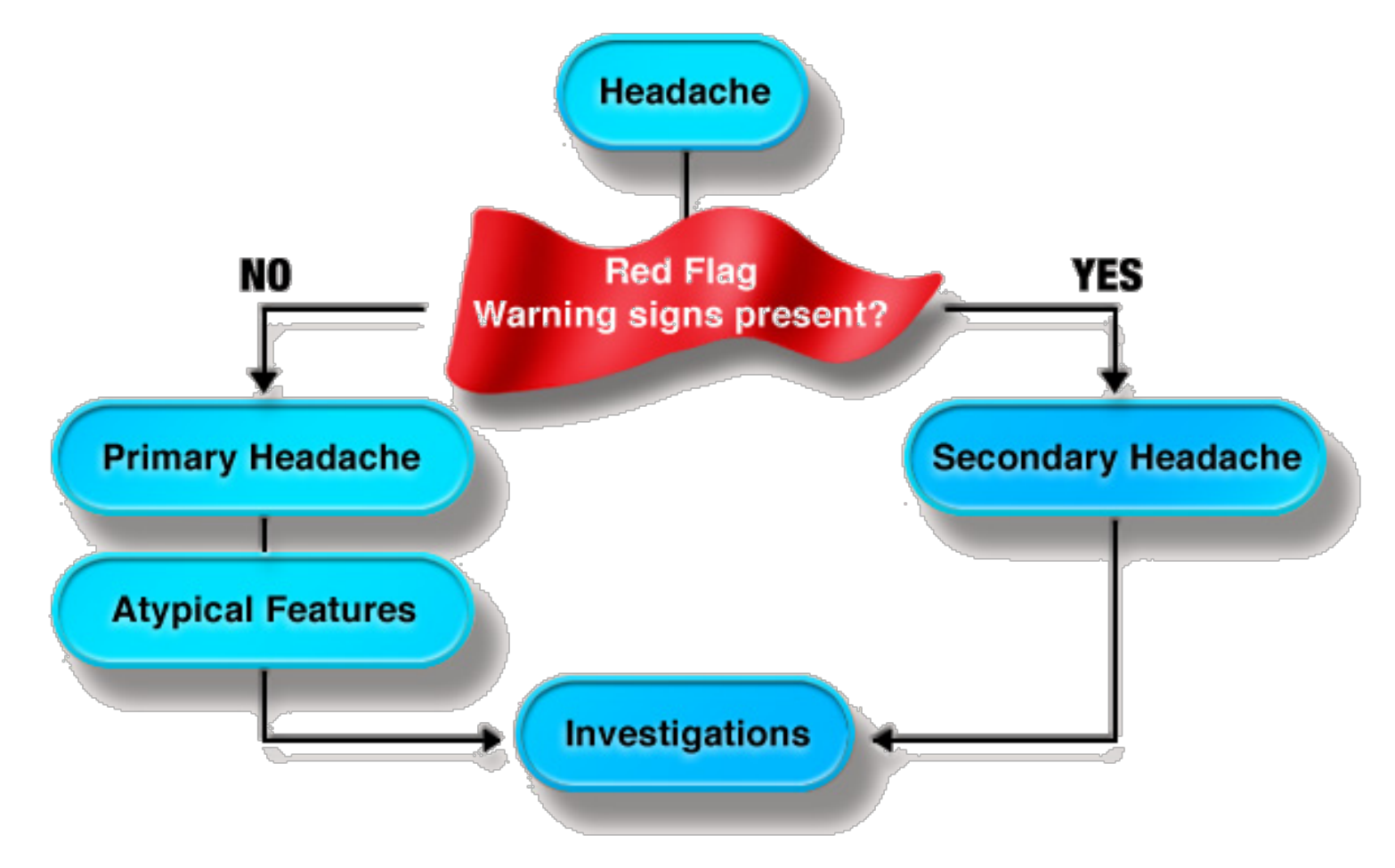
Secondary Headache: Clinical Presentation



A meta-analysis found that ***0.18% of patients*** with migraine and normal neurologic exam will have ***significant*** intracranial pathology.

Adapted from Frishberg BM, et al. www.aan.org. 1999

Initial Diagnostic Approach



Adapted from Silberstein SD et al., eds.
Headache in Clinical Practice. 2nd. August 2002.

SNOOP!

- **Systemic** symptoms (fever, weight loss) or Secondary risk factors (HIV, systemic cancer)
- **Neurologic** symptoms or abnormal signs (confusion, impaired consciousness)
- **Onset**: sudden, abrupt, or split-second
- **Older**: new onset & progressive headache, in middle-age >50 (giant cell arteritis)
- **Previous** headache history: first headache or different (change in attack frequency, severity, or clinical features)
- **Other:** positional, progressive.

Testing

- Primary headache is a clinical diagnosis
- Testing is useful to *rule out* other disorders
- No role for EEG
- LP and neuroimaging most useful

Neuroimaging: What test to get?

- MRI generally superior to CT
  - Better look at posterior fossa
  - Superior imaging of vascular structures
  - Radiation risks of CT are not minor
- Plain CT indicated if acute bleed is suspected
- Consult the radiologist!
  - Other tests may be helpful (MRV, MRA)

Managing headaches

- Abortive treatment
  - Virtually all patients require
- Preventive treatment
  - Only a subset of patients with migraine and TTH; essential all with CH
  - An underused intervention!

Reasonable lifestyle modifications

- Regular meals
- Adequate sleep; Standardized sleep and wake times
- Regular exercise and maintenance of normal weight
- Limit or avoid caffeine, watch alcohol
- No good evidence for dietary restrictions

Options for acute therapy

• **Disorder**	• **Common treatments**
Tension-type HA	NSAIDs, mild analgesics
Migraine	Ergot derivatives Triptans (barbiturates, combination analgesics)
Cluster HA	Injectable sumatriptan; oxygen 10-12 liters with NRB mask for 15 minutes at headache onset

Cohen et al. High-flow oxygen for cluster headache: a randomized controlled trial. JAMA 2009;22:2451-7.

A few words on triptans

- There are seven of them
  - All available orally (2 as orally disintegrating tablets)
    - Results are similar when comparable doses are used
    - Nonetheless, patients usually have a favorite
  - Two available as nasal sprays
  - One available as subcu injection
- Generic versions of three are available in the US
- Sumatriptan already available without prescription in some countries

Sumatriptan (generic)

Zolmitriptan

Naratriptan (generic)

Rizatriptan (generic)

Almotriptan

Eletriptan

Frovatriptan

Loder E . Triptan therapy in migraine. N Engl J Med 2010;363:63-70

Common Triptan Side Effects

- Tingling
- Warmth
- Flushing
- Chest discomfort
- Dizziness

Triptans: Contraindications

- Ischemic heart disease
  - Angina pectoris
  - History of myocardial infarction
  - Documented silent ischemia
- Coronary vasospasm (including Prinzmetal's angina)
- Poorly controlled hypertension
- Multiple risk factors for coronary artery disease, unless workup is fully negative

Optimizing abortive therapy

- Use adequate dose
- Use early/at mild stage of headache
- Monitor response and adjust therapy accordingly (eg combinations)
  - Anti-emetics
  - NSAIDs

On call!

- 36 year old woman with long history of occasional migraine that usually responds fabulously to rizatriptan 10 mg.
- This time, she is getting over a bout of norovirus and can’t keep rizatriptan down. Her headache has lasted 2 days. She wants to know if she should go to the ED.
- What do you do? (if you are being cost-conscious!)

Think rescue therapy

- Humane
- Necessary
- Practical
  - Keep patients out of the ED
- Nonoral formulations helpful

Options include:

- Injectable or nasal spray triptans
- Injectable or nasal spray DHE
- Phenothiazines
- Indomethacin suppositories
- Narcotics (not a sin)
- Sedatives
- Steroids

The ED is a bad place for migraineurs

- Fluorescent lights
- “Treated like a drug addict!”
- Danger of unnecessary workup (a fifth CT scan)
- At risk of receiving nonspecific treatments like meperidine that can set up a bad treatment paradigm

In the ED

- Hydration
- Parenteral therapy
  - Dihydroergotamine shines here: 1 mg IV or SC
  - Anti-emetics
  - Steroids
- Use of opioids should be minimized

Colman, et al. Parenteral dexamethasone for acute severe migraine headache: meta-analysis of randomised controlled trials for preventing recurrence.

BMJ 2008;336:1359-1361 doi:10.1136/bmj.39566.806725.BE (Published 9 June 2008)

When is preventive treatment indicated?

- For migraine or tension-type headache:
  - Headache frequency ≥ 1/week
  - Abortive therapy ineffective, contraindicated
  - Abortive treatments overused
- Cluster headache
  - Essentially everyone, but only during period of susceptibility

Goals of Preventive Therapy

- Reduce headache-related disability
- Reduce headache frequency, duration and intensity by at least 50%
- Improve response to abortive medications
- Reduce abortive medication requirements

Preventive Medications

- Tension-type HA
  - Tricyclics, NSAIDs
- Migraine
  - Propranolol, timolol, divalproex sodium, topiramate and onabotulinum toxin are FDA-approved. TCAs, Biofeedback, ACEIs, ARBs, Vitamin B2, gabapentin and others used
- Cluster headache
  - Lithium and verapamil (both off-label)

	AAN/AHS	Canadian	EFNS
Search dates	Through 5/09	Through 6/11	Through 1/09
Planned update	Not reported	“at least every 2 years”	“should be done every 3 years”
Inclusion criteria	“…randomized adult patients with migraine to agent under study or comparator”	“prospective, randomized, controlled trials…”	“Papers published in English or German..a review book..the German treatment recommendations…”
Methods of classification	Level A, B , C, U A: established efficacy, should be offered; B: Probably effective, should be considered; C: Possibly effective, may be considered.	Level of evidence rated high, moderate, low or very low; then graded strong or weak based on balance of benefits and harms	Grade A, B, C (drugs of first choice, drugs of second choice, drugs of third choice)

Results

- Areas of agreement: Highest level in all 3 guidelines:
  - Divalproex
  - Metoprolol
  - Propranolol
  - Topiramate

Common Preventive Medications

Evidence Level	Medication ✓ = FDA Indication	Usual Daily Dose	Comments
B	Atenolol	50-100 mg	
A	Propranolol ✓	80-240 mg	
A	Metoprolol	50-150 mg	
U	Verapamil	180-480 mg	Downgraded, favorable AE profile
A	Divalproex sodium✓	250-1500 mg	FDA pregnancy category X
U	Gabapentin	300-1800 mg	Downgraded, favorable AE profile
A	Topiramate✓	25-150 mg	FDA pregnancy category D
B	Amitriptyline	10-150 mg	Downgraded but strong clinical impression of benefit
B	Venlafaxine	37.5-150 mg	Well tolerated, not sedating
C	Cyproheptadine	2-8 mg	Pediatric population, sedating

Rizzoli, P. Acute and Preventive Treatment of Migraine, Continuum Neurol 2012;18(4):764-82

New options: ACEIs and ARBs

- AHRQ has commissioned a systematic review of the evidence for preventive migraine treatment
- They reach completely different conclusions
- They emphasize the overall benefits of ACEIs and ARBS…mostly driven by quality scores for individual studies and benign side effect profile

Shamliyan TA, Choi JY, Ramakrishnan R, Biggs Miller J, Wang SY, Taylor FR, Kane RL. Preventive pharmacologic treatments for episodic migraine in adults. Journal of General Internal Medicine 2013

Special considerations

- Use with caution in women of childbearing age:
  - Divalproex
  - Topiramate
  - Lisinopril/Candesartan

What is an adequate trial of prevention?

- Duration
- Dose
- Monitoring
- Combinations?

- 2 months
- At target dose
- Calendar or diary
- Previously ineffective drugs may still work in combination with others

Chronic Migraine

A Primary Headache Syndrome

(Organic causes of headache are excluded)

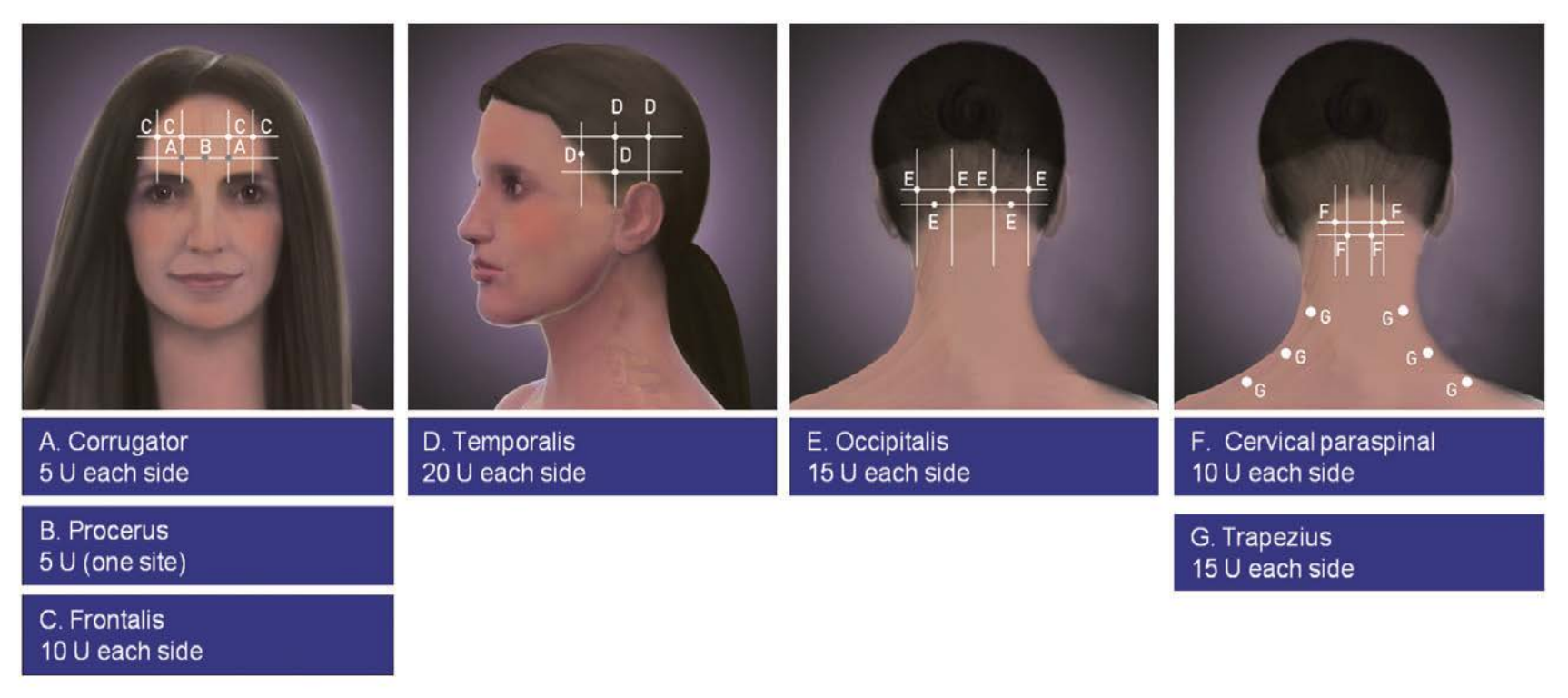
Headache occurs	>	15 days a month
Lasts	>	4 hours a day
Migrainous	>	8 days a month or more

1-3 % of the world's population: more common than epilepsy and virtually all other neuro diseases

Treatment of chronic migraine

- Prevention emphasized
- Watch use of abortive medication in order to avoid medication overuse headache
- Onabotulinum toxin type A FDA-approved for prophylaxis
  - The dose for treating chronic migraine is 155 Units IM, 0.1 mL (5 Units) per injection site.
  - Every 12 weeks

**Fig 1.—Fixed-site, fixed-dose injection site locations: the (A) corrugators, (B) procerus, (C) frontalis, (D) temporalis, (E) occipitalis,
(F) cervical paraspinal, and (G) trapezius muscle injection sites.**



Blumenfeld et al. Method of injection of onabotulinum toxin A for chronic migraine. Headache 2010; doi: 10.1111/j.1526-4610.2010.01766.x

Syndrome of medication overuse headache

- Occurs in patients with pre-existing headache
- Self-sustaining rhythm of predictable and escalating headache frequency and medication use
- Poor response to appropriate symptomatic and preventive treatments
- Medication withdrawal results in escalation of headache

Principles of MOH therapy

- Start prevention
- Taper medications most likely to cause rebound
- Substitute acute medications that do not cause rebound
- Address maladaptive coping skills, catastrophizing

Be aware of:

Opioid and barbiturate abstinence syndromes

Increasing headache during withdrawal period

What's in the pipeline?

- Devices
  - Transcranial Magnetic Stimulation
  - Implanted nerve stimulators
- CGRP monoclonal antibodies
- New ways to deliver old medications (DHE, sumatriptan)

Summary

- Diagnosis of primary headache is largely based on pattern recognition
- Appropriately applied testing rules out secondary headaches
- Many treatment options available!

- Thanks!
- rburch@partners.org

- Slides for reference based on comments from previous years
  - Largely based on clinical experience, but references included where applicable.

Strategies for Refractory Migraine

- Change the approach
  - Goal is improvement of quality of life and maintenance of function
  - Treatment is as much philosophical as medical for some patients: focusing on positives, mindfulness, reasonable expectations
  - “We are continuing to try different treatments, and I’m hopeful that we will find a way to make you feel at least a little better. But it’s important not to put your life on hold waiting for this problem to go away. I think it’s time to start focusing on how to make the best of your life as it is now.”

Strategies for Refractory Migraine

- Multidisciplinary care is essential
  - Headache specialist (most academic centers now have one) should coordinate
  - Treatment of psychiatric comorbidities (both anxiety and depression more common in chronic and refractory migraine)
  - Cognitive behavioral therapy (CBT) uniquely helpful in migraine – treats anticipatory anxiety and other maladaptive coping strategies

Strategies for Refractory Migraine

- Rational preventive polypharmacy
  - One trial evaluating combination of topiramate and propranolol was negative
  - Used for almost all refractory patients anyway
  - Combination of CBT and propranolol more effective than either alone
- Prevent symptomatic medication overuse
- Avoid opiates when possible

Strategies for Refractory Migraine

- Nonpharmacologic treatments helpful for some patients (no good evidence, however)
  - Acupuncture
  - Massage
  - Craniosacral therapy
  - Yoga, tai chi
- Focus on maintenance of activity and employment even if it worsens pain to some degree (generally avoid supporting disability)

Refractory migraine references

- Book: Refractory Migraine, Mechanisms and Management: Elliot A. Schulman, FACP, MD, Morris Levin, MD,Alvin E. Lake, III., PhD, and Elizabeth Loder, MPH, MD. August 2010
- Review article: Refractory migraine - a review. Schulman E. Headache. 2013 Apr;53(4):599-613.

Preventive medication titration suggestions

- Start at lowest dose, increase weekly.
  - May increase faster if well tolerated, slower if side effects are prominent
- Titration is stopped when:
  - Efficacy goal is reached (ie headaches improve)
  - Target dose is reached
  - Side effects prevent further increase
    - Better to maintain a partially effective subtherapeutic dose than to aggressively increase and “lose” medication due to side effects

Preventive medication titration suggestions

- - Amitriptyline. I typically start with a very low dose such as 5 mg and increase each week as follows: 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, or as tolerated.
- - Nortriptyline, started at 12.5 or 25 mg nightly, increased as tolerated to a maximum of 100 mg nightly.
- - Topiramate, started at 12.5 mg daily, increased to 25 mg, and then increased by 25 mg each week to a target of 100 mg daily/nightly
- - Propranolol, started at 20 mg daily and increased as tolerated to a target of 60-80 mg daily
- - Venlafaxine: I typically start venlafaxine XR 37.5 mg nightly, increased after two weeks to 75 mg nightly.
- - Depakote, started at 250 mg nightly and increased to 500 mg nightly after one week; may increase to 500 mg BID if tolerated and as needed

Preventive medication titration suggestions

- - Verapamil, started 40 mg TID or 120 mg QHS. Surveillance EKGs are necessary. May increase further if tolerated. (For migraine. For cluster headache, start 120 mg daily and increase as tolerated by EKG and cardiovascular parameters. Short acting verapamil may be more effective in cluster headache).
- - Gabapentin, started at 300 mg nightly and increasing as tolerated to a target of 600 mg BID-TID. May increase further if tolerated.
- - Candesartan, started at 4 mg daily and increased weekly to a target of 16 mg daily.
- - Lisinopril, started at 10 mg daily and increased weekly to a target of 40 mg daily.