Migraine and POTS

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Disclosures

- Consultant to
  - Emisphere pharmaceuticals
  - Quest Diagnostics

44yoF with POTS, migraine

- Dizzy, lightheaded with standing
- Used to work 60-70 hours per week in retail management
- In 2001, spent 2.5 years in bed following heat exhaustion at an airshow.
- Had intractable lightheadedness, fainting, migraine headaches, and confusion.
- Hx of panic attacks in childhood

evaluation

- Tilt testing showed HR rise >30 bpm within 10 minutes of standing, c/w POTS
- autonomic testing normal.
- Norepinephrine levels normal-supine 273 ng/dl, standing 462
- Rest of lab tests normal.
- Treatment-
- 50% improved with midodrine
- Began botox injections for chronic migraine following failure of 2 preventive agents.

After 3 years, Had Relapse

- Could no longer receive botox, lost insurance
- Migraine worsened
- POTS symptoms worsened dramatically
- Performed occipital, supraorbital, auriculotemporal nerve blocks to abort acute headache
- Patient assistance program to obtain drug

one patient's symptoms

-Fatigue
-Lethargy
-Take frequent naps
-Dizziness/lightheadedness
-Hot flashes-Feeling hot with faint
-Feeling of faint/blackouts/sense of falling, even sitting or at rest.
-Vertigo
-Disequilibrium
-Sensitivity to lights, sound and scents
-Sensitivity to all florescent lighting and other bright indoor lighting.
-Severe migraine pain-Eyes (mainly left), sinus, head, neck, between shoulder blades and upper back.
-Blurred vision-sparks/spots, isolated areas within vision are blurred or specific moving objects within sight. Vision change from minute to minute, hour to hour, day to day.
-Shooting pains in eyes. Mostly in left eye.
-Nausea
-Severe head, upper back, shoulder, between shoulder blades and neck pain- burning, throbbing and stabbing.
-Mid back pain
-Pain in ankles, wrists, fingers, toes, elbows, knees, hips and buttocks.
-Joint and muscle pain throughout body.
-Severe weakness in face, lips, neck, arms, hands, legs and feet.
-Numbness in extremities/slight paralysis
-Both arms will cramp from armpits to hands with numbness immediately following the feeling of faint, rapid heart rate and breathing.

- -Involuntary rapid eye movement.
-Change in vision
-Memory loss/confusion/poor concentration
-High blood pressure
-Low blood pressure
-High heart rate
-Low heart rate
-Heart palpitations
-Chest pain
-Hot or cold weather intolerance
-Exercise intolerance
-Low blood sugar or reactive.
-Frequent urination and/or can't fully empty bladder
-Diarrhea or constipation
-Gastronintestional discomfort
-Acid reflux
-Sharp stomach, rib and abdominal pains
-Feeling of bugs jumping or crawling on skin.
-Feeling of burning throughout my body. Mostly in joints and large muscles.
-Difficulty sleeping at night
-Dehydration (though I drink a lot of water)
-Strong salt cravings
-Dry eyes, hair, skin and nails.
-Disappearing moons on fingernails
-Poor circulation
-Hearing loss/ringing ears
-Facial, neck and chest flushing that has also broken facial blood vessels.
-Bloat including face
-Inner and/or outer body shakes
-Difficulty swallowing-choking on my own saliva even while sleeping. -Shortness of breath
-Frequent coughing
-Feeling of pins and needles in face, lips, arms, legs, hand

The Symptom Snowball

- Symptoms multiply and amplify with time
- “Somatic Hypervigilance”
- Why does this occur?
- Is there a connection to migraine?

J Cardiovasc Electrophysiol 2009;20: 352-358

Migraine is common in POTS

	# pts	%
Diffuse associated symptoms		
Fatigue	73	48
Sleep disturbance	48	32
Migraine headache	42	28
Myofascial pain	24	16
Neuropathic type pain	3	2

(From Thieben MJ, Sandroni P, Sletten DM, Benrud-Larson LM, Fealey RD, Vernino S, Lennon VA, Shen WK, Low PA. Postural Orthostatic Tachycardia Syndrome: The Mayo Clinic Experience. Mayo Clinic Proceedings 82:308-313, 2007. Modified with permission.)

Mayo Clin Proc 2007;82:308-313

Migraine

- 4 or more pounding/throbbing HA that limit activity, with light or sound sensitivity or nausea.
- Often accompanied by other symptoms
  - Visual disturbances –aura
  - Nausea
  - Vomiting
  - Diarrhea
  - Light, sound, smell sensitivity
  - Scalp sensitivity
  - Vertigo
  - Cognitive dysfunction- “brain fog”

Migraine Without Aura - Common Migraine

Mnemonic: SULTANS

- Headache has at least 2 of the following characteristics:
  - S = severe
  - UL = unilateral
  - T = throbbing
  - A = activity worsens HA

And at least 1 of the following during headache:

  - N = nausea or vomiting
  - S = sensitivity to light/sound

Headache Classification Subcommittee of the International Headache Society (2004), Cephalalgia 24:1-150

Diagnostic Criteria for Migraine With Aura (Classic Migraine)

- At least 2 attacks
- Aura must exhibit at least 3 of the following characteristics:
  - Fully reversible
  - Gradual onset
  - Lasts less than 60 minutes
  - Followed by headache within 60 minutes
  - HA may begin before or simultaneously with the aura
  - Normal neurologic exam and no evidence of organic disease that could cause headaches

Headache Classification Subcommittee of the International Headache Society (2004), Cephalalgia 24:1-150

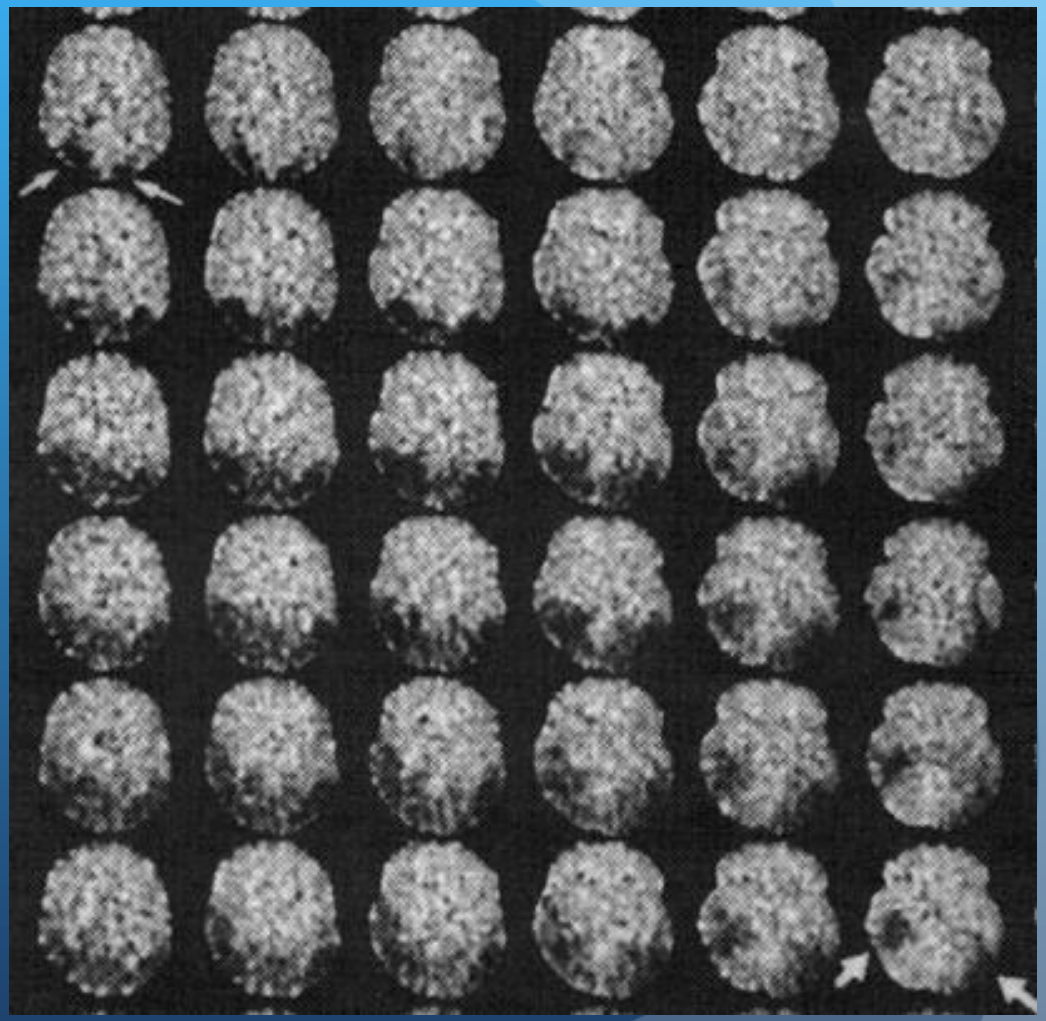
Functional Imaging of Migraine

- Spread of cortical depression from posterior occipital cortex
- May occur in migraine with warning (aura) or without aura

Archives of neurology. 1999

Spreading wave of reduced blood flow by PET/fMRI imaging

- Area of low blood flow in occipital cortex spreads at 3-6mm/min forward to the parietal and temporal lobes.



R P Woods; M Iacoboni; J C Mazziotta
The New England journal of medicine. 1994

Complicated Migraine

- Persistent neurologic residue of a migraine attack
- Migraine with dramatic focal neurologic features (include ophthalmoplegic, hemiplegic, basilar migraine)
- A frequent stroke mimic in the Emergency room
- look for “slow sensory march” of symptoms

Migraine: Abortive Therapy

Individual Attacks at Home

- Aspirin/APAP/caffeine (Excedrin®)
- Sumatriptan (Imitrex), eletriptan (Relpax), zolmitriptan (Zomig®), rizatriptan (Maxalt®)
- NSAIDs- ibuprofen, others
- Butalbital (Fioricet), opioids (codeine) not recommended due to abuse potential
- Do not exceed 2-3 days treatment in 1 week → rebound

Practical neurology. 2015

Triptans

- Major advance in migraine therapy
- 5-HT1B/1D agonists
- Vasoconstriction
- All act by suppressing nausea, confusion, autonomic dysfunction and pain associated with migraine attack
- Differ only in pharmacokinetics

Johnston MM, Rapoport AM. Triptans for the management of migraine. Drugs. 2010 Aug 20;70(12):1505-18

Triptans List

- Sumatriptan 25-100 mg po/6 mg sq/5 mg nasal at HA onset, rpt 1 hr sq, 2 hr po/nasal
- Zolmitriptan 2.5-5 mg
- Rizatriptan 10 mg SL
- Eletriptan (Relpax®), frovatriptan (Frova®), almotriptan (Axert®), others

Practical neurology. 2015

Johnston MM, Rapoport AM. Triptans for the management of migraine. Drugs. 2010 Aug 20;70(12):1505-18

Migraine Prophylaxis

First Line (Pregnancy Class)

- β-blockers (C): propranolol LA (Inderal-LA) **FDA** 60 mg qd, timolol 20 mg qd **FDA**
- Anticonvulsants: topiramate **FDA** (Topamax®) (was C, now D- 3/28/11 due to cleft palate) 25-100 mg bid
  - Lower toxicity than divalproex (Depakote®), **no weight gain**
- Tricyclics antidepressants (D): nortriptyline (Pamelor®) 10-60 mg
- NSAID: naproxen sodium (Anaprox DS®) (C) (menstrual migraine - 550 mg bid x 10 days)

Silberstein SD, Neurology 55(6):754-762

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Migraine Prophylaxis

Other Options

- Divalproex (Depakote®) (D) **FDA**
- Gabapentin (Neurontin®) (C)
- Baclofen (Lioresal®) (C)
- "MigreLief"[1,2] $20 /60 pills
  - Riboflavin (Vitamin B_2) 400 mg/day (A)
  - Magnesium oxide 360 mg/day (B)
  - Feverfew 100 mg/day
- Petadolex 1 tid (Butterbur extract) (A)

[1]*Pfaffenrath V, Wessely P, Meyer C, et al. Magnesium in the Prophylaxis of Migraine - A Double-Blind, Placebo-Controlled Study. Cephalalgia 1996;16:436-40.*

[2]*Schoenen J, Lenaerts M, Bastings E. High-dose Riboflavin as a Prophylactic Treatment of Migraine: Results of an Open Pilot Study. Cephalalgia 1994;I14:328-9*

Chronic Migraine (TM)

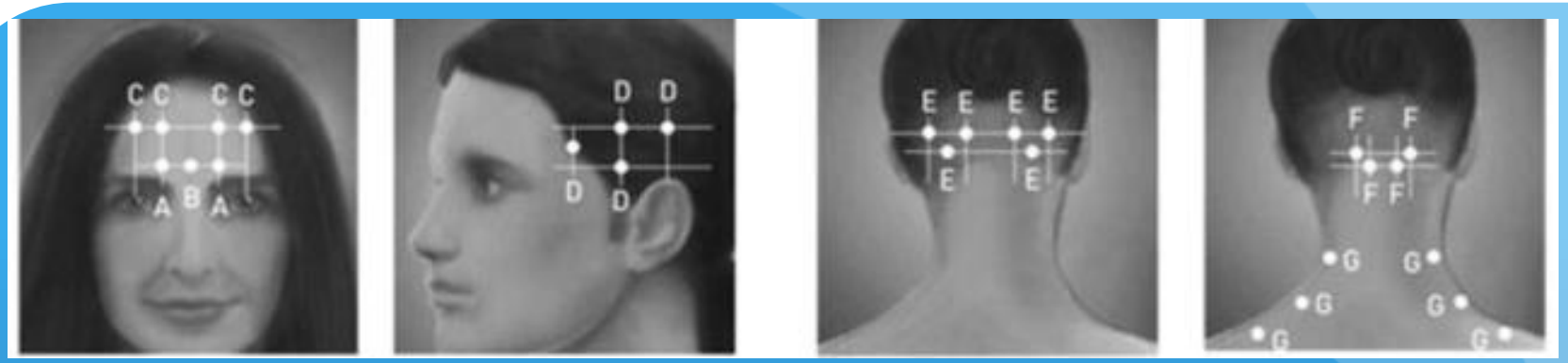
- > 15 days/month head pain
- Headache > 4 hours/day
- At least 1 of:
  - Previous HA fulfills IHS criteria for migraine
  - Increasing frequency > 3 months
- Medication overuse in 80% with TM

Recent Developments

Botulinum toxin 155 units

- Inhaled DHE
- Sumatriptan- patch; no-needle injection
- Memantine (Namenda)
- Combinations
  - Sumatriptan and naproxen (Treximet®) - (FDA)
- Occipital and supraorbital nerve stimulators
- CGRP monoclonal antibodies
- Anticonvulsants
  - Zonisamide
  - Levetiracetam
  - lamotrigine

CNS drugs. 2015 , DOI: 10.1007/s40263-015-0253-z
Cephalalgia 2015
Neurology 2013; 80:697-704



Botox for Chronic Migraine

- FDA approved for treatment refractory chronic migraine
- Must have tried and failed at least 2 other prevention meds (topirimate, nortryptiline, propranolol, etc)
- Must have >15 HA days per month, > 4 hours per day
- Every 3 months, 155 units injected in 31 locations on the scalp and neck (5 units/site)
- 70% of patients experience >50% relief of HA after 3 sets of injections

Cephalalgia. 2006;26:790–800.

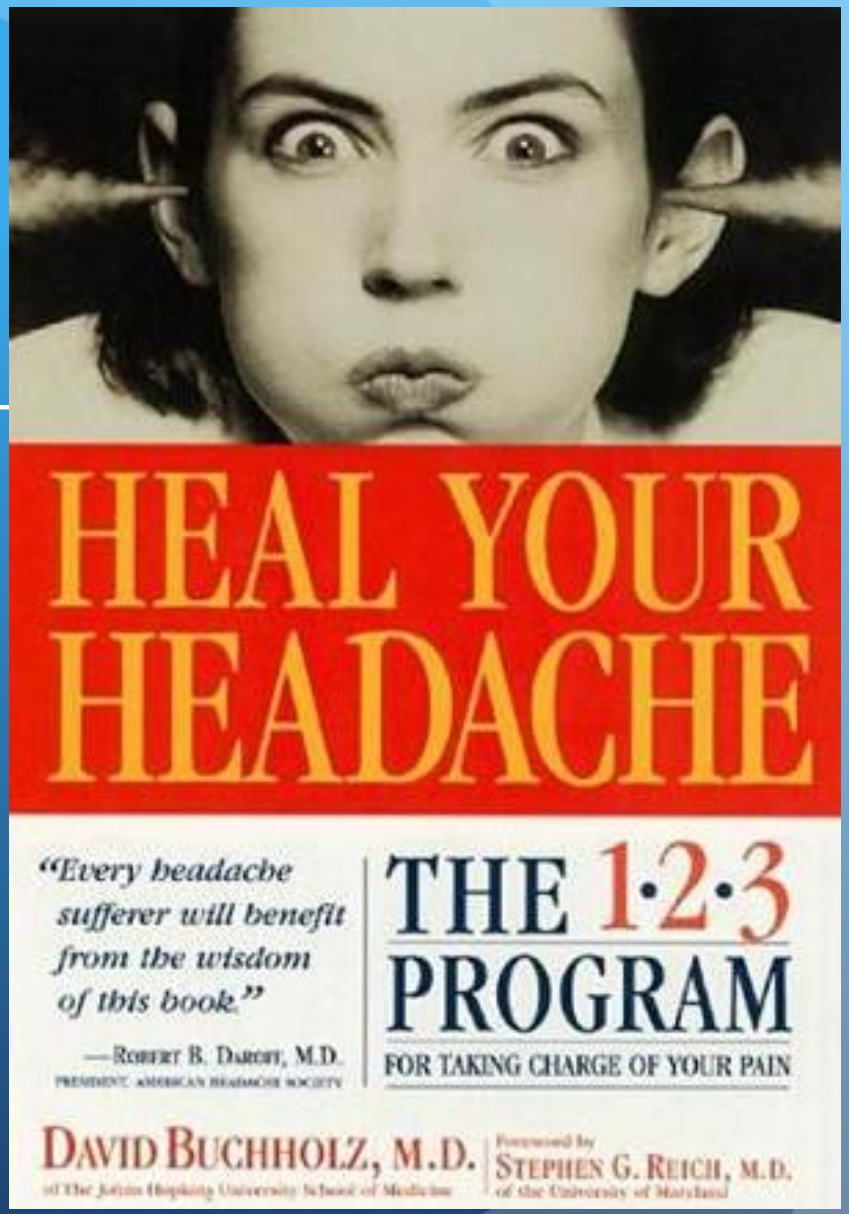
Breaking News! Immune Therapy for Migraine

- Calcitonin gene related peptide (CGRP)
- Bind to receptors that mediate headache pain and light sensitivity
- Initial attempts to use antagonists failed due to liver toxicity (telcagepant)
- Monoclonal antibody that blocks binding of CGRP to the ligand (receptor)
- Several candidate drugs in clinical trials
- Results promising
- First immunotherapy for migraine treatment

Current Neurology and Neuroscience Reports 2015, 15:25
CNS drugs. 2015 , DOI: 10.1007/s40263-015-0253-z

Dietary Triggers

- Caffeine
- Chocolate
- Alcohol
- Estrogen (BCPs)
- Aspartame
- Citrus, bananas
- Nuts
- Hard cheese, processed meats
- Many others



Transformed Migraine/Status Migrainosus

Treatment

- Withdraw all medication
- Raskin protocol: DHE IV 0.5 mg/metoclopramide (Reglan®) 10 mg IV q 8 hours for 3 days[1]
- Dexamethasone (Decadron-LA®) 10-24 mg IV x1
- Dexamethasone (Decadron®) 2 mg bid for 3-5 days

Am Fam Physician. 2011;83(3):271-280.

BMJ 2008 Jun 14; 336:1359

1Raskin NH (1986), Neurology 36(7):995-997

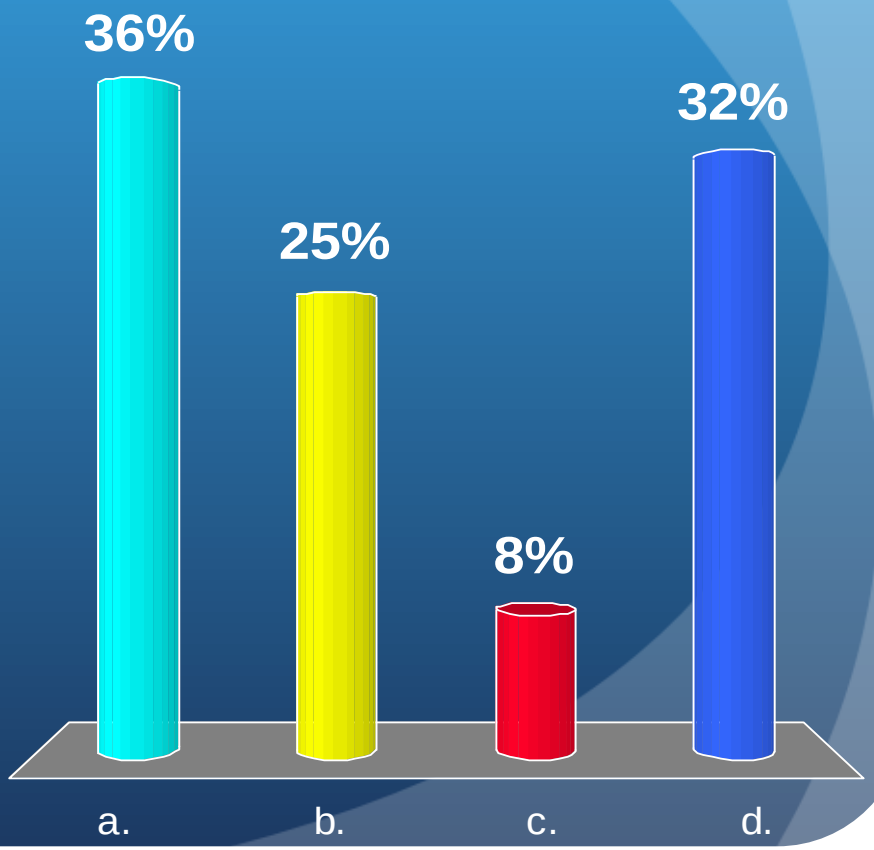
You Make the Call

- 37-year-old man with lifelong migraine and develops 6 weeks of unremitting headache (HA)
- Bitemporal, throbbing, 3-7/10, morning HA
- Relieved with acetaminophen/aspirin/caffeine (Excedrin Migraine®)
- No visual disturbances, scotomata, nausea, photophobia
- 3 months of cyclosporin (Neoral®) for alopecia universalis
- Exam is normal

Audience Question

What is the diagnosis?

a. Transformed migraine
b. Medication overuse headache
c. Cyclosporin induced headache
d. Chronic tension type headache



Medication Overuse Headache

- Prevalence 1-2%
- Morning headaches
- Chronic daily headache > 15 days/month
- Simple analgesics > 15 days/month
- Ergots, triptans, opioids, combo NSAIDS > 10 days per month
- Most have baseline migraine HA

Treatment of medication-overuse headache: A systematic review.

Cephalalgia 2015

Medication Overuse Headache

Treatment

- Stop all OTC analgesics, caffeine consumption
- Wean butalbital, opioids, benzodiazepines
- Ketorolac PO 60 mg x1, 10 mg q 6 hours x 3 days
- Tizanidine (Zanaflex®) 2-8 mg tid[1]
- Occipital Nerve blocks
- Raskin protocol: DHE 0.5-1 mg IV q 8 hours/ metoclopramide 10 mg for 3 days

Treatment of medication-overuse headache: A systematic review.

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Treatment of Transformed Migraine and Medication Overuse Headache

- Education, close followup for 8-12 weeks
- Lifestyle changes: stop caffeine and smoking, get regular sleep, exercise
- Diet modification- Heal Your Headache, Bucholz
- Biofeedback, Yoga, Cognitive Behavioral Therapy
- Abrupt withdrawal of analgesics **except:**
  - Barbiturates: wean over 1 month
  - Opioids: clonidine withdrawal

Non-pharmacologic guidelines for Migraine 2012

http://www.neurology.org/content/78/17/1346.full.html

Dodick DW (2006), N Engl J Med 354(2):158-165

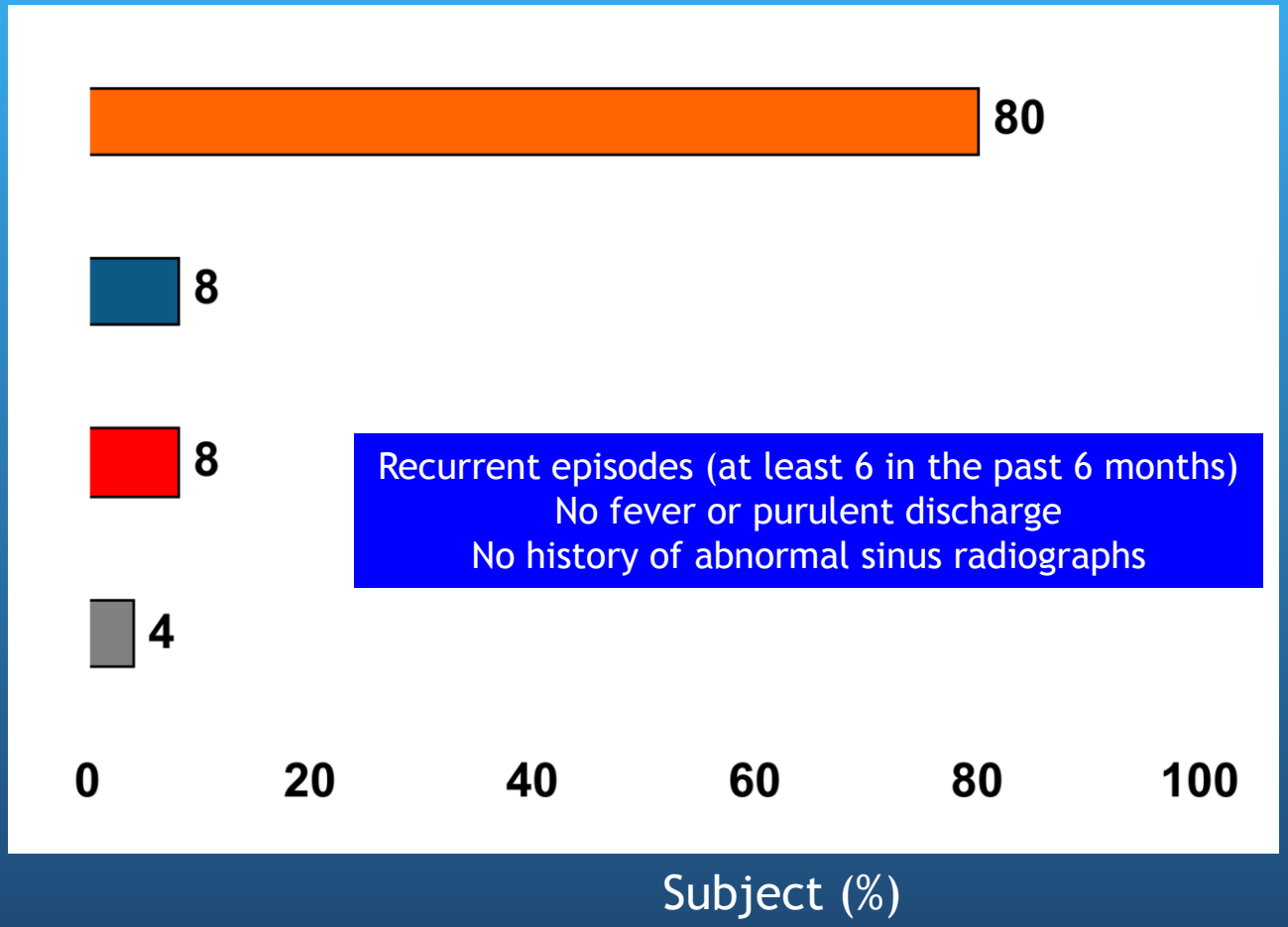
“Sinus Headaches”?

- Over-diagnosed and over-treated
- Not a recognized form of HA by the IHS except in setting of acute bacterial sinusitis
- 74% fulfill IHS migraine criteria
- 45-50% of asymptomatic adults have evidence of sinus mucosal thickening or edema
- Utility of routine CT sinuses not established

Gupta M, Silberstein SD. Expert Opin Pharmacotherapy 2005;6:715-722.

Mehle ME, Kremer PS. Sinus CT scan findings in “sinus headache “ migraneurs. Headache 2008;48:67.

How often is "Sinus" Headache Really Migraine?



Schreiber CP, et al. Arch Intern Med. 2004;164:1769-1772

Worrisome HA Red Flags

"SNOOPS"

- **S**ystemic symptoms: fever, weight loss
- **N**eurologic symptoms or signs: confusion, depressed alertness or consciousness
- **O**nset: sudden, abrupt, split-second
- **O**lder: new HA > 50 years old - temporal arteritis
- **P**revious HA history: change in usual HA pattern - change in frequency, character, severity
- **S**econdary risk factors: HIV, cancer

Summary

- Migraine occurs commonly with POTS
- May cause many symptoms besides head pain
- Most “Sinus Headaches” are actually migraine
- Avoid analgesics > 2 days per week to avoid Medication Overuse HA

Questions from the Audience?