OHSU Dept of Neurology

Migraine as a Chronic Neurovascular Disorder

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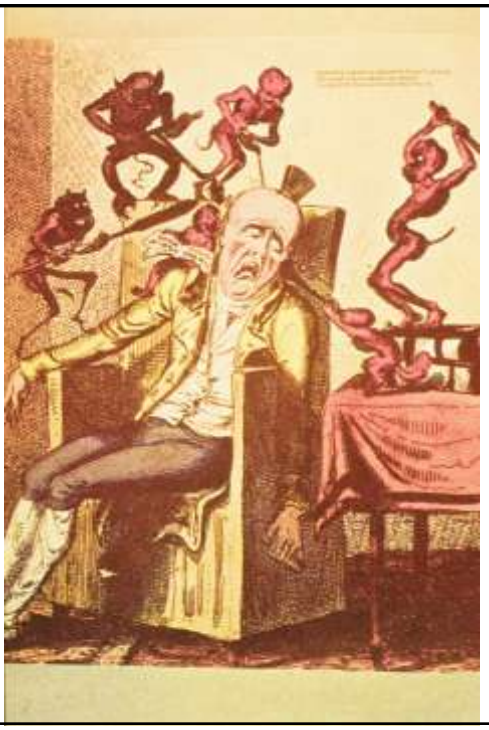
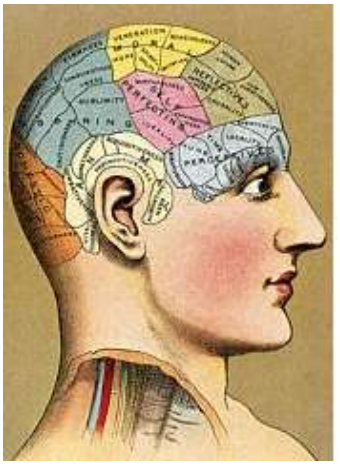


??? Headache "Triggers"???



- MSG
- Zucchini
- Dijon mustard
- Provolone cheese
- Peanut butter
- Chocolate
- Pizza

Warmed Goat Cheese Salad with Grilled Vegetables

- **Free of:**
  - **Caffeine**
  - **Chocolate**
  - **Citrus fruits**
  - **Red wine**
  - **Aged cheese**
  - **MSG and nitrates**
  - **Aspartame**
  - **Nuts**
  - **Onions and garlic**

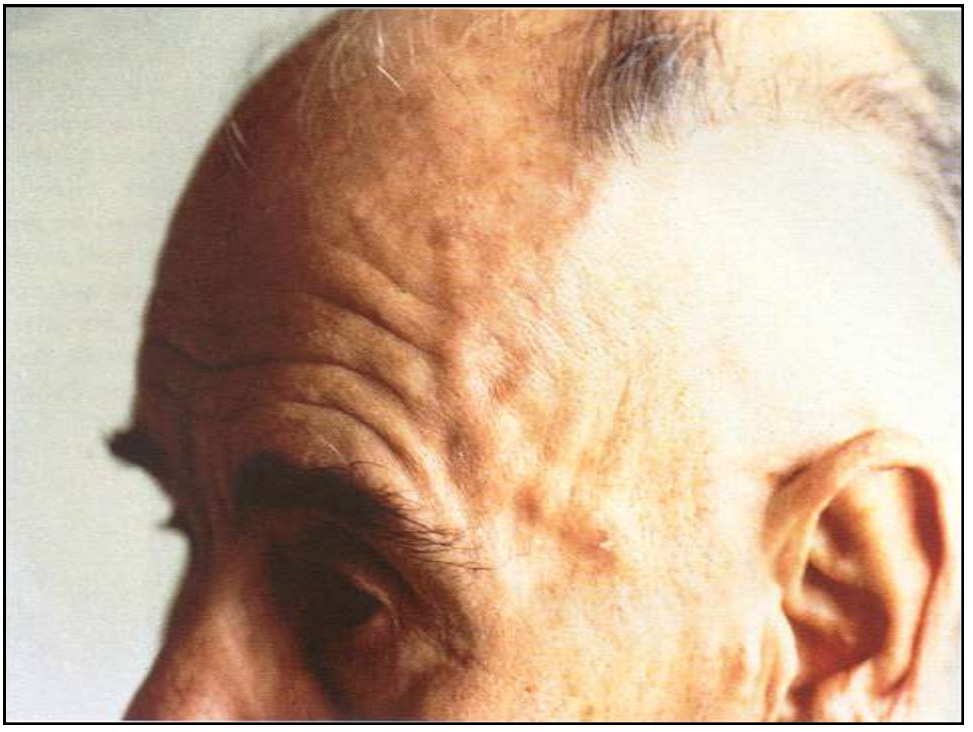
calories 184
protein 10 grams
fat 8 grams
carbohydrates 18 gm

Migaine Prodromes???

- Mood swings
- Urge to clean out closets
- Yawning
- Craving the new dark M&Ms
- Talkativeness
- Stomach discomfort
- Craving for sex

Recognition of Ominous Headache

- “First or worst” headache of my life
- New-onset headache in mid-life or older
- Change in character of longstanding headache
- Strictly unilateral headache
- Headache associated with fever, meningeal signs, cancer or immunosuppression
- Headache associated with abnormal neurological examination



Primary Headache Classification

- Migraine without aura (common)
- Migraine with aura (classic)
- Tension-type headache
- Cluster headache

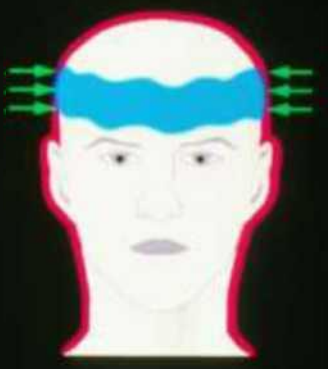
Criteria for office diagnosis of episodic tension-type headache

A. Headache pain accompained by two of the following symptoms:
- Pressing/tightening (nonpulsating) quality
- Bilateral location
- Not aggravated by routine physical activity

B. Headache pain accompanied by both of the following symptoms:
- No nausea or vomiting
- Photophobia and phonophobia absent or only one present

C. Fewer than 15 days per month with

D. No evidence of organic disease



IHS diagnostic criteria for migraine without aura

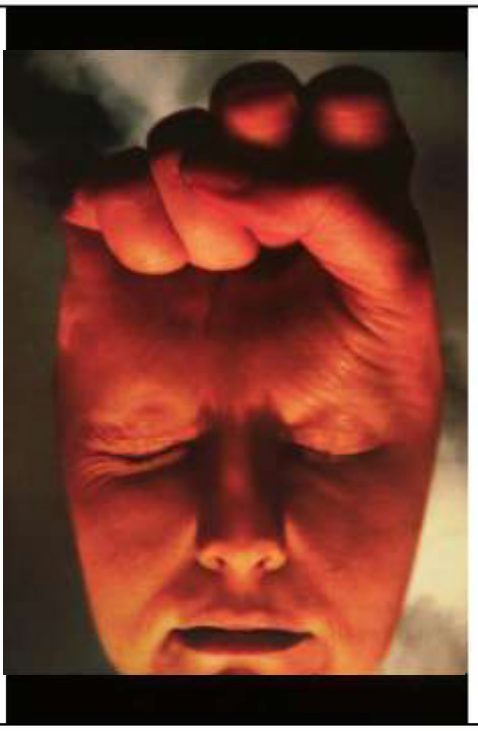
A. Lasting 4 to 72 hours

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

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

D. At least five attacks fulfilling A, B, and C

E. No evidence of organic disease



Common Symptoms of Migraine

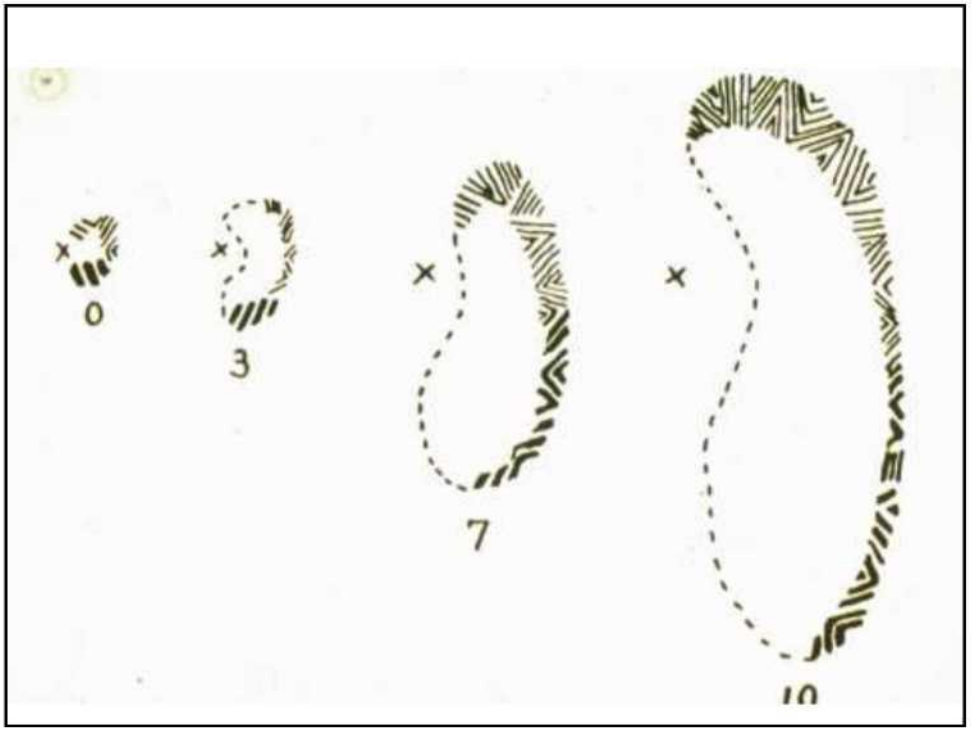
- Headache
- Visual or sensory aura
- Anorexia, nausea, vomiting, diarrhea
- Photophobia, phonophobia
- Mood changes

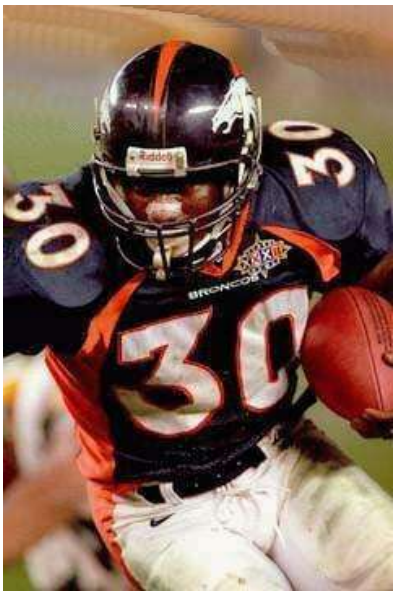
Criteria for office diagnosis of migraine with aura

A. Headache pain is preceded by at least one of the following neurologic symptoms:

- Visual
  - Scintillating scotoma
  - Fortification spectra
  - Photopsia
- Sensory
  - Paresthesia
  - Numbness
  - Unilateral weakness
  - Speech disturbance (aphasia)

B. No evidence of organic disease

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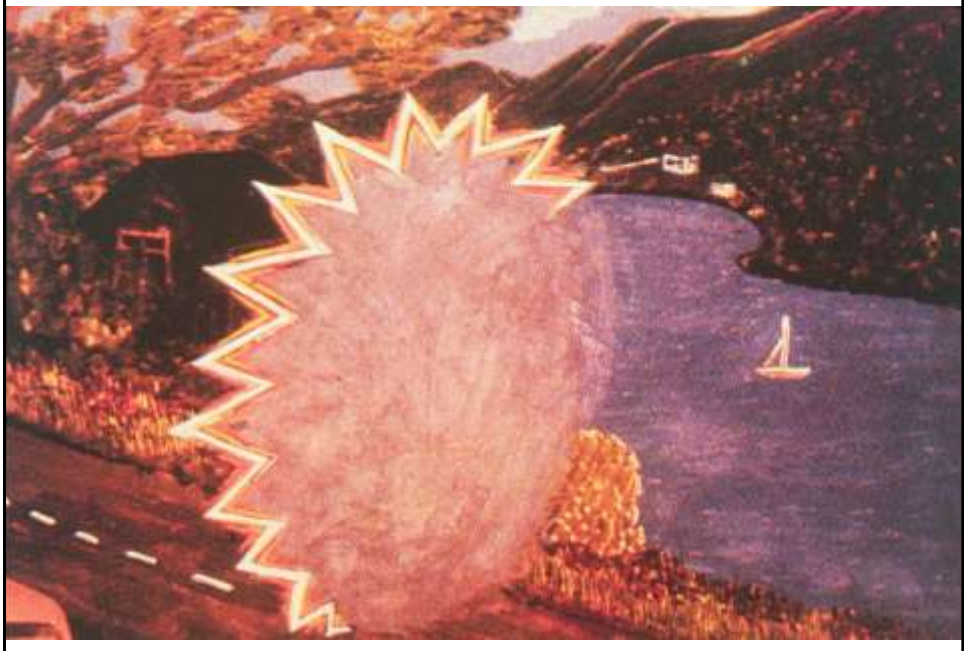


Migraine in Clinical Practice

- There are 28 million migraine sufferers in the US
  - Only half are diagnosed
  - Far fewer are receiving optimal care
- Clinicians interact with migraine patients
  - As primary consultations
  - Amidst other co-morbid medical conditions
- Often migraine goes unrecognized

Lipton RB, Diamond S, Reed ML, et al. Migraine diagnosis and treatment: American Migraine Study II. *Headache.* 2001;41:538-645.

Juanita – 27 yo Female with 2-3 HAs per Month

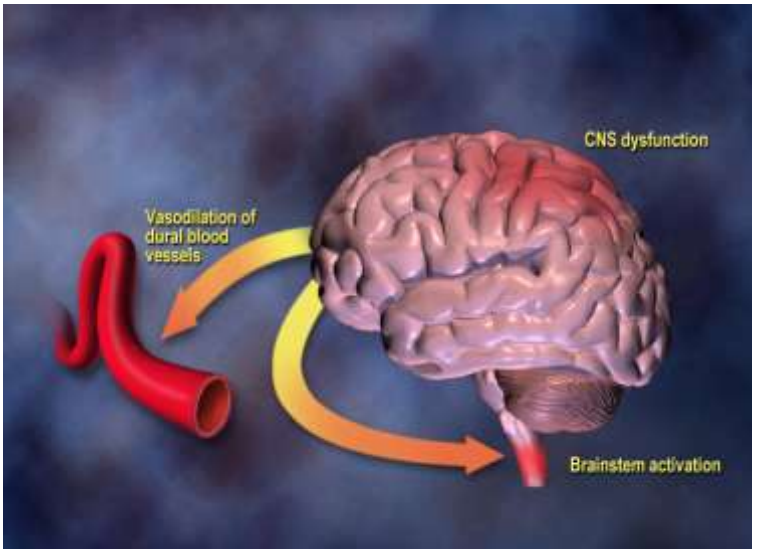
Clinical Assessment

- How many headache diagnoses does she have?
  - ☐ One?
  - ☐ Two?
  - ☐ Three?
  - ☐ More?

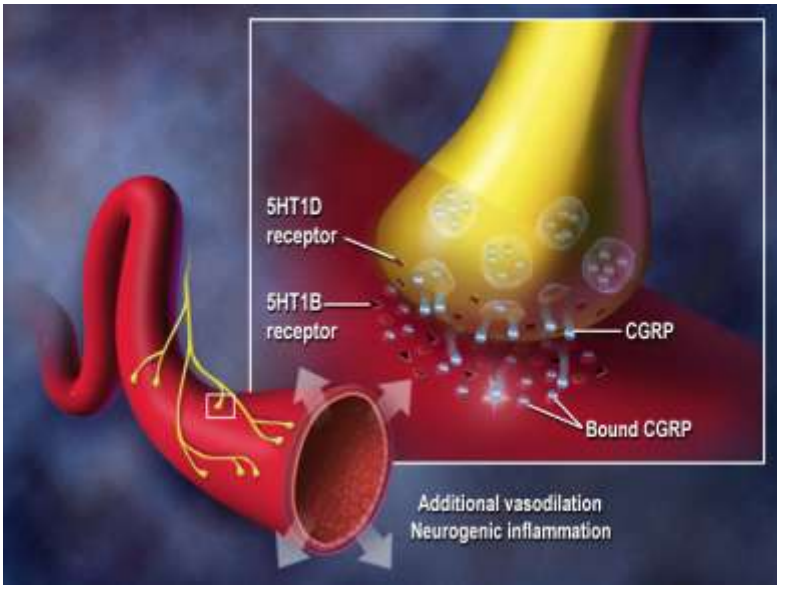
Clinical Assessment

- How many different headache treatments should this patient have?
  - ☐ One?
  - ☐ Two?
  - ☐ Three?
  - ☐ More?

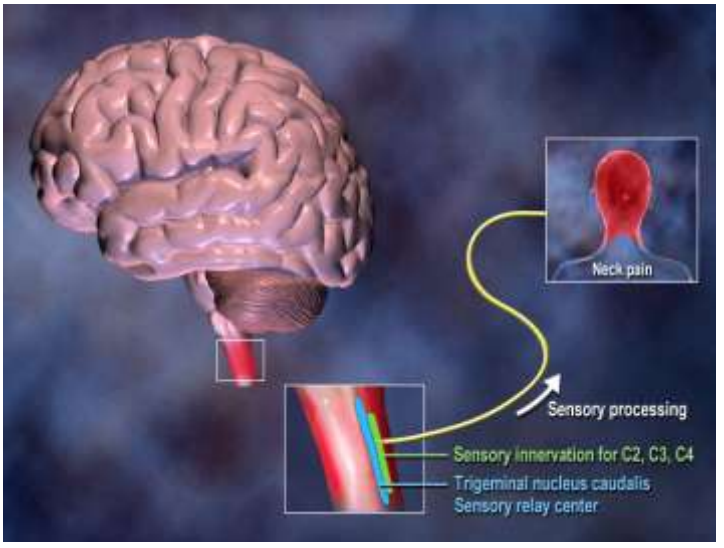
Pathophysiology of Migraine Evolution of the Vascular Theory



The Neurovascular Theory

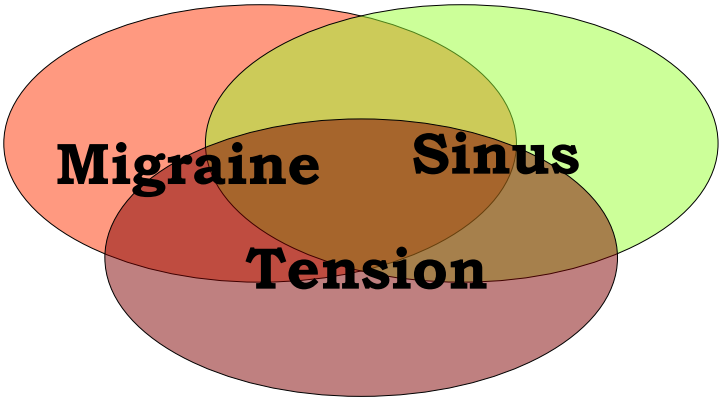


Trigeminal Nucleus Caudalis Extends to Dorsal Horn for C2, C3, and C4, Resulting in Neck and Posterior Head Pain



Cranial Parasympathetic Stimulation Can Result in "Sinus Symptoms" Which Often Leads to a Diagnosis of Sinus Headache

Common Clinical Presentations of Migraine



"ID Migraine Screener"

- Do you feel **nauseated** or sick to your stomach with your headache?
- Does **light** bother you?
- Do your headaches **limit your ability** to work, study or do what you need to do for at least a day?

Lipton et al, Neurology August 2003

Nausea

- Average Office Visit: 11-15 minutes
- Optimal single and three-variable models for the diagnosis of migraine
  - Only single-variable model: **nausea**
  - Best three-variable model: nausea/photophobia/pulsating pain
    - Best + likelihood ratios/ least – likelihood ratios *- Martin, V et al Headache 2005*

Brenda – 29 yo
Mother on Vacation

Symptomatic and Abortive Therapy for Migraine

- Analgesics/ Antiemetics
- NSAIDS
- Opiates
- Ergotamine/dihydroerotamine
- Isometheptene mucate
- **Serotonin (5-HT) (triptans) receptor agonists**

Symptomatic and Abortive Therapy for Migraine

- Analgesic combinations
  - Beware of overuse and “rebound”
  - Use of medications more than 15 days/month
  - Caffeine-combinations the culprit
  - Watch for acetominophen toxicity (3-4 grams per day)
    - Excedrin, Fioricet, Lortab,Percocet, Ultracet

When to Prevent Migraine

- Interference with work/school
- Acute meds fail or are contraindicated
- Medication overuse
- Adverse side effects
- Complicated migraine
  - (hemiplegic, basilar)

Colleen – 27 yo
Teacher and Single Mother

Terry – 45 yo
Female with Daily Headache

Preventative Therapy

- FDA-Approved Medications
  - Propranolol, Timolol
  - Methysergide (unavailable)
  - Valproic Acid
  - Topiramate (2004)
- NSAIDS (Cox-2/long-acting)
- Tricyclic Antidepressants
- Calcium Channel Blockers
- Anti-convulsants

PREVENTION of Headache

- Keep a headache diary
  - Food triggers, sleep schedule, stress
- Consider dietary supplement
  - Vitamin B2 (400 mg) and Magnesium (400 mg)
- Preventative Medicines
  - Beta blockers, Calcium channel blockers, Anti-convulsants (Topamax,Neurontin)
  - BCP without placebo (Seasonale)
- Reduce stress/barometric change
  - Move to Arizona
  - Change your boss/spouse/med scho dean

Botulinum Toxin

- **Several open-label and small placebo-controlled trials**
- **Recent abstract** ***Neurology 64: March 2005***
  - **355 patients with CDH (>15/mo)**
  - **Botox Type A/placebo every 90 days/9 mo**
  - **HA-free days: no significance**
  - **HA frequency reduction by >50% at day 180: p=0.027**

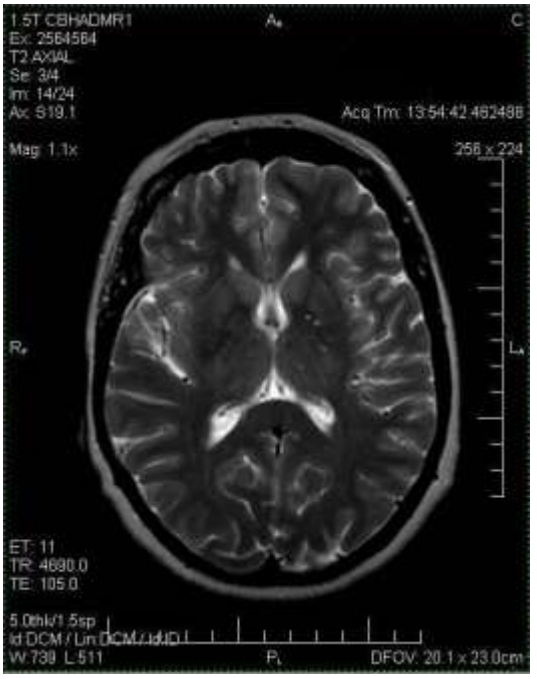
Preventive Therapy: Maxiums

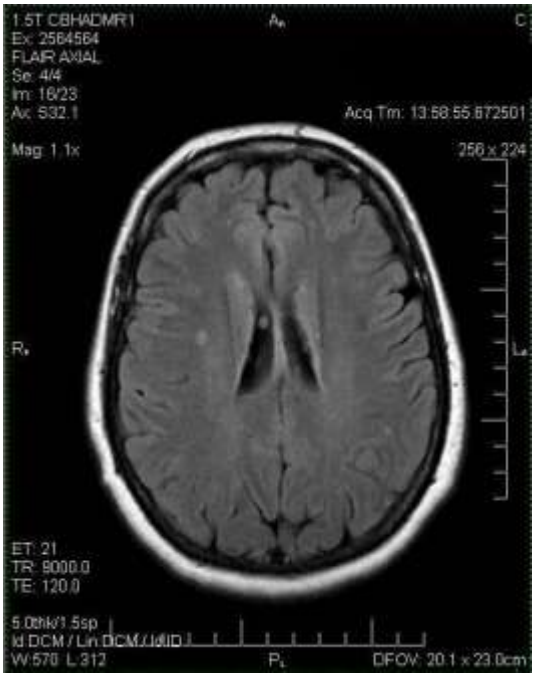
- "Start low and go slow"
  - 10 mg amitriptyline or nortriptyline
  - 80-120 mg verapamil (SR)
  - 40-80 mg propranolol
  - 500 mg valproic acid (ER)/topiramate 25 mg
  - Cox 2 inhibitors
- Hang on for 4-6 weeks/ Diary!!

Migraine as an Episodic Disorder
vs.
Migraine as a Disease

Migraine as a Risk Factor for Subclinical Brain Lesions

- The risk of deep white matter lesions on MRI brain scans is increased in patients with migraine with and without aura
- And the risk is further increased with attack frequency greater than one per month.
- - JAMA January 28, 2004





Reducing the Risk of Migraine Transformation to Chronic Daily Headache

Disease modification

- **Early diagnosis**
- **Early behavioral change**
- **Early prophylactic phamacotherapy**
  - **Only ½ of patients candidate for prevention receive it**
- **Analysis of pooled data from 3 topiramate trials: reduced the risk of development of chronic forms of headache**

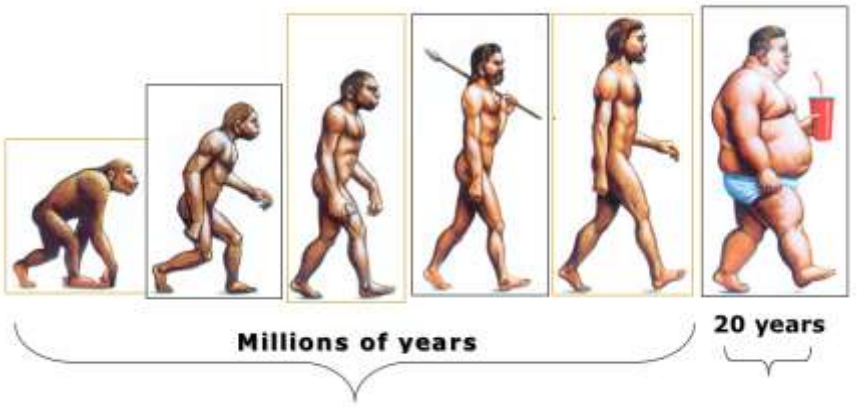
Limmroth, V. Headache 2007

Weight and Migraine Possible Mechanisms

- CGRP levels increased in obese women
  - CGRP: postsynaptic mediator of trigeminovascular inflammation
- Obesity is pro-inflammatory
  - High levels of IL-6 and TNF-a
- Migraine
  - Neurovascular inflammation
  - Like obesity, comorbid with cardiovascular disorders, and risk of stroke (with aura)

Weight and Migraine

- 12% of adults have migraine. 64% of US adults are overweight or obese (BMI 25-35)
- Overweight and obese individuals have increased frequency, not prevalence, of migraine
  - Significant associations: disability, photo- and phono-phobia
- Obesity is comorbid with CDH, fibromyalgia and chronic back pain

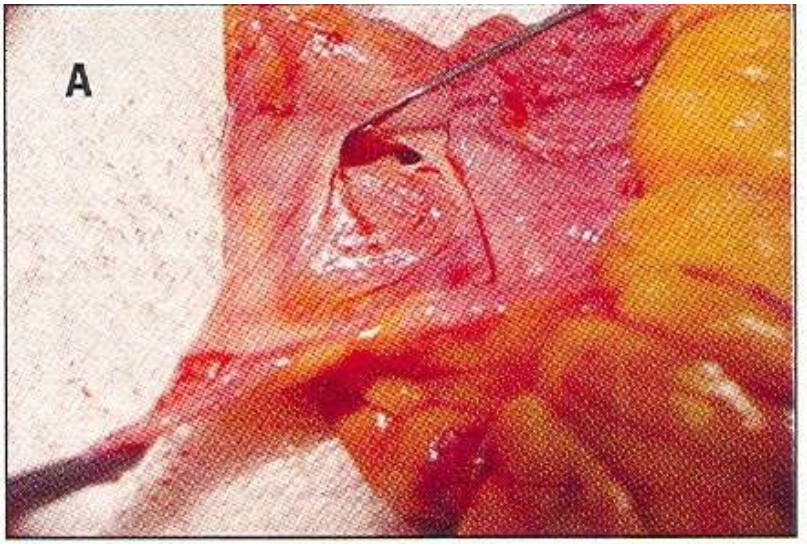


DEVOLUTION!!!

Percutaneous closure of patent foramen ovale reduces the frequency of migraine attacks

- Paradoxical emboli through right to left shunt…….stroke, ?migraine
- Prevalence of PFO and ischemic lesions in migraine cf to healthy controls
- 215 patients: 22% with migraine (cf 12%)
- Post closure HA freq decreased by 54%

- Neurology 2004;62:1399-1401 M. Schwerzmann et al, University Hospitals Bern, Switzerland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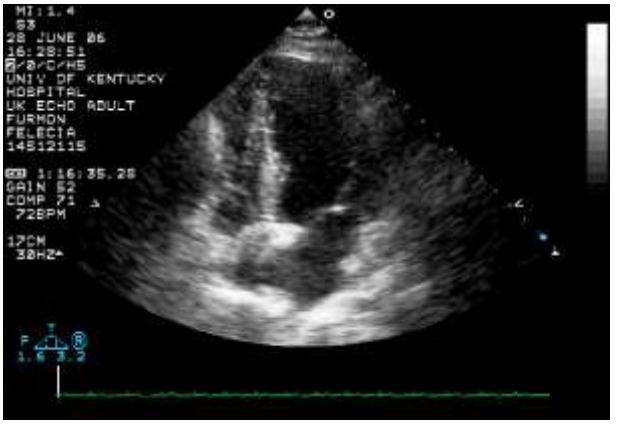
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1:16:35.28
GAIN 52
COMP 71
72BPM
17CM
32HZ

? Hypotheses?

- Transcranial Doppler sonography detects >10 microembolic signals/hr in PFO pts
- Arise from thrombi of venous circulation
  - Normally lysed in the pulmonary circulation
- Valsalva: microemboli reach brain

Central Sensitivity Syndromes

- Irritable Bowel
- Overactive Bladder
- Low Back Pain, TMJ Disorder
- Migraine and Chronic Tension Headaches
- Comorbid: mood disturbance
- Associated: Chronic Fatigue, Sleep Disturbance, “Fibro-Fog,” Endocrine Dysfunction

Central Sensitization

- Nociception *plus*
  - Modulation in the CNS
  - Emotional and affective components
  - Temporal summation ("wind up")
    - Second pain (C fibers stim > q 3 sec); inh by NMDA rec antagonists
- Pain amplification syndromes
  - Heightened sensitivity to non-painful stimuli as well: touch, heat, cold, light, sound, smell
  - HPA, high levels of sub P/ EAAs in CSF

Central Sensitization

- Excitability of spinal cord neurons after injury
  - Dorsal Horn neurons transmit nociceptive input to the brain
- Enlargement of receptive fields of sc neurons
- Reduction in pain threshold
- Recruitment of novel afferent inputs
  - A-beta fibers normally have no role in pain
- Pain generation by low threshold mechanoreceptors normally silent in pain processing

Pharmacologically Maintained Daily Headache

- Discontinuation of offending medication is paramount to success
  - No acute medication has been proven not to be associated with pharmacologically maintained CDH
- The goal is to return baseline neurological function to normal

Chronic Daily Headache and Analgesic Rebound Headache

1. Stop medications
2. Break Cycle with parenteral medications

   DHE, non-oral triptans

   3. Start Prophylaxis even before parenteral meds
   4. Behavioral intervention: biofeedback, diet, exercise

Chronic Daily Headache and Medication Overuse Headache

- DHE-45 0.5-1.0 mg SQ or IM q 8 h x 3 d
  - With Reglan 10 mg PO q 8h
- Naproxen 500 mg q 12 h
- Prednisone Six Day Taper
  - 60 mg x 2 d, 40 mg x 2d, 20 mg x 2d
- Frova or Amerge q 12 h x 3 d
- On Day 3: initiate Nortriptyline 10 mg x 7d or Topamax 25 mg hs x 7d and increase PRN

ER Headache

- 2.4 million of the 90.3 million emergency department visits in 1999 were headache-related
  - National Hospital Ambulatory Medical Care Survey
- 2.6% share of total visits
- Fourth most common cause of ED utilization

ER Headache Mgt

- IV compazine, thorazine, phenergan
- IV toradol preceded by reglan
- IV DHE preceded by reglan
- IV depacon (18-20 mg/kg) by IV push
- IV propofol
- SQ sumatriptan// 100% oxygen for cluster

Trigeminal Autonomic Cephalgias

- Cluster headache
- Paroxysmal hemicranias
  - Episodic and chronic
- Hypnic headache
- SUNCT (short-lasting unilateral neuralgiform headache with conjunctival injection and tearing)

SUNCT

- Exceedingly rare, more common in men
- Pain paroxysms of 5-250 seconds
- Lacrimation, red eye
- Transformation of trigeminal neuralgia to SUNCT: anectodal reports
  - V1 nociceptive input results in cranial parasypathetic activation

SUNCT, con't

- fMRI: increased posterior hypothalamic blood flow (as in cluster headache)
- Refractory to treatment
  - Not indomethacin-responsive
  - Intravenous lidocaine

Intriguing Headache Types

- “Brain-Freeze” cold-induced headache
  - Ice cream, slushies
- “Ice-Pick” Headache
  - Responds to Indocin 25-50 mg tid
- Exertion-induced Headache
  - Rule out Arnold Chiari I
- Coital Headache
  - Indocin 25-75 mg
  - 30 minutes preventatively