



Women's Health and Headache

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Objectives

- Discuss the epidemiology of migraines
- Discuss typical clinical symptoms of migraine and its subtypes
- Demonstrate competency in applying the clinical features discussed in the ICHD-3 for the diagnosis of migraine and its variants
- Demonstrate competency of the mechanism of action, side effects, utility and proper selection of abortive and prophylactic therapy for migraines
- Familiarize yourself with the symptoms, signs, diagnostic criteria, treatment options and prognosis for headache etiologies due to intracranial pressure variance.

MIGRAINE

Migraine Epidemiology

- >30 million Americans have 1 or more migraine headaches per year.
 - 75% of all persons who experience migraines are women
 - 1 in 6 American women has migraine headaches.
- The incidence of migraine with aura peaks in boys at around age 5 years and in girls at around age 12-13 years
- Migraine-related loss of productive time in the US workforce is more than \$13 billion per year

Enviromental Migraine Triggers

- Hormonal changes, such as those accompanying menstruation (common), pregnancy, and ovulation
- Stress
- Excessive or insufficient sleep
- Medications (many medications implicated but common include vasodilators and oral contraceptives)
- Smoking
- Exposure to bright or fluorescent lighting
- Strong odors (eg, perfumes, colognes, petroleum distillates)
- Head trauma
- Weather changes
- Motion sickness
- Cold stimulus (eg, ice cream headaches)
- Lack of exercise
- Fasting or skipping meals

Dietary Migraine Triggers

- Red wine
- Certain foods and food additives have been suggested as potential precipitants of migraine, including the following:
 - Caffeine
 - Artificial sweeteners (eg, aspartame, saccharin)
 - Monosodium glutamate (MSG)
- Citrus fruits
- Foods containing tyramine (eg, aged cheese)
- Meats with nitrites

ICHD-3



IHS CLASSIFICATION ICHD-3

Search ...



PART II

The Secondary Headaches

Secondary headaches develop as a secondary symptom due to another disorder that is known to cause headache. Examples are headaches attributed to bacterial meningitis, to trauma or medication overuse headache



Home

How to use the classification

Classification

Part one: the primary headaches

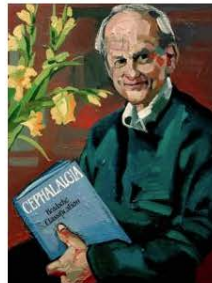
1. Migraine
2. Tension-type headache (TTH)
3. Trigeminal autonomic cephalalgias (TACs)
4. Other primary headache disorders

Part two: the secondary headaches

5. Headache attributed to trauma or injury to the head and/or neck
6. Headache attributed to cranial or cervical vascular disorder
7. Headache attributed to non-vascular intracranial disorder
8. Headache attributed to a substance or its withdrawal

Home

The International Classification of Headache Disorders 3rd edition



On behalf of the Classification Committee of The International Headache Society I am proud to present the **third edition of the International Classification of Headache Disorders (ICHD-3)**. This follows the publication of **ICHD-3 beta** in 2013. The idea behind the beta version was to promote more field testing before presentation of the final ICHD-3, and this has worked well. There have been excellent field-testing studies published, in migraine with aura, cluster headache, idiopathic intracranial hypertension and trigeminal neuralgia among others. It was, for example, documented that the Appendix criteria for A1.2 *Migraine with aura* were superior to the criteria for 1.2 *Migraine with aura* in the main body of ICHD-3 beta, better distinguishing this disorder from transient ischemic attacks. Field testing of the novel associated features in criterion C1 for 3.1 *Cluster headache*, facial flushing and aural fullness, revealed that they did not add to diagnostic discrimination. Consequently, these symptoms are included only in the Appendix of ICHD-3, where they invite further study. These are examples of the evidence-based process of disease classification that now underpins all future changes to the *International Classification of Headache Disorders*.

A contributing reason for the beta version was, as we thought, so that ICHD-3 could when published include the codes of the *International Classification of Diseases*, 11th edition (ICD-11), from the World Health Organization (WHO). We expected that ICD-11 would be finished in 2016, but unfortunately there have been long and unexpected delays so that the final codes are still not available. We therefore have to publish ICHD-3 without them.

ICHD-3 is published as the first issue of *Cephalalgia* in 2018, exactly 30 years after the first edition of the *International Classification of Headache Disorders*, ICHD-I as we now call it. This first version was based primarily upon the opinions of experts, but proved nevertheless to be largely valid. ICHD-II, published in 2004, included a number of changes prompted partly by new evidence and partly by revised opinions of experts. New scientific evidence played a relatively greater role in the changes made in ICHD-3 beta, and all the further changes included in ICHD-3 are based on such evidence. Thus headache classification is now and will in the future be driven entirely by research.

A long journey that started in 2010 has ended with the publication of ICHD-3, but the present committee has still much to do for a couple of years. ICHD-3 beta was translated into many languages.

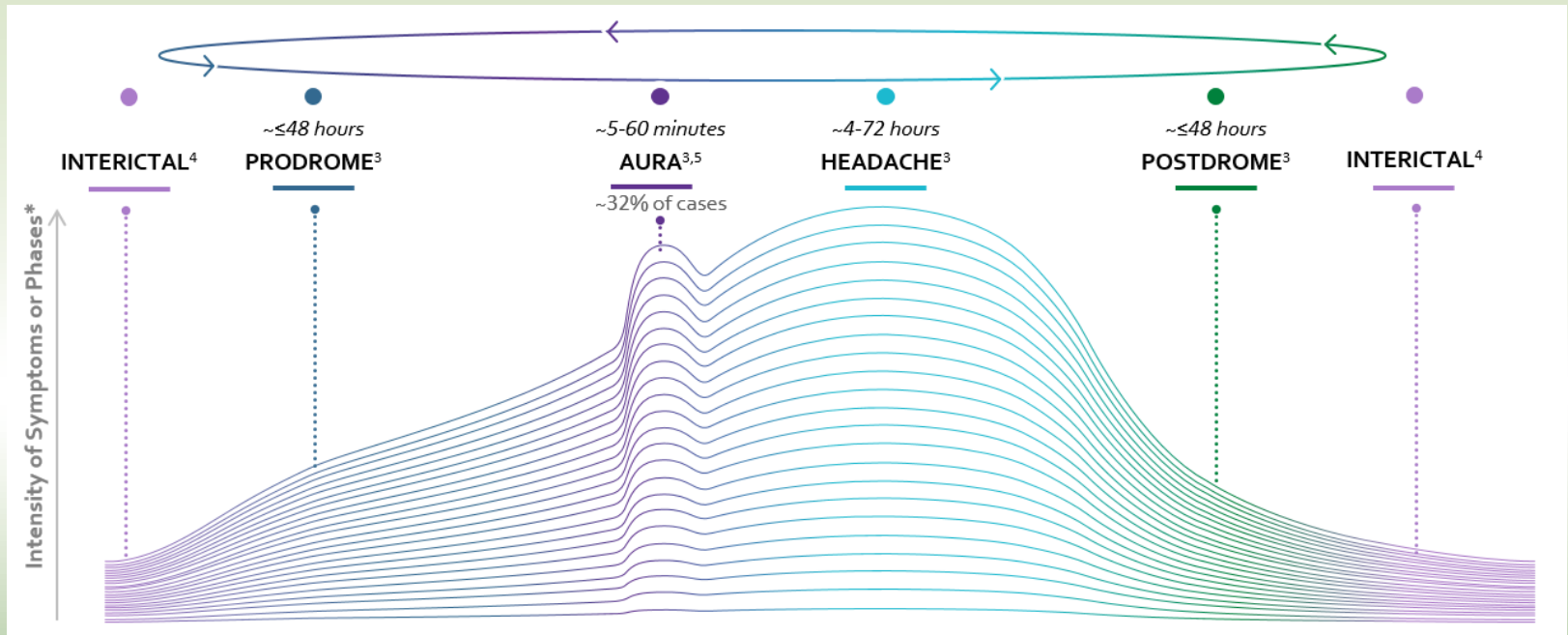
Migraine Diagnostic Criteria

- A. At least five attacks fulfilling criteria B-D
- B. Headache attacks lasting 4-72 hr (untreated or unsuccessfully treated)
- C. Headache has at least two of the following four characteristics:
 - 1. unilateral location
 - 2. pulsating quality
 - 3. moderate or severe pain intensity
 - 4. aggravation by or causing avoidance of routine physical activity (eg, walking or climbing stairs)
- D. During headache at least one of the following:
 - 1. nausea and/or vomiting
 - 2. photophobia and phonophobia
- E. Not better accounted for by another ICHD-3 diagnosis.

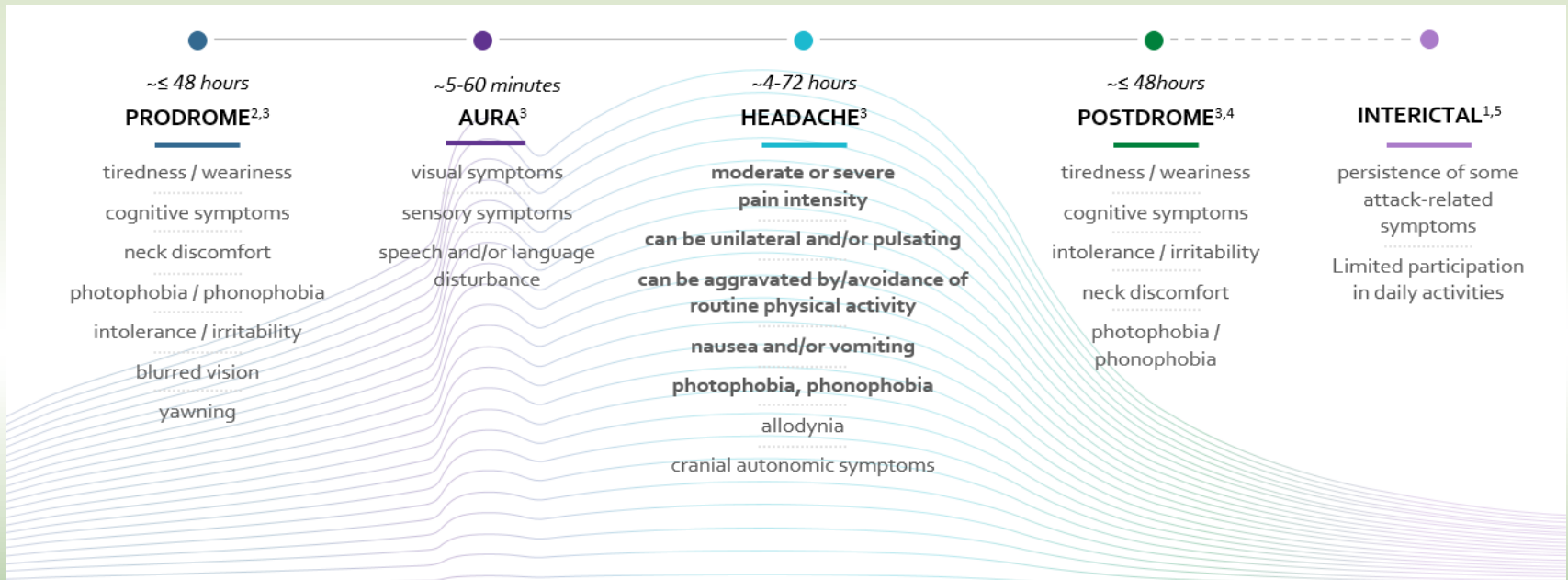
Migraine variants

- Common Migraine (no aura)
- Classic Migraine (w/ aura)
- Classic Migraine with Prolonged Aura (Complicated Migraine)
- Classic migraine with brainstem aura (Basilar Migraine)
- Hemiplegic Migraine
- Retinal Migraine (ophthalmic migraine)

Migraine Phases



Migraine Phases



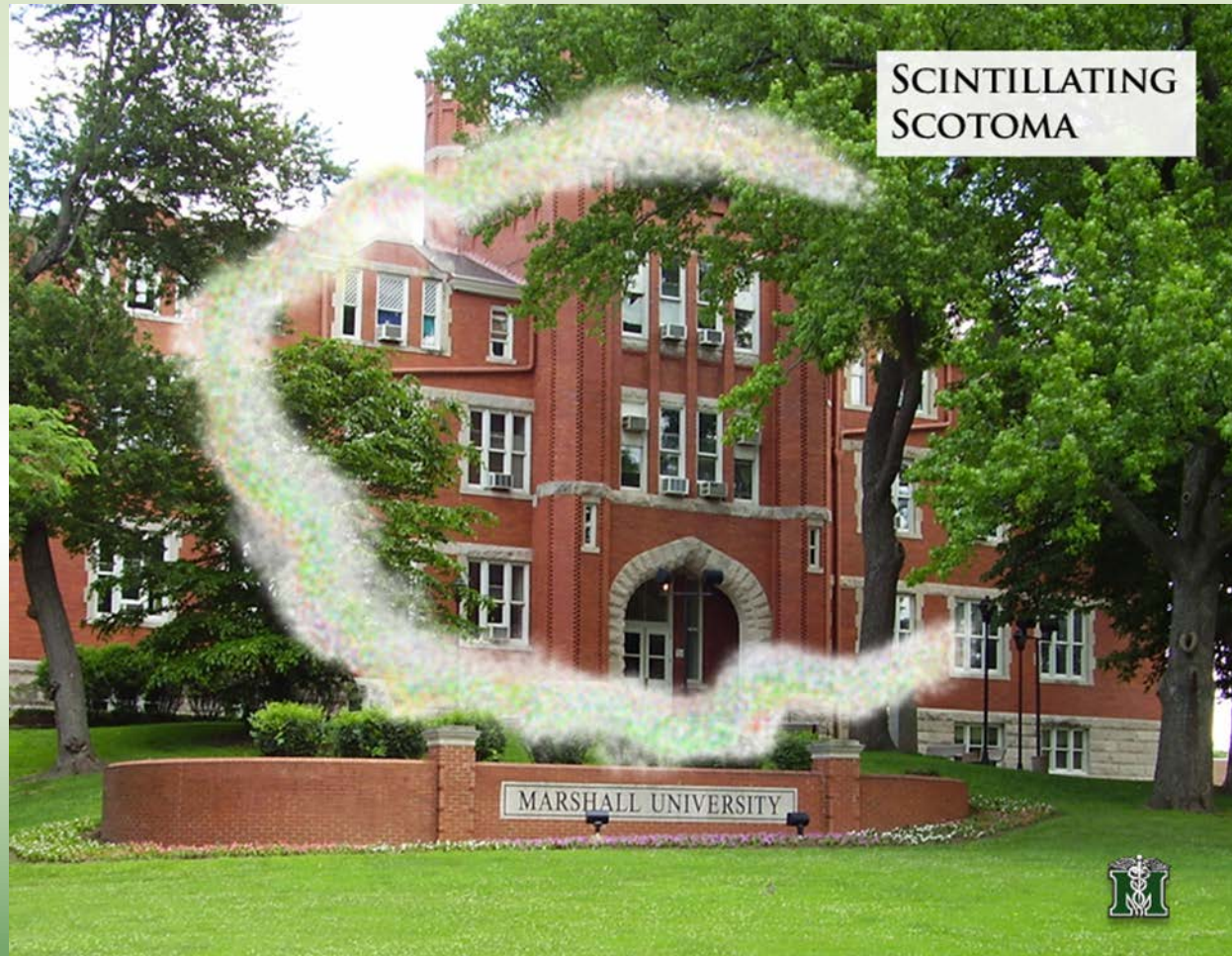
Common Migraine

- Fulfils ICHD-3 Criteria and has NO Aura

Classic Migraine

- Fulfils ICHD-3 Criteria and has aura with both of the following:
 - fully reversible visual, sensory and/or speech/language symptoms
 - no motor, brainstem or retinal symptoms.
 - Symptoms typically begin 20 minutes prior to migranous headache onset

Common Visual Aura



Common Visual Aura



Other Common Auras

- Parasthesia on face, arm/hand
- Confusion state (word finding difficulty)

Migraine with Prolonged Aura (complicated migraine)

- Symptoms same as migraine with aura but the aura is *quite dramatic* and can last for an extended period of time. Diagnosis is made by exclusion of other more serious underlying pathology.

Migraine with Brainstem Aura (Basilar Migraine)

- Must meet migraine headache criteria previously described
- Aura with both of the following:
 - at least two of the following fully reversible brainstem symptoms:
 - a) dysarthria
 - b) vertigo
 - c) tinnitus
 - d) hyperacusis
 - e) diplopia
 - f) ataxia not attributable to sensory deficit
 - g) decreased level of consciousness (GCS ≤ 13)
- No motor or retinal symptoms.

Hemiplegic Migraine

- Must meet migraine headache criteria previously described
- Aura consisting of both of the following:
 1. Fully reversible motor weakness
 - Motor symptoms generally last less than 72 hours but, in some patients, motor weakness may persist for weeks.
 2. Fully reversible visual, sensory and/or speech/language symptoms.

Retinal Migraine

- Recurrent attacks of unilateral visual disturbance or blindness lasting from minutes to 1 hour
 - Patients describe a gradual visual disturbance in a mosaic pattern of scotomata that gradually enlarge, producing total unilateral visual loss
- Associated with minimal or no headache.

Migraine Abortive Therapies

- Non-Pharmacologic Approach
 - **Avoid triggers:**
 - Red Wine
 - Certain foods (chocolate, some cheeses MSG heavy nitrite containing foods-ie highly processed meats)
 - hunger from missing meals
 - Sleep deprivation and irregular sleeping pattern
 - Stress

Migraine Abortive Therapies

- Treating in the first 20 minutes of symptoms is necessary for greatest efficacy
 - NSAID's
 - Triptans
 - Ergots
 - Dopamine antagonists

Triptans

- 5HT₁ Antagonists (Triptans) available in oral, inhaled and subcutaneous forms (examples below)
 - Sumatriptan* (very short onset and duration)
 - Multiple formulations: oral tabs, nasal spray and injections
 - Rizatriptan* (short onset and duration)
 - Elatriptan* (short onset and duration)
 - Almotriptan (short onset and duration)
 - Naratriptan* (intermediate onset and duration)
 - Zolmitriptan (intermediate onset and duration)
 - Frovatriptan (long onset and duration)

(*)Generic Available

Triptan Dosing Guide

Drug	Route	Dosing Size	Max Daily Dose	Onset	Half Life	Common Side effects	Contraindications	Comments
Almotriptan (Axert™)	Oral	6.25 mg 12.5 mg	25mg	30 min	4 hours	•nausea 2% •paresthesia 1%	Other triptans or Ergot derivatives	• Better tolerated than Sumatriptan
Eletriptan (Relpax™)	Oral	20 mg 40mg	80mg	30 min	4 hours	•dizziness 6%; •nausea 5%; •paresthesia 3%; •chest/ tightness/ pressure 2%	Other triptans or Ergot derivatives	• Good balance between fast onset and long duration ²
Frovatriptan (Frova™)	Oral	2.5 mg	7.5mg	2-3 hours	26 hours	•dizziness 8% •paresthesia 4%; •flushing 4%; •chest pain 2%	Other triptans or Ergot derivatives	• Longest half-life • Slow onset but low recurrence
Naratriptan (Amerge™)	Oral	1 mg 2.5 mg	5 mg	1-2 hours	6 hours	•nausea 5%; •paresthesias 2%; •throat pain 4%; •dizziness 2%	Other triptans or Ergot derivatives	• Better tolerated than Sumatriptan • Less headache recurrence than Sumatriptan
Rizatriptan (Maxalt™)	Oral ODT	5 mg 10mg	30 mg (15 mg per day if taking betablocker)	30 min	3 hours	•dizziness9% •nausea 6%; •paresthesia 4%; •chest pain 3%; •throat pain 2%	• Other triptans, Ergot derivatives, MAOIs • Use 5 mg dose if taken with propranolol	• <i>Maxalt-MLT</i> is an orally-disintegrating tablet and may be taken without water • Best efficacy at two hours among orals but high recurrence rate

Triptan Dosing Guide Continued

Sumatriptan (Imitrex™)	Oral	25 mg 50mg 100mg	200 mg	30 min	2.5 hours	<ul style="list-style-type: none"> •paresthesia 5%; •chest pain 2%; •throat pain 2%; 	Other triptans, ergot derivatives, MAOIs	<ul style="list-style-type: none"> • 100 mg dose may be more effective than 50 mg dose
Sumatriptan (Sumavel Injection™)	SQ	1 mg to 6 mg as a single dose (vial) 4 mg/0.5 mL or 6 mg/0.5mL prefilled cartridge	12 mg	10 min	2 hours	<ul style="list-style-type: none"> •injection site reactions 59%; •parasthesia 14%; •dizziness 12%; •flushing 7%; •chest pain 5%; •throat pain 2% 	<ul style="list-style-type: none"> • Other triptans, ergot derivatives • Use with MAOI not advised. MAOIs reduce sumatriptan clearance, resulting in significantly increased levels 	<ul style="list-style-type: none"> • Consider for patients who suffer from severe migraines, vomit early in the attack, or if migraines rapidly peak in intensity
Zolmitriptan (Zomig™)	Oral ODT	1.25 mg 2.5 mg 5 mg (not first line)	10 mg	45 min	3 hours	<ul style="list-style-type: none"> •nausea 9%; •dizziness 8%; •paresthesia 7%; •throat pain 7%; •chest pain 3% 	Other triptans, ergot derivatives, MAOIs	<ul style="list-style-type: none"> • <i>Zomig-ZMT</i> is an orally disintegrating tablet and may be taken without water
Zolmitriptan (Zomig™)	Nasal	2.5 mg 5 mg	10 mg	15 mins	3 hours	<ul style="list-style-type: none"> •unusual taste 21%; •paresthesia 10%; •throat pain 4%; •nausea 4%; •nasal cavity discomfort 3% 	Other triptans, ergot derivatives, MAOIs	<ul style="list-style-type: none"> • Rapid-acting alternative to injection • Taste and nasal route not acceptable to some patients?

Ergots

- Therapeutic activity attributed to agonist effect at 5-HT-1D receptors, which includes vasoconstriction of intracranial blood vessels, or activation of 5-HT1D may inhibit proinflammatory neuropeptide release
- Dihydroergotamine is used for severe refractory headaches such as status migranosis and a protocol is used to repeatedly dose in the inpatient setting for sustained relief.

Dopamine Antagonists

- Reduce nausea
- Dopamine Antagonists available in oral and subcutaneous forms
 - Metoclopramide (Reglan)
 - Prochlorperazine (Compazine)

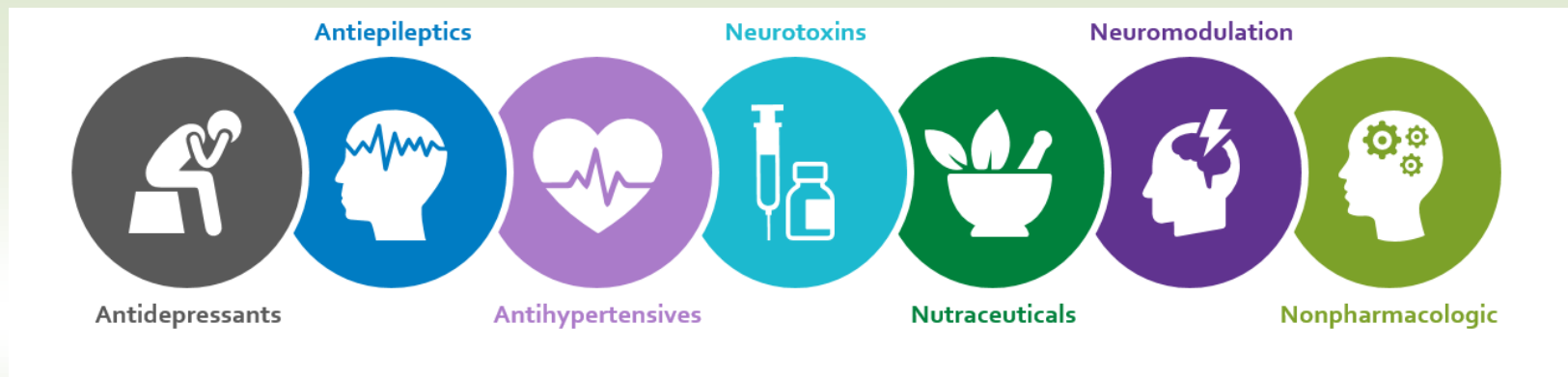
Combination Therapies

- Combinations
 - Acetaminophen, ASA, and Caffeine (**Excedrin Migraine**)
 - Works well when only used 2-3 x weekly
 - Acetaminophen, butalbital, and caffeine (**Fiorcet**)
 - Typically, only used for Post-LP headaches
 - Acetaminophen, Isometheptene and Dichloralphenazone (**Midrin**)

Migraine Prophylaxis

- Prophylaxis should be considered:
 - Sustained recurrent headaches of 4x per month
 - Significant medical comorbidity or economic impact with headaches
 - Recurrent missed days of school
 - Recurrent ED visits

Migraine Prophylaxis



Migraine Prophylaxis Options

- Antihypertensives
 - Beta Blockers
 - Calcium Channel Blockers
- Anticonvulsants
 - Gabapentin
 - Topiramate
 - Valproic Acid

Migraine Prophylaxis Options

- Antidepressants
 - TCA's
 - SSRI's
 - SNRI's
- Vitamins/Minerals/Supplements
 - Mg
 - B2
 - Butterbur

Refractory Migraine Prophylaxis

- Botulinum Toxin Injections
- CGRP Antagonists

Adult Migraine Prophylaxis Guide

Prophylactic Treatment of Migraines in Adults

Agent	Dosing	Comments
Amitriptyline (Elavil™)	<u>Starting dose:</u> 12.5 mg <u>Goal dose:</u> 50 to 100mg QHS	May be given at dinner time to avoid early-morning sleepiness. Can cause constipation and dry mouth.
Verapamil CR (Calan™)	<u>Starting dose:</u> 120 mg QHS <u>Goal dose:</u> 240-360 mg QHS	Tends to work better in men. Effective in some complicated migraines or basilar migraines. Can cause hypotension
Propranolol (Inderal™)	<u>Starting dose:</u> 20 mg BID <u>Goal dose:</u> 30mg BID and up	Avoid in patients with asthma. Can cause hypotension
Atenolol (Tenormin™)	<u>Starting dose:</u> 25 mg BID <u>Goal dose:</u> 50mg BID and up	Avoid in patients with asthma. Can cause hypotension. Less side effects than propranolol
Topiramate (Topamax™)	<u>Starting dose:</u> 25 mg qhs <u>Goal dose:</u> 50-100mg bid	Avoid if history of kidney stones. Can cause poor attention. Weight loss.
Valproate (Depakote™)	<u>Starting dose:</u> 250 mg BID <u>Goal dose:</u> 500mg BID	Must have baseline LFT's and Platelets and needs follow-up monitoring. Teratogenic (13% fetal malformation). Weight gain is an issue.
Gabapentin (Neurontin™)	<u>Starting dose:</u> 300 mg BID <u>Goal dose:</u> 300-900mg TID	Can cause pedal edema and fatigue.
Venlafaxine XR (Effexor™)	<u>Starting dose:</u> 37.5mg QD <u>Goal dose:</u> 75-150mg QD	Can cause nausea, insomnia and dizziness. Can worsen headaches in some settings. Warn men that is can cause delayed ejaculation
Duloxetine (Cymbalta™)	<u>Starting dose:</u> 30mg QD <u>Goal dose:</u> 30-60mg QD	Can cause nausea, somnolence, dry mouth and dizziness. Can worsen headaches.
Botulinum Toxin (Botox™)	<u>Starting dose:</u> 155 units	Reserved for patients with ≥15 headache days per month whom have failed at least 2-3 prior prophylaxis trials. Can only be dosed once every 90 days due to concern of antibody formation
Erenumab (Aimovig™)	Starting dose: 70mg once monthly Goal dose: 70-140mg monthly	Injectable CGRP antagonist. Must fail multiple (2-3 or more) other options due to cost (~\$6500 annually).
Magnesium	400mg BID	Seems to work well in menstrual cycle related migraine. May help with constipation
Riboflavin (Vitamin B2)	200mg BID	Can turn urine yellow/orange
Butterbur	150mg QD	Hard to find locally.

INTRACRANIAL PRESSURE HEADACHES

IIH Epidemiology

- IIH is a disorder of unknown etiology that predominantly affects obese women of childbearing age
- United States Incidence
 - More than 90% of patients with IIH are women of childbearing age
 - 0.9 cases per 100,000 in general population (both sexes)
 - 19 cases per 100,000 population in women 20% over ideal body weight
 - An 8:1 female-to-male ratio for a mean weight 38% over the ideal weight for height

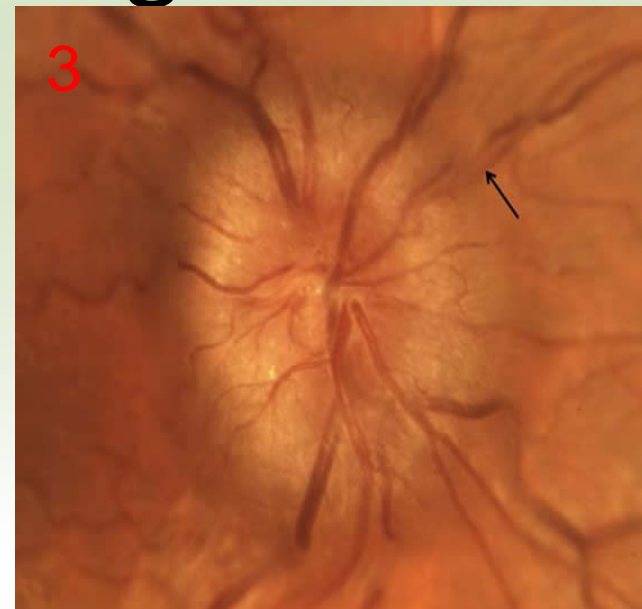
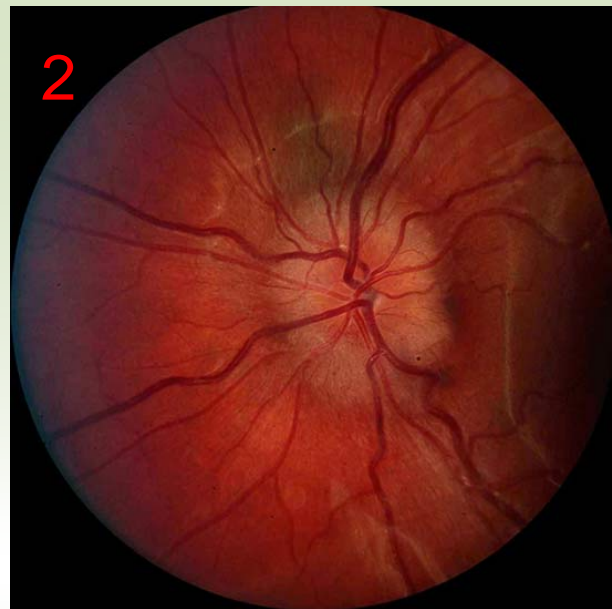
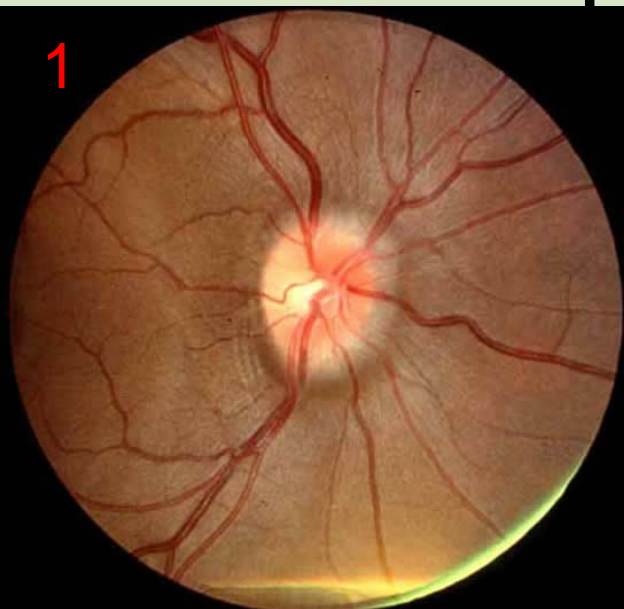
Symptoms

- Headaches
 - Nonspecific with variable location
 - Character: Throbbing and/or pressure type
 - Worsen with Valsalva
- Pulsatile tinnitus
 - Audible “whooshing”
- Vision impairment
 - Flashes and floaters
 - Diplopia
 - Due to either trochlear or abducens palsy
 - Decrease acuity and impaired visual fields
 - Typically, the vision loss starts in the nasal inferior quadrant and is followed by loss of the central visual field
 - Visual dimming with Valsalva

Papilledema

- Typically bilateral disc edema is noted secondary to the increased intracranial pressure
- Severity of disc edema does not help to distinguish underlying pathology
- Untreated increased intracranial pressure ultimately leads to optic atrophy and resultant loss of acuity

Papilledema-Grading

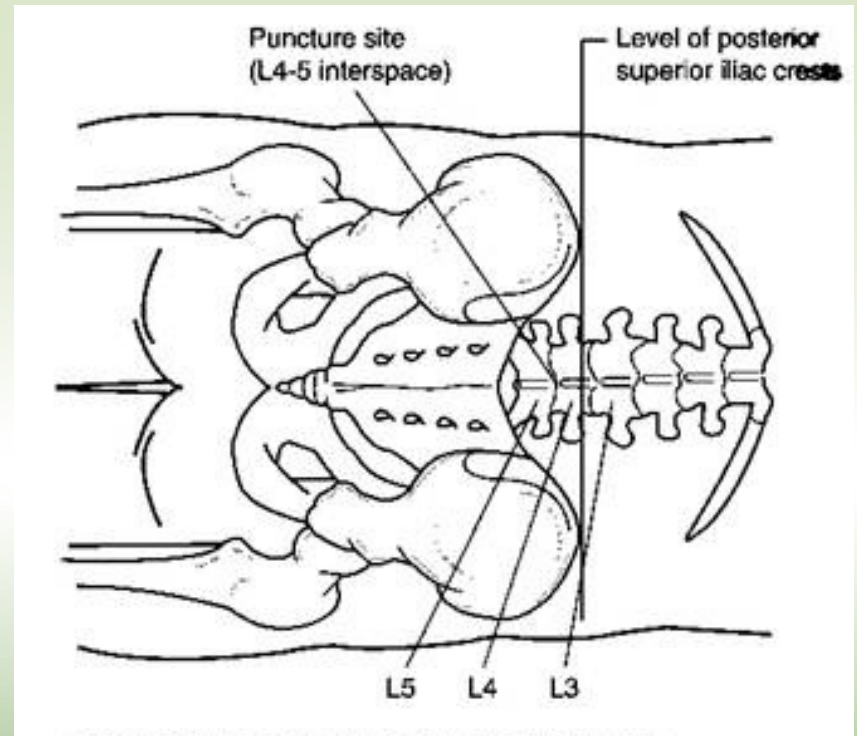


Neuroimaging Work-up

- Disc edema necessitates neuroimaging with MRI (with and without) and MRV to rule out mass or dural venous sinus thrombosis
- IIH findings on MRI:
 - normal ventricles
 - enlarged optic nerve sheaths
 - occasionally an empty sella

Lumbar Puncture

- **Localize the landmarks:** between spinous processes at L3-4 level.
 - This level corresponds to the level of the posterior superior iliac crest.
 - On obese patients, find the sacral promontory; the end of this structure marks the L5-S1 interspace.



CSF Data

- Normal opening pressures are typically 120-170mm H₂O
- Diagnosis of IIH requires pressures of >250mm H₂O
- CSF can be drained to normal closing pressures

Non-Pharmacologic Management

- Weight loss!!
 - Diet
 - As little as a 5-10% weight loss has been demonstrated to yield a reduction in ICP with accompanying resolution of papilledema.
 - Bariatric Surgery:
 - Review of case series/reports (62 total patients)
 - 52 (92%) experienced resolution of the presenting symptoms.
 - Of the 35 patients who underwent postoperative funduscopy, 34 had resolution of papilledema.
 - Of 12 patients who underwent pre- and postoperative visual field examinations, 11 showed resolution of visual field defects

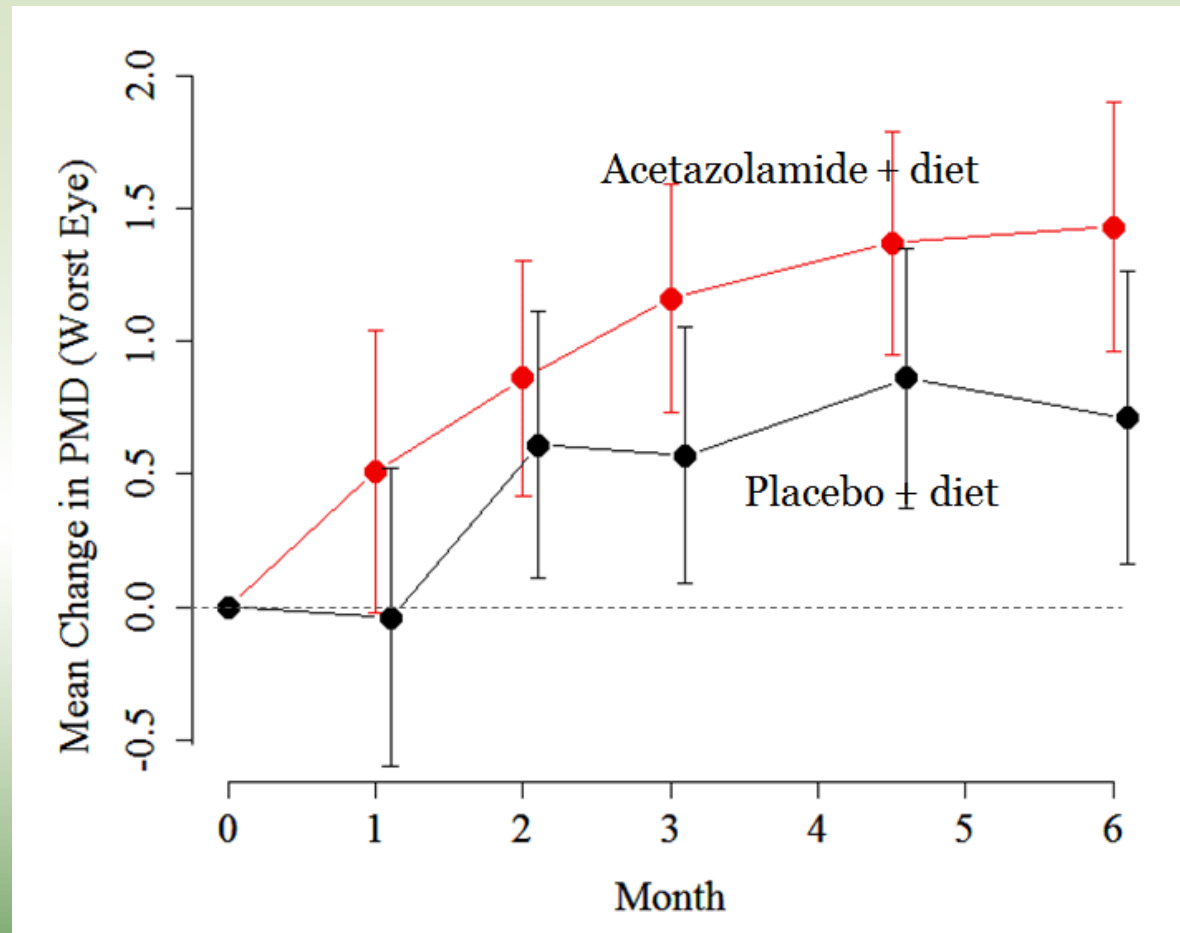
Pharmacologic Management

- Diuretics
 - Acetazolamide (good data- see next slides)
 - Furosemide (little data)
- Corticosteroid
 - Can be used transiently in rapidly progressing visual deterioration
- Anticonvulsants
 - Topiramate
 - Weak carbonic anhydrase inhibitor
 - side effect is weight loss (a necessary goal in most IIH cases), which can help put the disease in remission.

Acetazolamide

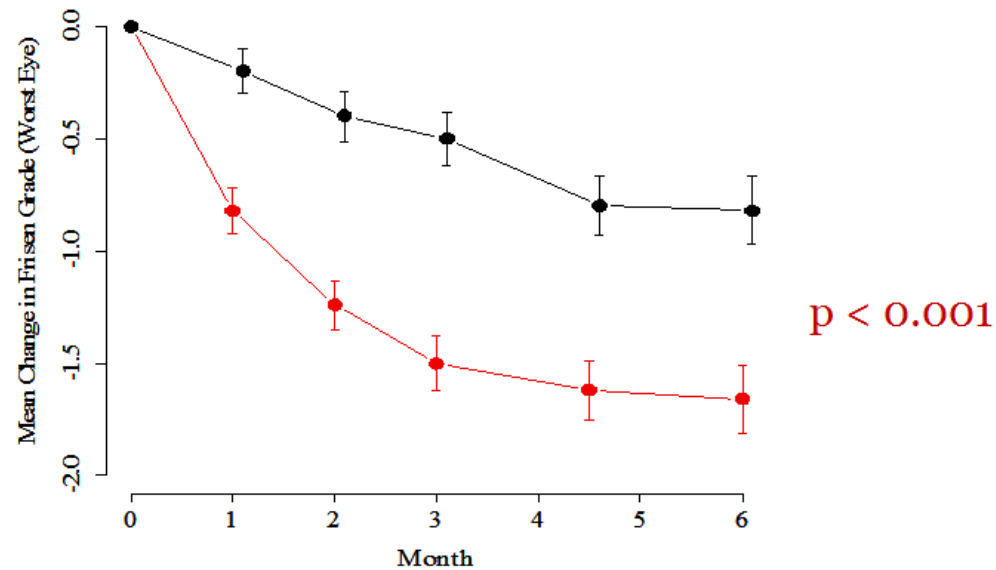
- NORDIC Trial
 - Primary endpoint: Determine efficacy of diet and acetazolamide vs diet and placebo with regard to visual field function
 - Secondary endpoint:
 - Change in disc edema, quality of life and CSF pressure
 - 165 enrolled (161 women 4 men)
 - 88% obese with mean BMI 39.9
 - 5% had first degree relative(s) with IIH
 - Dosing of 4g per day achieved by 93% with average patient adherence of 89%

Acetazolamide: NORDIC Trial

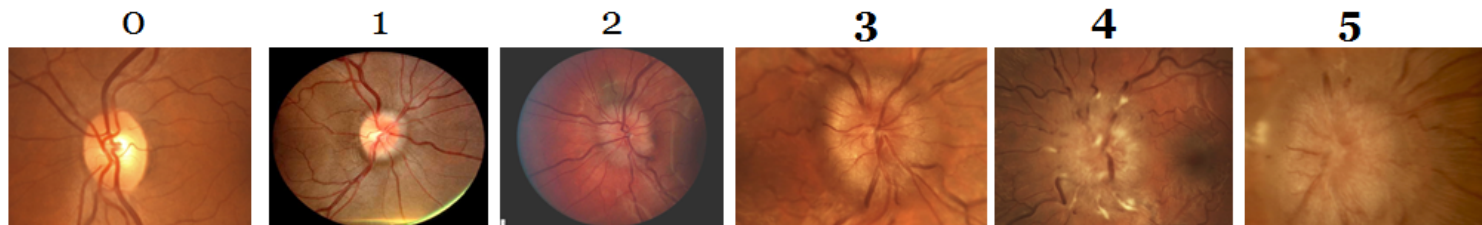


The acetazolamide-plus-diet group in red had a statistically significant improvement in visual field mean deviation with most of the change occurring in the first month

Acetazolamide: NORDIC Trial



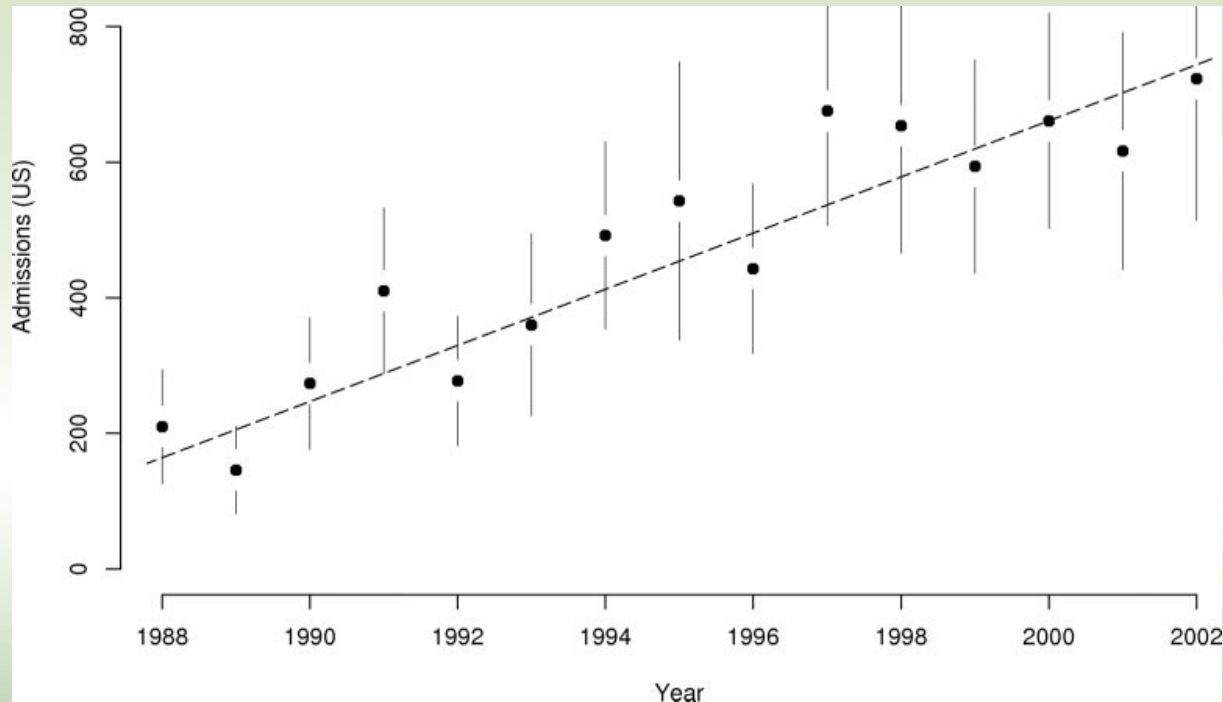
Grades of Papilledema



Surgical Indications

- Failed medical management resulting in:
 - Continued elevations in ICP
 - Progressive visual deterioration
 - Worsening disc edema /early signs of optic atrophy
- Fulminant IIH

Shunting Procedures



Graph showing rising annual aggregate caseload of placement of new CSF shunts for IIH in United States nonfederal hospitals. The aggregate annual caseload increased 350% during this 14-year interval, or 9.4% annually (P 0.001). Curry et al. 2005

SPONTANEOUS INTRACRANIAL HYPOTENSION

SPONTANEOUS INTRACRANIAL HYPOTENSION

- Misnomer as most events are spinal in etiology
- Implies one of the following:
 - Low CSF volume
 - Low CSF pressure
 - Low compliance of the caudal spinal dura.

Epidemiology

- Prevalence 1 per 50,000,
- Incidence of 5 per 100,000.6
- Women > men
- Typically presents in the fourth or fifth decades

Clinical Symptoms

- Variable location of the headache pain
- Headache is orthostatic, worsening in the upright posture
- Worsens as day progresses
- Can worsen with Valsalva, exercise or bending
- The following results in symptomatic improvement
 - Caffeine
 - Lying flat or in Trendelenburg
 - High Altitude

Diagnosis

- You must get a great history
- Exam is typically normal
- Patients may be slim with an elongated, slender neck.
- Improvement of symptoms in the Trendelenburg position (10- to 20-degree head-down tilt for 5 to 10 minutes) is highly suggestive of spontaneous intracranial hypotension
- LP Opening pressure <6cm H₂O

Treatment

- A nontargeted, autologous, high-volume epidural blood patch is often the first step in management
 - successful approximately 30% of the time
- Other options
 - Bed rest
 - Abdominal binder
 - Caffeine
 - Corticosteroids- prednisone taper beginning at 50mg/d
- Surgical Correction

Autologous Blood Patch

- The mechanism of epidural blood patches leading to improvement is uncertain and may be related to any of the following:
 - Tamponade and sealing of the leak
 - Restriction of CSF egress into the epidural space
 - Mild compression of the thecal sac by the epidural blood secondary increased CSF pressure rostral to the injection
- Decreasing the elasticity of the thecal sac.

Surgical Mitigation

- Surgery may be needed in cases of a calcified disk or osteophyte causing a dural defect.
- Leaking meningeal diverticula can be ligated or clipped.
- Larger dural defects are closed with a muscle or fat pledget, with gelatin sponge and fibrin sealant, or sutured