Headaches in Primary Care

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Educational Objectives

By completing this educational activity, the participant should be better able to:

1. Increase awareness and interest of primary headaches in primary care and provide a clinical framework for the diagnosis, prophylaxis, and treatment of migraine.
2. Discuss the distinction between primary and secondary headaches.
3. Identify risk factors for migraine progression and develop a plan for headache treatment based upon migraine staging.

Speaker Disclosure

Dr. Ready disclosed that he is on the advisory board for Theranica, and he is on the speaker's bureau for Allergan, Amgen, Biohaven, Lilly, and Teva.

Headaches in Primary Care

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Put on Your Radar Screen

- Stanford Neuroscientist
- Started Podcast in January
- When you understand the mechanism, you know how to maintain the machine
- Topics include Sleep, Pain, Learning, Performance

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Additional Primary Care Resources

National Headache Foundation
Headaches.org
Outstanding resources for Patients & Clinicians

Podcasts series

American Headache Society
AmericanHeadacheSociety.org
Recently started program for Primary Care Outreach

First Contact – multiple resources for Clinicians

Southern Headache Society -- https://southernheadache.org/
Great listserv discussion where cases are posted and discussed.

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Objectives

By completing this educational activity, the participant should be better able to:

- Increase awareness and interest of headache in primary care.
- Provide a clinical framework for the diagnosis, prophylaxis, and acute migraine treatment.
- Identify risk factors for migraine progression and develop a plan for treatment using migraine staging.

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First Things First
Primary or Secondary Headache

- **Primary** – nervous system you are born with or acquire (trauma) & the environment you are in
  - Migraine, Cluster, Tension Type
  - **Headache as the Condition**
- **Secondary –** headaches that are caused by something else
  - Infection, Mass, Vascular, Trauma
  - **Headache as a Symptom**

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SNOOP4

Ruling Out Secondary Headaches

Systemic symptoms and signs

Neurologic symptoms or signs

Onset: peak at onset or <1 minute

Older: after age 50 years

Previous headache: pattern change

Postural, positional aggravation

Precipitated by valsalva, exertion, etc.

Papilledema

Silberstein SD, Lipton RB. In: Silberstein SD et al, eds. *Wolff's Headache and Other Head Pain*. 8th ed. New York: Oxford University Press; 2008:315-377.
Dodick D. *N Engl J Med*. 2006;354:158-165.
Bigal ME et al. *J Headache Pain*. 2007;8:263-272.

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Headache Imaging Indications — ACR Guidelines

Clinical Features/Red Flags	Suspected Condition	Recommended Imaging*
Associated with trauma	Bleed	CT head without contrast
New feature or neurologic deficit	Neoplasm, vascular malformation, aneurysm	MRI brain
Thunderclap (sudden onset; severe)	Bleed (esp SAH)	CT head without contrast; MRI brain, MRA head and neck, MR venogram head (if CT negative)
Sudden unilateral, and/or pain radiating to the neck	Vascular (e.g., arterial dissection)	CTA head and neck; MRA head and neck
Pain due to trigeminal autonomic cephalgia	Neoplasm	MRI brain with/without gadolinium
Persistent or positional pain	CSF leak/IIH	MRI brain with/without gadolinium
Immunocompromised state	Infection; malignancy	MRI brain with/without gadolinium
Temporal pain in older individuals	Giant cell arteritis	MRI brain

*Additional imaging may be recommended based on initial findings.
ACR=American College of Radiology; CT=computed tomography; MRI=magnetic resonance imaging; SAH=subarachnoid hemorrhage; IIH=idiopathic intracranial hypertension.
Douglas AC et al. *J Am Coll Radiol*. 2014;11:657-667.

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Migraine: More Than a Headache

- Tension Type HA & Migraine 2nd & 3rd most prevalent medical disorder worldwide
- Migraine accounts 30% of global burden of disability & 50% of all Neuro disability
- 4th leading cause of disability in women & 7th overall

Lancet 2012

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Why Migraine?
Why Should I Care?

- 6% ♂, 18% ♀, 33-37% reproductive ♀, 4% CDH
- Returning armed forces 38% ♂, 58% ♀, 20% CDH
- Most common 25 – 55yr (most productive years)

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Battle of the Migraine Screens

ID Migraine™ (PIN)

1. Does light bother you when you have a headache? (**P**hotophobia)
2. Has a headache limited your activities for a day or more in the last three months? (**I**mpairment)
3. Are you **N**auseated or sick to your stomach when you have a headache?

Positive result: ≥2 "yes" responses
PPV: 93%

P.O.U.N.D.

Pulsatile quality
Duration 4–72 h**O**urs
Unilateral location
Nausea or vomiting
Disabling intensity

Number of Features	Probability of Migraine
1–2	17%
3	64%
4–5	92%

PPV=positive predictive value.
Lipton RB et al. *Neurology*. 2003;61:375-382; Lipton RB et al. *Headache*. 2004;44:387-398; Detsky ME et al. *JAMA*. 2006;296:1274-1283; Ebell MH. *Am Fam Physician*. 2006;74:2087-2088.

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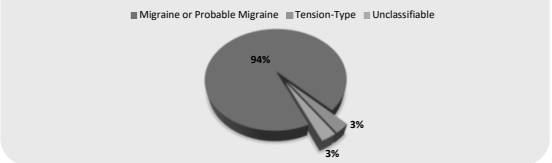
Migraine is the Most Common Episodic Headache Seen in Primary Care

Multisite, prospective Landmark Study of adults consulting their physician (93% primary care) with episodic headache

- IHS diagnosis based on diary review (n=377)



Tepper SJ et al. *Headache*. 2004;44:856-864.

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Migraine Stages

Stage 1 – Infrequent Episodic ≤ 1 Migraine/month	Education plus effective acute treatment
Stage 2 – Frequent Episodic 2 – 6 headache days/month	Education plus effective acute treatment with back up; medications limits; preventive measures
Stage 3 – Transforming Migraine 7 – 14 headache days/month	Education; preventive pharmacology; acute pharmacology with back up & rescue; behavioral interventions
Stage 4 – Chronic Migraine - ≥15 headache days/month	Education; preventive pharmacology; judicious acute pharmacology with back up and rescue; behavioral interventions

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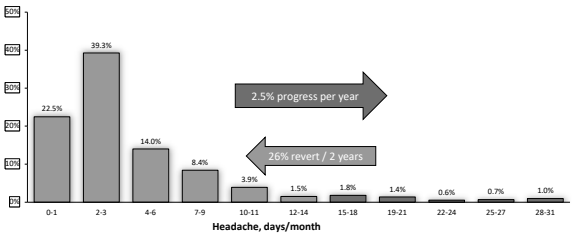
Migraine Frequency



1. Lipton RB. *Neurology*. 2009;72(5 suppl):S3-S7. 2. Manack A et al. *Neurology*. 2011;76(8):711-718. 3. Blumenfeld AM et al. *Headache*. 2013;53(4):644-655. 4. Bigal ME et al. *Headache*. 2008;48:1157-1168.

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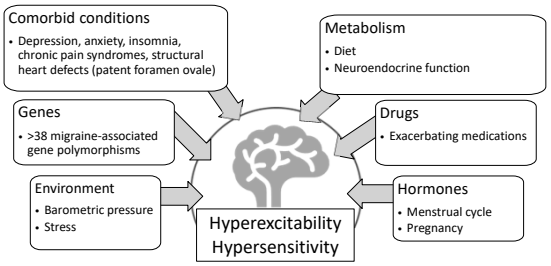
Migraine: A Sensitive Brain That Doesn't Like Change



Charles A. *Lancet Neurol*. 2018;17:174-182; Akerman S et al. *Pharmacol Ther*. 2017;172:151-170.

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Taking Care of the Sensitive Brain: SEEDS

- **Sleep** – Make standard sleep hygiene recommendations to maximize sleep quantity/quality
- **Exercise** – 30 to 60 minutes a day 3 to 5 times a week
- **Eat** – Regular healthy meals, adequate hydration, and low or stable caffeine intake
- **Diary** – Records baseline pattern, assess response to treatment, monitors analgesia to improve accuracy of migraine diagnosis
- **Stress** – Cognitive behavioral therapy, mindfulness, relaxation, biofeedback, and provider-patient trust to minimize anxiety

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Headache Diaries

- Days with headache
- Some measure of intensity
  - A scale based on **functional** level may be easiest
- Acute medication use and response
- Suspected potential triggers
- Apps
  - Migraine Buddy
  - Migraine Monitor
  - N-1 Headache

Example

1	Pain but activities possible
2	Activities are slowed
3	Activities are not possible
4	Patient is bedridden

Becker WJ. *Headache*. 2017;57:1471-1481.

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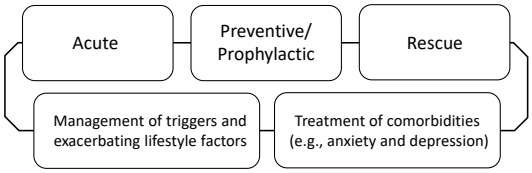
Individualized Migraine Treatment Plans



Becker WJ. *Headache*. 2017;57:1471-1481; Silberstein SD et al. *Neurology*. 2012;78:1337-1345.

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Headache Treatments

Abortive – pain freedom in 2 hours

Preventive – reduce frequency, intensity and improve response to acute meds

Rescue – when the stop medicine didn't

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Acute Migraine Therapy

- Goal is pain freedom in 2 hours
- Treat at mild pain (prior to central sensitization)
- May use polypharmacy

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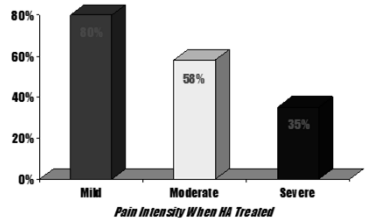
Triptan Pearl: Treat @ Mild Pain

Early Intervention Improve Efficacy

2 Hour Pain Free Response



Cady RK, et al. *Headache* 38:173-83; Pascual J, et al. *Headache* 42[supl 1]:S10-S17

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Oral Therapies: Which One?

What ever works!

There is no medication that is perfect for all migraine attacks or all circumstances in which treatment is needed.

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Triptans: What's the Difference?

Triptan	$T_{1/2}$	$	Pearl
Sumatriptan	2.5h	9/$12	Multiple formulation
Rizatriptan	2-3h	9/$16	Reduce dosed with propranolol
Eletriptan	4h	9/$37	Typically better response
Almotriptan	3h	12/$126	Good tolerability
Zolmotriptan	3h	6/$38	Best tolerated NS
Naratriptan	26h	9/$26	Scheduled dosing for Menstrual Related Migraine
Frovatriptan	6h	9/$160	Scheduled dosing for Menstrual Related Migraine

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Early GI Symptoms

Augment with antiemetic
Metoclopramide
Prochlorperazine
Bypass Gut
IN spray or powder
Injectable

Migraine Recurrence
Long Duration Migraine

Polypharmacy
NSAID/Antiemetic
Long ½ life Nara/Frova
Scheduled Dosing

Choosing Triptans

Failure to one doesn't predict response to other
Use over at least 3 attacks
Limit to 10 days/month

Rapid onset of Pain

Fast acting PO Ele/Riza/Zolmi
Bypass gut
IN – Suma liquid /powder
Subcut Suma
Antiemetic PO / PR

Triptan Nonresponder

Start Migraine Preventive
Use Max dosage
Alternate triptan/formulation
Polypharmacy

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Triptan Safety

Triptan CV Safety Expert Panel Consensus Statement
PC trials data evaluation, long-term, open-label studies, and post-marketing surveillance

Summary of evidence

- Modestly elevated incidence of chest tightness, heaviness, pain, or pressure (i.e., triptan sensations) relative to placebo in well-controlled clinical trials that excluded patients with significant cardiac risk factors or known ischemic heart disease
- Symptoms are generally transient, mild, and nonserious

Conclusions

- Determinants of cardiovascular AEs are poorly defined; several nonischemic mechanisms have been proposed
- Among pts without known/suspected CAD, triptan safety profile is well defined & appears to reflect a very low risk of serious CV AEs
- In pts at low CAD risk, triptans can be prescribed confidently /s prior cardiac status evaluation

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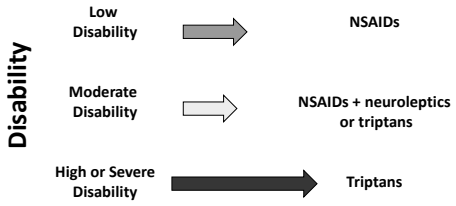
Stratified Care



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New Kids on the Block

Dtans

- $5HT_{1F}$ receptor antagonist
- No vasoconstriction
- Lasmiditan
- Schedule V
- Eight-hour post dosing driving restriction
- May take early or late

Gepants

- CGRP receptor blockers
- No vasoconstriction
- Ubrogepant / Rimegepant

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Ditans / Gepants Clinical Trials

	Lasmiditan		Ubrogepant		Rimegepant	
$T_{1/2}$	≈ 5.5h		α 3h β 5-7h		10-12h	
Pain Relief Severe/Moderate to mild/no pain Therapeutic Gain	100mg 200mg	14 15	50mg	13	75mg	16
Pain Freedom Severe/Moderate to no pain Therapeutic Gain	100mg 200mg	13 17	50mg	7.5	75mg	10
Adverse Events	Dizziness Sedation Paresthesia		100mg Nausea Sedation		Nausea	

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eTNS

FDA cleared Acute Migraine Treatment & Prevention

Acute: one hour PRN
Prevention: 20 minutes nightly
Cost: $500 – 60-day money back guarantee

Replacement electrodes $25 q2-3 months

US VA coverage

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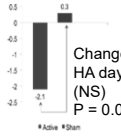
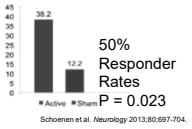
eTNS Prevention (PREMICE) / Acute Migraine Treatment (ACME)



Change in HA days (NS)
P = 0.054

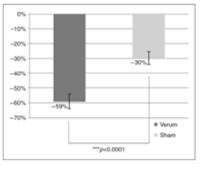
Prevention



50% Responder Rates
P = 0.023

Schoenen et al. *Neurology* 2013;80;697-704.

Acute



Reduction in VAS pain score,1 hour
P <0.0001

Chou et al. *Cephalalgia*. 2019;39:3-14.

Slide courtesy of Stew Tepper, MD

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Remote Nonpainful Electrical Stimulation (RNES) for Acute Migraine Treatment (Nerivio)

- 3 prospective, DBRC crossover, sham-controlled trials
- MOA: activates descending inhibitory pathways via conditioned pain modulation (CPM) effect, an endogenous 5-HT brainstem pain mechanism
- Premise: Pain inhibits pain
- Once there is a noxious stimulus at any body location (migraine), it may be inhibited by a second stimulus at a different location (device) with high intensity, not perceived as painful
- FDA cleared/approved May 2019
- $49 to treat 12 migraine attacks
- VA & some insurance coverage

Yarntisky et al. *Neurology* 2017;88:1250-1255.
Nir et al. *EJ Pain* 2011;15: 491-497.
Goadsby. *Ann Indian Acad Neurol* 2012;15(Suppl 1):S15-S22.

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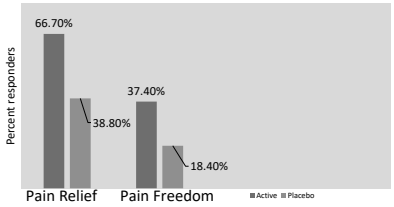
Remote Electrical Neurostimulation (REN) Pivotal Trial for Acute Migraine Treatment

Two Hours post treatment Pain Response



Yarnitsky et al. *Headache* 2019;59:1240-1252.

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Combined Trigeminal (Supra-orbital/trochlear) & Cervical (Greater Occipital Nerve) Stimulation for Acute Migraine Treatment in Adults (RELIVION)

- **Acute** Pivotal RCT, N=131, **Treat for 60m**
- 2h Pain Freedom Active: 46% vs.
  - Sham: 11.86% (p-value: <0.0001)
- 2h Pain Relief Active: **60%** vs.
  - Sham: **37%** (P=0.0018)
- 2-hour MBS freedom 2-hours Active: 75%
  - Sham: 46.7% (p=0.009)
- 2h Complete Pain/MBS relief @ 2-hours Active: 47.2%
  - Sham: 11.1% (p=0.0003)

Tepper SJ and Sharon R. *Headache* 2021; 61 (S1): 105 (abstract).

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What I Do

- Soooooo Off-label & remember my patients aren't yours
- Effervescent ASA 1000mg + Mg 500mg or
- Ibuprofen (liquid gels better) 1000-1200mg + Mg
- Naproxen 500mg + Mg
- Augment /c Metoclopramide or Prochlorperazine
- Triptan – All generic now
- Timoptic 1 – 2 drops sublingual daily PRN Drink H_2O 1st
- Triptan non-responders or contraindicated – Ditans/Gepants
- Neuromodulation

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Headache Treatments

Abortive – pain freedom in 2 hours

Preventive – reduce frequency, intensity and improve acute med response

Rescue – when the stop medicine didn't

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American Migraine Prevalence and Prevention (AMPP) Study Guidelines

Should Offer

- ≥6 headache days/month
- ≥4 headache days with some impairment
- ≥3 headache days with severe impairment or bed rest

Should Consider

- 4 or 5 migraine days/month with normal functioning
- 3 migraine days with some impairment
- 2 migraine days with severe impairment

Not Indicated:

- <4 headache days/month with no impairment
- ≤1 headache day/month regardless of impairment

Lipton RB et al. *Neurology.* 2007;68:343-349.

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Traditional Oral Preventive Therapies

Established Efficacy Level A recommendation; Should be offered	Probably Effective Level B recommendation; Should be considered	Possibly Effective Level C recommendation; May be considered	Efficacy Uncertain Level U recommendation; Not supported or refuted
Antiepileptic drugs Divalproex sodium Valproate sodium Topiramate **Beta-blockers** Metoprolol Propranolol Timolol **Triptans** Frovatriptan (short-term for menstrual migraine)	**Antidepressants** Amitriptyline Venlafaxine **Beta-blockers** Atenolol Nadolol	**Antiepileptic drugs** Carbamazepine **Beta-blockers** Nebivolol Pindolol **Alpha-agonists** Clonidine Guanfacine **Antihistamines** Cyproheptadine **Angiotensin receptor blockers** Candesartan	**Antiepileptic drugs** Gabapentin **Beta-blockers** Bisoprolol **Antidepressants** Fluoxetine; fluvoxamine Protriptyline **Calcium-channel blockers** Nicardipine; nifedipine; nimodipine; verapamil Coumadin Acetazolamide Cyclandelate

Silberstein SD et al. *Neurology*. 2012;78:1337-1345; American Headache Society. *Headache*. 2019;59:1-18.

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CGRP Antibodies

	Erenumab Amgen	Galcanezumab Lilly	**Fremanezumab** **Teva**	Eptinezumab Alder
Pharmacologic Target	CGRP Receptor	CGRP Ligand	CGRP Ligand	CGRP Ligand
Condition	EM CM	EM CM ECH	EM CM ECH	EM CM
Dosing	70mg / 140mg	120mg / 240mg	675mg →225mg X 2	100mg / 300mg
Notes	EM 140mg 50% ↓ 50% 75% ↓22.0% CM 140mg 50% ↓ 41.2% 75% ↓ 21.0%	EM months 1-6 120mg 50% ↓ 20.5 240mg 50% ↓ 19.2 @ month 6 – 50%↓	EM 50% ↓ 40.8	CM 100mg ↓ 57.6% 300mg ↓ 61.4% 75% ↓ 33.1% Shown to ↓ from 1d

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Indications for CGRP Antibodies
American Headache Society

CGRP monoclonal antibodies are appropriate for adults who experience				
Migraine With or Without Aura	4-7 MHD AND BOTH of the following:	Intolerability to at least 2 prior preventive txt due to side effects OR	Inadequate response to 6w trial of at least 2 prior preventive txt AND	≥ Moderate Pt reported disability
Migraine With or Without Aura	8-14 MHD	As Above		No disability requirement
Chronic Migraine		As Above		onabotulinumtoxinA intolerance or nonresponse /p 2 injection cycles

American Headache Society. *Headache*. 2019;59:1-18.

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Side Effects and Cautions With Anti-CGRP/CGRP-R mAbs

Drug	Notable Side Effects/Cautions
Erenumab	Constipation (October 2019 warning of serious complications); latex allergy; injection site reactions; upper respiratory symptoms
Fremanezumab	Injection site reactions; upper respiratory symptoms
Galcanezumab	Injection site reactions; upper respiratory symptoms
Eptinezumab	Nasopharyngitis; hypersensitivity

All USPIs include warnings and contraindications about hypersensitivity reactions

- Data on long-term safety are limited
  - Over 3 years of exposure in a 5-year open-label extension study of erenumab, rates and types of adverse events were consistent with those reported in shorter-term randomized controlled trials
  - No cases of discontinuation due to constipation

TEAE=treatment emergent adverse event.
Tepper DE. *Headache*. 2019;59:477-480; Dodick DW et al. *Cephalalgia*. 2019;39:1075-1085; FDA. https://www.accessdata.fda.gov/scripts/cder/daf/. Accessed March 3, 2020; Ashina M et al. *Cephalalgia*. 2019;39:1455-1464; Ashina M et al. Presented at the 61st American Headache Society Annual Meeting; July 11-14, 2019; Philadelphia, PA; IOR10.

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New and Emerging Preventive Agents: Gepants

Pros
- Migraine specific
- ~50% efficacy in reducing monthly migraine days in clinical trial
- Rapid onset
- Good safety (No CV risk)
- Good tolerability
- Oral administration

Cons
- These agents are relatively new, so few real-world data on safety and efficacy are available

Croop R, et al. *Lancet*. 2021;397(10268):51-60; Ailani J, et al. *N Engl J Med*. 2021;385(8):695-706.

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Gepants for Migraine Prevention

Available Gepants	Route	Forms	Dosing	Most Common Side Effects
Rimegepant	Oral (ODT)	75 mg	Every other day	Nausea
Atogepant	Oral (tablet)	10 mg, 30 mg, 60 mg	Once daily	Nausea

Pros
- Migraine specific
- ≈50% efficacy in ↓MMD in clinical trial
- Rapid onset
- Good safety (No known CV risk)
- Good tolerability
- Oral administration
- Out of system in 5 days

Cons
- The Gepants are relatively new, so few real-world data on safety and efficacy are available

Rimegepant prescribing information. https://biohaven-nurtec-consumer-assets.s3.amazonaws.com/nurtec-prescribing-information.pdf ; Atogepant prescribing information. https://www.rxabbvie.com/pdf/QULIPTA_pi.pdf; Ailani J, et al. *NEJM*. 2021;385(8):695-70.

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Prevention – Pound of Cure

- Start low & go slow
- Supplements – **Mg^{++} 500mg**, Riboflavin 400mg, **CoQ-10 200mg BID**, Butterbur (should be PA free – HA docs starting to avoid Butterbur) Melatonin 3 – 5mg (2 hours before bed)
- Membrane Stabilizing medications-Valproate, Topiramate, **Zonisamide**, Gabapentin
- Anti-HTN Beta Blockers, CCB, ACE, **Candesartan 16mg**
- TCA (off label) most data is with amitriptyline – SSRIs not thought to be effective
- **Scheduled Nerve Blocks (Occipital or Pericranial)**
- OnabotuliniumtoxinA -- FDA approved for Chronic Migraine Oct 2010
- Enurenumab CGRP ab approved for EM/CM in May 2018
- Frenunezumab & Galcanezumab CGRP ab approved in Sept 2018
- Rimegepant QOD dosing / Atogepant Daily dosing

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Risk Factors for Progression

Modifiable

- Attack frequency
- Poorly treated acute HA
- Obesity
- Snoring/OSA
- Stressful life events
- Medication overuse
- Caffeine overuse

Not Modifiable

- Age
- Female sex
- Low education or SES
- Genetic factors
- Head injury

OSA=obstructive sleep apnea
Ashina S, et al. *Curr Treat Options Neurol.* 2008;10:36-43.

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Migraine Progression Risk Factors
Attack Frequency

- Them that gots, gets!
- The Brain learns Pain
- Inflection point starts at about 5 attacks a month
- Use a Bridge Therapy to suppress Headaches
  - Naproxen BID X 30 days
  - Steroids burst or taper
  - Repeated Blocks
  - Methergonivine 0.2mg 1-2 PO TID X 14 – 28 days -- $$$$
  - CGRP mab / Gepants

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Ineffective Acute Therapy Leads to Migraine Progression

- Results from AMPP study
- Episodic Migraine to Chronic Migraine: 3.1% / 1 year
- Acute treatment evaluated as
  - Moderately effective, Poor, Very Poor

- Moderately effective 2.7% progressed
- Poor 4.4% progressed
- Very Poor 6.8% progressed

Neurology. 2015 Feb 17; 84(7) 688-695

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Migraine Progression Risk Factors
Poor Acute Migraine Treatment

- Use Stratified Care
- Suit the treatment to the attack
  - Mild – Distract, ignore, eat, rest, ice…
  - Moderate – NSAID +/-Triptan
  - Severe – Nasal or Parental; bypass the gut. Olanzapine 10 or 20mg PO & go to bed
- Augment with Magnesium, Metoclopramide, Prochlorperazine

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Migraine Progression Risk Factors
Obesity/Dietary

- Weight loss shown ↓HA frequency; intensity, disability & acute med usage @ 60 months /c improvement thru 12 months
- Improvement also seen /p bariatric surgery
- Calorie restricted diets enhance neuroplasticity affecting pain sensation & cognitive function
  - Believed to stimulate neuroplasticity & increased resistance to oxidative stress

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Migraine Progression Risk Factors

Obesity/Dietary
Diet as Medicine – Prevention

- Chronic Migraine pts randomized to
  - Diet high on Omega 3
  - Diet low in Omega 6
  - Both groups improved but Omega 3 group better 8.8 days vs 4.6 days
- 30% improvement in HA days/attacks /c IgG elimination diet
- Additional support in small trial in pts /c comorbid migraine & IBS showed improvement with IgG elimination diet was observed antibodies were eliminated

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Migraine Progression Risk Factors

Sleep Disorders

- Poor sleep (not rested most mornings)
  - Worsen additional migraine comorbidities
    - Depression/anxiety/fibromyalgia
- May mean the difference between success & failure
- Simple behavioral instructions provided to chronic female migraineurs
  - 58% remission to episodic migraine @ 12 weeks
  - No remission in sham group @ 6 weeks, then crossover
  - Crossover 43% remission to episodic migraine @ 6 weeks
  - Improvement correlated /c adherence to instructions

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Reference: Simple Sleep Hygiene

- Eliminate stimulants (caffeine, nicotine). Initially, no caffeine after 13:00. If still with sleeping difficulties, then keep moving back the last caffeine intake.
- Discontinue naps
- Regular exercise improves sleep. However, exercise within 5 hours of bedtime may raise core body temperature & delay sleep. If that is the only time you can exercise, then take a cool shower to cool off.
- Move dinner to at least 4 hours before bedtime.
- Curtail liquids within 2 hours of bedtime. Limit alcohol intake.
- Prepare a dark sleeping environment. Limit nocturnal light. If nightlights are needed to prevent falls, use the dimmest light possible.

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Reference: Simple Sleep Hygiene

- Schedule an initial consistent bedtime and awakening that allows for eight hours in bed, seven days a week — weekdays & weekends
- The bed is only for sleep and adult intimacies
- No distractions while in bed, No television, reading, smart phones, pets or other children while in bed
- White noise such as a fan or relaxing music is OK
- Search www.youtube for "Weightless" by Marconi Union
  - This song has been shown to help people fall asleep faster
- Use visualization technique (guided imagery), autogenic phrases, or progressive muscle relaxation to start to get to sleep
- **YouTube – Michael Sealey – get him on your radar screen**

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Reference: Huberman Sleep Cocktail

Magnesium Threonate
300-400mg

- Typically 144mg elemental MG ~ 2 capsules
- Crosses the blood-brain barrier
- Enhances ability of mitochondria to "recharge"
- ↑ neuroplasticity (via BDNF)
- Magnesium Glycinate an option

Apigenin
50mg

- Chamomile derivative
- Acts as a Cl channel agonist – shuts down forebrain
- ↑ sleep time/rate in mice
- Promotes more restful sleep
- Can ↓ cortisol

Theanine
200 – 400mg

- AA found in green tea
- ↑α brain waves: REM Sleep
- ↑GABA release (relaxation)
- Stimulates Dopamine release
- Improved sleep
- Enhances mental discipline & focus
- **Use care with Dream d/o - nightmares**
- Start with a low dose
- No caffeine within 6 hours of Theanine

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Reference: Later Huberman Suggestions

Huberman Lab Podcast
Mathew Walker, Ph.D.

- **Tart Cherry Juice**
- Time Stamp 2:01
- BID dosing 1 – 8oz
- Improved sleep 34 – 84 minutes (dose dependent)
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5617749/pdf/nihms854648.pdf
- Also available as a supplement capsule

Jocko Podcast

- Inositol 900mg
- Time Stamp 4:31
- Used in Anxiety / Insulin Sensitivity, PCOS
- Acts as a sedative
- Beneficial with low carb diet or difficulty with sleep onset

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Migraine Progression Risk Factors
Stressful Life Events

- Leading Single Migraine Trigger
- Adverse Childhood Experiences increase risk
- What is Stress? – anything that acts on you to provoke a response
- Goal of "Stress Management" is to build resilience
  - Timex watch – take a lickin'

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Migraine Progression Risk Factors
Stressful Life Events

- They Can't Find Anything Wrong – David Clarke MD
  - www.stressillness.com
- Breathe2Relax app
  - No Charge
  - Available in multiple formats
  - ≥ 10min/Day associated with ↓ BP
- Calm app
- Headspace app
- DawnBuse.com
  - Relaxation exercises download for free
- The Relaxation and Stress Reduction Workbook – M. Davis
- You Tube – Michael Sealey & Binaural Beats

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Migraine Progression Risk Factors
Stressful Life Events

- Above all, do not lose your desire to walk.
- Everyday, I walk myself into a state of well-being & walk away from every illness.
- I have walked myself into my best thoughts, and I know of no thought so burdensome that one cannot walk away from it.
- But by sitting still, & the more one sits still, the closer one comes to feeling ill.
- Thus, if one just keeps on walking, everything will be all right."

Soren Kierkegaard

Walking ≥ 3 Kilometers a day is associated with positive neuroplastic changes

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Getting Patients to Move

- 3 Km associated with Brain Derived Neurotrophic Growth Factor (BDNF)
- Promotes new neuronal connections to deal with encountered stress

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Give a Goal

- Goal is really self-care
- Movement towards a goal is associated with increase in positive emotion
- Positive emotion inhibits pain
- Miles for Migraine
- 2 Mile, 5K, 10K

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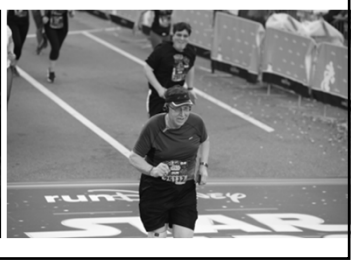
If I can do it…



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Migraine Progression Risk Factors
Symptomatic Medication Overuse

- AKA "Rebound" – not best term
  - Overuse isn't much better
  - Migraine frequency ↑ /c increasing acute medication use
- HA that occurs in an individual with a pre-existing 1' HA when in the presence of MO develops a new type of HA or a marked worsening of their pre-existing HA – ICHD III
- Pts do not understand this condition
  - See usage as a direct response to their headaches
- Incidence in Primary Care Clinic ≈ 21%
  - Much higher in specialty clinic

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Migraine Progression Risk Factors
Symptomatic Medication Overuse

- Patient must be educated about limits on acute medications
  - Max 10-12 days / month
- Need to know that HAs unlikely to get better if continue to overuse
- May need to withdraw in a controlled setting
- Headaches worsen during withdrawal
  - Use a "Bridge" therapy

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Commentary on Medication Overuse Headache (MOH)

"An entrenched idea in need of scrutiny"

- Evidence of cause and effect is weak
  - Especially weak for simple analgesics (e.g., aspirin, ibuprofen)
- Medication withdrawal or limitation may benefit some patients
  - Withdrawal studies have been mostly uncontrolled with high dropout rates
  - Ethics of withholding symptom-relieving medication?

*"The concept of MOH should be **viewed with more skepticism**. Until the evidence is better, we **should avoid dogmatism** about the use of symptomatic medication. Frequent use of symptom-relieving headache medications should be **viewed more neutrally**, as an indicator of poorly controlled headaches, and not invariably a cause."*

Scher AI et al. *Neurology.* 2017;89:1296-1304.

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Migraine Progression Risk Factors
Caffeine Overuse

- Just say no!
- If you must…
  - Limit to two servings a day
  - ≤ 200mg/day

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Headache Treatments

Abortive – pain freedom in 2 hours

Preventive – reduce frequency, intensity and improve response to acute meds

Rescue – when the stop medicine didn't

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Why Should I Treat Acute Headaches?

- Have to keep our patients out of the ED
- Primary HAs are not an emergency
- Not the best place – too bright, too loud, often ignored
- Can't risk exposure to opiates
- More likely to V.O.M.I.T. in ED

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No Opiates for Headaches

- Major risk factor for Medication Overuse HA
- Once established it's a self-fulfilling prophesy
- Jakubowsk, et al. 2005, Wolfe Award paper
  - 64%-71% Migraine pts pain-free 1' /p ketorolac iv
- Only factor that predicted ketorolac failure: hx of opioid txt in the nonresponders
- Rewires the brain to perpetuate the HA state by inhibiting the breakdown of glutamate

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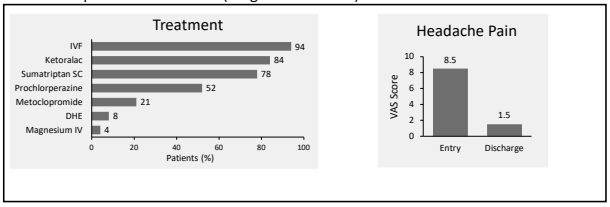
Clinical Headache Rescue

AHS Poster: Associated Neurologists of Southern CT
- Drop-in headache clinic
- 500 patients seen between 9/05 and 8/07

- Time to present = 104 hours (range 8–240 hours)



DHE= dihydroergotamine; VAS=visual analog scale.
McAllister PJ et al. *Headache*. 2008;48(Suppl 1):S1-S72. Abstract FS6.

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Clinical Headache Rescue
UAB Experience

200 pts. Randomized Optimal Self Admin or
Optimal Self Admin + Optional in-clinic Headache rescue

Optimal Self-Admin		Clinic Rescue
		423 visits
		33.6K **($80**)
73	ED Visits	**27**
147.9K**($2027**)	ED Direct Cost	45.3K (**$1609**)
		79% no d/a > 24'

Morey V, Rothrock JF. *Headache.* 2008;48:939-943

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Clinical Headache Rescue
UAB Experience

89% very satisfied

Drug	#	Drug Cost
Droperidol 2.75mg	218	3.00
Diphenhydramine 50mg	201	1.25
DHE 1mg	167	42
Prochlorperazine 5-10mg	141	11.5
Promethazine 50mg	68	4.
Ketorolac 30mg	38	9 + 11 (saline)

Morey V, Rothrock JF. *Headache.* 2008;48:939-943

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Rescue Headache Interventions

- IV >> IM >> PO
- Sumatriptan 6mg IM/SC
- Dihydroergotamine 1mg IM/SC/IV
- Ketorolac 30mg IV / 60mg IM
- Neuroleptics – Dopamine Antagonists (Droperidol, Metoclopramide, Prochlorperazine)
- Steroids
- Others – Mg^{++}, Valproic Acid, Diphenhydramine
- Procedures – Occipital Nerve Block, Lower Cervical Intramuscular Injections

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Procedures

- Lower Cervical Intramuscular Injections
- Occipital Nerve Block
- Sphenopalatine Ganglion Block
- Pericranial Injections

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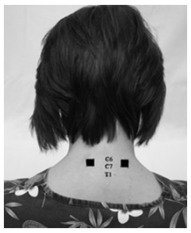
Lower Cervical Intramuscular Injections



- Headache 10/06
- 417 ED Pts / 1 yr
- 65% relief in 15m
- Repeat injection brought additional relief
- Worsened HA in 1%

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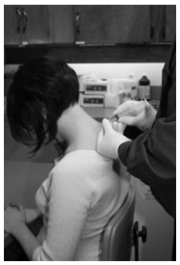
Lower Cervical Intramuscular Injections



- 3mL bupivacaine 0.5%
- 25g 1.5" / 27g 1.25"
- 2-3cm lateral to the spinous processes between C6 & C7
- AE /CI – Vasovagal, neck stiffness, usual injection risks

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Occipital Nerve Block

- Local anesthetic (bupivacaine) .5% lidocaine 1%
  - -- Duration of anesthesia doesn't correlate to duration of relief
- Steroid (triamcinolone 40mg/mL) evidence doesn't support general use
- 3mL total per side
- 25- or 27-gauge needle
- May place as a "ridge" or point of maximum tenderness

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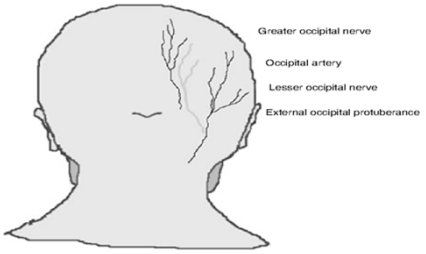
Occipital Nerve Block



Marcus DA, Ready DM. *Discussing Migraine*. Springer 2017

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Occipital Nerve Block

44 CM / 2 groups GON weekly X 4

Followed @ 4 weeks, 2 months, 3 months

	Baseline HA Frequency	One Month	Two Months	Three Months
Bupivacaine	21.0 +/-4.4	10.9 +/- 7.1	6.1 +/- 2.4	6.3 +/- 1.9
Saline	20.9 +/- 5.0	15.5 +/- 7.3	18.2 +/- 6.1	19.1 +/- 6.3
		4.6	**12.1**	**12.8**

No serious AEs

Bupivacaine – significant ↓months 1,2,3

Saline – decrease @ month 1 only

Gul HL, et. al. *Acta Neurol Scand*. 2016 Dec 2.

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Greater Occipital Nerve Block

PGON: 25 Chronic Migraine patients on oral prophylaxis

GON: 53 Chronic Migraine patients medically refractive to oral medications

	Baseline HA Days	Month 3 HA Days	Δ	Baseline HA Severity	Month 3 HA Severity	Δ
PGON- 25	13.76±8.07	3.28±2.15	**10.48**	8.08±0.90	5.96±1.20	**2.12**
GON - 53	15.73±7.21	4.52±3.61	**11.21**	8.26±1.32	5.16±2.64	**3.10**

Inan N, et. al. *Noro Psikiyatr Ars*. 2016 Mar;53(1):45-48.

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Occipital Nerve Block

- Adverse Events / Contraindications
- Prior hx of craniotomy over injection site
- AEs primarily related to steroid – fat atrophy, alopecia, pigment a change
- Vagal response – Happened to me X 4 in over 18K blocks

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Pericranial Bupivacaine Injections

Robert Kaniecki, MD University of Pittsburgh

- 218 Subjects
- 34 sites – 0.25% Bup
- Q 12 weeks
- 87.1% Female
- Age – 40.4 years
- Migraine for 18 .5 years
  - 21.4 / 28 days /c HA
  - 15.5 Severe HA days
  - 18.3 Treatment days
- 55.2 % > 50% reduction
  - 35.3% achieved by 4 wk
- ↓HA days 22.8d to 9d
- ↓ Severe 15.9d to 6.1d
- ↓ Treatment 18.1d to 7.9d
- 11.5% no response/Lost-FU

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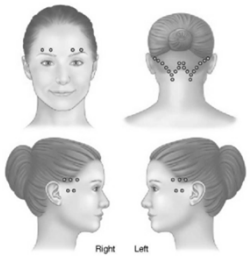
Pericranial Bupivacaine Injections

Robert Kaniecki, MD University of Pittsburgh



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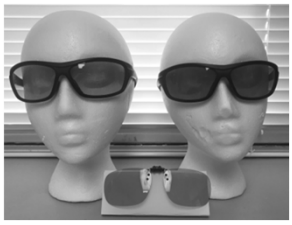
New Kids on the Block
Migraine Sunglasses

- People with Migraine are sensitive to specific wavelengths
- Specific Tint FL-41
- Most online vendors have money back guarantee
- Theraspecs, Axon Optics, Somnilight (only one with clip-on)
- MigraineReady code for 10% off



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Barometric Pressure Headaches

- Comes with App to notice when to put in
- 4.1 / 5 stars – 819 ratings
- May also use Acetazolamide BID/TID

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Migraine in 4 Sentences

or Less

It is Neurological

Its is Genetic

It is Highly Disabling

It is infinitely treatable

And it is by far the most fascinating neurological condition you can treat!

Peter Goadsby, MD

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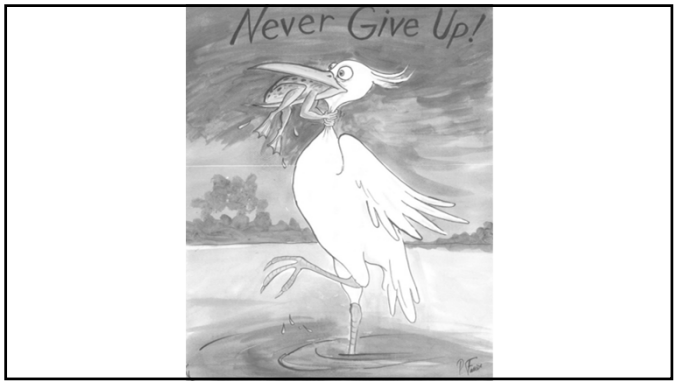

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Notes