Migraine

Prophylaxis and Treatment

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Disclosure

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

By the end of this educational activity, the learner should be better able to:

1. Increase awareness and interest of headache in Primary Care
2. Provide a clinical framework for the diagnosis, prophylaxis, and acute migraine treatment
3. Identify risk factors for migraine progression and develop a plan for treatment using migraine staging
Why Should I Care?

- **New Mexico**
  - State pop.: 1,713,160
  - Headache spec.: 1

- **Oklahoma**
  - State pop.: 3,124,091
  - Headache spec.: 3

- **Texas**
  - State pop.: 20,188,012
  - Headache spec.: 25

- **Arkansas**
  - State pop.: 2,441,535
  - Headache spec.: 1

- **Louisiana**
  - State pop.: 3,787,641
  - Headache spec.: 6
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
SNOOP4
Ruling Out Secondary Headaches

S Systemic symptoms and signs
N Neurologic symptoms or signs
O Onset: peak at onset or <1 minute
L Older: after age 50 years
P Postural, positional aggravation
P Precipitated by valsala, exertion, etc.
P Papilledema
P Previous headache: pattern change

I Infectious
N Neoplasm
V Vascular
T Temporal Arteritis
C CSF Leak
M Mass / CSF Leak
↑ ↑ CSF Pressure
A Above

# Headache Imaging Indications — ACR Guidelines

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

*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.
Migraine: More Than a Headache

• Tension Type HA & Migraine 2\textsuperscript{nd} & 3\textsuperscript{rd} most prevalent medical disorder worldwide

• Migraine accounts 30\% of global burden of disability & 50\% of all Neuro disability

• 4\textsuperscript{th} leading cause of disability in women & 7\textsuperscript{th} overall

    \textit{Lancet} 2012
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)

### Battle of the Migraine Screens

**ID Migraine™ (PIN)**

1. Does light bother you when you have a headache? (Photophobia)
2. Has a headache limited your activities for a day or more in the last three months? (Impairment)
3. Are you Nauseated 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**
- **Unilateral location**
- **Nausea or vomiting**
- **Disabling intensity**

<table>
<thead>
<tr>
<th>Number of Features</th>
<th>Probability of Migraine</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–2</td>
<td>17%</td>
</tr>
<tr>
<td>3</td>
<td>64%</td>
</tr>
<tr>
<td>4–5</td>
<td>92%</td>
</tr>
</tbody>
</table>

PPV=positive predictive value.
Migraine – Most Common Episodic Headache 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)

Migraine Treatment Target: 5HT & CGRP Receptors

Triptans & ergots prevent CGRP release and constrict CGRP-dilated vessels; Lasmiditan prevents CGRP release.

OnabotulinumtoxinA prevents CGRP release.

Anti-CGRP receptor MAB: erenumab

Anti-CGRP ligand MABs: fremanezumab, galcanezumab, eptinezumab

CGRP receptor antagonists (gepants): Ubrogepant, Rimegepant, Atogepant, Vazegepant

Cerebrovascular smooth muscle cell

Vasodilation


Slide courtesy of Stew Tepper, MD
CGRP and Migraine

- CGRP levels are increased during migraine
- CGRP infusions can trigger migraine
- CGRP inhibitors block migraine progression
  - Reduces migraine frequency, intensity, duration
- CRRP inhibition allows brain to recover more fully from a migraine event

- A brain which has not fully recovered from a migraine attack is more reactive. Leaving it more vulnerable for a subsequent attack.
Staging Migraine

• Developed by Lipton, Cady, Farmer, & Bigal

• 1st doctor/patient book

• Based on Migraine frequency not severity

• http://www.managingmigraine.org/online-books/patient/flash.html
## Migraine Stages

<table>
<thead>
<tr>
<th>Stage 1 – Infrequent Episodic</th>
<th>Education plus effective acute treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 1 Migraine/month</td>
<td>Education plus effective acute treatment</td>
</tr>
</tbody>
</table>

| Stage 2 – Frequent Episodic   | Education plus effective acute treatment with back up; medications limits; preventive measures |
| 2 – 6 headache days/month     | Education plus effective acute treatment with back up; medications limits; preventive measures |

| Stage 3 – Transforming Migraine | Education; preventive pharmacology; acute pharmacology with back up & rescue; behavioral interventions |
| 7 – 14 headache days/month     | Education; preventive pharmacology; acute pharmacology with back up & rescue; behavioral interventions |

| Stage 4 – Chronic Migraine   | Education; preventive pharmacology; judicious acute pharmacology with back up and rescue; behavioral interventions |
| - ≥ 15 headache days/month   | Education; preventive pharmacology; judicious acute pharmacology with back up and rescue; behavioral interventions |
Migraine Frequency

- 22.5%: Headache days/month 0-1
- 39.3%: Headache days/month 2-3
- 14.0%: Headache days/month 4-6
- 8.4%: Headache days/month 7-9
- 3.9%: Headache days/month 10-11
- 1.5%: Headache days/month 12-14
- 1.8%: Headache days/month 15-18
- 1.4%: Headache days/month 19-21
- 0.6%: Headache days/month 22-24
- 0.7%: Headache days/month 25-27
- 1.0%: Headache days/month 28-31

2.5% progress per year
26% revert / 2 years

References:
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
Migraine Outcomes: Acute therapy vs. No Acute Therapy
Acute Therapy

• Goal is pain freedom in 2 hours
• Treat at mild pain (prior to central sensitization)
• May use polypharmacy
Triptan Pearl: Treat @ Mild Pain
Early Intervention Improve Efficacy

2 Hour Pain Free Response

Pain Intensity When HA Treated

Acute Oral Therapies

Non-triptan
• NSAIDS
• Combinations
  • APAP/ASA/caffeine
  • Analgesics
  • Antiemetics

Triptans / Ergotamines

Ditans / Gepants

When to consider
• First-line therapy
• Adjunctive therapies

There is no medication that is perfect for all migraine attacks or all circumstances in which treatment is needed.
# Triptans: What’s the Difference?

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

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

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

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

Migraine Recurrence
Long Duration Migraine
Polypharmacy
NSAID/Antiemetic
Long ½ life Nara/Frova
Scheduled Dosing

Triptan Nonresponder
Start Migraine Preventive
Use Max dosage
Alternate triptan/formulation
Polypharmacy
Stratified Care

- Low Disability: NSAIDs
- Moderate Disability: NSAIDs + neuroleptics or triptans
- High or Severe Disability: Triptans Parental Gpant/Dtans
New Kids on the Block
Dtans & G-pants

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
# Ditans / Gepants Clinical Trials

<table>
<thead>
<tr>
<th></th>
<th>Lasmiditan</th>
<th>Ubrogepant</th>
<th>Rimegepant</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T_{1/2}$</td>
<td>≈ 5.5h</td>
<td>α 3h</td>
<td>β 5-7h</td>
</tr>
<tr>
<td></td>
<td>100mg</td>
<td>50mg</td>
<td>75mg</td>
</tr>
<tr>
<td>Pain Relief</td>
<td>200mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Severe/Moderate to mild/no pain) Therapeutic Gain</td>
<td>14 15</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>100mg</td>
<td>50mg</td>
<td>75mg</td>
</tr>
<tr>
<td>Pain Freedom</td>
<td>200mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Severe/Moderate to no pain) Therapeutic Gain</td>
<td>13 17</td>
<td>7.5</td>
<td>8.1</td>
</tr>
<tr>
<td></td>
<td>100mg</td>
<td>50mg</td>
<td></td>
</tr>
<tr>
<td>Adverse Events</td>
<td>Dizziness</td>
<td>100mg</td>
<td>Nausea</td>
</tr>
<tr>
<td></td>
<td>Sedation</td>
<td>Nausea</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Paresthesia</td>
<td>Sedation</td>
<td></td>
</tr>
</tbody>
</table>
New Kids on the Block
Sunglasses & Neuromodulation

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

Prevention

Change in HA days (NS)  
P = 0.054

Acute

50% Responder Rates  
P = 0.023

Reduction in VAS pain score, 1 hour  
P < 0.0001


Slide courtesy of Stew Tepper, MD
Remote Nonpainful Electrical Stimulation (RNES) for Scute Migraine Treatment (Nerivio)

- 3 prospective, double-blinded, randomized, crossover, sham-controlled trials
- MOA: activates descending inhibition 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
- $99 to treat 12 migraine attacks
- No commercial insurance coverage

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

Two Hours post treatment Pain Response

<table>
<thead>
<tr>
<th>Percent responders</th>
<th>Pain Relief</th>
<th>Pain Freedom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>66.70%</td>
<td>38.80%</td>
</tr>
<tr>
<td>Placebo</td>
<td>37.40%</td>
<td>18.40%</td>
</tr>
</tbody>
</table>

What I Do

• Sooooo Off-Label & remember my patients aren’t yours
• 3 tablets Effervescent ASA + Mg 500mg or
• Ibuprofen (liquid gels better) 1000-1200mg + Mg
• Naproxen 500mg + Mg
• Augment /c Metoclopramide or Prochlorperazine
• Triptan – All generic now
  • Generic Sumatriptan ≤$2/pill, GoodRX.com
Headache Treatments

Abortive – Pain freedom in 2 hours

Preventive – Reduce frequency, intensity and improve acute med response

Rescue – When the stop medicine didn’t
# American Migraine Prevalence & Prevention on Prevention

**Should Offer**

- $\geq 6$ HA days/month;
- $\geq 4$ HA days /c some impairment;
- $\geq 3$ HA days /c severe impairment / bed rest

**Should Consider**

- 4-5 migraine days/month /c nl fxn
- 2-3 migraine days/month with some impairment;
- 2 migraine days /c severe impairment.

**Not indicated** $\leq 4$ HA days & no impairment or 1 HA day/month regardless of impairment
Prevention Saves You Money!

18-month comparison study
Acute vs. acute/preventive therapies
  • Office visits ↓ 51%
  • ED visits ↓ 82%
  • CT scans ↓ 75% MRI scans ↓ 88%
  • Medication costs ↓ $48-$138/month/patient

## Migraine Progression Risk Factors

<table>
<thead>
<tr>
<th>Modifiable</th>
<th>Not Modifiable</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Attack frequency</td>
<td>• Age</td>
</tr>
<tr>
<td>• Poorly treated acute HA</td>
<td>• Female sex</td>
</tr>
<tr>
<td>• Obesity</td>
<td>• Low education or SES</td>
</tr>
<tr>
<td>• Snoring/OSA</td>
<td>• Genetic factors</td>
</tr>
<tr>
<td>• Stressful life events</td>
<td>• Head injury</td>
</tr>
<tr>
<td>• Medication overuse</td>
<td></td>
</tr>
<tr>
<td>• Caffeine overuse</td>
<td></td>
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</tbody>
</table>

OSA=obstructive sleep apnea
Migraine Behavior Basics
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.
Traditional Oral Preventive Therapies

<table>
<thead>
<tr>
<th>Established Efficacy</th>
<th>Probably Effective</th>
<th>Possibly Effective</th>
<th>Efficacy Uncertain</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Level A recommendation; Should be offered</strong></td>
<td><strong>Level B recommendation; Should be considered</strong></td>
<td><strong>Level C recommendation; May be considered</strong></td>
<td><strong>Level U recommendation; Not supported or refuted</strong></td>
</tr>
<tr>
<td><strong>Antiepileptic drugs</strong>&lt;br&gt;Divalproex sodium&lt;br&gt;Valproate sodium&lt;br&gt;Topiramate</td>
<td><strong>Antidepressants</strong>&lt;br&gt;Amitriptyline&lt;br&gt;Venlafaxine</td>
<td><strong>Antiepileptic drugs</strong>&lt;br&gt;Carbamazepine</td>
<td><strong>Antiepileptic drugs</strong>&lt;br&gt;Gabapentin</td>
</tr>
<tr>
<td><strong>Beta-blockers</strong>&lt;br&gt;Metoprolol&lt;br&gt;Propranolol&lt;br&gt;Timolol</td>
<td><strong>Beta-blockers</strong>&lt;br&gt;Atenolol&lt;br&gt;Nadolol</td>
<td><strong>Beta-blockers</strong>&lt;br&gt;Nebivolol&lt;br&gt;Pindolol</td>
<td><strong>Beta-blockers</strong>&lt;br&gt;Bisoprolol</td>
</tr>
<tr>
<td><strong>Triptans</strong>&lt;br&gt;Frovatriptan (short-term for menstrual migraine)</td>
<td><strong>Alpha-agonists</strong>&lt;br&gt;Clonidine&lt;br&gt;Guanfacine</td>
<td><strong>Alpha-agonists</strong>&lt;br&gt;Fluoxetine; fluvoxamine&lt;br&gt;Protriptyline</td>
<td><strong>Calcium-channel blockers</strong>&lt;br&gt;Nicardipine; nifedipine; nimodipine; verapamil</td>
</tr>
<tr>
<td><strong>Triptans</strong>&lt;br&gt;Frovatriptan (short-term for menstrual migraine)</td>
<td><strong>Antihistamines</strong>&lt;br&gt;Cyproheptadine</td>
<td><strong>Angiotensin receptor blockers</strong>&lt;br&gt;Candesartan</td>
<td><strong>Coumadin</strong>&lt;br&gt;Acetazolamide&lt;br&gt;Cyclandelate</td>
</tr>
<tr>
<td><strong>Antibiotics</strong>&lt;br&gt;Penicillin</td>
<td><strong>Antibiotics</strong>&lt;br&gt;Cephalosporins</td>
<td><strong>Antibiotics</strong>&lt;br&gt;Macrolides</td>
<td><strong>Antibiotics</strong>&lt;br&gt;Quinolones</td>
</tr>
<tr>
<td><strong>Antimotility agents</strong>&lt;br&gt;Loperamide</td>
<td><strong>Antimotility agents</strong>&lt;br&gt;Olsalazine</td>
<td><strong>Antimotility agents</strong>&lt;br&gt;Yates</td>
<td><strong>Antimotility agents</strong>&lt;br&gt;Metronidazole</td>
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<td><strong>Antimotility agents</strong>&lt;br&gt;Metronidazole</td>
</tr>
</tbody>
</table>

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
• Membrane Stabilizing medications-Valproate, Topiramate, Gabapentin...
• Anti-HTN Beta Blockers, CCB, ACE, Candesartan 16mg
• TCA (off label) most data is with amitriptyline – SSRIs not thought to be effective
• OnabotulinumtoxinA – 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
• Eptinezumab CGRP ab I.V. approved February 2020
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
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.
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](http://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.
Autogenic Training

• My mind is quiet and at peace.
• I am calm and at peace.
• It is time to sleep and restore.
• My right arm is heavy.
• My left arm is heavy.
• I am calm and at peace.

• My shoulders are heavy.
• My jaw is heavy and relaxed.
• I am calm and at peace.
• My right leg is heavy.
• My left leg is heavy.
• It is time to sleep and restore.
• I am calm and at peace.
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’
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 smart phone application
• Headspace smart phone application
• DawnBuse.com
  • Relaxation exercises download for free

• The Relaxation and Stress Reduction Workbook – M. Davis
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
Getting Patients to Move

- 3 Km associated with Brain Derived Neurotrophic Growth Factor (BDNF)
- Promotes new neuronal connections to deal with encountered stress
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
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
Why Should I Treat Acute Headaches?

- Have to keep these people 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
Clinical Headache Rescue

- Assoc. Neurologist of S. CT AHS Scientific Assembly Poster
- Drop-in HA Clinic – 9/05 - 8/07 500 pts
- Time to Present = 104 hours (8-240h)
- VAS pain: Entry 8.5 Discharge 1.5
- Txt: IVF (94%), Ketorolac (84%), Suma sq (78%), Prochlorperazine (52%), Metoclopramide (21%), DHE (8%), Mg++ (4%)

Clinical Headache Rescue
UAB Experience

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

<table>
<thead>
<tr>
<th>Optimal Self Adm</th>
<th>Clinic Rescue</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>423 visits</td>
</tr>
<tr>
<td></td>
<td>33.6K ($80)</td>
</tr>
<tr>
<td>73</td>
<td>ED Visits</td>
</tr>
<tr>
<td>147.9K($2027)</td>
<td>ED Direct Cost</td>
</tr>
<tr>
<td></td>
<td>45.3K ($1609)</td>
</tr>
<tr>
<td></td>
<td>79% no d/a &gt; 24’</td>
</tr>
</tbody>
</table>

Morey V, Rothrock JF. *Headache*. 2008;48:939-943
Clinical Headache Rescue
UAB Experience

89% very satisfied

<table>
<thead>
<tr>
<th>Drug</th>
<th>#</th>
<th>Drug Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Droperidol 2.75mg</td>
<td>218</td>
<td>3.00</td>
</tr>
<tr>
<td>Diphenhydramine 50mg</td>
<td>201</td>
<td>1.25</td>
</tr>
<tr>
<td>DHE 1mg</td>
<td>167</td>
<td>42</td>
</tr>
<tr>
<td>Prochlorperazine 5-10mg</td>
<td>141</td>
<td>11.5</td>
</tr>
<tr>
<td>Promethazine 50mg</td>
<td>68</td>
<td>4.</td>
</tr>
<tr>
<td>Ketorolac 30mg</td>
<td>38</td>
<td>9 + 11 (saline)</td>
</tr>
</tbody>
</table>

Morey V, Rothrock JF. *Headache*. 2008;48:939-943
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
Procedures
Can I Stick a Needle in That?

• Lower Cervical Intramuscular Injections
• Occipital Nerve Block
• Sphenopalatine Ganglion Block
• Pericranial Injections
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%
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
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.
Occipital Nerve Block

Marcus DA, Ready DM. Discussing Migraine. Springer 2017
Occipital Nerve Block

44 CM / 2 groups GON weekly X 4
Followed @ 4weeks, 2 months, 3 months

<table>
<thead>
<tr>
<th></th>
<th>Baseline HA Frequency</th>
<th>One Month</th>
<th>Two Months</th>
<th>Three Months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bupivacaine</strong></td>
<td>21.0 +/-4.4</td>
<td>10.9 +/- 7.1</td>
<td>6.1 +/- 2.4</td>
<td>6.3 +/- 1.9</td>
</tr>
<tr>
<td><strong>Saline</strong></td>
<td>20.9 +/- 5.0</td>
<td>15.5 +/- 7.3</td>
<td>18.2 +/- 6.1</td>
<td>19.1 +/- 6.3</td>
</tr>
</tbody>
</table>

No serious AEs
Bupivacaine – Significant ↓ months 1,2,3
Saline – Decrease @ month 1 only

Greater Occipital Nerve Block

PGON: 25 Chronic Migraine pts on oral prophylaxis
GON: 53 Chronic Migraine pts medically refractive to oral medications

<table>
<thead>
<tr>
<th></th>
<th>Baseline HA Days</th>
<th>Month 3 HA Days</th>
<th>Δ</th>
<th>Baseline HA Severity</th>
<th>Month 3 HA Severity</th>
<th>Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGON-25</td>
<td>13.76±8.07</td>
<td>3.28±2.15</td>
<td><strong>10.48</strong></td>
<td>8.08±0.90</td>
<td>5.96±1.20</td>
<td><strong>2.12</strong></td>
</tr>
<tr>
<td>GON-53</td>
<td>15.73±7.21</td>
<td>4.52±3.61</td>
<td><strong>11.21</strong></td>
<td>8.26±1.32</td>
<td>5.16±2.64</td>
<td><strong>3.10</strong></td>
</tr>
</tbody>
</table>

Occipital Nerve Block

• Adverse Events / Contraindications
• Prior hx of craniotomy over injection site
• AEs primarily related to steroid- fat atrophy, alopecia, pigment change
• Vagal response – Happened to me X 4 in over 12K blocks
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 wks
• ↓ HA days 22.8d to 9d
• ↓ Severe 15.9d to 6.1d
• ↓ Treatment 18.1d to 7.9d
• 11.5% no response/Lost-FU
Pericranial Bupivacaine Injections
Robert Kaniecki, MD, University of Pittsburgh
Pericranial Bupivacaine Injections
Robert Kaniecki, MD, University of Pittsburgh
Pericranial Bupivacaine Injections
Robert Kaniecki, MD, University of Pittsburgh
# Who Should Get CGRP Antibodies

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Strongly Consider for Pts /c</strong></td>
<td></td>
</tr>
<tr>
<td>Severe disability with lack of benefit from existing alternatives or inability to tolerate existing alternatives</td>
<td>Safety concerns are outweighed by the possibility that treatment will be effective.</td>
</tr>
<tr>
<td>Difficulty adhering to regimens requiring daily medications.</td>
<td>The long duration of action and monthly or quarterly administration obviates the need for daily pills.</td>
</tr>
<tr>
<td>Polypharmacy in the context of multiple comorbid conditions</td>
<td>Antibodies offer a low risk of drug interactions.</td>
</tr>
</tbody>
</table>

Loder EW, Burch RC. *JAMA Neurology*, 2018.
Who Should Get CGRP Antibodies

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoid in Pts /c</td>
<td></td>
</tr>
<tr>
<td>Infrequent headaches that respond to abortive treatment.</td>
<td>These patients are not candidates for prophylaxis, and it is safer to treat headaches individually.</td>
</tr>
<tr>
<td>Existing pregnancy or likelihood of becoming pregnant.</td>
<td>The levels of CGRP are lower in women with preeclampsia than normal pregnancy.</td>
</tr>
<tr>
<td>Known cardiovascular disease or high risk of cardiovascular disease.</td>
<td>The use of CGRP may have a cardioprotective effect and be a vasodilatory fail-safe mechanism during vasoconstrictive or ischemic emergencies.</td>
</tr>
</tbody>
</table>

Loder EW, Burch RC. *JAMA Neurology*, 2018.
# Who Should Get CGRP Antibodies

<table>
<thead>
<tr>
<th><strong>Recommendation</strong></th>
<th><strong>Rationale</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exercise Caution for Pts who are</strong></td>
<td></td>
</tr>
<tr>
<td>Doing well on current treatments with acceptable tolerability.</td>
<td>The long-term safety risk is not worth taking.</td>
</tr>
<tr>
<td>Members of a group that was excluded from clinical trials.</td>
<td>Trial findings have uncertain generalizability.</td>
</tr>
<tr>
<td>Concomitantly, regularly exposed to vasoconstrictive drugs or substances associated with the development of reversible cerebral vasoconstrictive syndrome.</td>
<td>Use in the context of prolonged CGRP blockade may be risky</td>
</tr>
</tbody>
</table>

Loder EW, Burch RC. *JAMA Neurology* 2018.
Side Effects and Cautions with Anti-CGRP/CGRP-R mAbs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Notable Side Effects/Cautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erenumab</td>
<td>Constipation (October 2019 warning of serious complications); latex allergy; injection site reactions; upper respiratory symptoms, HTN</td>
</tr>
<tr>
<td>Fremanezumab</td>
<td>Injection site reactions; upper respiratory symptoms</td>
</tr>
<tr>
<td>Galcanezumab</td>
<td>Injection site reactions; upper respiratory symptoms</td>
</tr>
<tr>
<td>Eptinezumab</td>
<td>Nasopharyngitis; hypersensitivity</td>
</tr>
</tbody>
</table>

- 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.

All USPIs include warnings and contraindications about hypersensitivity reactions
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
Never Give Up!
The following slides are listed within this handout for your consideration. These slides highlight important information for management of migraine.
## Headache Imaging Indications — ACR Guidelines

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

*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.
<table>
<thead>
<tr>
<th>Stage 1 – Infrequent Episodic ≤ 1 Migraine/month</th>
<th>Education plus effective acute treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 2 – Frequent Episodic 2 – 6 headache days/month</td>
<td>Education plus effective acute treatment with back up; medications limits; preventive measures</td>
</tr>
<tr>
<td>Stage 3 – Transforming Migraine 7 – 14 headache days/month</td>
<td>Education; preventive pharmacology; acute pharmacology with back up &amp; rescue; behavioral interventions</td>
</tr>
<tr>
<td>Stage 4 – Chronic Migraine 15 headache days/month</td>
<td>Education; preventive pharmacology; judicious acute pharmacology with back up and rescue; behavioral interventions</td>
</tr>
</tbody>
</table>
### Triptans: What’s the Difference?

<table>
<thead>
<tr>
<th>Triptan</th>
<th>T&lt;sub&gt;1/2&lt;/sub&gt;</th>
<th>$</th>
<th>Pearl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sumatriptan</td>
<td>2.5h</td>
<td>9/$12</td>
<td>Multiple formulation</td>
</tr>
<tr>
<td>Rizatriptan</td>
<td>2-3h</td>
<td>9/$16</td>
<td>Reduce dosed with propranolol</td>
</tr>
<tr>
<td>Eletriptan</td>
<td>4h</td>
<td>9/$37</td>
<td>Typically better response</td>
</tr>
<tr>
<td>Almotriptan</td>
<td>3h</td>
<td>12/$126</td>
<td>Good tolerability</td>
</tr>
<tr>
<td>Zolmitriptan</td>
<td>3h</td>
<td>6/$38</td>
<td>Best tolerated NS</td>
</tr>
<tr>
<td>Naratriptan</td>
<td>26h</td>
<td>9/$26</td>
<td>Scheduled dosing for Menstrual Related Migraine</td>
</tr>
<tr>
<td>Frovatriptan</td>
<td>6h</td>
<td>9/$160</td>
<td>Scheduled dosing for Menstrual Related Migraine</td>
</tr>
</tbody>
</table>
Choosing Triptans

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

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

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

Migraine Recurrence
Long Duration Migraine
Polypharmacy
NSAID/Antiemetic
Long ½ life Nara/Frova
Scheduled Dosing

Triptan Nonresponder
Start Migraine Preventive
Use Max dosage
Alternate triptan/formulation
Polypharmacy
Migraine Behavior Basics
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.
# Traditional Oral Preventive Therapies

<table>
<thead>
<tr>
<th>Established Efficacy</th>
<th>Probably Effective</th>
<th>Possibly Effective</th>
<th>Efficacy Uncertain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level A recommendation; Should be offered</td>
<td>Level B recommendation; Should be considered</td>
<td>Level C recommendation; May be considered</td>
<td>Level U recommendation; Not supported or refuted</td>
</tr>
</tbody>
</table>

- **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

---

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.
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.
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