TREATMENT OF PRIMARY HEACHES IN PRIMARY CARE

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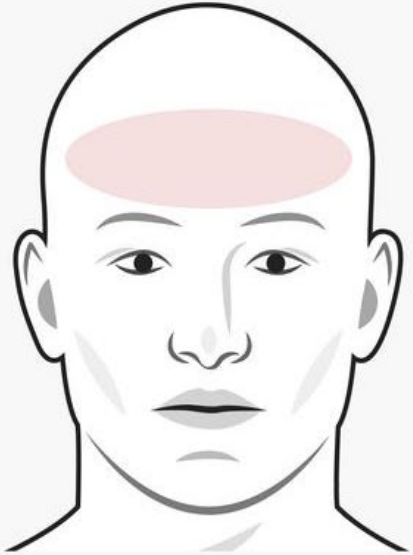
OBJECTIVES

1. Briefly discuss the different types of primary headaches
2. Describe current evidenced-based guidelines for the proper treatment of acute primary headaches
3. Classify the most effective abortive treatments for primary headaches
4. Demonstrate the proper development of a treatment plan utilizing abortive and preventive therapies to decrease headache morbidity

Speaker has no relevant relationships with commercial interest and is not receiving commercial support for any of this educational activity.

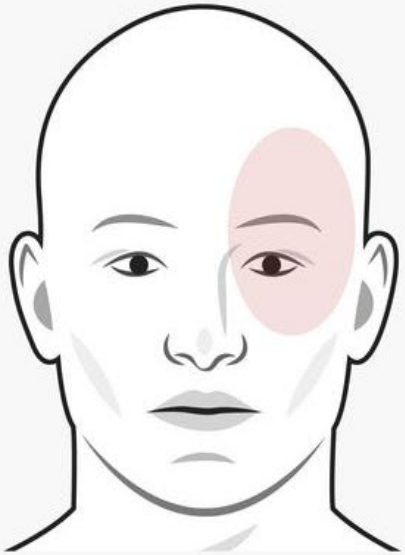
PRIMARY HEADACHE ASSESSMENT

Common types of headaches



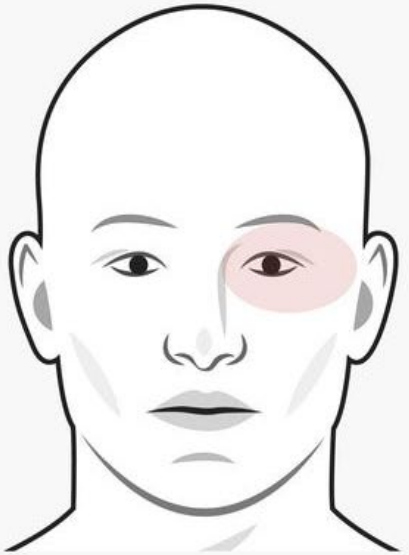
Tension

Tight band of squeezing pressure around your head



Migraine

Throbbing or pulsing pain on one side of your head



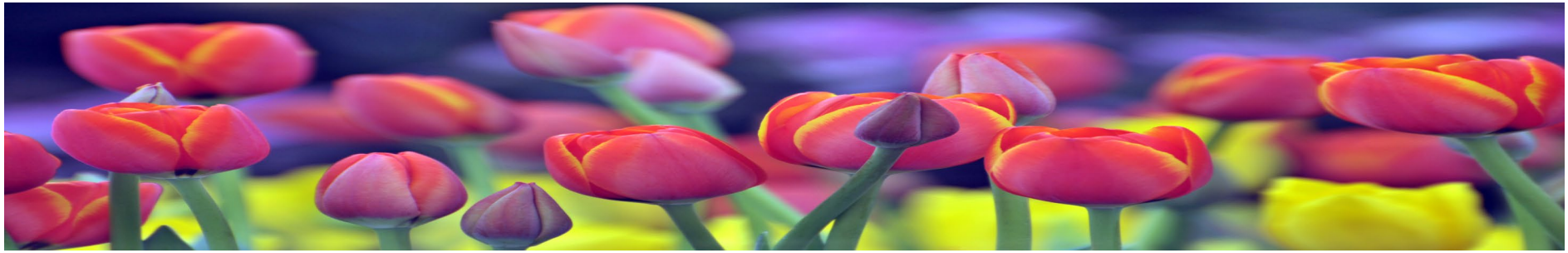
Cluster

Severe pain concentrated around one eye

SOURCE: U.S. NATIONAL LIBRARY OF MEDICNE

POUND mnemonic for Migraine Dx

P	Is the headache Pulsatile in quality?
O	Is the headache present for ONE day? (between 4-72 hours)
U	Is it Unilateral in location?
N	Is there associated Nausea or vomiting?
D	Is the headache disability in intensity?



INTERNATIONAL CLASSIFICATION OF HEADACHE DISORDERS – 3

DEFINE & CLASSIFY ALL KNOWN HEADACHE DISORDERS

MIGRAINE DISABILITY ASSESSMENT SCALE

In the last 3 months how many days:

1. Missed work
2. Productivity reduced by half or more
3. Household work incomplete
4. Household work reduced by half of more
5. Miss family, social or leisure activities
6. Headache was present
7. How painful were the headaches

MIDAS SCORE = # DAYS/MONTH 1-5

MIDAS GRADE	DEFINITION	MIDAS SCORE
I	LITTLE OR NO DISABILITY	0-5
II	MILD DISABILITY	6-10
III	MODERATE DISABILITY	11-20
IV	SEVERE DISABILITY	21+

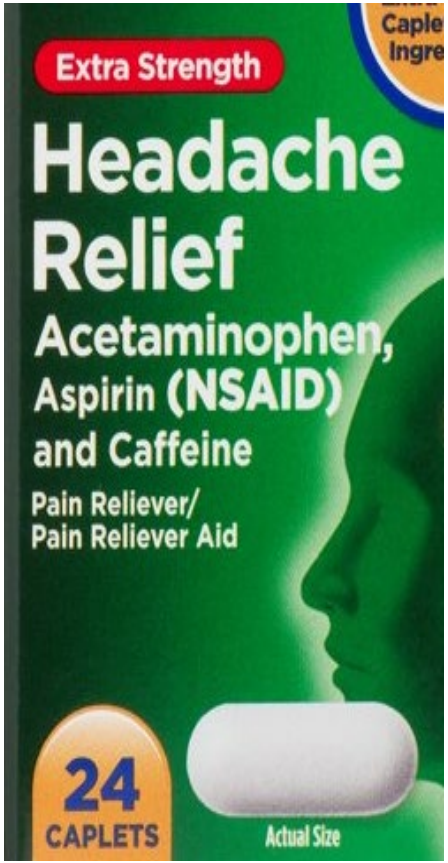
TREATMENT

KNOW WHAT YOU ARE TREATING BEFORE PRESCRIBING: ICHD-3 Diagnostic Criteria

TENSION-TYPE HEADACHES

ABORTIVE THERAPIES

ANALGESICS	TYLENOL NSAIDS (IBUPROFEN, KETOPROFEN) KETOROLAC INDOMETHACIN
COMBINATION ANALGESICS/CAFFEINE	EXCEDRIN MIGRAINE, GOODY'S HEADACHE POWDER, NODOZ MAXIMUM STRENGTH, VANQUISH CAPLETS
COMBINATION ANALGESICS W/BUTALBITAL & CODEINE	BUTALBITAL/ACETAMINOPHEN, CAFFEINE, CODEINE (Fioricet with codeine) BUTALBITAL/ASPRIRIN/CAFFEINE/CODEINE (Fiorinal with codeine)
TRIPTANS	ALMOTRIPTAN, FROVATRIPTAN, RIZATRIPTAN
MUSCLE RELAXERS	CYCLOBENZAPRIN, TIZANIDINE



PARENTERAL TREATMENTS

- CHLORPROMAZINE
- METOCLOPRAMIDE
- METOCLOPRAMIDE + DIPHENHYDRAMINE
- KETOROLAC

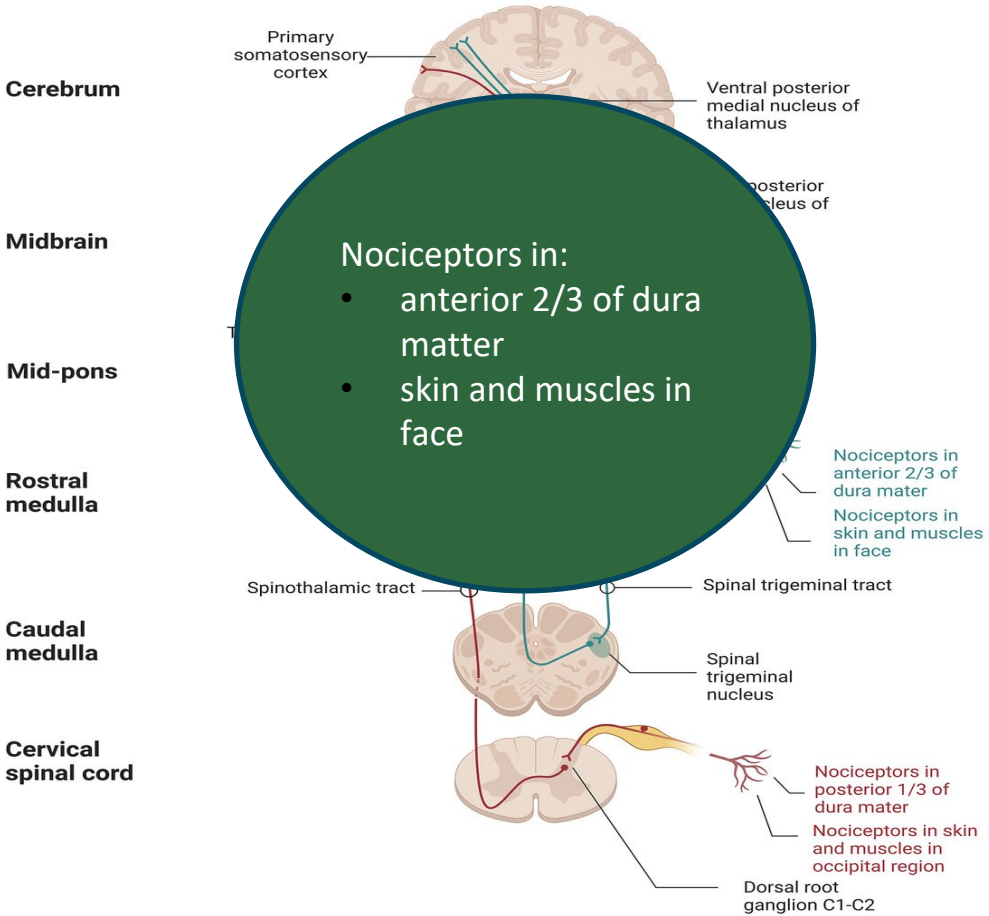
Chronic TTH: PROPHYLACTIC TREATMENT

- ≥ 10 headaches per month
- Evidence is limited/nonspecific
- Start low
- Max dose/min side effects
- Adequate trials

OFF-LABEL

1. AMITRIPTYLINE
2. MIRTAZAPINE
3. VENLAFAXINE (EFFEXOR)
4. TIZANIDINE

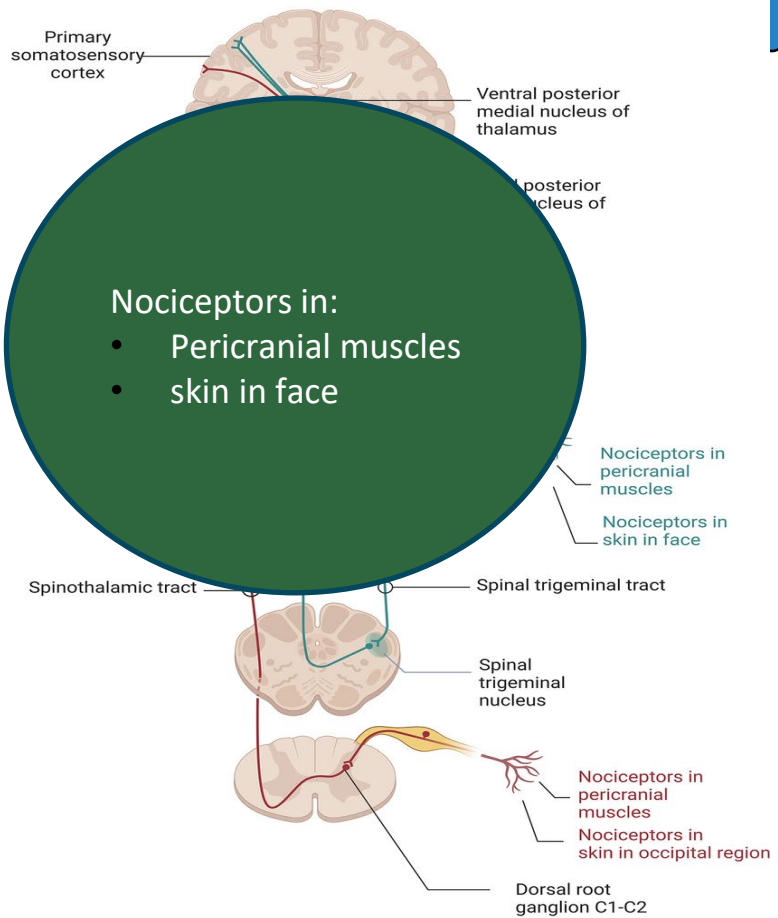
Migraine



Nociceptors in:

- anterior 2/3 of dura matter
- skin and muscles in face

Tension-type headache



Nociceptors in:

- Pericranial muscles
- skin in face

THE BEST TREATMENT

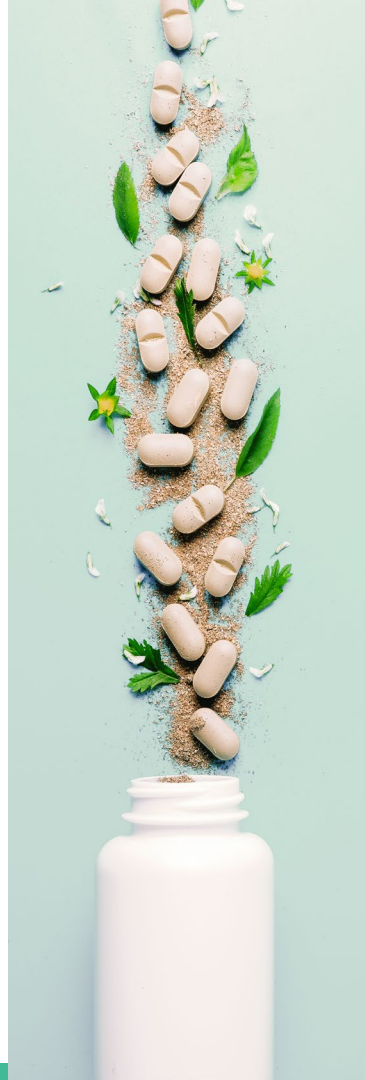
COMBINED BEHAVIORAL + TCA

BEHAVIORAL:

- BIOFEEDBACK
- COGNITIVE BEHAVIORAL THERAPY
- RELAXATION/STRESS REDUCTION

DURATION OF TREATMENT

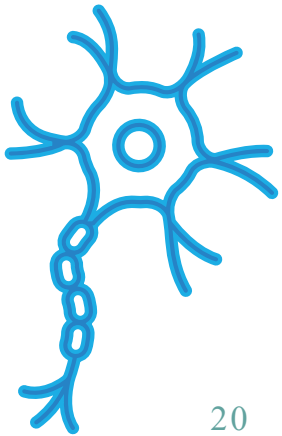
- PATIENT COMPLIANCE
- HEADACHE DIARY
- DURATION 3-6 MONTHS
  - CONSIDER SLOW TAPER



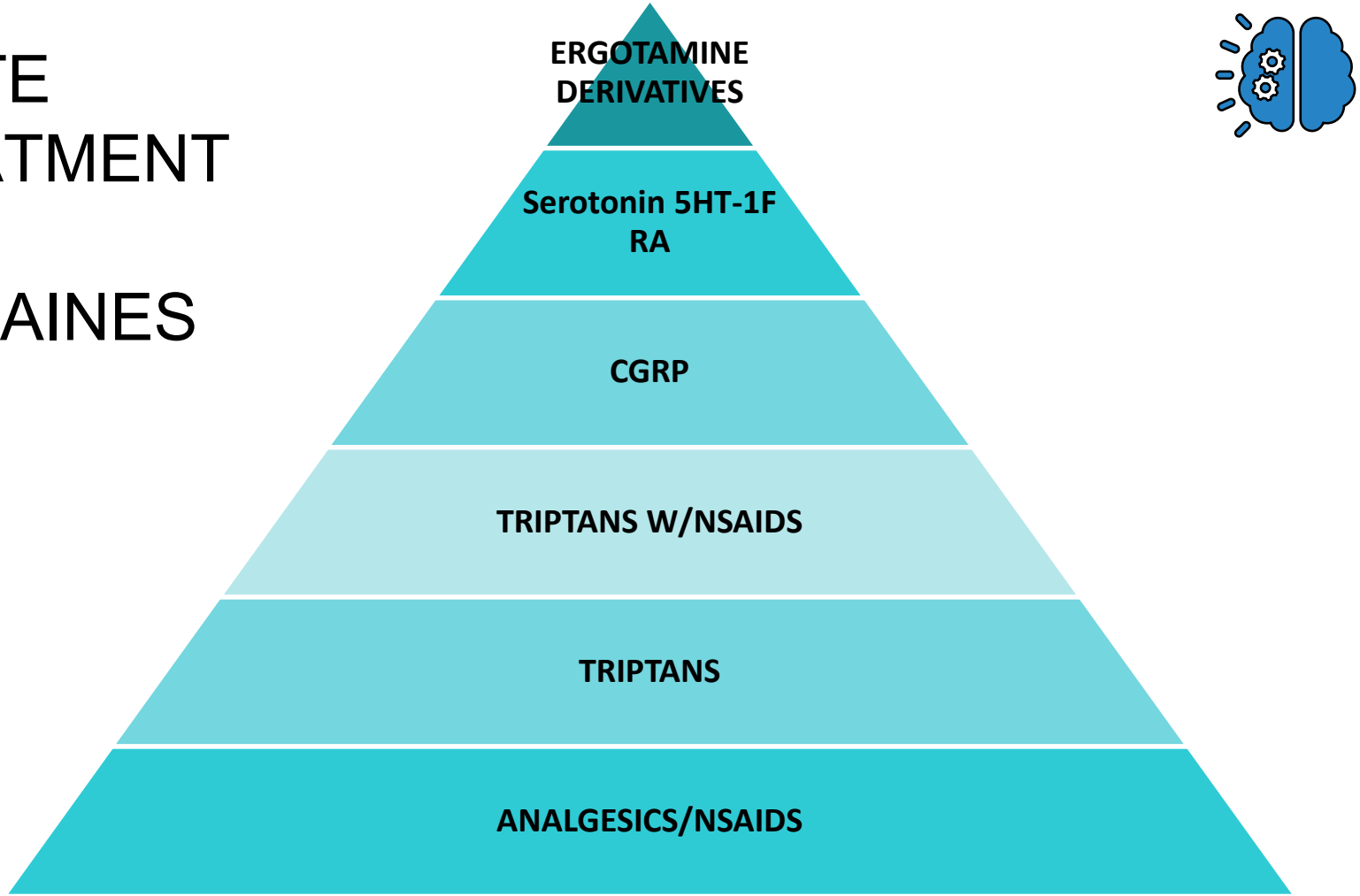
MIGRAINES

MIGRAINES

- 12-15% of the population
- Migraine w/o Aura – 75%
- Migraine w/Aura – 25%
- 2ND only to backpain as a disability
- Predictive symptoms: nausea, photophobia, phonophobia, and exacerbation by physical activity



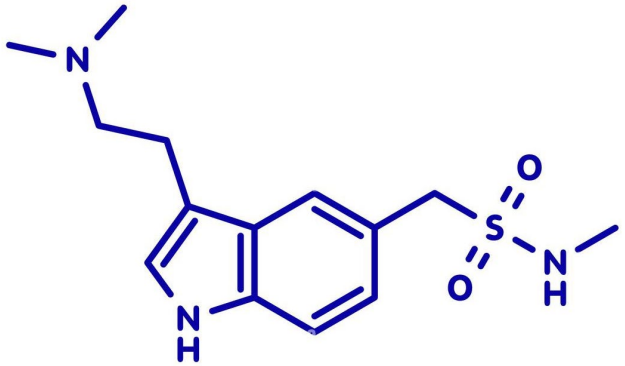
ACUTE TREATMENT OF MIGRAINES



ANALGESICS

- NSAIDS Proven Efficacious
- Ketorolac (Parenteral) = Efficacy With Triptans
- Indomethacin (Oral Or Suppository)
  - 50 Mg
  - May Be Halved/Thirds
- Acetaminophen Effective @ 1000mg
- Combination Acetaminophen-aspirin-caffeine Abortive In Uncomplicated Migraines

TRIPTANS

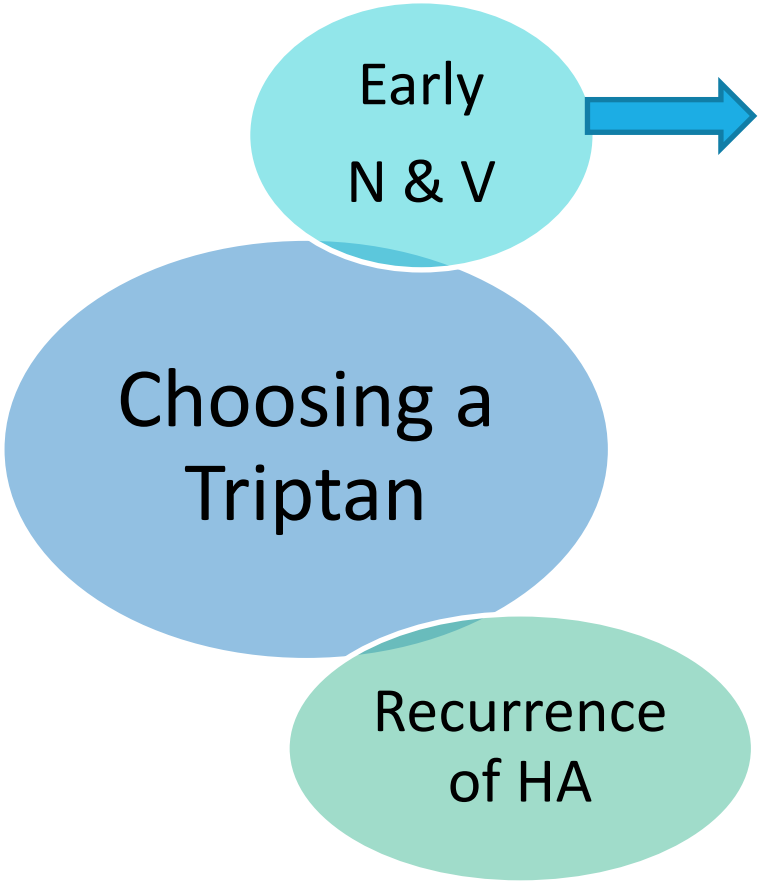


- Serotonin 1b/1d agonists
- Serotonin 5-HT receptors
- Late 1980’s
- Work by:
  - Inhibiting the release of vasoactive peptides
  - promote vasoconstriction
  - block pain pathways in the brainstem
  - inhibition of neuronal inflammation

TRIPTANS

- SUMATRIPTAN (IMITREX) – SQ, Nasal spray, Nasal powder
- ZOLMITRIPTAN (ZOMIG) – Nasal
- NARATRIPTAN (AMERGE) – Slower onset/Lower efficacy
- RIZATRIPTAN (MAXALT) – Downward dose w/propranolol
- ALMOTRIPTAN (AXERT)
- ELETRIPTAN (RELPAX) – Heavily metabolized by CYP450
- FROVATRIPTAN (FROVA) - Slower onset/Lower efficacy

RESPONSIVENESS TO TRIPTANS DOES NOT EQUAL DIAGNOSIS



Nasal Spray: Sumatriptan or Zolmitriptan
Wafer: Rizatriptan
Melt: Zolmitriptan
SQ: Sumatriptan

\+

Antiemetics

Add a NSAID **OR**
Longer acting Triptan
- Naratriptan
- Almotriptan
- Frovatriptan

Choosing a Triptan

Rapidly progressing migraine attack

- Consider preventative
- Higher dose
- Alternative Triptan
- Alternative formulation (SQ, intranasal)
- Combination triptan + NSAID

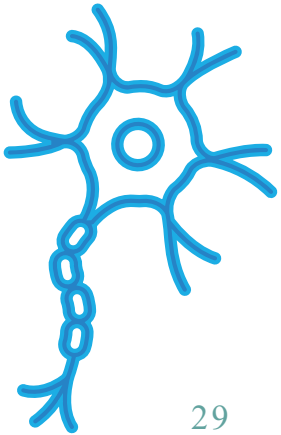
Lack of triptan response

- Sumatriptan SQ
- Zolmitriptan Intranasal
- Fast Acting: Eletriptan, Rizatriptan, Zolmitriptan

FAILURE OF ONE TRIPTAN DOES NOT EQUAL FAILURE OF THE CLASS!

LIMITATIONS

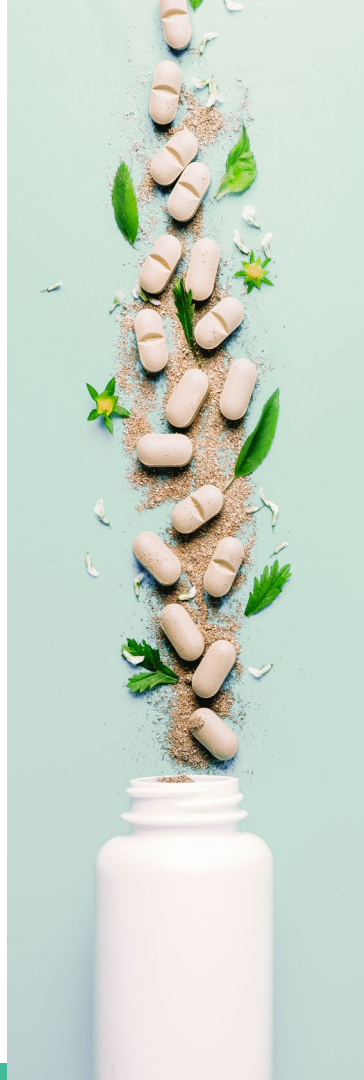
- <10 DAYS USE/ MONTH
- AVOID USE IN:
  - Hemiplegic migraine
  - Basilar migraine
  - Ischemic stroke
  - Ischemic heart disease
  - Prinzmetal's angina
  - Uncontrolled hypertension
  - Pregnancy



TRIPTANS W/ NSAIDS

DURATION

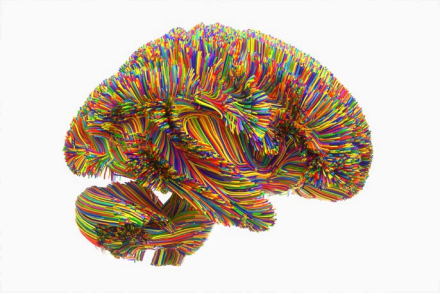
- Sumitriptan/Naproxen (Treximet)
  - 10 mg/60 mg – Peds
  - 85 mg/500 mg
- 2016 Meta-analysis
  - More effective than either alone
  - Assumes generalizability



CALCITONIN-GENE RELATED PEPTIDE (CGRP)

SMALL MOLECULE CGRP (Gepants)

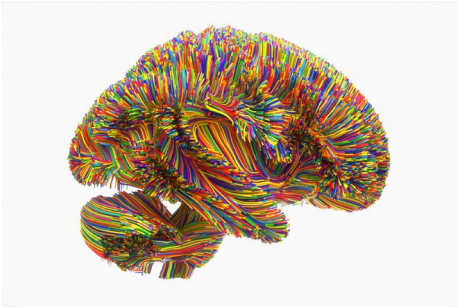
Rimegepant (Nurtec odt)	Ubrogepant (Ubrelvy)	Atogepant (Qulipta)	**Zavegepant (Zavzpret)**
ACUTE • 75mg daily **Prophylaxis** • 75 mg qod	**ACUTE** • 50-100 mg • 200 mg/24 hour max • Repeat dose after 2 hours	**Prophylaxis** • 10-60 mg qd	**ACUTE** • 10 mg/spray



LARGE MOLECULE CGRP (monoclonal antibodies)

Erenumab (Aimovig)	Fremanezumab (Ajovy)	Galcanezumab (Emgality)	Eptinezumab (Vyepti)
• 70-140 mg SC monthly	• 225 mg SC monthly • 675 mg SC q3 months	• 120 mg SC q month	• 100 mg q 3 months • 300 mg q 3 months

GEPANTS: MOA/ADVERSE ACTIONS



- Mediate trigeminovascular pain transmission
- Generally well tolerated
- Limited evidence (eg, children, older adults, and pregnant or lactating patients)
  - Long-term studies needed
- MOST COMMON adverse reactions
  - Nausea, somnolence, dry mouth

Small Molecule CGRP (Gepants)

Indicated if: insufficient response or contraindication (eg, coronary artery disease) to triptans

Differ from triptans:

- Do not cause vasoconstriction
- Do not lead to medication overuse headache

Differs from the CGRP monoclonal antibodies

- Oral or dissolvable tablets rather than injectable
- Elimination rates: Gepants clear in a few days

DITANS

LASMIDITAN (Reyvow)

- Selective serotonin 1F receptor agonist
- Block CGRP
- Inhibits trigeminal nerve firing
- Approved October 2019

DOSAGE:

50-100mg in one oral dose
No benefit of second dose
Max 200mg in 24 hours

- Most common adverse effect was dizziness

DITANS DIFFER FROM TRIPTANS

- Triptans work on sensory nerve & blood vessel receptors
- Ditans only work on sensory nerve receptors

ADVERSE ACTIONS/RESTRICTIONS

- Potentially sedation
- 8 - hour driving restriction
- CDS Schedule V

ERGOTAMINE DERIVATIVES

ABORTIVE

ERGOTS

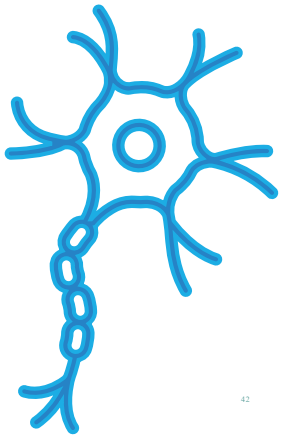
- Both ergotamine and dihydroergotamine bind to 5HT 1b/d receptors, just as triptans do.
- Do not use within 24 hours of a triptan or other ergot derivatives
- Contraindicated:
  - HTN
  - Ischemic heart disease
  - Pregnancy
  - Breastfeeding

ERGOTAMINE

- Questionable individual effectiveness
- Suppository + Caffeine
  - Increased efficacy & side effects
- Risks outweigh benefits

Dihydroergotamine

- Fewer side effects than ergotamine
- IV, IM, SQ, Intranasal
- Combine with antiemetic



ANTIEMETICS

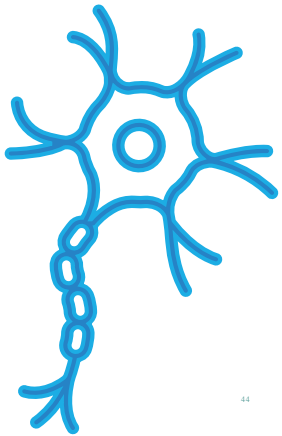
ABORTIVE

ANTIEMETICS

- **DOPAMINE RECEPTOR AGONISTS**

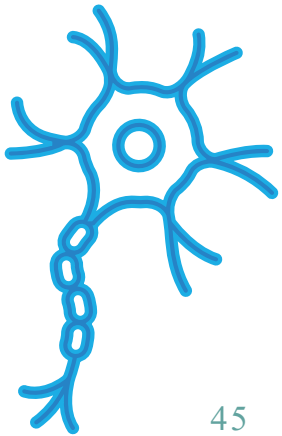
- Metoclopramide (Reglan) (iv)
- Prochlorperazine (Compazine) (iv or im)

- Give with diphenhydramine (to prevent akathisia & acute dystonia)



ANTIEMETICS

- PROCHLORPERAZINE
  - > Effective than metoclopramide
    or SQ sumatriptan
    or hydromorphone
- METOCLOPRAMIDE less effective than chlorpromazine & prochlorperazine
- Chlorpromazine, Ondansetron, Haloperidol: limited evidence
  - Rebound headaches
  - Qt-segment prolongation



PREVENTIVE THERAPIES

WHEN DO YOU INITIATE PREVENTIVE?

>4 headaches/month

OR

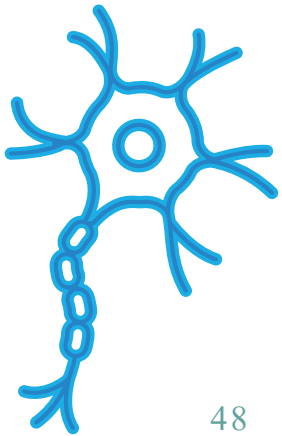
Headaches >12 hours

OR

>8 headache days/month

Other Considerations

- Failure of acute therapies
- Debilitating despite acute treatment
- Acute treatment intolerability or contraindications
- Overuse of acute medication
- Menstrual migraines



PREVENTIVE TREATMENT OF MIGRAINES

CGRP

- Erenumab (Aimovig)
- Fremanezumab (Ajovy)
- Galcanezumab (Emgality)
- Eptinezumab (Vyepti)
- Atogepant (Qulipta)

BETA BLOCKERS

- Metoprolol
- Propranolol
- Timolol

ANTICONVULS-ANTS

- Topiramate
- Valproate

ANTIDEPRES-SANTS

- Amitriptyline
- Venlafaxine

CPRG PROPHYLAXIS – FIRST LINE

Generic (Brand)	Dosage	Implications/Adverse Events
Erenumab (Aimovig)	140 mg SC q mo	• Hypertension
Fremanezumab (Ajovy)	225 mg SC q mo	• Injection site reactions
Galcanezumab (Emgality) 2018	240 mg SC x 1; 120 mg SC monthly	

CPRG – PROPHYLAXIS cont.

Generic (Brand)	Dosage	Implications/Adverse Events
Eptinezumab (Vyepti) 2020	100-300 mg q 3 months	• upper respiratory tract infections, hypersensitivity, and fatigue.
Rimegepant (Nurtec)	75 mg ODT QOD	Avoid in severe hepatic dx & ESRD Abdominal pain, nausea
Atogepant (Qlipta)	60 mg po QD	• Weight loss, constipation, nausea • Severe hepatic dx & ESRD

CPRG Characteristics

- Generally, well tolerated
- Angioedema/Anaphylaxis
- Limited data on special populations
  - Less than 18 years
  - Pregnancy/breast feeding
  - Significant cardiovascular disease or other serious comorbidities

How do you choose?

Level A (Efficacy Established)	Level B (Probably Effective)	Level C (Less evidence/possibly effective)
Divalproex	Amitriptyline	Candesartan
Propranolol	Atenolol	Carbamazepine
Timolol	Nadolol	Lisinopril
Topiramate	Naratriptan	Nebivolol
Frovatriptan	venlafaxine	Nicardipine
Metoprolol	Zolmitriptan	

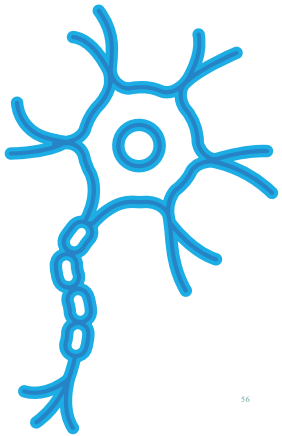
Conflicting/Inadequate Data	Ineffective
Bisoprolol Fluoxetine Gabapentin Nifedipine Nimodipine Pindolol Protriptyline Verapamil	Acebutolol Lamotrigine Oxcarbazepine Telmisartan

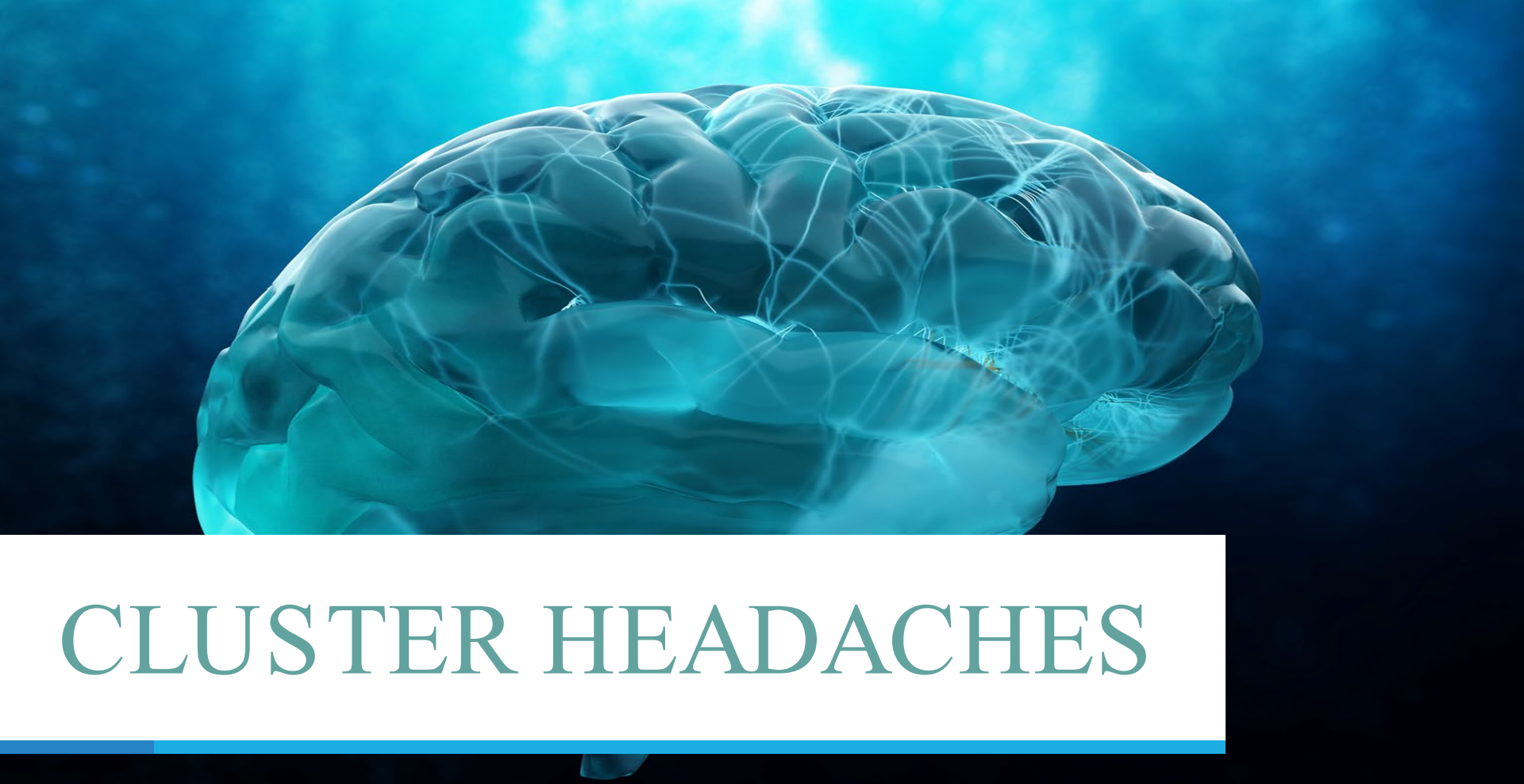
Provided no contraindications & Shared Decision Making

Scenario	Drug Choice
<60 y.o. non-smoker w/HTN	Metoprolol, Propranolol, Timolol
25-year-old with asthma	Avoid beta blockers
Depression or mood disorder	Amitriptyline or venlafaxine
Insomnia	Amitriptyline
Obesity	Topiramate
Child-bearing female	AVOID VALPROATE!!!

Principles

- Start low, go slow
- Adequate trial
  - 4 weeks
  - 3-6 months
- Consider slow taper if migraine well controlled

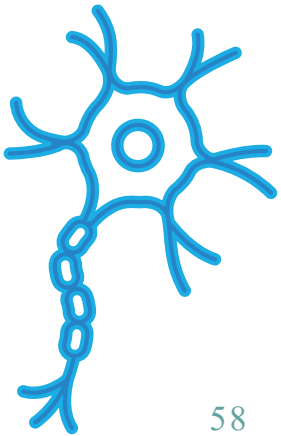




CLUSTER HEADACHES

Acute Interventions

- Initial
  - Oxygen
  - Triptans
- Alternative acute therapies
  - Lidocaine
  - Ergots
  - Octreotide



Cluster HA Preventive interventions

Episodic:

- Long-lasting active periods (≥2 months)

Chronic:

- continuous HA
- remissions < 3months

- Verapamil (240-480 mg daily)
- Glucocorticoids (alone or with verapamil)
  - 60-100mg daily for 5 days, then 10mg/day taper

Alternative:

- Galcanezumab (Emgality) CGRP MA
- Topiramate (w/verapamil)
- Lithium

MEDICATION OVERUSE HA

INTERNATIONAL CLASSIFICATION OF HEADACHE DISORDERS-3 (ICHD-3)

Diagnostic criteria:

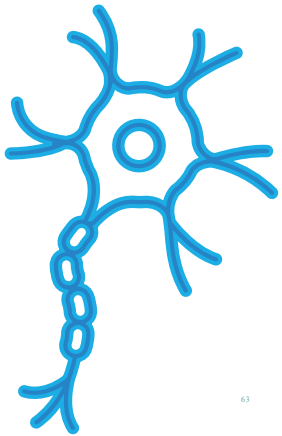
- Headache occurring on ≥15 days/month in a patient with a pre-existing headache disorder
- Regular overuse for >3 months of one or more drugs that can be taken for acute and/or symptomatic treatment of headache
- Not better accounted for by another ICHD-3 diagnosis.

CHRONIC DAILY HEADACHE

- CHRONIC MIGRAINE
- CHRONIC TENSION-TYPE HEADACHE
- HEMICRANIA CONTINUA
- **MEDICATION OVERUSE HEADACHE**
  - Pre-existing headache disorder
  - Daily headache lasting >4 hours
  - Acute medications used >2-3 days/week
  - Clinical diagnosis

MOH: Drug class & Duration

- Ergotamine: >10 days/month for >3 months
- Triptan: >10 days/month for >3 months
- ASA: >15 days/month for >3 months
- NSAIDs: >15 days/month for >3 months
- Opioids: >10 days/month for over 3 months



Drug Dependency

- Outpatient or Inpatient?
- What medication is being overused?
  - Barbiturates, Opioids, Benzodiazepines
  - Consider inpatient
    - Patient motivation
    - Medical stability/comorbidities
    - Mental health comorbidities
- Pace of taper depends on
  - Amount/frequency of use

OUTPATIENT

1. D/C overused medication
2. Taper if withdrawal is a concern (i.e. Opioids)
3. Switch to an alternative from a different class
   - Limit use to no more than 2 days per week
   - Steroids, NSAIDs
   - Prochlorperazine
4. Initiate preventive medication, then taper acute medication
5. Bridge therapy with a long-acting NSAID

BRIDGE THERAPY

If patient is unlikely to be successful with a taper

- Long-acting NSAID
  - i.e. Naproxen 500mg BID x 2-4 weeks
- Tizanidine plus NSAID
  - Titrate tizanidine up by 2mg q 3-5 days until therapeutic effect or sedation
  - Give QHS
  - PRN abortive for severe headache
- Glucocorticoids (60mg daily x 5 days)

Case studies, chart reviews

Few controlled studies

PREVENTIVE THERAPY

- Initiate/Optimize preventive therapy with withdrawal
  - Depending on the primary headache disorder
- Best outcomes at 6 months
- Relapse prevention
  - Limit NSAIDs to 14 or fewer days per month
  - Limit butalbital to ≤3 days/month
- Patient Education!!

EVALUATION - APPs

- Duration, Severity, Aura, Stress
- Medication Tracker (including effectiveness)
- Trigger Tracker
- Connect with Provider
- Share headache, medication, and trigger reports
- Detailed reports and insights

MIGRAINE BUDDY

BONTRIAGE

MIGRAINE MONITOR

N1-HEADACHE APP

Questions

References

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