Management of Migraine

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Disclosures

- I have received honoria, consulting fees, and/or speaking fees from
  - Allergan Canada
    - Onabotulinum Toxin A (Botox ™)
    - FDA & Health Canada approved for the prophylactic treatment of Chronic Migraine
  - Tribute Pharmaceuticals
    - Diclofenac Potassium (Cambia ™)
    - FDA & Health Canada approved for the acute treatment Migraine
  - Aralez
    - Sumatriptan + Naproxen Sodium (Treximet ™)
    - FDA approved for the acute treatment of Migraine
  - TEVA
    - Fremanezumab (Ajovy ™)
    - FDA approved for the prophylactic treatment of Migraine
  - Novartis
    - Erenumab (Aimovig ™)
    - FDA & Health Canada approved for the prophylactic treatment of Migraine
  - Eli Lilly
    - Galcanezumab (Emgality ™)
    - FDA approved for the prophylactic treatment of Migraine

I will be mentioning these treatments

Migraine

- 10-15 % of the population
- underdiagnosed
- 100x more common than MS
- More common that DM + OA + Asthma
- In the top 10 of diseases with years lost to disability – world wide
  - More than stroke, brain tumors, dementia, Parkinsons, MS, Epilepsy
- 10% would make different choices about having children
- 40% would be a better parent

Chronic Migraine

- 0.9% and 1.4% of the population
- 11,678 in Nova Scotia
- Less than 1/3 work full time
- 1 in 5 can’t work
- Use a lot of resources
  - Family MD, specialist visits, pain clinic visits, ERs
  - $1,884 per patient per year
    - $22 million a year to the Nova Scotia health care system

4 questions of Neurology

- Is it neurological?
- Where in the neuro-axis is the problem?
- What is causing the problem?
- What can we do about it?

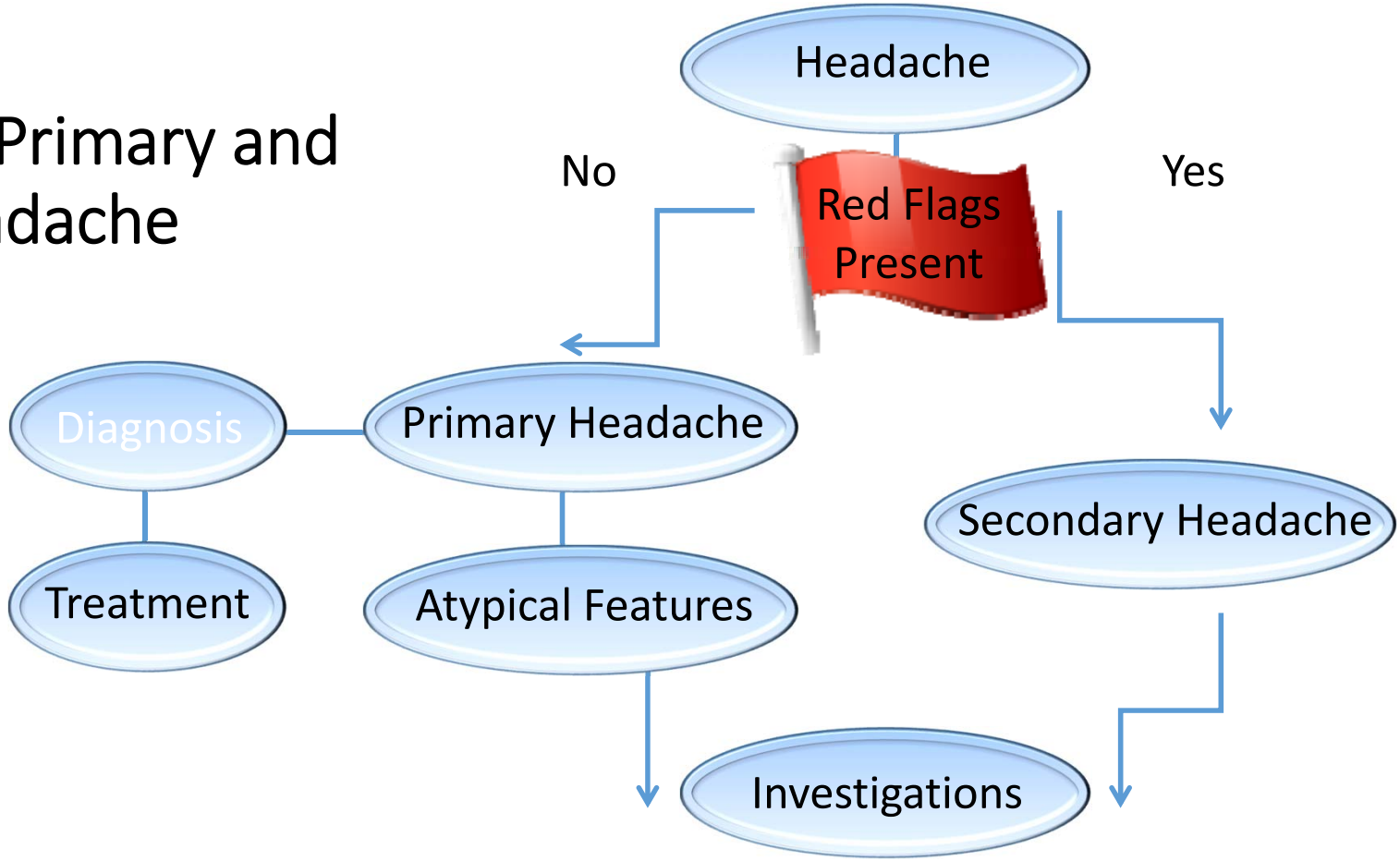
Additional 2 questions of Headache

PRIMARY

OR

SECONDARY

Distinguishing Primary and Secondary Headache Disorders



Adapted from Dodick DW. Adv Stud Med. 2003;3(6C):S550-S555

Red Flags– SNOOP[5] - Secondary Causes

S	**Systemic or 2º Risks**	**Fever, weight loss, night sweats, other systemic symptoms** **Secondary Risk Factors: Cancer, HIV**
N	**Neurologic Deficits** ***or abnormal signs***	**Focal neurologic deficit** **Confusion** **Impaired/altered LOC** **Side locked headache**
O	**Onset**	**Thunderclap**
O	**Older**	**> 50 yo** **> 60 yo is GCA until proven otherwise**
P_1	**Previous Headache History**	**First Headache** **Different Headache – change in Hz, severity, clinical features**
P_2	**Postural or Positional Aggravation**	**CSF pressure too high or too low**
P_3	**Precipitated by Valsalva**	**Cough, bend, sneeze, lift, other bearing down** **Exertional headaches**
P_4	**Papilledema/Pulsatile Tinnitus**	**Vision Change and/or loss – IIH, increased ICP**
P_5	**Pregnancy/Peri Partem**	**Preeclampsia, Hypercoagulable, CSF leaks, treatment selection**

Thunderclap Headache

- **Subarachnoid Hemorrhage**
  - **Sentinel headache**
- **Reversible Cerebral Vasoconstriction Syndrome**
- **Cerebral venous thrombosis**
- **Cervical artery dissection**
- **Spontaneous intracranial hypotension**
- Pituitary apoplexy
- Retroclival hematoma
- Stroke, Ischemic or Hemorrhagic
- Acute hypertensive crisis
- Colloid cyst of the third ventricle
- **Infections**
- ~~Primary thunderclap headache~~

GCA

Most common in patients >70 yrs (85%), F > M

- Presentation:
  - Constitutional symptoms (fever-50%, weight loss, fatigue) - Systemically UNWELL
  - Amaurosis, can progress to bilateral (33% within first few days)
  - NB: Can present with isolated other cranial neuropathy
  - Intermittent diplopia
  - Headache (67%)
  - Jaw/tongue claudication (50%), scalp tenderness
  - PMR (50%) - stiffness and pain (NOT weakness) in the proximal muscles (often in the morning),
- Fundoscopic exam:
  - pale “chalky white edema”, swollen discs, peripapillary hemorrhages, branch or central retinal artery occlusions, cotton wool spots (retinal ischemia)

GCA

- Diagnosis:
  - temporal artery bx is gold standard
  - ESR - elevated in 98%
  - Thrombocytosis
- Treatment

  Corticosteroids (DO NOT delay for the biopsy) - consider IV if vision loss

  ASA

  Screen for aortic aneurysm
- Prognosis
  - Thrombocytosis is associated with higher risk of permanent vision loss in patients with GCA
  - Permanent partial/complete vision loss in up to 20%

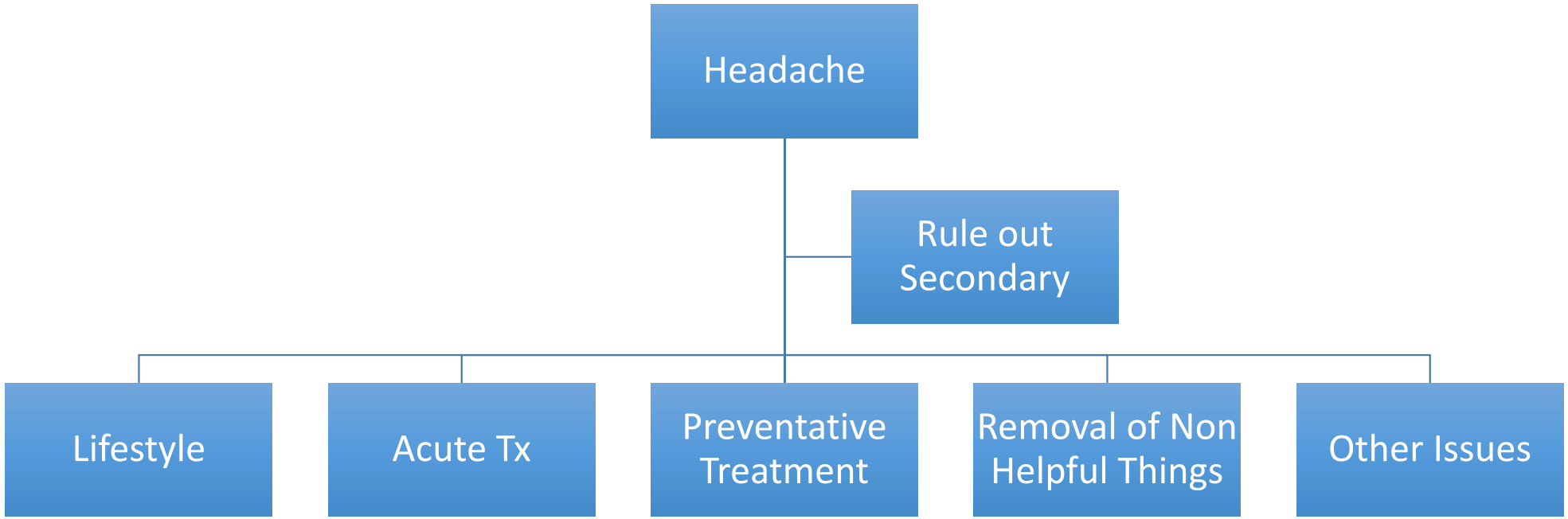
Top 5 Keys to Success!

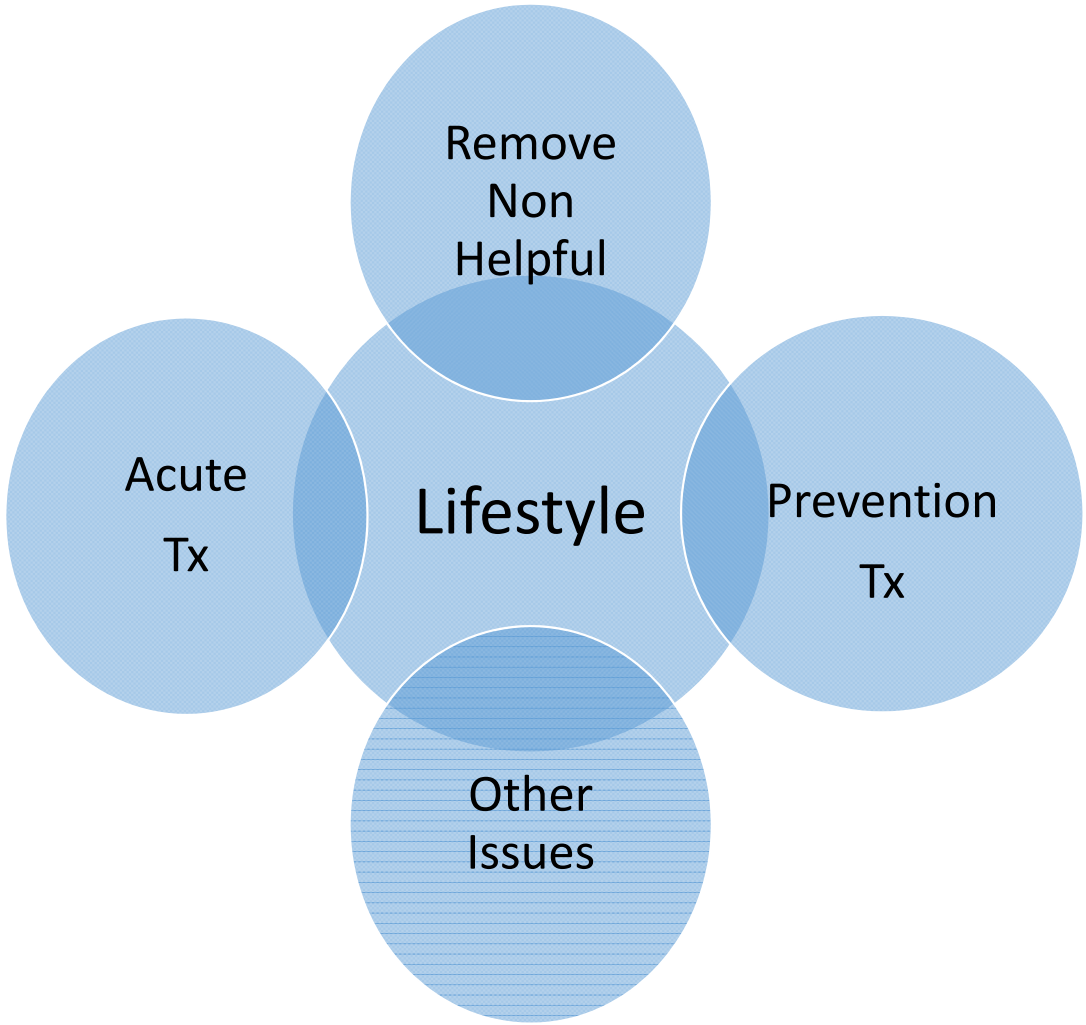
1. Rule out Secondary Causes
    - Identify contributing factors
2. Establish a diagnosis
3. Select an appropriate treatment
4. Set realistic goals and expectations
5. Follow up

Some contributing factors to consider

- OSA
- TMJD / Bruxism
- Cervical spine DDD
- occipital neuronitis
- Psychiatric comorbidities
- Caffeine ingestion
- Supine hypertension
- Abuse History
- Other pain disorders
- Medication overuse
- Obesity

Migraine management




Remove
Non
Helpful
Acute
Tx
Lifestyle
Prevention
Tx
Other
Issues

Start with a case

Case : Rebecca

- 18 y.o. with 5 year history of recurrent intermittent stereotyped headaches
- Increasing frequency for the last 18 months
  - Initially 1 per month
  - Current 3-4 headaches per week (12-16 per month)
- Bifrontal and periorbital, occasionally left temporal
  - Throbbing
- Severe pain lasting 4-6 hours
  - Pain peaks within 30 minutes
- Nausea, no vomiting, avoids light and noise, prefers to lie down
- Moderate to severe disability, missing 1-2 days of school per week and requiring bed rest with some headaches

Case : Rebecca

- Other Associated Symptoms
  - “Blurry” vision during headaches
  - X 6 months
    - wiggly lines and bright round spots over peripheral vision, bilateral
    - 10-15 minutes prior to headache onset
- Headaches triggers
  - Dehydration
  - prolonged computer work
  - sleeping in
  - menses (2 days prior to menstrual period)
- She has a past history of motion sickness, no head injury

Case : Rebecca

- Recently started using a birth control pill
- Currently on Alesse 21, no known drug allergies
- Family history of migraine (mother, maternal grandmother)
- Parents have recently divorced, no bullying in school, has a boyfriend and is sexually active
- Drinks cola every day, irregular sleep schedule, drinks < 1.5 L per day, only eats breakfast 2-3 days per week
- No tobacco, no street/recreational drugs

Case: Rebecca

- Tired OTC Analgesics
  - Acetaminophen 500 mg
  - Naproxen 220 mg
- Dimenhydrinate 50 mg
- Propranolol caused exertional SOB
- Amitriptyline caused morning somnolence

- Vitals normal, BMI 30
- General and neurological physical exams were normal

Migraine – ICHD 3

A. At least five attacks fulfilling criteria B–D

B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)

C. Headache has at least two of the following four characteristics:
   1. unilateral location
   2. pulsating quality
   3. moderate or severe pain intensity
   4. aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs)

D. During headache at least one of the following:
   1. nausea and/or vomiting
   2. photophobia and phonophobia

E. Not better accounted for by another ICHD-3 diagnosis

3-item ID Migraine™ Screener *

During the last three months, did you have any of the following with your headaches:

Item	Yes / No
You felt nauseated or sick to your stomach when you had a headache?	Yes □ No □
Light bothered you (a lot more than when you don't have headaches?)	Yes □ No □
Your headaches limited your ability to work, study or do what you need to do for at least one day?	Yes □ No □

*** A positive response on 2 of 3 questions yields a predictive value of 93%.**

Lipton RB *et al., Neurology*. 2003;61(3):375–382.

Migraine with Aura – ICHD 3

A. At least two attacks fulfilling criteria B and C

B. One or more of the following fully reversible aura symptoms:

1. visual
2. sensory
3. speech and/or language
4. motor
5. brainstem
6. retinal

C. At least two of the following four characteristics:

1. at least one aura symptom spreads gradually over 5 minutes, and/or two or more symptoms occur in succession
2. each individual aura symptom lasts 5-60 minutes
3. at least one aura symptom is unilateral
4. the aura is accompanied, or followed within 60 minutes, by headache

D. Not better accounted for by another ICHD-3 diagnosis, and transient ischemic attack has been excluded.

Chronic Migraine

A. Headache (tension-type-like and/or migraine-like) on ≥15 days per month for >3 months and fulfilling criteria B and C

B. Occurring in a patient who has had at least five attacks fulfilling criteria B-D for 1.1 Migraine without aura and/or criteria B and C for 1.2 Migraine with aura

C. On ≥8 days per month for >3 months, fulfilling any of the following
   1. criteria C and D for 1.1 Migraine without aura
   2. criteria B and C for 1.2 Migraine with aura
   3. believed by the patient to be migraine at onset and relieved by a triptan or ergot derivative

D. <u>Not better accounted for by another ICHD-3 diagnosis.</u>

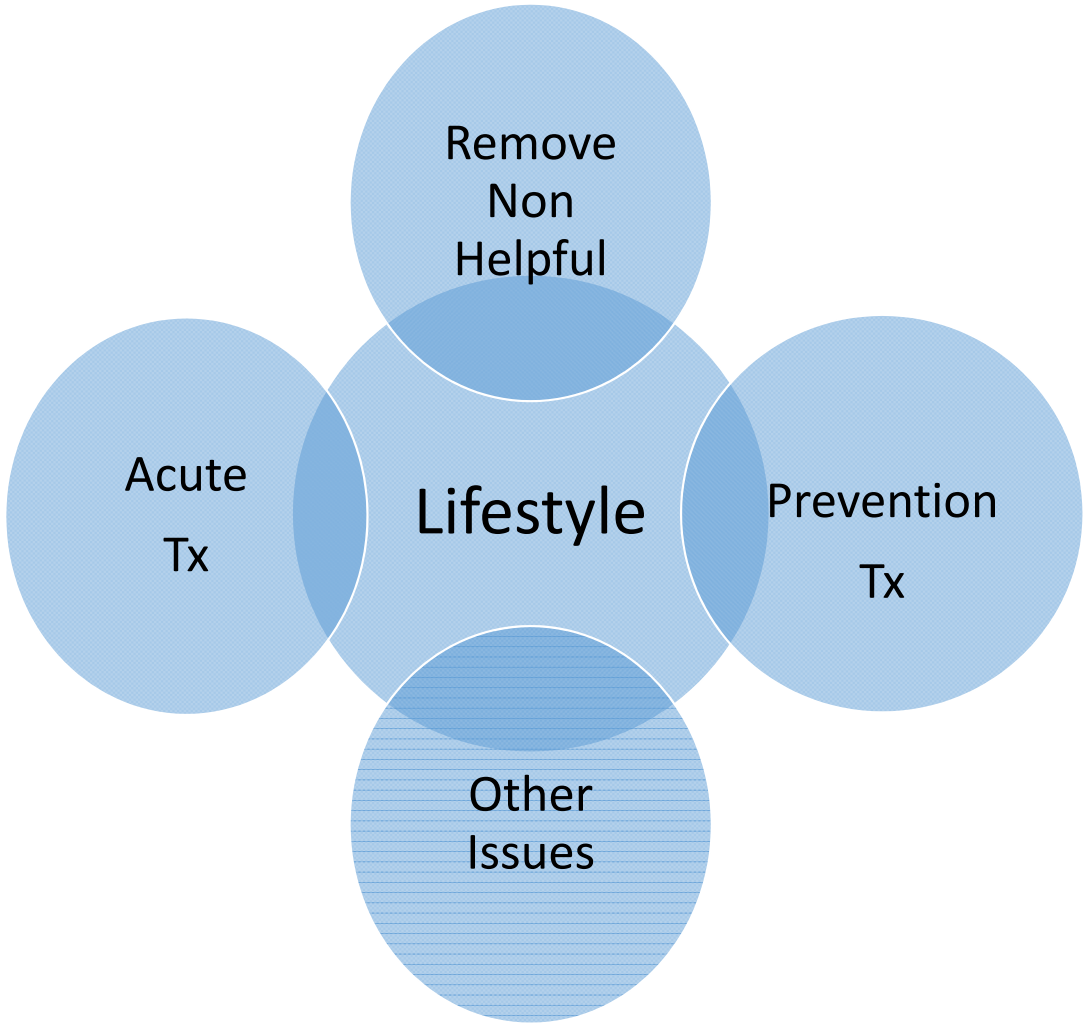
Menstrually-related migraine

A. Attacks, in a menstruating woman, fulfilling criteria for Migraine and criterion B below

B. Occurring on day 1 ± 2 (*ie*, days −2 to +3) of menstruation in at least two out of three menstrual cycles, and additionally at other times of the cycle

Other issues

- Excess caffeine
- Possibly dehydrated
- Poor Sleep
- Psychosocial stressors
- Skipping meals
- Pain peaks early
  - 30 minutes
  - Lots of Disability
- OTC not working
- On OCP – and Dx of Migraine with Aura
  - Sexually active with male partner


Remove
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Other
Issues

Lifestyle

Non Pharmacologic Treatments

Exercise

- Regular aerobic exercise
- Daily
- 20 minutes
  - Huffing and puffing

Diet

- No specific diet
- Well balanced
- Canada's Food Guide
- Fresh fruits, vegetables, all food groups
- Portion control
- No skipping meals
  - Protein at every meal
- Avoid food triggers
  - Usually figure out easily
    - Detailed diaries don't add a lot
- Mediterranean diet

Dehydration

- Headache Trigger
- Goal
  - Urine mostly colourless by mid-morning

Sleep

- Migraines are negatively affected by sleep alterations
- Too little
- Too much
- Recommend same bedtime and same awake time
  - Everyday!

Stress

- Stress is one of the biggest / most ubiquitous migraine triggers
- Elimination is impossible
- Management is key
- Mindfulness
- Meditation
- Yoga, Tai Chi
- Psychology
  - CBT, biofeedback
- Paced Breathing
- www.dawnbuse.com

Headache Diary

- Very Helpful
- Mostly for objective information on:
  - Frequency
  - Severity
  - Medication Use
- Less helpful for:
  - Triggers
- Patients are typically biased based on their most recent history
  - Few weeks

- Paper
- Electronic
  - iHeadache
  - My Migraine Buddy

Acute Treatment

Canadian Guidelines

Canadian Headache Society Guideline: Acute Drug Therapy for Migraine Headache

Irene Worthington[1], Tamara Pringsheim[3], Marek J. Gawel[1,8,9], Jonathan Gladstone[1,2], Paul Cooper[4], Esma Dilli[5], Michel Aube[6], Elizabeth Leroux[7], Werner J. Becker[3] on behalf of the Canadian Headache Society Acute Migraine Treatment Guideline Development Group

Can J Neurol Sci. 2013; 40: Suppl. 3 - S1-S3

Column A - NSAID

- Acetaminophen
  - 1000 mg
- ASA
  - 325-1000 mg
- Naproxen
  - 440-500 mg
- Ketoprophen ER
  - 200 mg
- Diclofenac
  - 50 mg
- Celecoxib
  - 100-200 mg

Column B - Triptan

- Rizatriptan
  - 5-10 mg PO or melt
- Sumatriptan
  - 25, 50, 100 mg
  - 20 mg Nasal, 6 mg S/C
- Eletriptan
  - 20, 40 mg
- Almotriptan
  - 6.25, 12.5 mg
- Zolmitriptan
  - 2.5, 5 mg PO or nasal
- Naratriptan
  - 1, 2.5 mg
- Frovatriptan
  - 2.5 mg

Column C Anti-emetic/Neuroleptic

- Metoclopromide
  - 10 mg
- Prochlorperazine
  - 10 mg PO
  - 25 mg PR
- Promethazine
  - 25 mg
- Domperidone
  - 10 mg
- Dimenhydrinate
  - 25-50 mg
- Ondansetron
  - 4-8 mg

What about Rebecca?

- **Pain peaks early!**
- Failed an OTC
  - Inadequate dose?
- Nausea
- Significant disability

- Diclofenac Potassium (Cambia)
- Sumatriptan sub cut
  - Nasal sumatriptan or zolmitriptan
- Antiemetic – Domperidone or metoclopramide

Medication Overuse

- Significant confounder
- 15 days per month for single simple analgesic
- 10 days per month for others or combinations
- Leads to central sensitization
    - Difficult to undo and takes time

Preventative Treatment

Canadian Guidelines

Canadian Headache Society Guideline for Migraine Prophylaxis

Canadian Journal of Neurological Sciences

Volume 39 Number 2 (Supplement 2) March 2012

Tamara Pringsheim[1], W. Jeptha Davenport[1], Gordon Mackie[2], Irene Worthington[3], Michel Aubé[4], Suzanne N. Christie[5], Jonathan Gladstone[6], Werner J. Becker[1] on behalf of the Canadian Headache Society Prophylactic Guidelines Development Group

Prophylactic Treatment of Migraine

- Medications
  - Supplements or nutraceuticals
  - Optimize selection based on co-morbidities or contributing factors
  - Exploit side effects based on co-morbidities or contributing factors
- Onabotulinum Toxin A (Botox)
- Nerve Blocks
- Devices
  - Cefaly, TMS
- NKOTB – anti CGRP MAb

Migraine Prevention Oral Tx

- Anti-seizure
  - Sodium divalproex
  - Topiramate
- TCA
  - Amitriptyline
  - Nortriptyline
- SNRI
  - Venlafaxine
  - Duloxetine
- CCB
  - Flunarizine
  - Verapamil
- Beta Blocker
  - Metoprolol
  - Nadolol
  - Propranolol
- ACEi/ARB
  - Ramipril, Lisinopril
  - Candesartan
- Neutraceuticals
  - Mg
  - B2
  - CoQ10
  - Butterbur
  - Feverfew

What about Rebecca?

- Failed Amitriptyline
- Failed Propranolol

- Could Try Nortriptyline
- Likely Topiramate
  - 25 mg QHS for 2-4 weeks
  - 50 mg QHS for 4 weeks
  - Introduce in AM in similar fashion if needed
- I try almost everyone on Mag, Vit B2, ± CoQ10

Plan B and C for Rebecca

Migraine Prevention – Onabotulinum Toxin a - Botox

- Onabotulinum Toxin Type A
- RCT evidence of effectiveness – PREEMPT Trials
- Chronic Migraine
- 155 Units of Onabotulinum Toxin Type A injected
  - 31 sites: Head, Neck and Shoulders

Newest addition to migraine prevention

Anti CGRP MAbs

4 currently

- Erenumab
  - Amgen, Novartis in Canada
- Eptinezumab
  - Alder
- Galcanezumab
  - Lily
- Fremanezumab
  - TEVA

CGRP Receptor

CGRP

Anti CGRP mabs

- Bottom Line
- All showed significant improvement over placebo for episodic and chronic migraine
  - Reduction in migraine days
  - Reduction in acute medication treatment
  - Decreased disability
- 50% responder rates
  - 25-60%
- 75% responder rates
  - 10-40%
- Few super responders

Nerve Blocks

Migraine Prevention - Stimulator

Neurology®

Migraine prevention with a supraorbital transcutaneous stimulator: A randomized controlled trial

Jean Schoenen, Bart Vandersmissen, Sandrine Jeangette, et al.

Neurology 2013;80;697-704 Published Online before print February 6, 2013
DOI 10.1212/WNL.0b013e3182825055

Transcranial magnetic stimulation

Other issues

- **Excess caffeine**
- Possibly dehydrated
- Poor Sleep
- Psychosocial stressors
- Skipping meals
- Pain peaks early
  - 30 minutes
  - Lots of Disability
- OTC not working
- **On OCP – and Dx of Migraine with Aura**
  - **Sexually active with male partner**

Excess Caffeine

- Caffeine has pain relieving properties
- Headache/migraine relieving properties
- Component of OTC combo analgesics
- Therefore it can be overused
- Medication Overuse Headache

- Gradual cessation
  - caffeine withdrawal is unpleasant and a migraine trigger
  - Over 1-2 months

OCP and Migraine

- Migraine with Aura
  - Doubles stroke risk
  - Women only
    - Women's Health Study
- Young woman with no vascular risk factors have a low stroke risk
- OCP and stroke risk
  - Best evidence from older OCP data (100 μg Estrogen era)
- Migraine with Aura + smoking + OCP
  - NO GO
- Migraine with Aura + HRT
  - NO GO

Rebecca

- Followed lifestyle recommendations
- Cambia + Sumatriptan + Metacloperamide
  - Worked really well
- Topiramate failed after about 6 months
- Onabotulinum Toxin A
  - Reduced headache frequency to 4-6 per month
  - All responsive to acute treatment
- Weaned off Caffeine
- She and her boyfriend elected to use barrier methods
  - IUD

Top 5 Keys to Success!

1. Rule out Secondary Causes
    - Identify contributing factors
2. Establish a diagnosis
3. Select an appropriate treatment
4. Set realistic goals and expectations
5. Follow up

Rebecca - continued

- Does well on the treatment recommendations

- Presents to the local emergency department
- Prolonged headache
- Started as her usual migraine
- Did not respond to her acute treatments
- Has had a headache for 4 days
  - Functioning poorly
- No new illness, not pregnant, no new meds, normal exam

Status migrainosis

Description:

- A debilitating migraine attack lasting for more than 72 hours.

Diagnostic criteria:

A. A headache attack fulfilling criteria B and C

B. Occurring in a patient with 1.1 *Migraine without aura* and/or 1.2 *Migraine with aura*, and typical of previous attacks except for its duration and severity

C. Both of the following characteristics:
   1. unremitting for >72 hours
   2. pain and/or associated symptoms are debilitating

D. Not better accounted for by another ICHD-3 diagnosis.

Notes:

- Remissions of up to 12 hours due to medication or sleep are accepted

Approach

- Outpatient strategy
  - NSAIDS +/- long acting Triptan
  - Steroid Taper
- Emergency Department strategy
  - Parentral access and monitoring available

Outpatient

- NSAID +/- Long Acting Triptan

- Naproxen 500 mg BID for 14 days
- Nabumetone 500 mg PID for 14 days
- Mefanamic Acid 500 mg TID for 14 days

- Frovatriptan 2.5 mg BID for 5 days

Outpatient

- Steroids

- Prednisone
  - 60 mg for 3-5 days
  - 50 mg 2d, 40 mg 2d, 30 mg 2d, 20 mg 2d, 10 mg 2 d, 5 mg 2d, stop

- Dexamethasone
  - 10 mg 2 d, 8 mg 2d, 6 mg 2d, 4 mg 2d, 2 mg 2d, 1 mg 2d, stop

- Side effects
- Consider PPI or H2 Blocker

Emergency Department - ParentraL

- First Line
  - Fluids
    - NS 1-2 L
  - Magnesium Sulfate 1 g
  - Toradol 30 mg
  - Benadryl 25 mg
  - Maxeran 10 mg
- Second line
  - ECG for QT
  - Dexamethasone 10 mg IV
  - Stemetil 10 mg IV
  - DHE
    - 0.5 mg in 50 mL D5W x 10 min
      - If no rise SBP >20 mmHg x 15 min
    - 0.5 mg in 50 mL D5W x 10 min
- Third Line
  - Repeat Toradol
    - Timing
  - ECG for QT
  - Haldol
    - 5 mg in 500 cc NS
      - Over 1 hr

Dexamethasone can be given as first line
Lorazepam 1 mg IV can be added to second or third line
DHE can be added to first line

Let’s discuss your cases

Thank you for your attention

Questions?

Concerns?

Comments?

Discussion?

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