



Migraine, menopause and HRT

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Declarations of interest: Asarina Pharma, Eli Lilly, Novartis, and Theramex

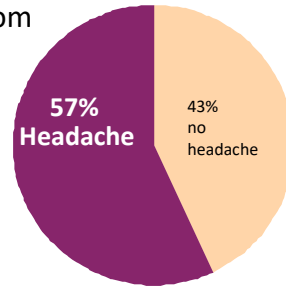


Overview

- Epidemiology
- Diagnosing headaches
- Relationship between menopause and migraine
- HRT for women with migraine
- Practical recommendations

Headache in a Menopause Clinic

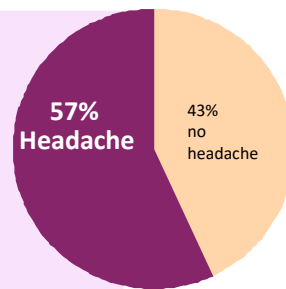
Women do not spontaneously report headache as a menopause symptom



MacGregor EA, Barnes DS. *Climacteric* 1999;2:218-23

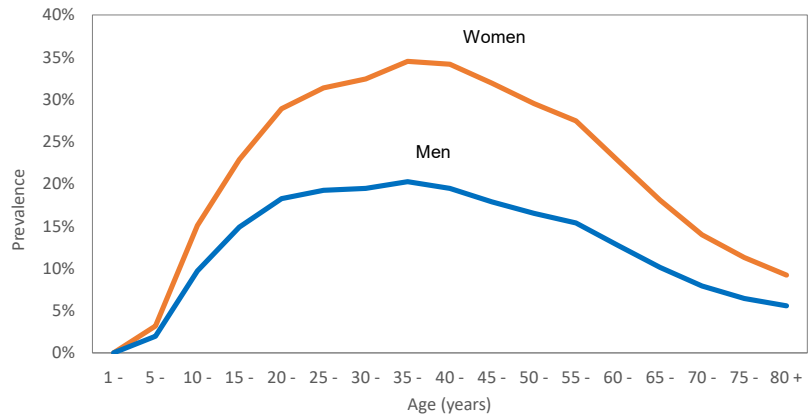
Headache in a Menopause Clinic

29% migraine
10% daily headache



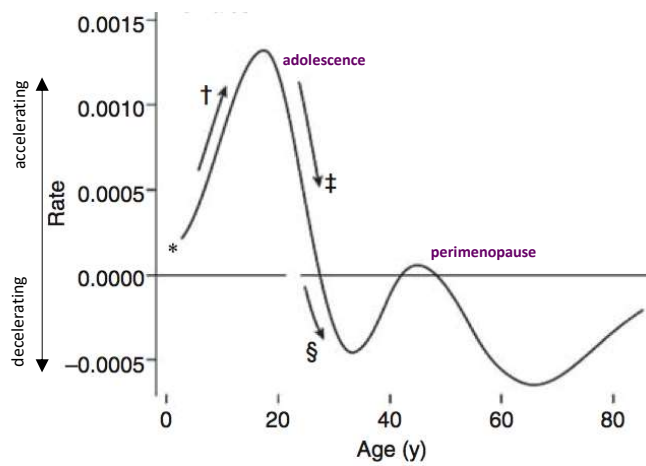
MacGregor EA, Barnes DS. *Climacteric* 1999;2:218-23

Prevalence of migraine



Global Burden of Disease Study 2017 (GBD 2017), IHME, Seattle, WA: 2018
Available from <http://ghdx.healthdata.org/gbd-results-tool>

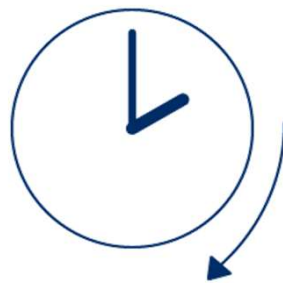
Rate of change of migraine prevalence over age continuum in females



Victor et al. *Cephalalgia* 2010;30(9):1065-72



Diagnosing headaches



**Headaches last 4-72 hours
'fine' between attacks**

Do you have the following with your headaches?

- Light bothers you more than usual?
- Your headaches limit your ability to work, study or do what you need to do for at least one day?
- You feel nauseated or sick?

Lipton et al Neurology 2003;61:375-82

Do you have the following with your headaches?

- Light bothers you more than usual?
- Your headaches limit your ability to work, study or do what you need to do for at least one day?
- You feel nauseated or sick?

Positive predictive value for migraine:

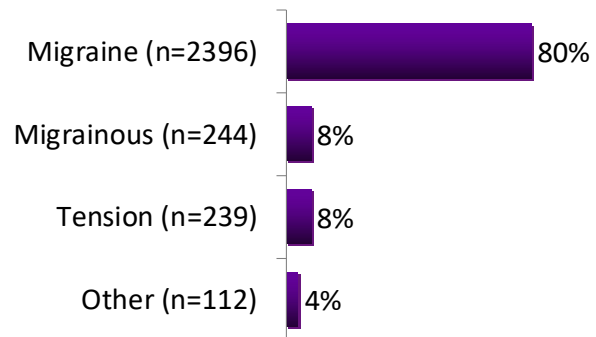
2 positive answers = 93%

3 positive answers = 98%

Lipton et al Neurology 2003;61:375-82

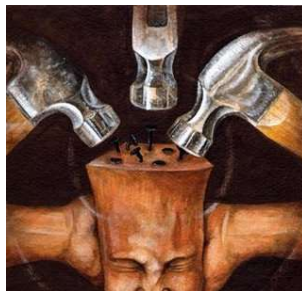
Sinus headache or migraine?

Correct diagnosis of 2991 patients with previous diagnosis of sinus headache

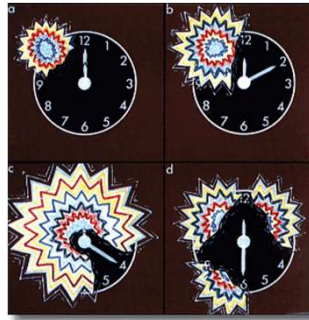


Schreiber et al. Arch Intern Med 2004;164:1769-72

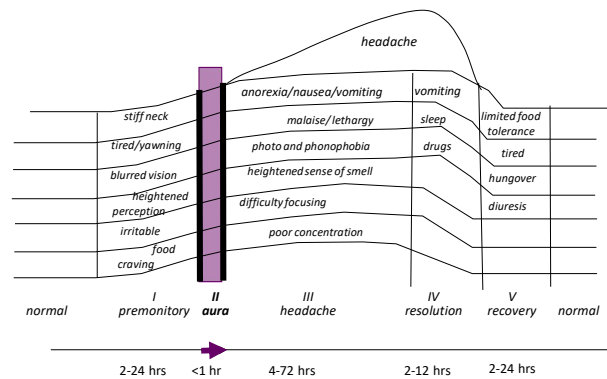
Migraine without aura 70-80% attacks



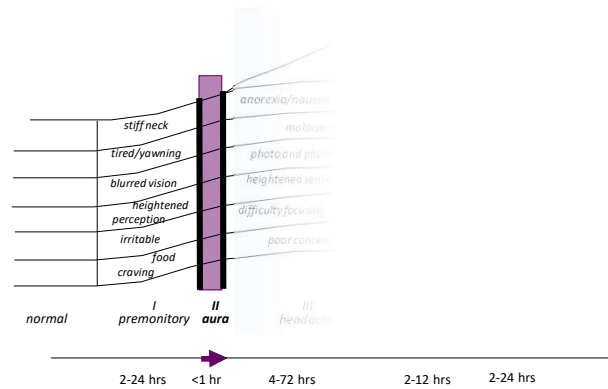
Migraine with aura 20-30% attacks



Migraine aura

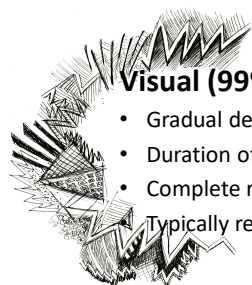


Migraine aura without headache 1% attacks



Blau JN Lancet 1992;339:1202-7

Migraine aura



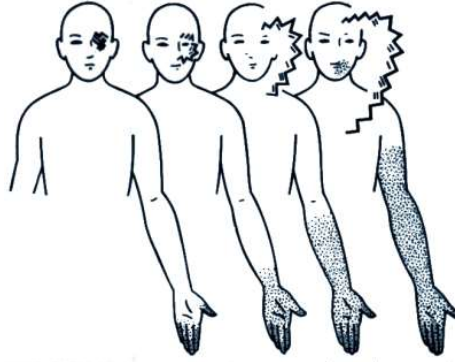
Visual (99%) +/- sensory +/- speech

- Gradual development
- Duration of <1 hr (typically 20-30 mins)
- Complete reversibility

Typically resolves BEFORE headache

Sensory aura

rarely occurs in
absence of visual
aura



Diagnosing typical migraine aura

- Do you ever have visual disturbances that
 - **Start** before a headache?
 - **Last** less than one hour?
 - **Resolve** before the onset of headache?
 - **Persist** with eyes closed?



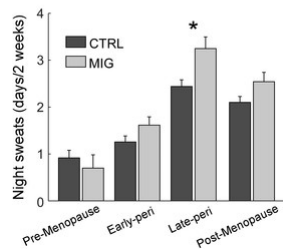
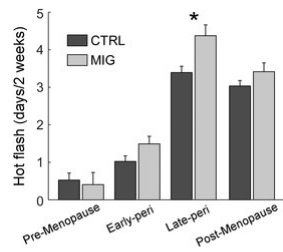
MacGregor EA. J Fam Plann Reprod Health Care 2016;42:380-6

Migraine and menopause

Migraine
is a risk factor for
onset of menopause
symptoms

HR 1.11
[95% CI 1.07-1.16]
p<0.0001

Sabia et al. *Maturitas* 2008;60:108-121



Migraine predicts
more frequent
vasomotor
symptoms

Maleki et al. *Annals of Neurology* 2019;85:865-74

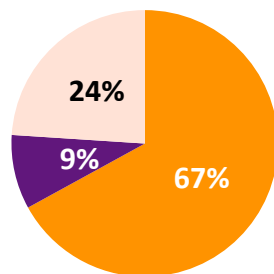
More frequent vasomotor symptoms associated with:

- severe depression
- anxiety
- sleep disturbance

Maleki et al. *Annals of Neurology* 2019;85:865-74

Effect of type of menopause

natural
■ improvement ■ worsening
■ no change

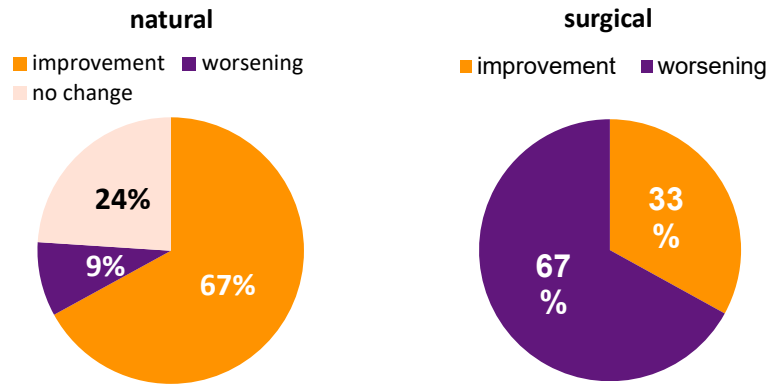


Improvement = >50% reduction in the frequency of attacks

- Prevalence improves with time since last menstrual period
- Mirrors decline in ovarian function

Neri et al. *Maturitas* 1993;17:31-7, Wang et al. *Headache* 2003;43:470-8

Effect of type of menopause



Improvement = >50% reduction in the frequency of attacks
Physiological vs. surgical menopause: P = 0.003

Neri et al. *Maturitas* 1993;17:31-7, Wang et al. *Headache* 2003;43:470-8

Migraine and HRT

Route of delivery

Oral estrogen

- ↑ frequency of attacks
- ↑ days with headache

Transdermal estrogen

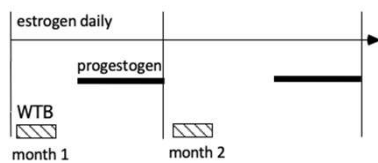
- no change



Nappi RE et al. *Maturitas* 2001;38:157-63

Regimen

Cyclical combined



Continuous combined



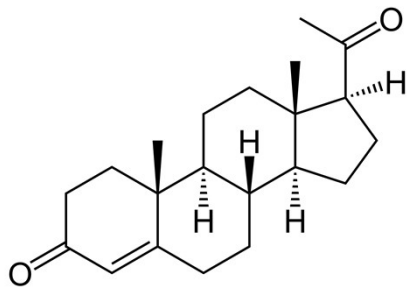
Continuous progestogens Perimenopause



LNG-IUS

- Provides contraception
- Manages bleeding

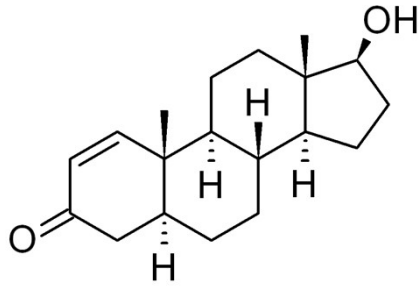
Continuous progestogens Postmenopause



Micronised progesterone

- breast 'neutral'
- sedative
- anxiolytic

Testosterone



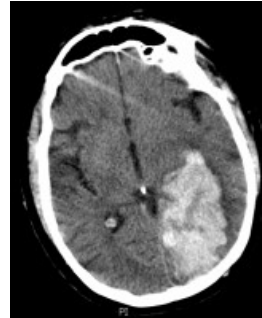
Greenblatt RB and Bruneteau DW. *J Am Geriatr Soc* 1974;22:186-90
Moehlig RC. *J Mich State Med Soc* 1955;54:577-9
Glaser R et al. *Maturitas* 2012; 71: 385-8

What about aura?

Migraine aura and ischemic stroke

Migraine aura is a marker for increased risk of ischemic stroke

Age matters



Risk of ischemic stroke in women with migraine

Age and type of migraine

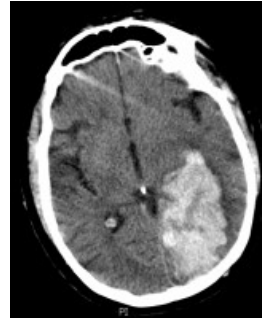


*p<0.01 Migraine (n=119,017) vs. control no migraine (n=119,017)

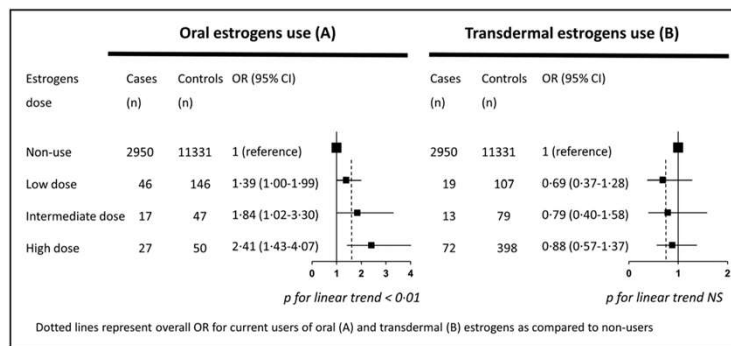
Migraine aura and ischemic stroke

Migraine aura is a marker for increased risk of ischemic stroke

Additional risk factors matter



Risk of ischemic stroke oral vs transdermal estrogen



SIGNIFICANT INCREASED RISK

NO INCREASED RISK

low: 51 mg oral or <50 µg transdermal
intermediate: 1.5 mg oral or 50 µg transdermal
high: 22 mg oral or >50 µg transdermal

Canonica M et al. *Stroke* 2016;47:1734-41

Practical recommendations

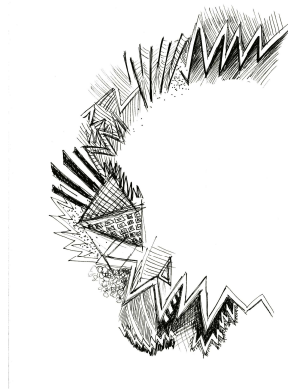
Pre-existing/new onset migraine



Migraine **with** or **without** aura does NOT contraindicate **transdermal** estrogen

Practical recommendations

New onset migraine with aura



- exclude TIA
- reassure
- change to transdermal
- lowest effective dose of estrogen to control vasomotor symptoms
- consider non-hormonal options if aura does not resolve or increases in frequency

Alternatives to HRT (also help migraine)

- SSRI
 - Escitalopram 10-20mg daily
- SNRI
 - Venlafaxine 37.5-150mg daily
- Alpha agonist
 - Clonidine 50-75mcg twice daily

Alternatives to HRT (also help migraine)



- Exercise
- Weight loss
- Cognitive Behavioural Therapy

Further reading

Post Reproductive Health
2018;24(1):11-18

Chronic conditions and menopause

Migraine, menopause and hormone replacement therapy

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2018, Vol. 24(1) 11-18
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Abstract

Perimenopause marks a period of increased migraine prevalence in women and many women also report troublesome vasomotor symptoms. Migraine is affected by fluctuating estrogen levels with evidence to support estrogen 'withdrawal' as a trigger of menstrual attacks of migraine without aura, while high estrogen levels can trigger migraine aura. Maintaining a stable estrogen environment with estrogen replacement can benefit estrogen-withdrawal migraine particularly in women who would also benefit from relief of vasomotor symptoms. In contrast to contraceptive doses of ethinylestradiol, migraine aura does not contraindicate use of physiological doses of natural estrogen. In women with migraine with or without aura, using only the lowest doses of transdermal estrogen necessary to control vasomotor symptoms minimizes the risk of unwanted side effects. Cyclical progestogens can have an adverse effect on migraine so continuous progestogens, as provided by the levonorgestrel intrauterine system or in continuous combined transdermal preparation, are preferred. There are no data on the effect of micronized progesterone on migraine, either cyclical or continuous. Non-hormonal options for both conditions are limited but there is evidence of efficacy for escitalopram and venlafaxine.

Keywords

Estrogen, hormone replacement therapy, menopause, migraine, vasomotor symptoms