

# **Cluster Headache and Paroxysmal Hemicrania**

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International Headache Society

# Cluster Headache and Paroxysmal Hemicrania



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# Disclosure

- **Research**
  - Mayo Clinic, NINDS, Advanced Bionics, Medtronic, Advanced Neurostimulation Systems, Alexza, St Jude
- **Consulting**
  - Allergan, Ortho-McNeil, GSK, Merck, Eli Lilly, Neuralieve, Solvay

## Objectives

- Identify the diagnostic criteria, clinical features, and pathogenesis of cluster headache and chronic paroxysmal hemicrania
- Develop evidence-based approach to the treatment of cluster headache and chronic paroxysmal hemicrania
- Identify emerging treatment options for medically intractable cluster headache and chronic paroxysmal hemicrania

## IHS Classification: Cluster HA and Other Trigeminal Autonomic Cephalalgias

### 3.1 Cluster headache

3.1.1 Episodic cluster HA

3.1.2 Chronic cluster HA

### 3.2 Paroxysmal hemicrania

3.2.1 Sporadic paroxysmal  
hemicrania

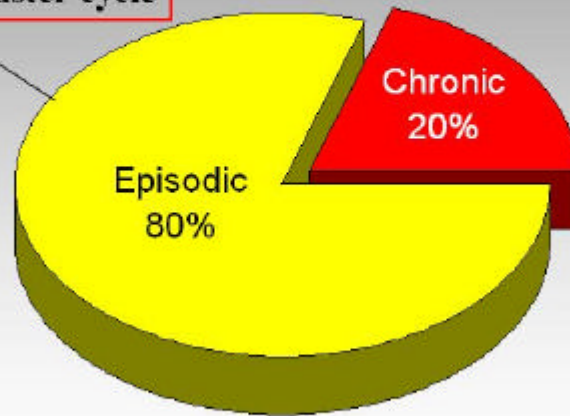
3.2.2 Chronic paroxysmal hemicrania

## IHS Classification: Cluster HA and Other Trigeminal Autonomic Cephalalgias

- 3.3 Short-lasting unilateral  
neuralgiform HA attacks with  
conjunctival injection and tearing  
(SUNCT)
- 3.4 Probable trigeminal autonomic  
cephalgia

## Cluster Headache

**27% only 1 cluster cycle**





## Cluster Headache Diagnostic Criteria

- At least 5 attacks
- Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15-180 minutes if untreated
- Headache is accompanied by at least one of the following:
  - ipsilateral conjunctival injection and/or lacrimation
  - ipsilateral nasal congestion and/or rhinorrhoea
  - ipsilateral eyelid oedema
  - ipsilateral forehead and facial sweating
  - ipsilateral miosis and/or ptosis
  - a sense of restlessness or agitation
- Attacks have a frequency from one every other day to 8 per day
- Not attributed to another disorder

# Cluster headache Epidemiology

- Prevalence 240/100,000
  - Multiple sclerosis  
177/100,000
- Incidence 9.8/100,000
  - Multiple sclerosis  
7.5/100,000
- Mean age of onset 31.5  
years (27-37)
- Male:Female ~ 3:1



Swanson JW et al *Neurology* 1994; D'Alessandro R et al *Cephalalgia* 1986; Elkjorn K *Headache* 1978; Rasmussen BK Thesis 1994; Sjaastad O et al *Cephalalgia* 2003; Kudrow L, *Cluster Headache* 1980; Manzoni GC, *Cephalalgia* 1998

## Cluster and other Trigeminal Autonomic Cephalgias

Severe, short-lasting,  
exclusively unilateral,  
*trigeminal* (orbital - temporal  
pain) *pain*.

Prominent attack-related  
cranial *autonomic*  
(*parasympathetic*) features.

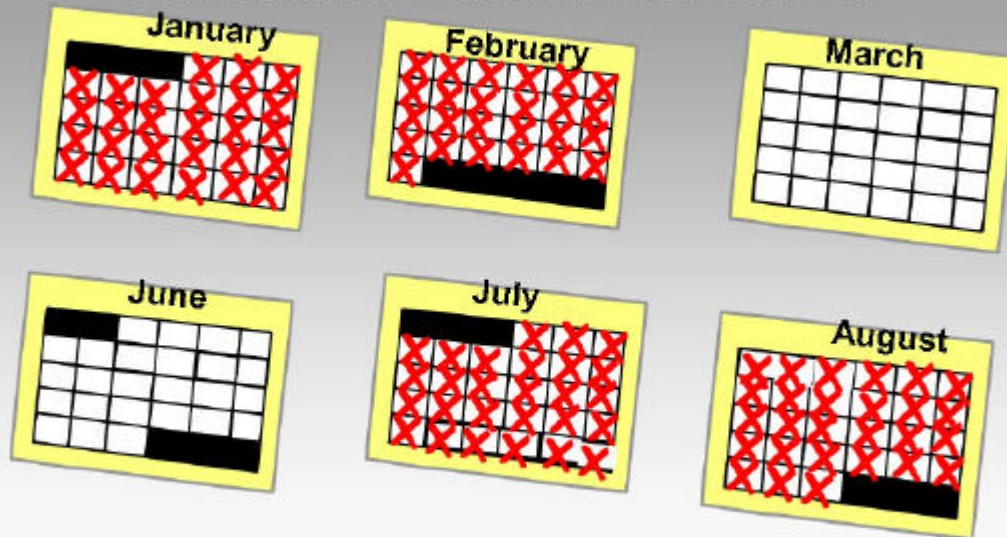


## Clinical Manifestations

- **Attack profile**
  - Pain and associated cranial autonomic symptoms
- **Periodicity**
  - Circannual
  - Circadian



## Circannual Periodicity Attack and Remission Phases



Adapted from Neurology Ambassador Program 2003  
Waldenlind E. *Cluster Headache and Related Conditions*. 1999.  
Kudrow L. *Cephalalgia*. 1987.

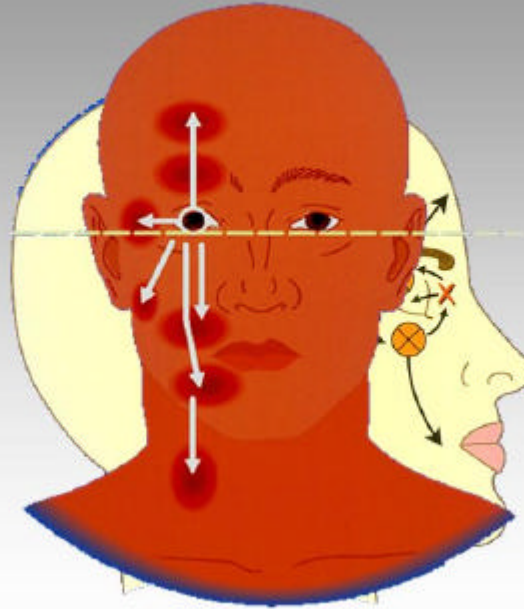
## Circadian Periodicity

- 1 to 3 attacks daily (up to 8 attacks/day)
- Peak time periods



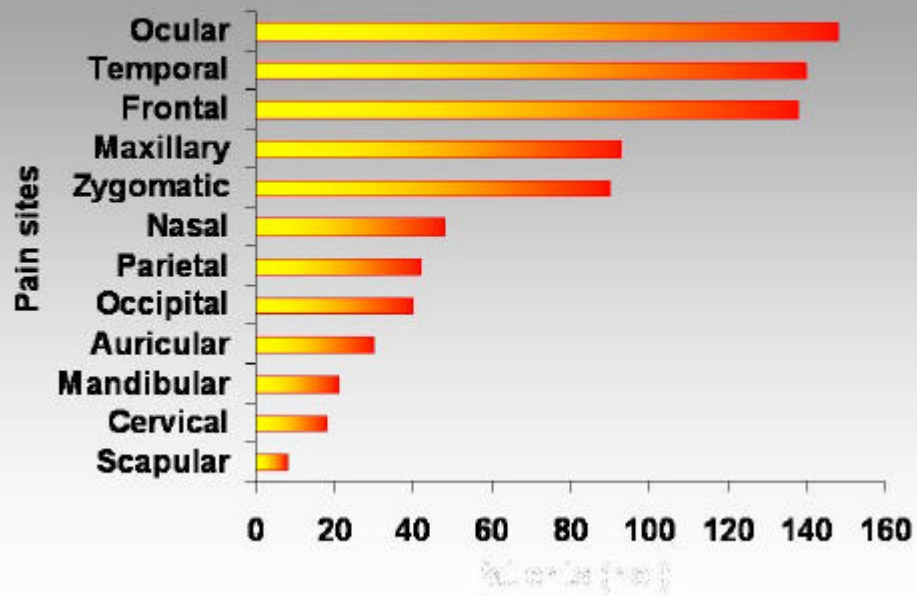
With permission Neurology Ambassador Program 2003  
Trucco M, Waldenlind E. *Cephalalgia*. 1993; Chervin RD et al. *Neurology*. 2001.

## Pain Location



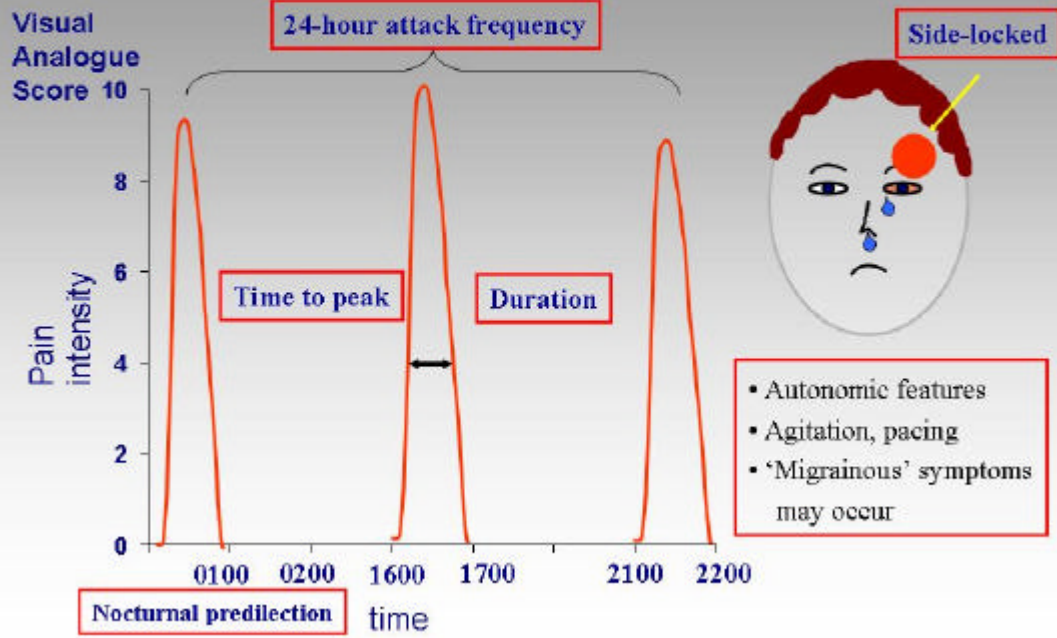
Raskin NH: Headache 2<sup>nd</sup> Ed p230

## Location of Maximal Pain During Cluster Attacks in 180 Patients





# Headache Phenotype



## Cluster headache Associated Clinical Features

- Motor restlessness (93%)
- Lacrimation (91%)
- Conjunctival injection (77%)
- Nasal congestion (75%)
- Ptosis or eyelid swelling (74%)
- Rhinorrhea (72%)
- Horner's syndrome (30%)
- Nausea (50%)/Vomiting (23%)
- Photophobia (56%)
- Phonophobia (43%)
- Aura (14%)—mostly visual, 36% of these also had migraine

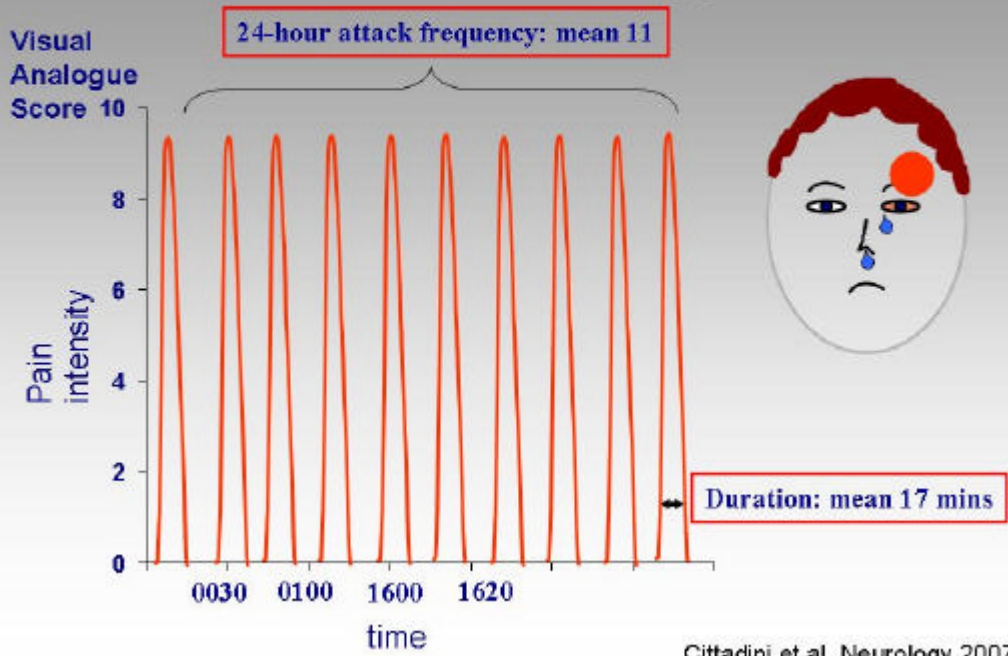
## Cluster Headache Comorbidities and Mimics

- Obstructive sleep apnea (58%)
  - 8-fold increased risk
  - 24X (BMI > 24)
  - 13X (Age >40)
- Tobacco (85%) and alcohol abuse
- Arterial dissection
- Sinusitis
- Glaucoma
- Cervical cord lesions
- Intracranial lesions
  - Pituitary / parasellar

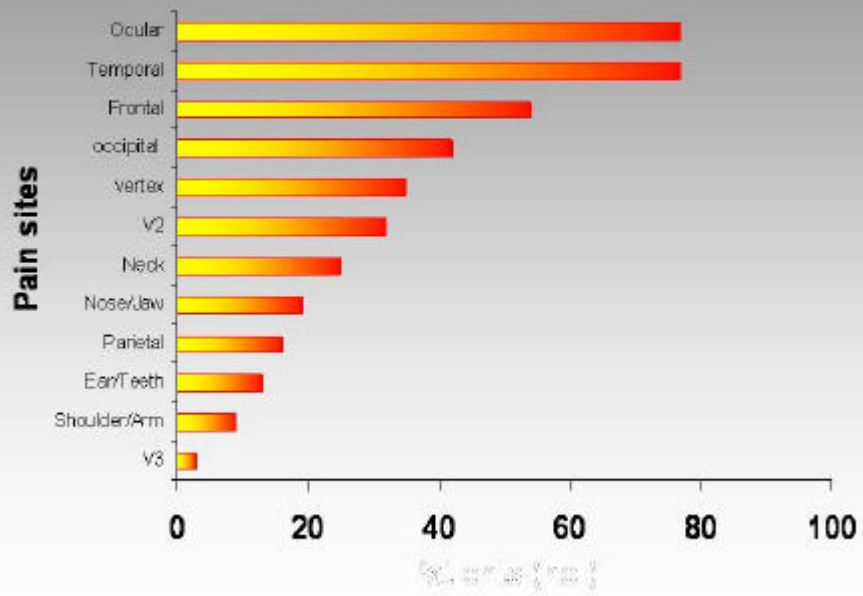
## Trigeminal Autonomic Cephalgias

<b>Feature</b>	<b>PH</b>	<b>SUNCT</b>	<b>Cluster</b>
Sex F:M	2:1	1:2	1:3
Attack duration	~15 mins	~ 1 min	60 mins
Attack frequency	11	~ 30	1
Treatment of choice	Indomethacin	Lamotrigine	Verapamil

# Chronic Paroxysmal Hemicrania Headache Phenotype



## Location of Maximal Pain During CPH Attacks in 31 Patients



Cittadini et al. Neurology 2007

# Chronic Paroxysmal Hemicrania

## Age at onset

- Mean 36 yrs (5-68)

## Behaviour

- Agitation/restlessness (80%) or aggression (26%)

## Background pain

- 18 (58%)

## Migrainous symptoms

- Phonophobia (64%)
  - ◆ ipsilateral (25%)
- Photophobia (64%)
  - ◆ ipsilateral (40%)
- Osmophobia 7 (22%)
- Nausea/vomiting 12 (38%)
- Motion sensitivity 16 (51%)

# Paroxysmal Hemicrania



## Current Criteria

- A. At least 20 attacks fulfilling criteria B-D
- B. Attacks of unilateral *orbital, supraorbital or temporal pain* lasting 2-30 minutes
- C. Headache is accompanied by at least one of the following:
  1. ipsilateral conjunctival injection and/or lacrimation
  2. ipsilateral nasal congestion and/or rhinorrhoea
  3. Ipsilateral eyelid oedema
  4. Ipsilateral forehead and facial sweating
  5. Ipsilateral miosis and/or ptosis
- D. Attacks frequency > 5/d for more than half of the time, although periods with lower frequency may occur
- E. Attacks are prevented completely by therapeutic doses of indomethacin
- F. Not Attributed to another disorder

## Proposed Criteria

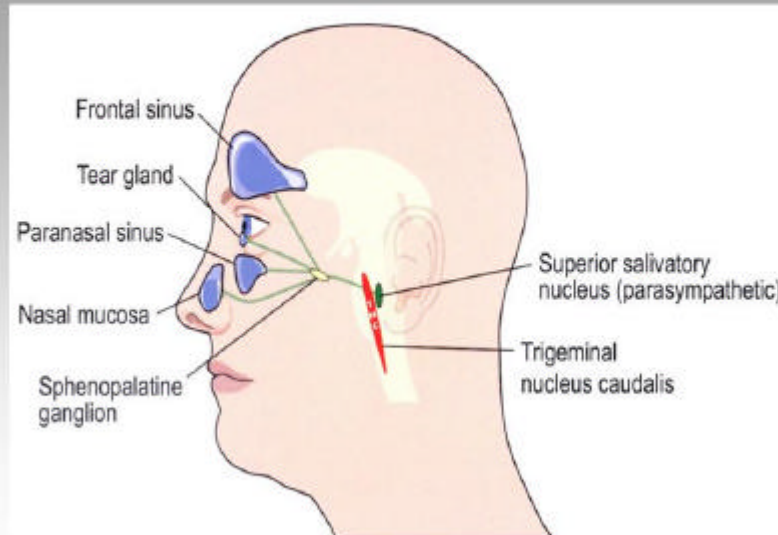
- B. Attacks of unilateral *head pain* lasting 2-30 minutes
- 6. *Ipsilateral forehead and facial flushing (54%)*
- 7. *Ipsilateral sense of aural fullness and/or peri-aural swelling (38%)*



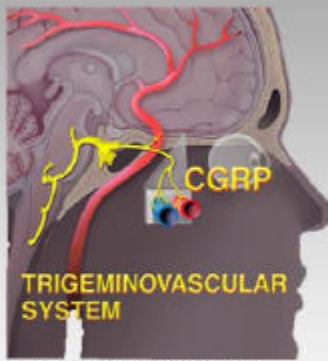
# Paroxysmal Hemicrania Treatment

- **Indomethacin**
  - 25mg tid with meals; 150mg often required
  - Dose can be lowered to find lowest effective dose
  - Intermittent discontinuation useful as remissions occur
- **Other treatments reported effective [anecdotal cases]**
  - (COX-2 inhibitors, other NSAIDs, AEDs [gabapentin, topiramate], acetazolamide, verapamil)

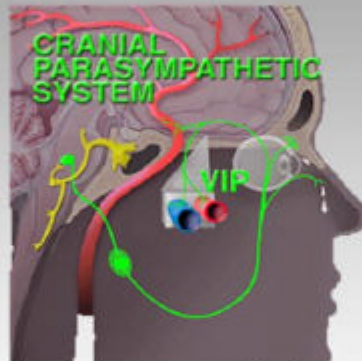
## Pathogenesis of Pain and Autonomic Features



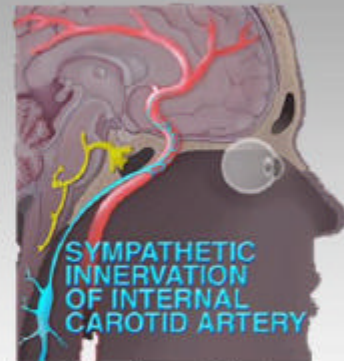
## Pathogenesis of Pain and Autonomic Features



Trigeminovascular activation (CGRP)



Cranial parasympathetic activation (VIP)

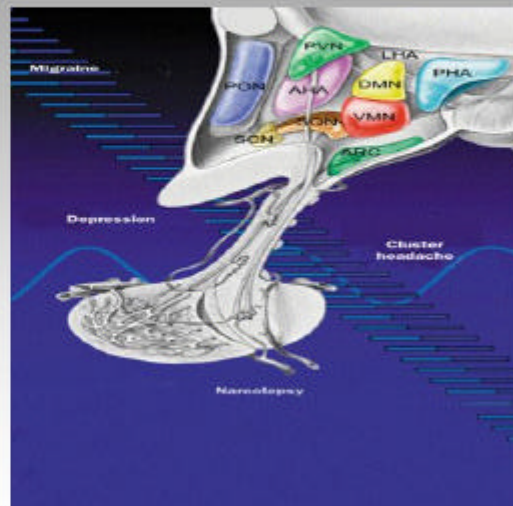


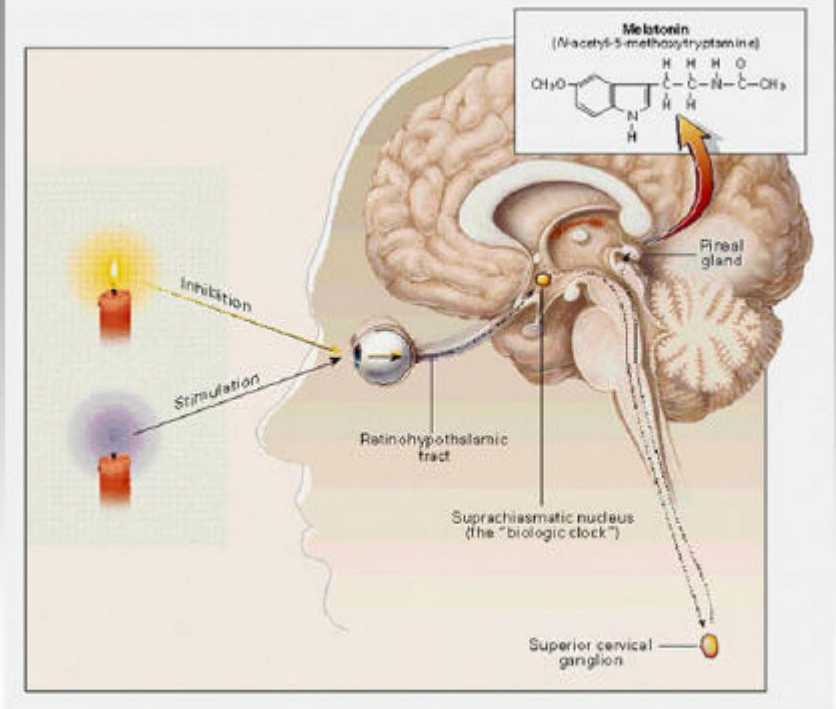
Internal carotid artery dilation (cavernous)

With permission Neurology Ambassador Program 2003  
Edvinsson L, Goadsby PJ. *Eur J Neurol.* 1998.

## Periodicity: Dysfunctional Hypothalamic Pacemaker

- Disordered circadian rhythms (melatonin, cortisol, etc)
- Circannual and circadian rhythmicity
- Seasonal predilection of cluster periods
- Functional imaging

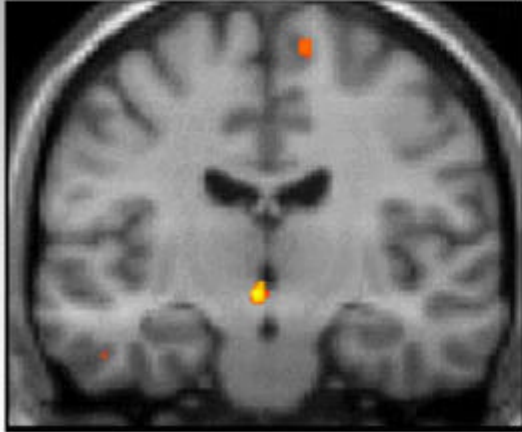




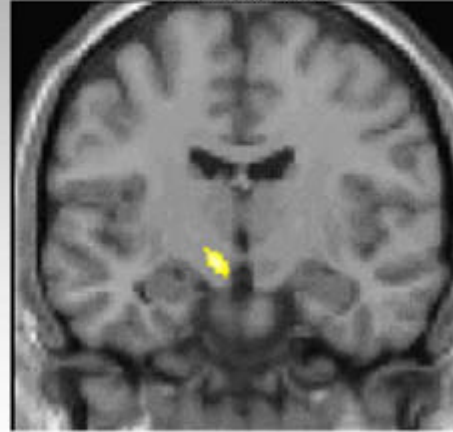
Brzezinski. N Engl J Med. 1997

## Hypothalamus Abnormal – Function and Structure

Function



Structure



With permission, Neurology Ambassador Program 2003:  
May A et al. *Lancet*. 1998; *Nat Med*. 1999.



## Therapy of Cluster HA

Acute  
therapy

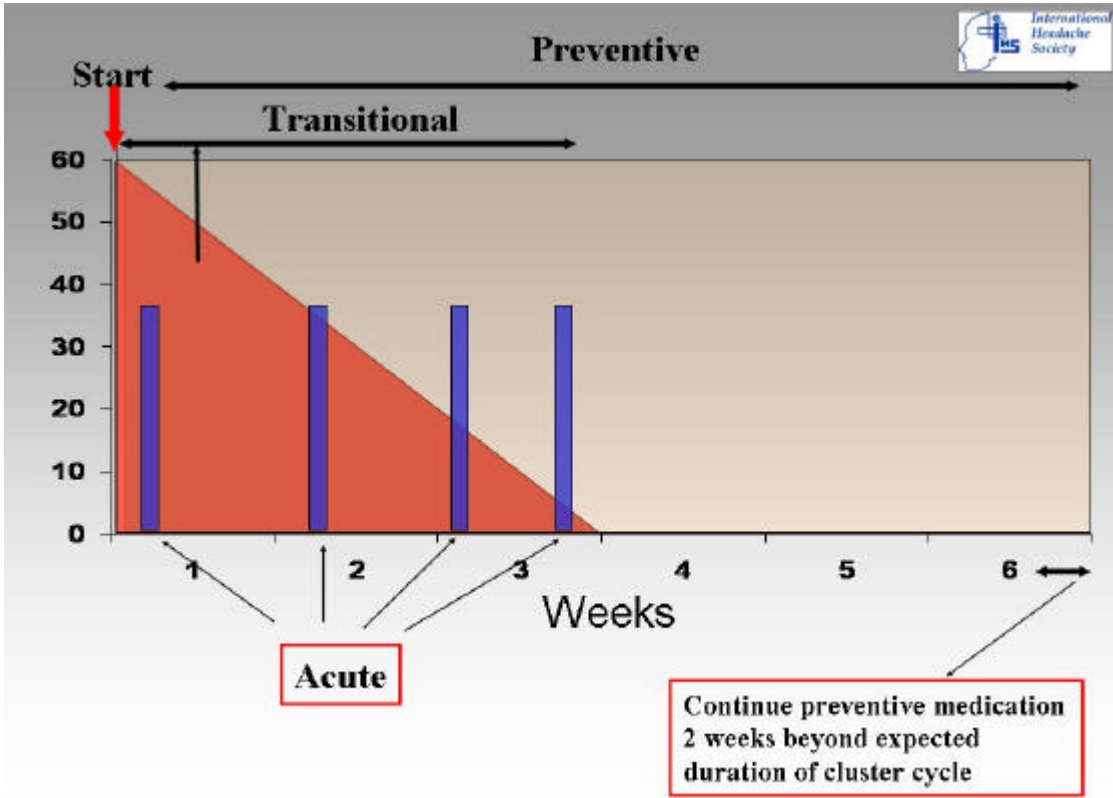


Preventive  
therapy

Transitional  
therapy

**Avoid triggers: Alcohol, nitroglycerin, altitude, sildenafil**





## Trigeminal Autonomic Cephalgias Evidence-Based Treatment

Therapy	Treatment of choice		
	Cluster headache	Paroxysmal hemicrania	SUNCT syndrome
<b>Acute</b>	100% O <sub>2</sub> , 15 l/min (A)	None	None
	Suma 6 mg s.c. (A)		
	Suma 20 mg nasal (A)		
	Zolmi 10 mg nasal (A)		
	Zolmitriptan 10 mg oral (B)		
	Lidocaine nasal (B)		
	Octreotide (B)		

A denotes effective, B denotes probably effective, C denotes possibly effective.  
(suma=sumatriptan; zolmi=zolmitriptan)

## Trigeminal Autonomic Cephalgias Evidence-Based Treatment

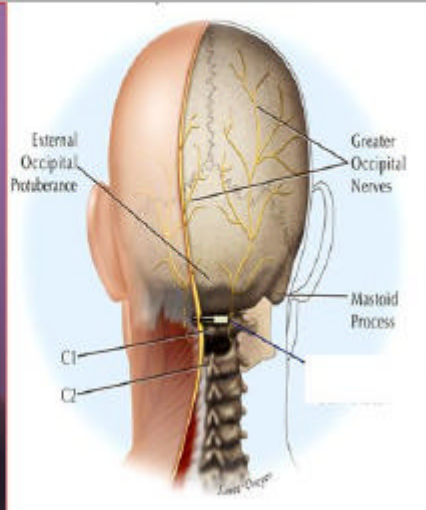
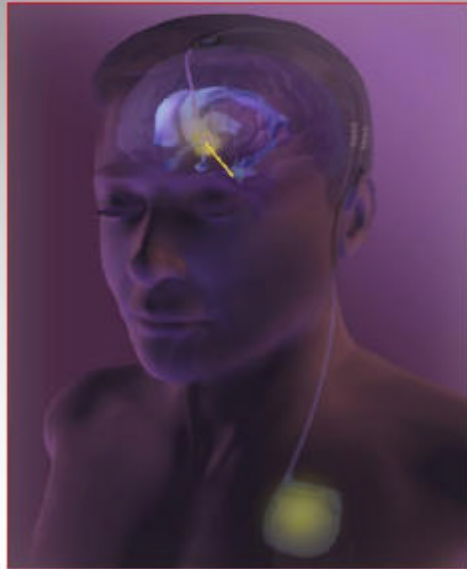
Therapy	Treatment of choice		
	Cluster headache	Paroxysmal hemicrania	SUNCT syndrome
Preventative	Verapamil (A)	Indomethacin (A)	Topiramate (B) *
	Corticosteroids (A) (PO/ONB)*	Verapamil (C)	Lamotrigine (C)
	Lithium carbonate (B)	NSAIDs (C)	Gabapentin (C) *
	Methysergide (B)		
	Topiramate (B)		
	Ergotamin tartrate (B)		
	Valproic acid (C)		
	Melatonin (C)		
	Gabapentin (C) *		

A denotes effective, B denotes probably effective, C denotes possibly effective.

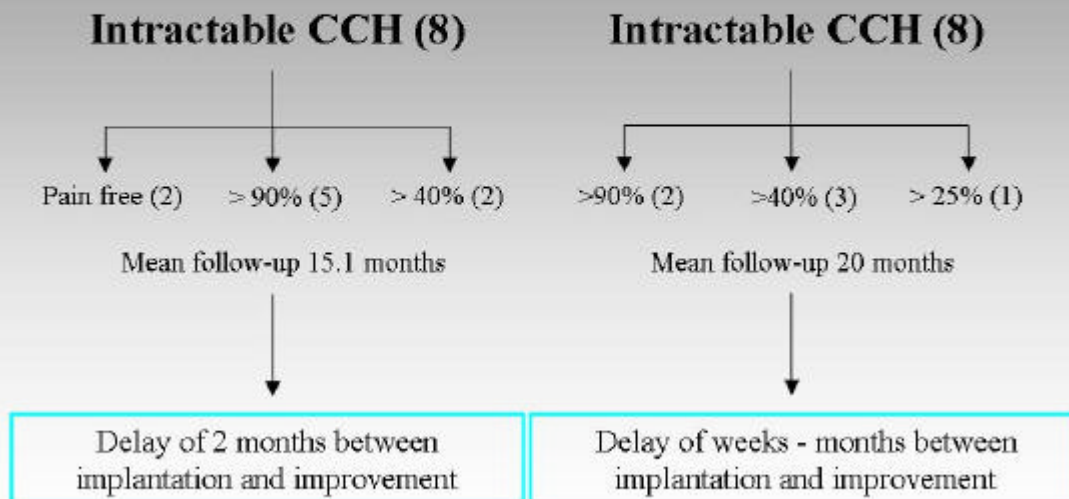
\*adapted

EFNS Guidelines. May A et al, Eur J Neurol 2006;13 (10):1066–1077

## Emerging Treatment Options for Refractory Trigeminal Autonomic Cephalalgias



## Occipital Nerve Stimulation for Intractable Cluster Headache



Magis D, et al. Lancet Neurology 2007;6(4):314-321

Burns B, et al. Lancet 2007; doi:10.1016/S0140-6736(07)60328-6

## Occipital Nerve Stimulation for Chronic Cluster Headache

Placement	Gender	Age	ONS Use (hrs/day)	FU (mo)
Unilat	F	51	18-20	12
Bilat	M	45	24	39
Unilat	F	49	24	10
Pre/Post Freq Per 90 d	Pre/Post Severity	Pre/Post BECK-II	Pre/Post HIT-6	Pre/Post MIDAS
72/90	6/6	11/12	63/65	92/166
90/90	8/5	13/17	69/61	230/90
90/90	8/3.5	NA	NA	270/89

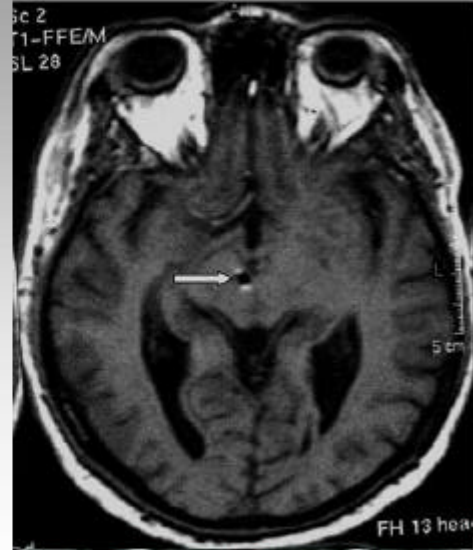
Schwedt TJ, Dodick DW et al. Cephalalgia 2007;27:153-157.

## ONS Adverse Events

- Surgical revision required 9 of 15 (60%)
  - Lead Revisions(8)
  - IPG Revision (1)
  - Infection (1)
- Mild-moderate
  - Stiff neck (2)
  - Incision pain (2)
  - IPG-site pain (1)

## DBS for *Refractory* Chronic Cluster Headache

- **16 patients CCH (Leone et al)**
  - 'cure' = 10
  - 'major' improvement = 6
  - mean follow-up = 23 mo
  - mean time to stable benefit 42d
- **6 patients CCH**
  - excellent = 3 (2PF)
  - unsatisfactory = 1
  - **1 terminated due to panic attack**
  - **1 died during procedure (ICH)**



Leone, et al. *Neurology* 2006;67(1):150-152

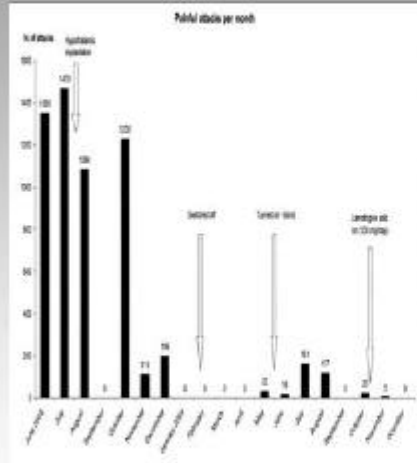
Schoenen et al. *Brain* 2005;128:940-947.



## DBS for Refractory Chronic Paroxysmal Hemicrania

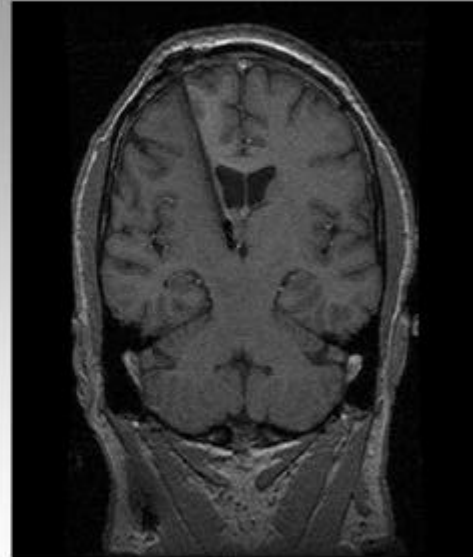
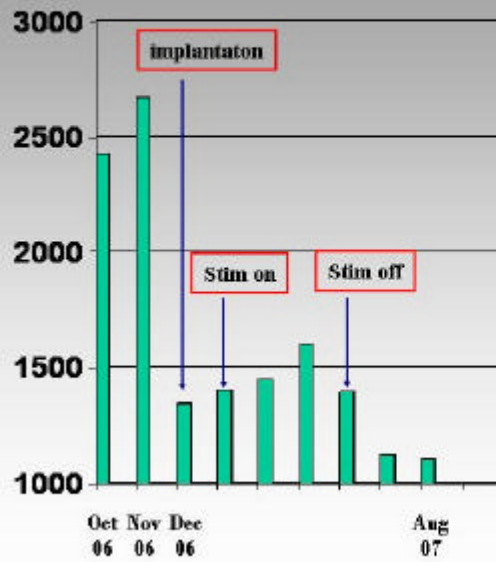
- 43 year-old woman with 20 month history
- 10-20 attacks per day; indomethacin responsive
- 3 months attack-free after DBS ('hypothalamus')
  - stimulation adjustment due to panic attacks

## DBS for *Refractory* SUNCT



Leone, M et al. Ann Neurol 2005;57:924-927

## DBS for SUNCT



Dodick et al. Unpublished

Adverse events: Severe decrease libido; diplopia; jaw contraction

## Cluster Headache and Other Trigeminal Autonomic Cephalalgias

- **How they are similar**
  - Pain characteristics and associated symptoms
  - Pathophysiology
  - Potential for secondary mimics
- **How they differ**
  - Attack duration and frequency
  - Treatment

## **CONTENT DISCLAIMER**

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