Cluster Headache and Chronic Paroxysmal Hemicrania

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CLUSTER HEADACHE

Old synonyms - Raeder syndrome, Horton cephalalgia, histamine cephalalgia, sphenopalatine neuralgia.

PATHOPHYSIOLOGY

- not fully determined.

Theories

A) **circadian pacemaker alterations** (due to ***hypothalamic dysfunction***).
- attacks increase following beginning and end of *daylight savings time*.
- there is *loss of circadian rhythm* (for blood pressure, temperature, hormones - prolactin, melatonin, cortisol, beta endorphins).
- recently, functional neuroimaging have identified **posterior hypothalamic grey matter** as key area for basic defect.
- pain is generated at PERICAROTID / CAVERNOUS SINUS COMPLEX.

B) **neurogenic inflammation**

C) carotid body **chemoreceptor dysfunction**

D) central **parasympathetic & sympathetic imbalance**

E) increased **responsiveness to histamine**.

EPIDEMIOLOGY

PREVALENCE 0.01-1.5% (≈ 0.3%)
- higher in **men** (male : female ≈ 6-8:1) and in **blacks**.
- family history is rare.

ONSET - any age (generally - in ***late twenties***).
- ≈ 10% patients develop cluster in their sixties.

Peptic ulcer disease is only known associated medical disorder.
- strong associations with ***smoking***, ***alcohol*** use, and previous ***head / face trauma***.
- certain *personality and physical characteristics* have been associated with cluster headache (e.g. tall and rugged-looking body, leonine facial appearance, multifurrowed and thickened skin with prominent folds, broad chin, vertical forehead creases, nasal telangiectasias).

CLINICAL FEATURES

A. **EPISODIC cluster headache** - remission periods lasting **≥ 14 days** (usually 6 months ÷ 2 years).
B. **CHRONIC cluster headache** (≈ 10%) - no remissions or remissions last **< 14 days**; headache is occurring for > 1 year.

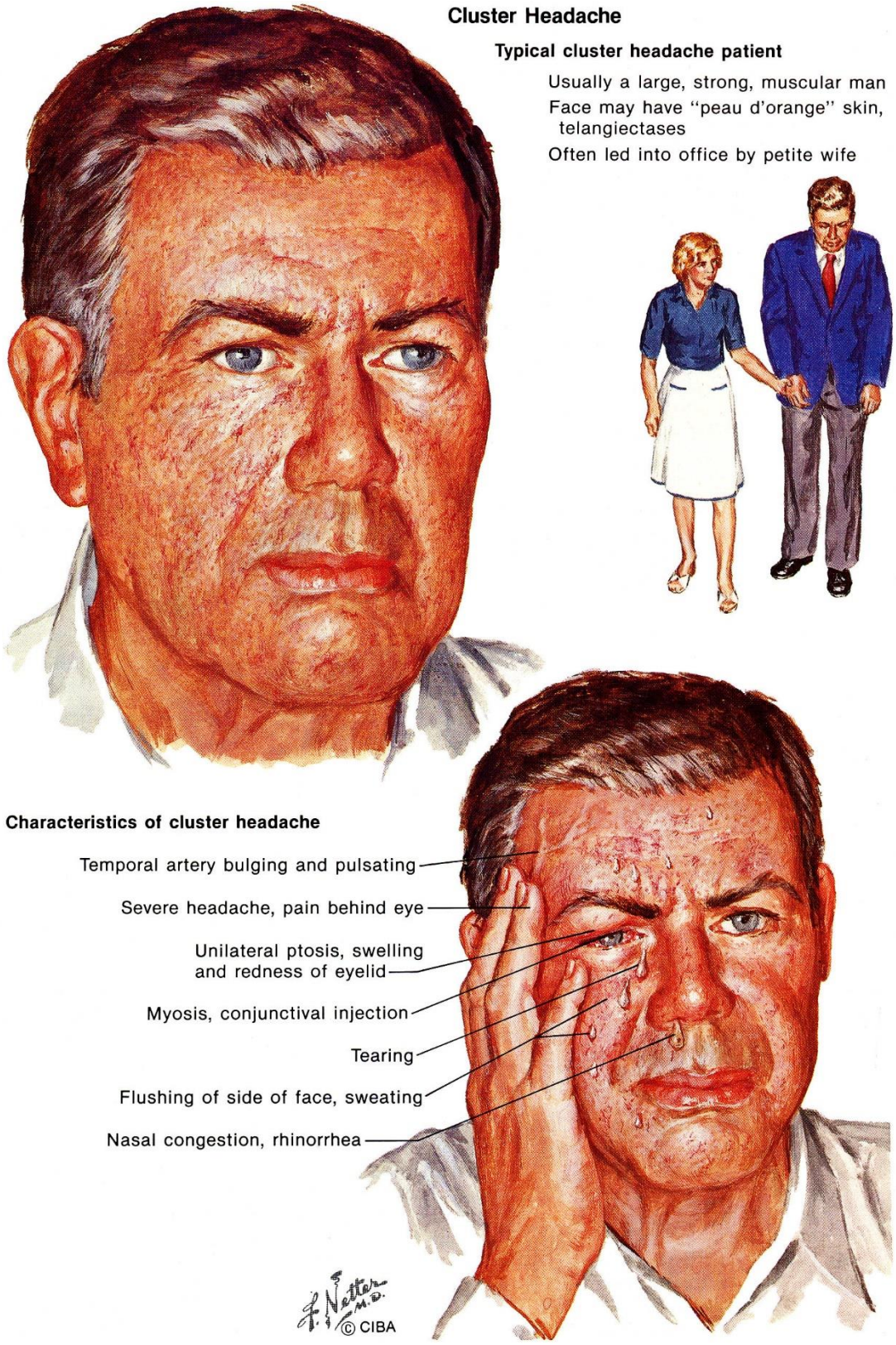
Either type may transform into other! (in 4-13% patients, **episodic CH** transforms into **chronic CH**)

Multiple episodes of headache:
1) pain begins ***without warning***.
2) **severe** – pain rapidly increases (within 5-15 minutes) to ***excruciating levels***.
3) **short-lived** – if left untreated, attacks usually last 30-90 minutes (15-180 minutes).
4) strictly **unilateral***, **periorbital** (orbital / supraorbital / temporal) – distribution of 1st or 2nd divisions of trigeminal nerve. *usually affects same side in subsequent months
5) ***may radiate*** to forehead, temples, jaws, nostrils, ears, neck, or shoulder.
6) pain is **deep**, **constant** (not throbbing), boring, piercing, burning, explosive.
7) at least one symptom of **unilateral (ipsilateral) autonomic dysfunction**:
    a) conjunctival injection ("red eye")
    b) lacrimation
    c) miosis
    d) ptosis
    e) eyelid edema
    f) nasal congestion
    g) rhinorrhea
    h) facial sweating
        - in variant of cluster headache, full Horner's syndrome can be seen.
8) patients feel ***agitated*** or restless with need to isolate themselves and move around (most sufferers assume upright position to relieve discomfort!); patients have been known to become violent or bang their heads against wall.
9) GI symptoms uncommon.

Attack frequency varies (8 attacks per day ÷ 1 attack every 2 days).

PERIODICITY is hallmark of cluster headache! - attributed to hypothalamic (particularly suprachiasmatic nuclei) hormonal influences

- attacks often ***occur at same time each day*** ("alarm clock headache"); onset is nocturnal in 50% cases (may awaken patients from sleep).
- attacks occur in **CLUSTER periods** that last 1 week ÷ 1 year (usually 1-3 months) separated by periods of headache-free remission.
- cluster episodes often appear at ***characteristic times of year*** (particularly around vernal and autumnal equinoxes).
- attacks may cease *during pregnancy* (but attacks seldom correlate with menses).



DIFFERENTIAL DIAGNOSIS

1. Secondary cluster-like headache (due to structural lesions near cavernous sinuses).
2. Chronic paroxysmal hemicrania
3. Migraine
4. Trigeminal neuralgia
5. Temporal arteritis
6. Raeder paratrigeminal syndrome - pain is constant (no distinct attacks)

7. Tolosa-Hunt syndrome
8. Sinusitis
9. Glaucoma

EVALUATION

- strictly clinical diagnosis - careful **history** is all that is needed.
- **MRI** is justified only in ***atypical cases*** or ***abnormal neurological examination*** (except when abnormality is Horner's syndrome!).

ABORTIVE THERAPY

Oral preparations are not recommended - absorbed too slowly.

1. Inhaled high-flow OXYGEN (**12 L/min 100% by mask for full 15 minutes** following headache onset) - treatment of first choice (70-80% effective); postulated mechanism – O_2 is vasoconstrictor and increases serotonin synthesis.
2. Parenteral SUMATRIPTAN 6 mg s/c
3. Parenteral DHE
4. Topical (intranasal) **local anesthetics** (2-4% LIDOCAINE) - to most caudal aspect of inferior nasal turbinate (patient in supine position) - can deliver *sphenopalatine ganglion block* - remarkably effective!
5. Parenteral **narcotics**
6. **Sphenopalatine ganglion stimulation** with implantable system
   - at 15 minutes following stimulation, 55% of treatment group had pain relief compared with 6% in sham treatment group ($P < .0001$); pain relief was maintained to 90 minutes (50% pain relief for treatment group vs 13% for sham). http://www.medscape.com/viewarticle/807281

PREVENTIVE THERAPY

- required for almost all patients!:
  - attacks are too short and too severe to treat with only abortive medication;
  - prophylactic treatment is most effective among all primary headache disorders! (except **chronic CH** - notoriously resistant to standard prophylactic agents)

- avoid ***alcohol*** and ***nitroglycerin***.
  Alcohol provokes attacks in 70% patients but has no effect when cluster bout remits ("***on-off vulnerability to alcohol***" - pathognomonic of cluster headache!!!).
- **Peripheral Nerve Blocks** see p. S24 >>

In order of preference (begin early in cluster period and continue until headache-free for at least 2 weeks):

1) ERGOTAMINE (orally 2 mg × 2/d) - **classic treatment** - most effective when given 1-2 hours before expected attack (for patients with single nocturnal episode, 1 mg suppository at bedtime may be all that is necessary)
   Educate regarding early symptoms of ergotism (limb claudication) when ergotamine is used daily (H: weekly limit of 14 mg).
2) VERAPAMIL

3) METHYSERGIDE (no longer available in USA)
4) LITHIUM (300 mg bid or tid titrated according to serum lithium level) – esp. useful in chronic cluster headache!
5) PREDNISONE (10-day course, beginning at 60 mg/d for 7 days and rapidly tapering); long-term use not recommended.
6) DIVALPROEX
7) CAPSAICIN drops to ipsilateral nostril - induces **substance P** release (principal mediator of pain); after repeated applications, depletes neuron of substance P.
8) INDOMETHACIN

N.B. PROPRANOLOL and AMITRIPTYLINE are largely ineffective!

- new approach: in refractory CCH + low risk for anticoagulant-related hemorrhagic complications, low-intensity anticoagulation with WARFARIN (to achieve INR 1.5–1.9) is associated with significantly higher incidence of remission lasting ≥ 4 weeks, as well as significantly less impact of headache on patients' quality of life as compared to placebo.

Surgical therapy:

1) new promising approach - DBS into ***posterior inferior hypothalamus***.
2) **surgical intervention** (for strictly unilateral chronic cluster) - ablation of sensory input of ***trigeminal nerve*** and ***autonomic pathways*** (e.g. percutaneous RF trigeminal gangliorhizolysis, rhizotomy) - effective in 75%.
3) SRS – methodology ***as for trigeminal neuralgia*** but results not as good (no sustained pain relief beyond 2 years F/U); some authors tried to add 8 mm shot to ***sphenopalatine ganglion*** (Pollock BE & Kondziolka D. J Neurosurg 87:450-453, 1997).

PROGNOSIS

- chronic headache that *may last for patient's life*.

- drug therapy may convert from chronic to episodic cluster.
- prolonged, spontaneous remissions have been described in up to 12% patients.

CHRONIC PAROXYSMAL HEMICRANIA

- as **CLUSTER HEADACHE** (2% prevalence of cluster headache) with following differences:

- dramatic response to INDOMETHACIN – diagnostic criterion!
- **women** > men (7:1)
- shorter headache duration ≈ 13 (5-30) minutes.
- headaches occur ≈ 5-11 times/day.
- 10% attacks may be triggered by flexing / rotating / pressing ***upper portion of neck***.
- typically, no remissions! (rarely, episodic paroxysmal hemicrania with remissions lasting weeks or months).
- MRI / CT should be undertaken to exclude symptomatic causes.
- treatment of choice - INDOMETHACIN (up to 200 mg/d); aspirin may also be beneficial, but relief is usually not complete.
- prognosis - may last indefinitely (with frequently reduced indomethacin requirement); spontaneous cures have been described.

HEMICRANIA CONTINUA

- exclusively 1-sided, **constant** moderate ÷ severe headache exquisitely responsive to INDOMETHACIN.

BIBLIOGRAPHY see p. S24 >>