MIGRAINE:
The invisible burden

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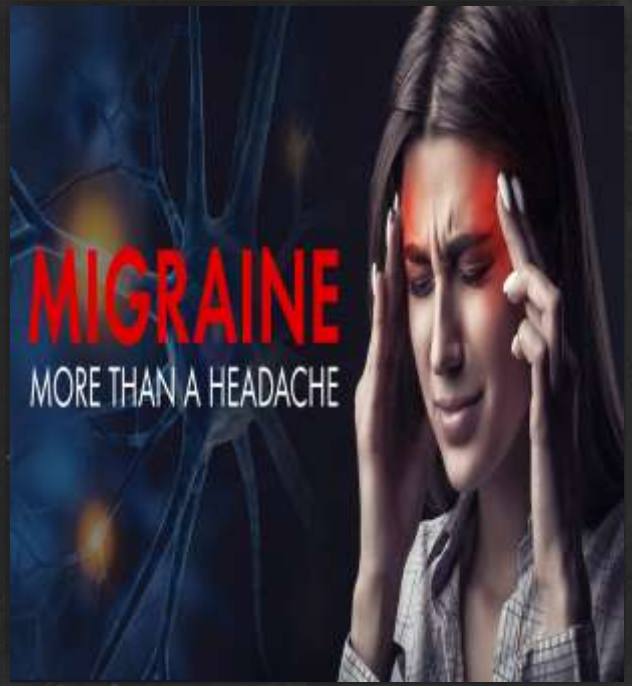
Contents of this presentation

Case Presentation

- Early one morning, a **26-year-old woman** suddenly notices that the **right side of her vision becomes blurry**. Within a few minutes she starts seeing **shimmering zig-zag lines and flashing lights** moving across her visual field.
- She becomes anxious because she feels something is wrong with her brain. About **20 minutes later**, the visual disturbance disappears — but it is followed by a **severe throbbing headache on the left side of her head**.
- The pain gradually worsens, she develops **nausea, vomiting, and extreme sensitivity to light and sound**, and she is forced to lie down in a dark room for several hours.
- Neurological examination later is completely normal.
- What happened to this patient?



01

Definition and Epidemiology

Definition and Epidemiology:

- Migraine is an episodic headache disorder characterized by recurrent attacks of moderate to severe pulsating pain often accompanied by nausea ,vomiting ,photophobia and phonophobia due to neurogenic inflammation
- 2nd most common cause of headache.
- Afflicts approximately 15% females and 6% males.

SYMPTOMS ACCOMPANYING SEVERE MIGRAINE ATTACKS IN 500 PATIENTS

SYMPTOM	PATIENTS AFFECTED, %
Nausea	87
Photophobia	82
Lightheadedness	72
Scalp tenderness	65
Vomiting	56
Visual disturbances	36
Paresthesias	33
Vertigo	33
Photopsia	26
Alteration of consciousness	18
Diarrhea	16
Fortification spectra	10
Syncope	10
Seizure	4
Confusional state	4

02

Classification and Etiology

Classification Of Migraine

- Migraine without aura or common migraine: No aura, seen in about 70-80% of patients.
- Migraine with Aura or Classical migraine: Seen in 20-30% migraine patients. The most common aura is visual and may include both positive and negative(visual field defects) features.
- Retinal Migraine: Involves attacks of monocular scotoma or even blindness of one eyes for less than an hour and associated with headache.
- Childhood periodic syndrome: Involves cyclical vomiting, abdominal migraine and benign paroxysmal vertigo of childhood. They may be precursors of migraine.

Complicated Migraine: Migraine headaches and or auras that are unusually long or unusually frequent or associated with a seizure or brain lesion.

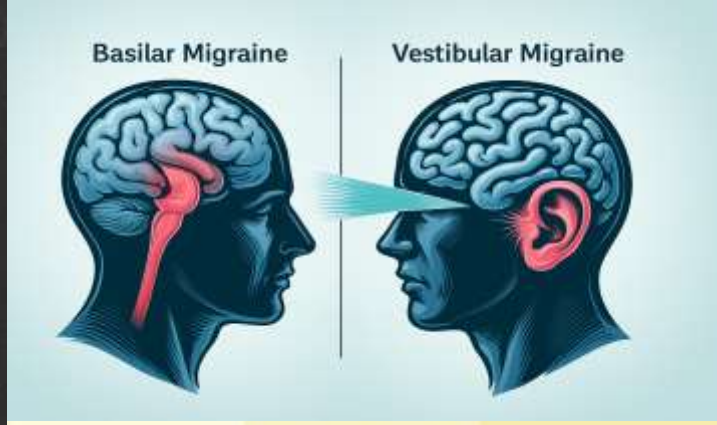
Basilar Migraine: Occipital headache, preceded by vertigo, diplopia and dysarthria +- visual and sensory symptoms (brainstem symtoms).

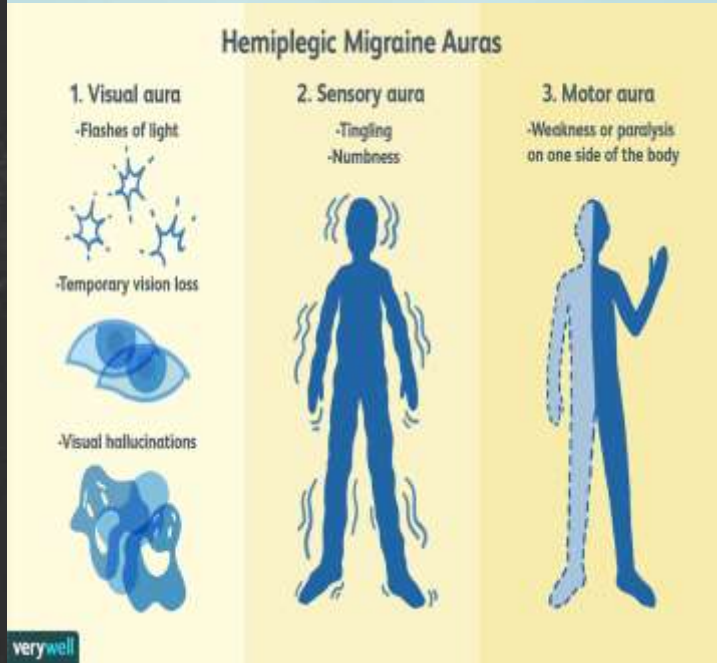
Hemiplegic migraine: Rare autosomal dominant disorder characterized by prolonged headache lasting hours or days, followed by hemiparesis and or coma that recovers slowly over days.

Opthalmoplegic migraine: Associated with transient 3rd nerve palsy with or without involvement of pupil, sometimes also affects 4th and 6th nerve.

Vestibular migraine

Catamental migraine: associated with menstruation





Etiology Or Risk Factors:

Genetic factors:

- Familial hemiplegic migraine genes:

  FHM1- CACNA1A: Neuronal P/Q calcium channel- increase neurotransmitter release.

  FHM2-ATP1A2: Astrocyte sodium pump- dysfunction increases extracellular K+.

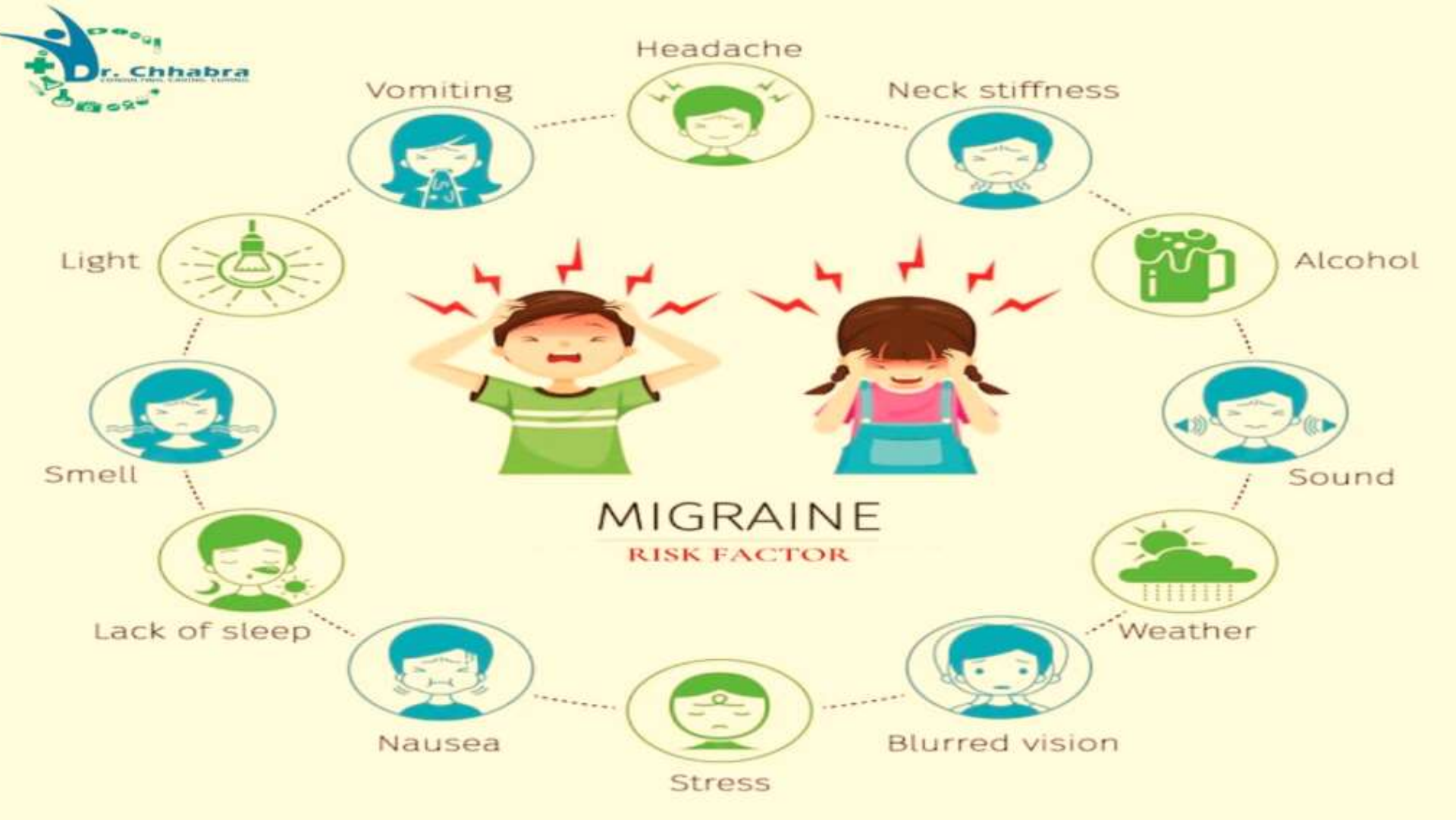
  FHM3- SCN1A: Neuronal sodium channel- increase action potential firing

Environmental triggers

- Stress
- Sleep deprivation
- Hormonal changes
- Certain foods (cheese, chocolate, alcohol)
- Bright light
- Strong smells

Lifestyle factors

- Irregular meals
- Dehydration


Dr. Chhabra
Headache
Vomiting
Neck stiffness
Light
Alcohol
Smell
Sound
MIGRAINE
RISK FACTOR
Lack of sleep
Weather
Nausea
Blurred vision
Stress

03

Pathophysiology and Phases Of Migraine

Pathophysiology

1. **Brainstem Dysfunction:**
   Migraine begins due to **abnormal sensory processing in the brainstem and thalamus.**
   These areas normally **control pain signals**, but in migraine they become **overactive**, leading to increased sensitivity to pain, light, sound, and smell.

2. **Trigeminovascular System Activation**
   The **trigeminal nerve** plays a major role.

Steps:

- Trigeminal nerve gets activated.
- It releases **vasoactive neuropeptides**, especially **CGRP (Calcitonin Gene-Related Peptide)**.
- CGRP causes:
- **Vasodilation of cranial blood vessels**
- **Neurogenic inflammation**
- **Transmission of pain signals**

These signals travel:
From **trigeminal nucleus → thalamus → cerebral cortex**, where pain is perceived.

Clinical importance:
Drugs that block CGRP can **treat acute migraine**.

3. Descending Pain Modulation Failure

Normally the brain suppresses pain through descending pathways from areas like:

Periaqueductal gray

Locus coeruleus

Rostroventromedial medulla

In migraine, this **pain inhibition system is defective**, so pain signals become stronger.

4. Role of Serotonin (5-HT)

Serotonin is very important in migraine.

Reduced or altered **serotonin activity** contributes to attacks.

Drugs like **triptans** stimulate **5-HT1B and 5-HT1D receptors**.

Effects of triptans:

Constrict cranial blood vessels

Reduce CGRP release

Block pain transmission

This is why **triptans stop migraine attacks**.

5. Role of Dopamine

People with migraine have **dopamine receptor hypersensitivity**.
This causes symptoms such as:
Yawning
Nausea
Vomiting
Hypotension
Because of this, **dopamine antagonists (e.g., metoclopramide)** help treat migraine.

6. Genetic Factors

Certain **ion channel mutations** increase neuronal excitability and predispose to migraine.
Examples (seen in familial hemiplegic migraine):
CACNA1A gene – calcium channel mutation
ATP1A2 gene – Na^+/K^+ ATPase mutation
SCN1A gene – sodium channel mutation
These changes make neurons **more easily activated**, triggering migraine.

Cortical spreading depression :

A causal association between migraine aura and headache is supported by evidence that both are linked to the phenomenon known as cortical spreading depression of Leão

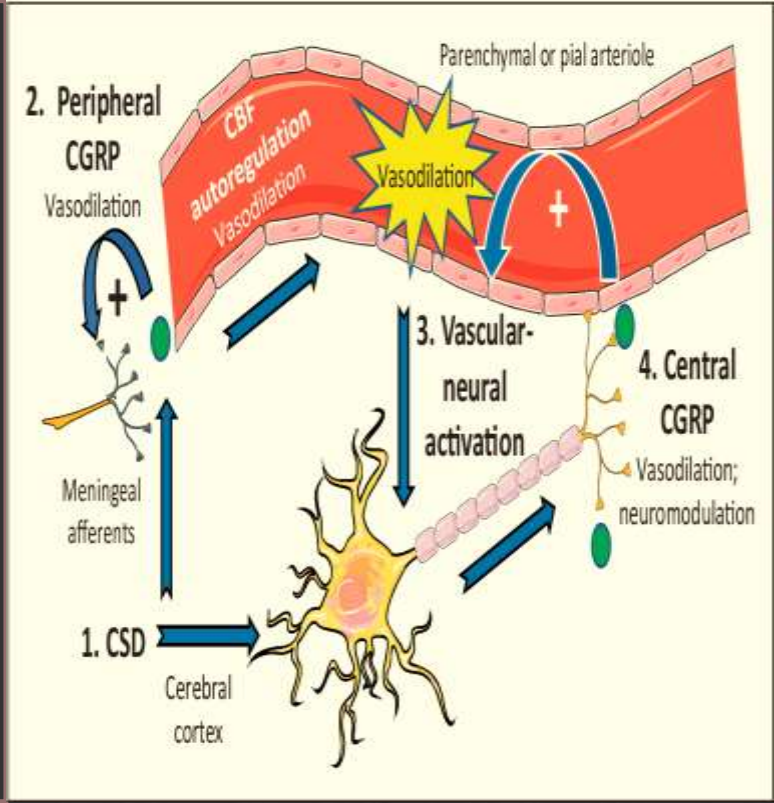
It is a self-propagating wave of neuronal and glial depolarization that spreads across the cerebral cortex.

Is hypothesized to

:●Cause the aura of migraine

●Activate trigeminal nerve afferents

●Alter blood-brain barrier permeability by matrix metalloproteinase activation.



Phases Of Migraine:

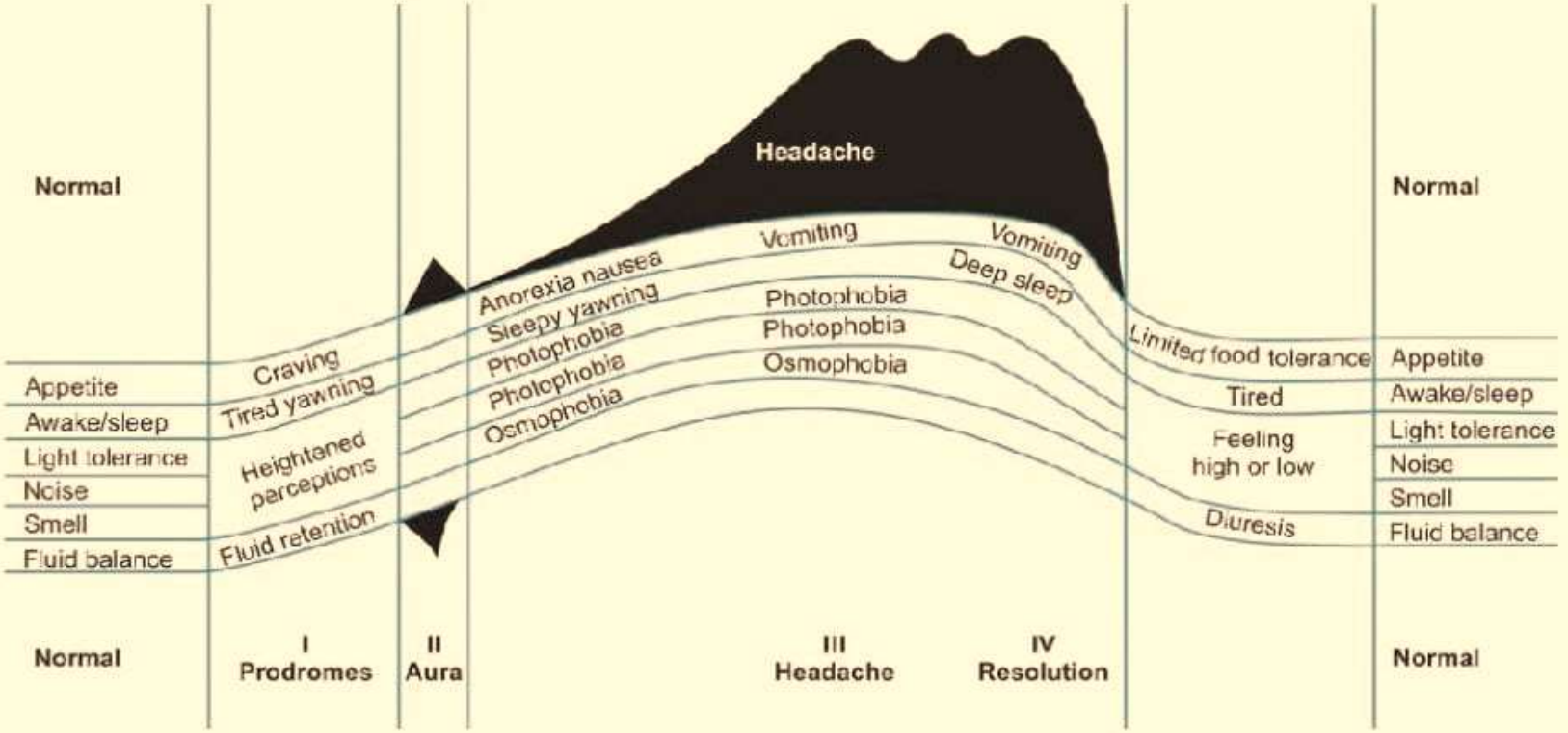


FIG. 16.8: Migraine phases.

TIMELINE OF A MIGRAINE ATTACK

PRODROME
FEW HOURS TO DAYS

- IRRITABILITY
- DEPRESSION
- YAWNING
- INCREASED NEED TO URINATE
- FOOD CRAVINGS
- SENSITIVITY TO LIGHT/SOUND
- PROBLEMS IN CONCENTRATING
- FATIGUE AND MUSCLE STIFFNESS
- DIFFICULTY IN SPEAKING AND READING
- NAUSEA
- DIFFICULTY IN SLEEPING

AURA
5-60 MIN

- VISUAL DISTURBANCES
- TEMPORARY LOSS OF SIGHT
- NUMBNESS AND TINGLING ON PART OF THE BODY

HEADACHE
4-72 HRS

- THROBBING
- DRILLING
- ICEPICK IN THE HEAD
- BURNING
- NAUSEA
- VOMITING
- GIDDINESS
- INSOMNIA
- NASAL CONGESTION
- ANXIETY
- DEPRESSED MOOD
- SENSITIVITY TO LIGHT, SMELL, SOUND
- NECK PAIN AND STIFFNESS

POSTDROME
24-48 HRS

- INABILITY TO CONCENTRATE
- FATIGUE
- DEPRESSED MOOD
- EUPHORIC MOOD
- LACK OF COMPREHENSION

04

Clinical Features and Diagnostic features

Clinical Features:

General Characteristics Of Headache:

- Location: Usually hemicranial (on one side of the head).
- Quality: Throbbing pain.
- Associated Symptoms: Nausea and vomiting are common.
- Sensitivity: Patients often prefer to be still in a dark, quiet environment.
- Allodynia: Scalp tenderness (pain from normally nonpainful stimuli).

The Aura:

A warning period consisting of focal neurological symptoms that usually evolve over 5–20 minutes and rarely last longer than 60 minutes.

- Visual Aura: Most common; includes shimmering, flashing lights (scintillating spots), zigzag lines (fortification spectra), or patchy visual field loss (scotomas).
- Sensory Aura: Tingling followed by numbness, spreading from one part of the body to another.
- Language Aura: Transient speech disturbance.
- Motor Aura: Transient weakness.

Migraine With Aura Symptoms

Seeing sparks and flashes

Ringing in ears and other noises

Tingling limbs

Loss of vision or visual hallucinations

Numbness or inability to move a part of body

Speech difficulties


AMF

Diagnostic Features

Migraine without aura

A. At least five attacks fulfilling criteria B-D
B. B. Headache attacks lasting 4-72 hours (when untreated or unsuccessfully treated)
C. 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 (eg, walking or climbing stairs)
D. 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.

1.2 Migraine with aura

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 three of the following six characteristics:

1. at least one aura symptom spreads gradually over ≥5 minutes 2. two or more aura symptoms occur in succession 3. each individual aura symptom lasts 5-60 minutes 4. at least one aura symptom is unilateral 5. at least one aura symptom is positive 6. the aura is accompanied, or followed within 60 minutes, by headache

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

1.3 Chronic migraine

A. Headache (migraine-like or tension-type-like) on ≥15 days/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/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. Not better accounted for by another ICHD-3 diagnosis.

Differential Diagnosis:

Table 2. Differential Diagnosis of Headache

Diagnosis	*Symptoms*	*Patient characteristics*	*Symptom relief*	*Associated symptoms*	*Notes*
Cluster headache	Sudden onset, unilateral severe headache lasting 15 to 180 minutes and occurring at the same time each day	More common in men; onset at 20 to 40 years of age	Activity, medication, oxygen, pacing	Ipsilateral cranial autonomic symptoms	May begin during sleep
Migraine	Unilateral throbbing headache, often with sudden onset	More common in women; onset typically in adolescence or young adulthood	Lying in a dark room, medication, sleep	Fatigue, nausea, photo- or phonophobia, vomiting; 50 percent of patients have bilateral autonomic symptoms[7]	Worse with activity
Paroxysmal hemicrania	Unilateral headache lasting two to 30 minutes	More common in women; onset typically at 34 to 41 years of age	Reliably responds to indomethacin	—	—
Short-lasting unilateral neuralgiform headaches with conjunctival injection and tearing	Unilateral headache lasting five to 240 seconds and occurring three to 200 times per day	More common in men; onset typically at 35 to 65 years of age	Usually refractory to treatment	Ipsilateral eye symptoms	Rare
Tension headache	Gradually developing, constant bilateral dull ache or squeezing band-like headache	Slightly more common in women	Analgesics, stress relief	Fatigue, pericranial muscle tenderness, sleep disturbance	Typically starts midday
Trigeminal neuralgia	Paroxysmal, electrical, sharp, stabbing pain in trigeminal nerve distribution, lasting a few seconds; episodes last weeks to months	Slightly more common in women; onset after 50 years of age	Carbamazepine (Tegretol)	Inconsistent pattern of headaches	Often triggered by cold air or light touch in the nerve distribution area

Information from reference 7.

Red Flags Of Headache

- "Worst" headache ever
- First severe headache
- Subacute worsening over days or weeks
- Altered level of sensorium/consciousness
- Abnormal neurologic examination
- Fever or unexplained systemic signs
- Significant weight loss
- Vomiting that precedes headache
- Pain induced by bending, lifting, cough, worsens with Valsalva maneuvers
- Pain which disturbs sleep or presents
- immediately upon awakening
- Known systemic illness, history of trauma, cancer or HIV
- New-onset headache in a patient
- >50 years of age
- Focal neurologic deficits, jaw claudication
- Morning headache associated with nausea and vomiting
- Pain associated with local tenderness (e.g., region of temporal artery)

Mnemonic SNNOOP10

- **S**ystemic symptoms including fever
- **N**eoplasm history
- **N**eurologic deficit (including decreased consciousness)
- **O**nset is sudden or abrupt
- **O**lder age (onset after age 50 years)
- **P10:**
  1. **P**attern change or recent onset of new headache
  2. **P**ositional headache
  3. **P**recipitated by sneezing, coughing, or exercise
  4. **P**apilledema
  5. **P**rogressive headache and atypical presentations
  6. **P**regnancy **or p**uerperium
  7. **P**ainful eye with autonomic features
  8. **P**ost-traumatic onset of headache
  9. **P**athology of the immune system such as HIV
  10. **P**ainkiller (analgesic) overuse (e.g., medication overus headache) or new drug at onset of headache

Investigations

- Migraine is **mainly a clinical diagnosis.**

Investigations if atypical features:

- MRI brain
- CT scan
- Lumbar puncture
- Blood tests

Migraine Disability Assessment Score (MIDAS)

INSTRUCTIONS: Please answer the following questions about all headaches you have had in the last 3 months. Write your answer in the box next to each question. Write zero if you have not done the activity in the last 3 months.

1	How many days in the last 3 months have you missed work or school because of your headaches?		days
2	How many days in the last 3 months has your performance at work or school been reduced by half or more because of your headaches? (Do not include the days you counted in question 1 that you missed work or school)		days
3	How many days in the last 3 months have you not done housework because of your headaches?		days
4	On how many days in the last 3 months has your housework performance been reduced by half or more due to your headaches? (Do not include the days you counted in question 3 when you did not do housework)		days
5	How many days in the last 3 months have you missed family, social or leisure activities because of your headaches?		days
	TOTAL		days
A	How many days in the last 3 months have you had headaches? (If the headache lasted more than 1 day, count each day)		days
B	On a scale of 0 to 10, on average, how intense were these headaches? (Where 0 = no pain, and 10 = maximum possible pain)		days

Scoring: After completing the questionnaire, add up the total number of days for questions 1-5. Do not include answers to questions A and B in the overall score

Grading system for the MIDAS Questionnaire

MIDAS Degree	Definition	MIDAS Score
I	Minimal or no disability	0-5
II	Mild disability	6-10
III	Moderate disability	11-20
IV	Severe disability	>21

05

Management

Treatment:

NON-PHARMACOLOGIC MANAGEMENT-

- Most patients benefit by the identification and avoidance of specific headache triggers.
- A regulated lifestyle is helpful, including a healthful diet, regular exercise, regular sleep patterns, avoidance of excess caffeine and alcohol, and avoidance of acute changes in stress levels.
- Patients with migraine do not encounter more stress than headache-free individuals; overresponsiveness to stress appears to be the issue.
- Since the stresses of everyday living cannot be eliminated, lessening one's response to stress by various techniques is helpful for many patients.
- These may include yoga, transcendental meditation, hypnosis, and conditioning techniques such as biofeedback. For most patients, this approach is, at best, an adjunct to pharmacotherapy

Pharmacological Treatment

TREATMENT OF AN ACUTE ATTACK:

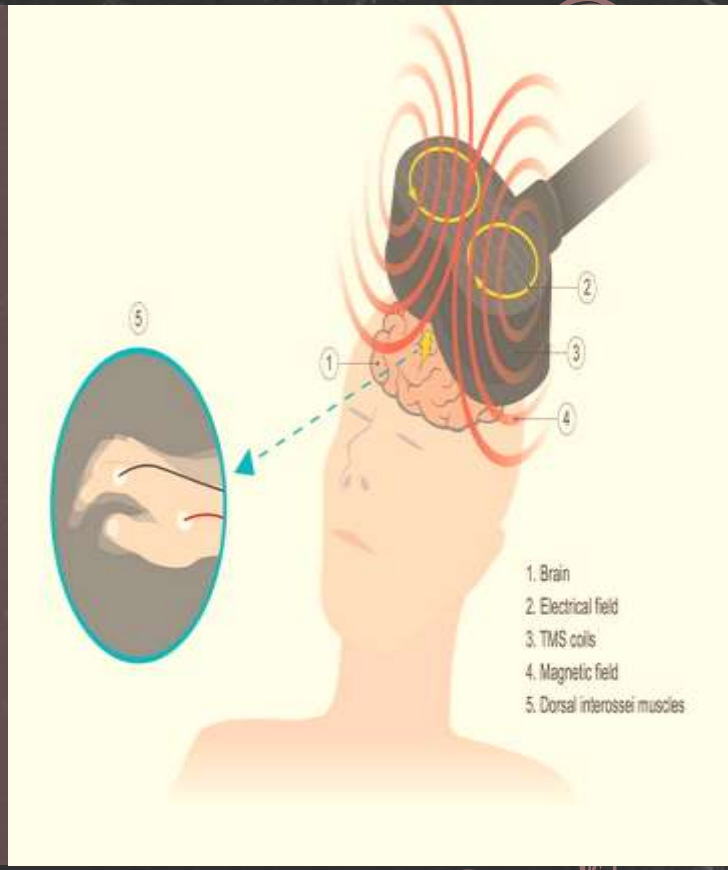
Analgesic: Simple analgesia such as aspirin, paracetamol or nonsteroidal anti-inflammatory agents.

Nausea may be treated by an antiemetic (metoclopramide or domperidone).

Severe attacks: If there is previously no relief with a nonsteroidal anti-inflammatory drug (NSAID), use "triptans".

- **Triptans** (e.g., sumatriptan: 50-100 mg tablet/5-20 mg nasal spray/6 mg S/C; rizatriptan: 5-10 mg tablet, frovatriptan: 2.5 mg oral; naratriptan: 2.5 mg oral; almotriptan: 12.5 mg oral; eletripton: 40-80 mg oral; zolmitriptan: 2.5 mg oral/5 mg intranasal spray)
- **Mode of action**: Potent 5-HT1B/1D agonists, inhibit release of CGRP and substance P, inhibit activation of the trigeminal nerve, and inhibit vasodilation in the meninges.
- **Administration**: Triptans are available as oral preparations, nasal spray, and subcutaneous injections.

- **Contraindications of Triptan**: Ischemic heart disease or stroke, high risk for coronary artery disease, pregnancy, hemiplegic or basilar migraine and use with ergots.
Calcitonin gene-related peptide antagonists (eg, erenumab, fremanezumab, galcanezumab) are very effective for acute treatment of migraine.
Lasmiditan, a selective serotonin 1F receptor agonist has been tried.
Single-pulse transcranial magnetic stimulation (TMS) has shown good benefit



Drug Prophylaxis

- Patients who have very frequent headaches (>2–3 weeks)
- Attack duration >48 hours
- Migraine-related disability >3 days/month
- Headache extremely severe
- Migraine accompanied by severe aura
- Contraindication to acute treatment
- Unacceptable adverse effects with acute migraine treatment
- Patients preference

Drug Prophylaxis

- Various drugs can be used and the most frequently used are:
- Anticonvulsants [antiepileptic drugs (AEDs)): Valproate (800 mg)or topiramate (100-200 mg daily) is the most effective option.
- B-adrenoceptor antagonists (l-blockers) (e.g. propranolol slowrelease 40-120 mg daily).
- Tricyclic antidepressants [e.g., amitriptyline 10 mg increasing weekly in 10 mg steps to 50-60 mg or Dosulepin (25-75 mg at night)].
- Methysergide 1-2 mg TID in resistant cases (prolonged use may produce retroperitoneal and mediastinal fibrosis).
- Botulinum toxin has been tried as a treatment for chronic migraine.
- Vasoactive drugs and calcium channel blockers: These include flunarizine (5-10 mg OD at bedtime), verapamil (80-160 mg 3 times a day), and methysergide and are used in refractory cases. Pizotifen is rarely used.
- Memantine-N-methyl-D-aspartate (NMDA) receptor antagonist, blocks glutamate.

References:

- Harrison's Neurology in Clinical Medicine: 3rd edition
- Davidson's Practice of Medicine
- Archit Baloor's Textbook of Medicine:Treatment and tables
- Grepmed: Table of Differential Diagnosis of Headache
- ICHD -3RD Edition for diagnosis of Migraine

Thankyou for listening