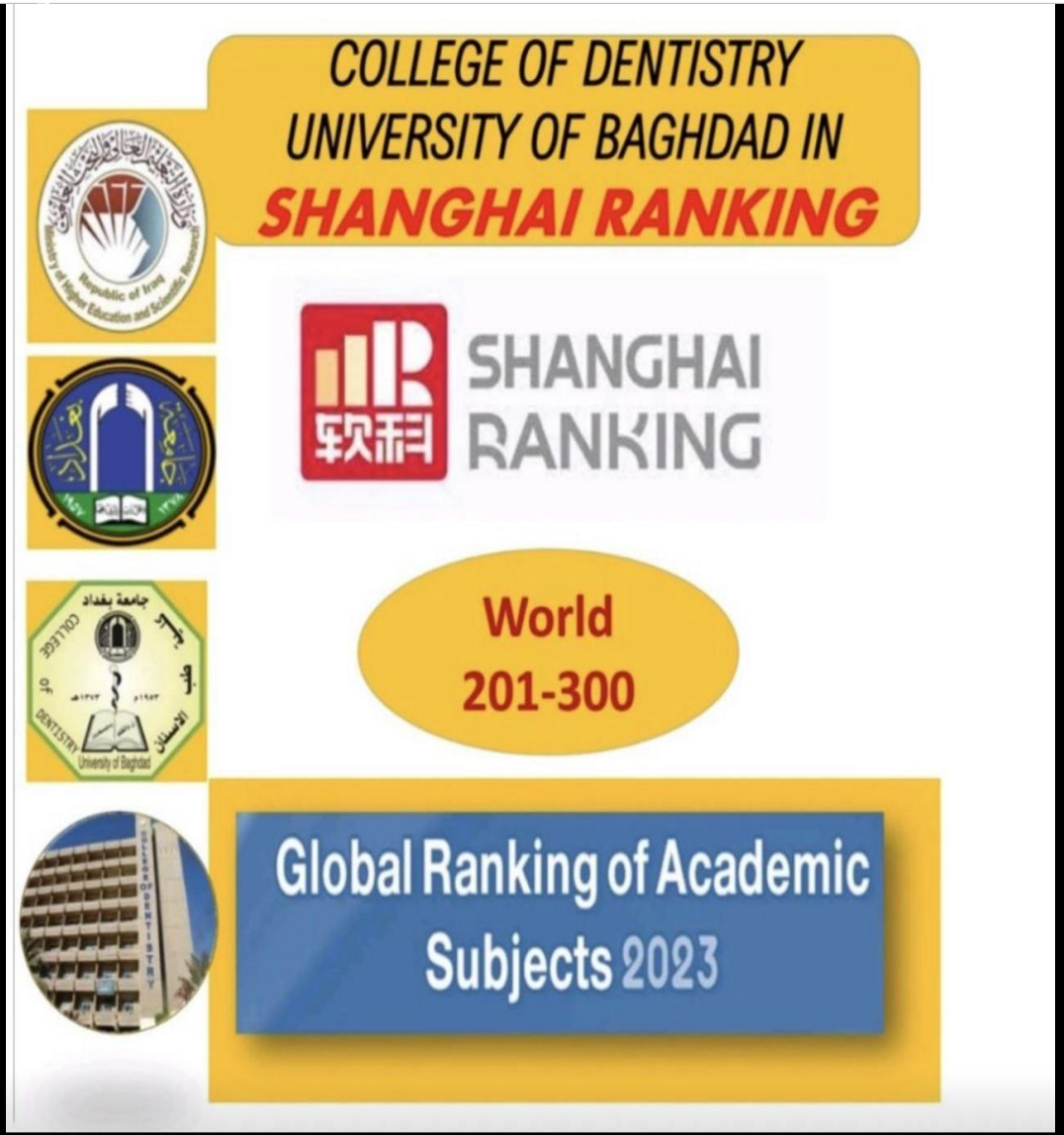
Migraine, types and treatment



Dr.Wafaa mansor

EPIDEMIOLOGY AND IMPACT

- Migraine is a common, often disabling disease of the nervous system
- The burden of migraine is greatest for the most severely affected people
- Despite improvements, migraine remains underdiagnosed and undertreated
- Resolving barriers to care requires several interventions

MIGRAINE PREVALENCE (American Migraine Study II)

- There are currently 36 million people with migraine age 12+ in the United States
  - 27 million female
  - 9 million male
- Nearly 1 in 4 households has at least 1 person with migraine
- Migraine prevalence peaks between the ages of 25–55

BURDEN OF MIGRAINE

- Individual burden
- Societal burden
  - Direct costs
    - $2.5 billion per year
  - Indirect costs
    - $13-31 billion per year
    - Absenteeism
    - Reduced effectiveness
  - Burden disproportionately distributed
    - 51% females with migraine → 93% of work loss due to migraine
    - 38% males with migraine → 85% work loss due to migraine

Hu HX et al. *Arch Intern Med*. 1999.
Stewart WF et al. *Cephalalgia*. 1996.

WHAT IS MIGRAINE?

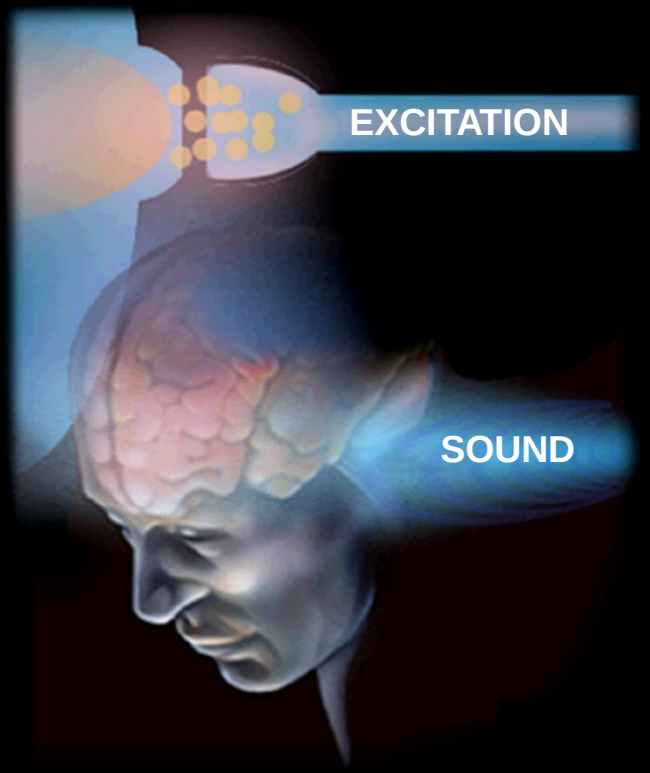
- Disorder characterized by episodic attacks of head pain and associated symptoms, such as nausea, sensitivity to light, sound, or intolerance to head movement
- Inherited tendency
- Neurobiologically based, common clinical problem

GENETIC BASIS

- Twin studies: MZ > DZ
- Ion channelopathy –

  <u>Familial hemiplegic migraine</u>

  - α_{1A} subunit of the P/Q voltage-gated Ca^{2+} channel on chromosome 19 (~50% of cases)
  - Mutation in gene *ATP1A2* (encodes alpha2 subunit of Na^{+}/K^{+} pump) results in loss of function of single *ATP1A2* allele (chromosome 1)
  - Linked to regular migraine
- Genetically heterogeneous



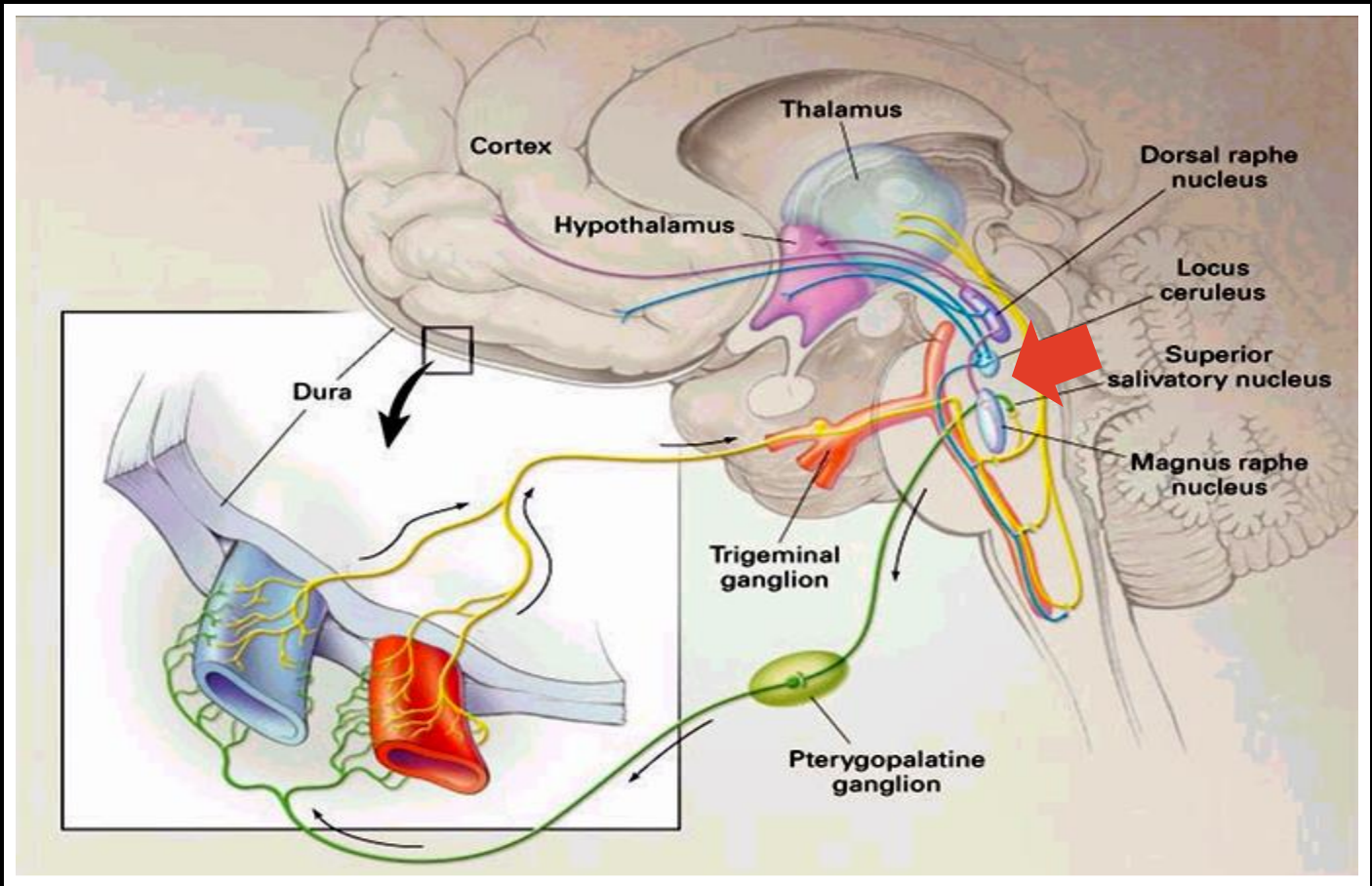
SENSITIVE BRAIN

- People with Migraine have altered neuro-physiologic responses between attacks
- Stabbing headache
  ("ice-pick" pains)
- Enhanced sensory processing
  - visual
  - auditory

TRIGGERING MIGRAINE

- Episodes may recur regularly as if initiated by an internal clock located in the hypothalamus
- Attacks may originate in the nervous system in response to stress or excessive afferent stimulation, such as flickering light or noise
- Some triggers act primarily on the cranial blood vessels; craniovascular afferents may then excite central pathways
- For many patients no factor can be identified

THE NEUROVASCULAR THEORY



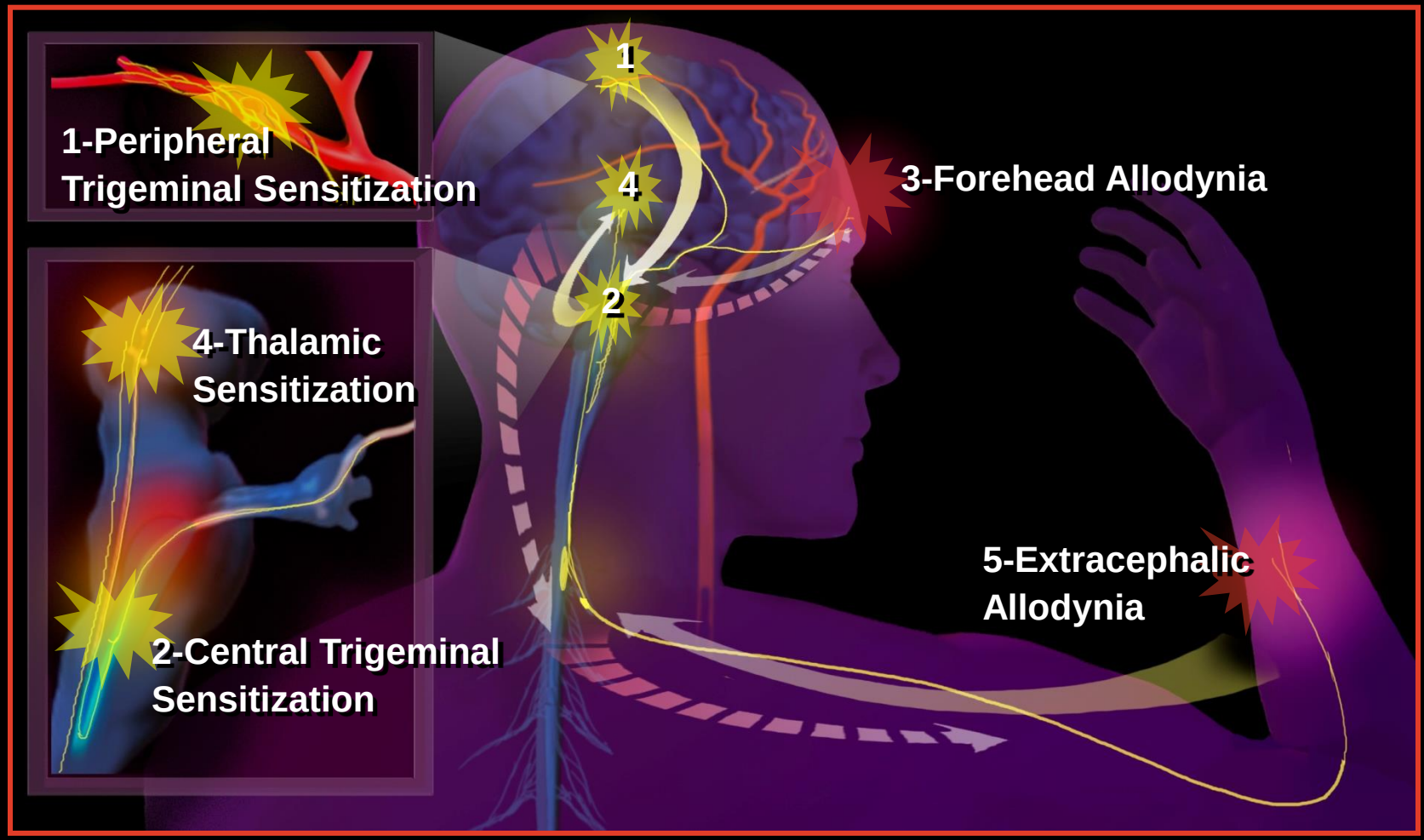
Goadsby PJ et al. *N Engl J Med.* 2002.

THE NEUROVASCULAR THEORY

Migraine is a neurovascular pain syndrome

- Referred pain from dura mater and blood vessels
- Peripheral neural processing
  - Neurogenic plasma protein extravasation (PPE)
  - Neuropeptides
- Central neural processing

CUTANEOUS ALLODYNIA



Burstein R et al. *Brain*. 2000.

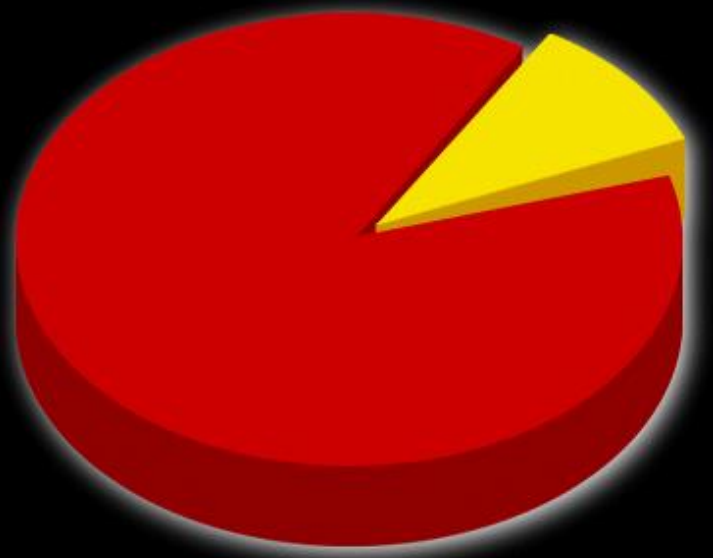
CLINICAL PRESENTATION OF HEADACHES

Primary

- **Migraine**
- **Tension-type (TTH)**
- **Cluster**
- **Other**
  (eg, benign cough headache)

Secondary

- **Infection**
- **Hemorrhage**
- **Increased ICP**
- **Brain tumor**



WORRISOME HEADACHE RED FLAGS "SNOOP"

- **S**ystemic symptoms (fever, weight loss) or **S**econdary risk factors (HIV, systemic cancer)
- **N**eurologic symptoms or abnormal signs (confusion, impaired alertness, or consciousness)
- **O**nset: sudden, abrupt, or split-second
- **O**lder: new onset and progressive headache, especially in middle-age >50 (giant cell arteritis)
- **P**revious headache history: first headache or different (change in attack frequency, severity, or clinical features)

ICHD-3 Beta Diagnostic Criteria
Migraine without Aura

- 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

IHS *MIGRAINE* AND *TENSION*-TYPE HEADACHE

CEPHALALGIA
An International Journal of Headache

Migraine

- ≥5 attacks lasting 4–72 h
- ≥2 of the following 4
  - Unilateral
  - Pulsating
  - Moderate or severe intensity
  - Aggravation by routine physical activity
- ≥1 of the following
  - Nausea and/or vomiting
  - Photophobia and phonophobia
- Not attributable to another disorder

Tension

- ≥10 attacks lasting 30 min–7 days
- ≥2 of the following 4
  - Bilateral
  - Pressing/tightening (Not pulsating)
  - Mild or moderate intensity
  - Not aggravated by routine physical activity
- No nausea or vomiting
- One or neither photophobia or phonophobia
- Not attributable to another disorder

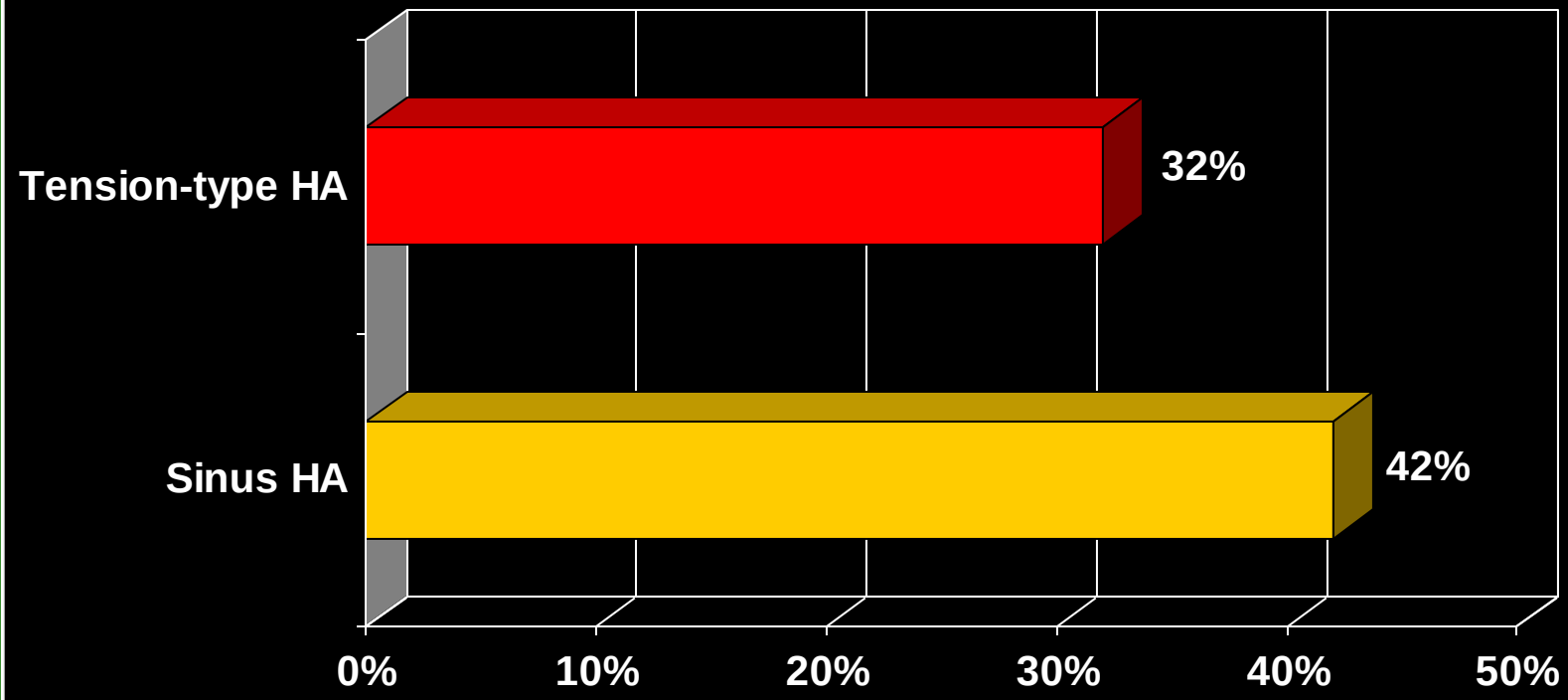
IMPORTANT DIAGNOSTIC CONSIDERATIONS

- No single criterion necessary nor sufficient for diagnosis
- 15% of patients have a neurological aura
- IHS criteria do not require GI symptoms
- Vomiting occurs in < 1/3 of patients
- 41% of migraine patients report bilateral pain
- 50% of the time, pain is non-pulsating

Recurring moderate-to-severe headache is migraine until proven otherwise

Russell MB et al. *Cephalalgia*. 1996.
Pryse-Phillips WEM et al. *Can Med Assoc J*. 1997.

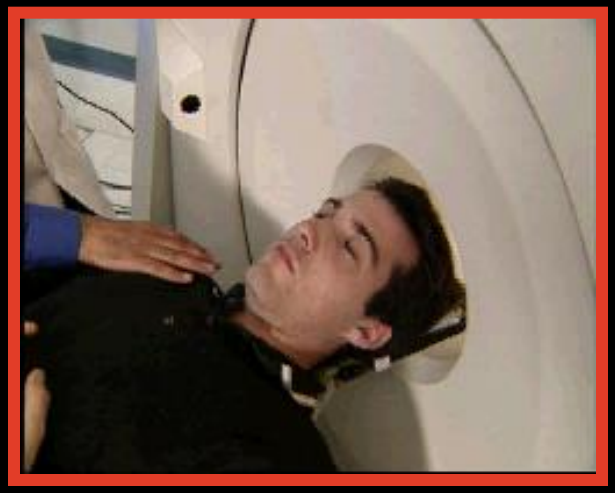
UNDIAGNOSED MIGRAINE SUFFERERS OFTEN RECEIVE OTHER MEDICAL DIAGNOSES



Lipton RB et al. *Headache*. 2001.

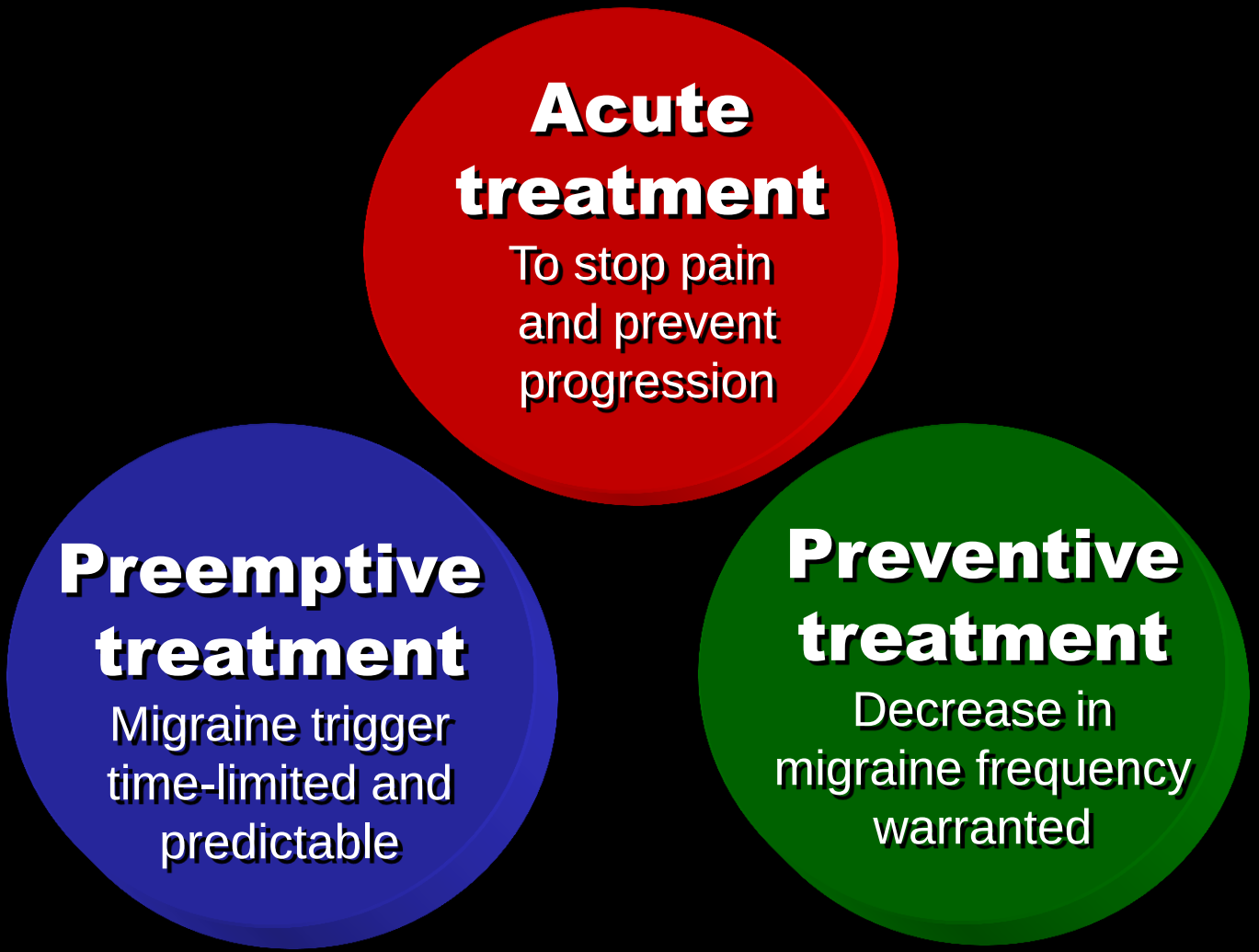
DIAGNOSIS TESTING CT AND MRI

- In patients with recurrent migraine, neither CT nor MRI is warranted except in cases with:
  - Recent substantial change in headache pattern
  - History of seizures
  - Focal neurologic symptoms or signs
- Role of CT or MRI in patients with nonmigraine headache is unclear
- Consensus expert opinion
  - MRI is more sensitive



Report of Quality Standards Subcommittee of AAN. *Neurology*. 1994.

STRATEGIES FOR MIGRAINE TREATMENT



Silberstein SD, Goadsby PJ. *Cephalalgia*. 2002.

ACUTE MIGRAINE MEDICATIONS

- Nonspecific
  - NSAIDs
  - Combination analgesics
  - Opioids?
  - Neuroleptics/antiemetics
  - Corticosteroids
- Specific
  - Ergotamine/DHE
  - Triptans
  - CGRP antibodies?

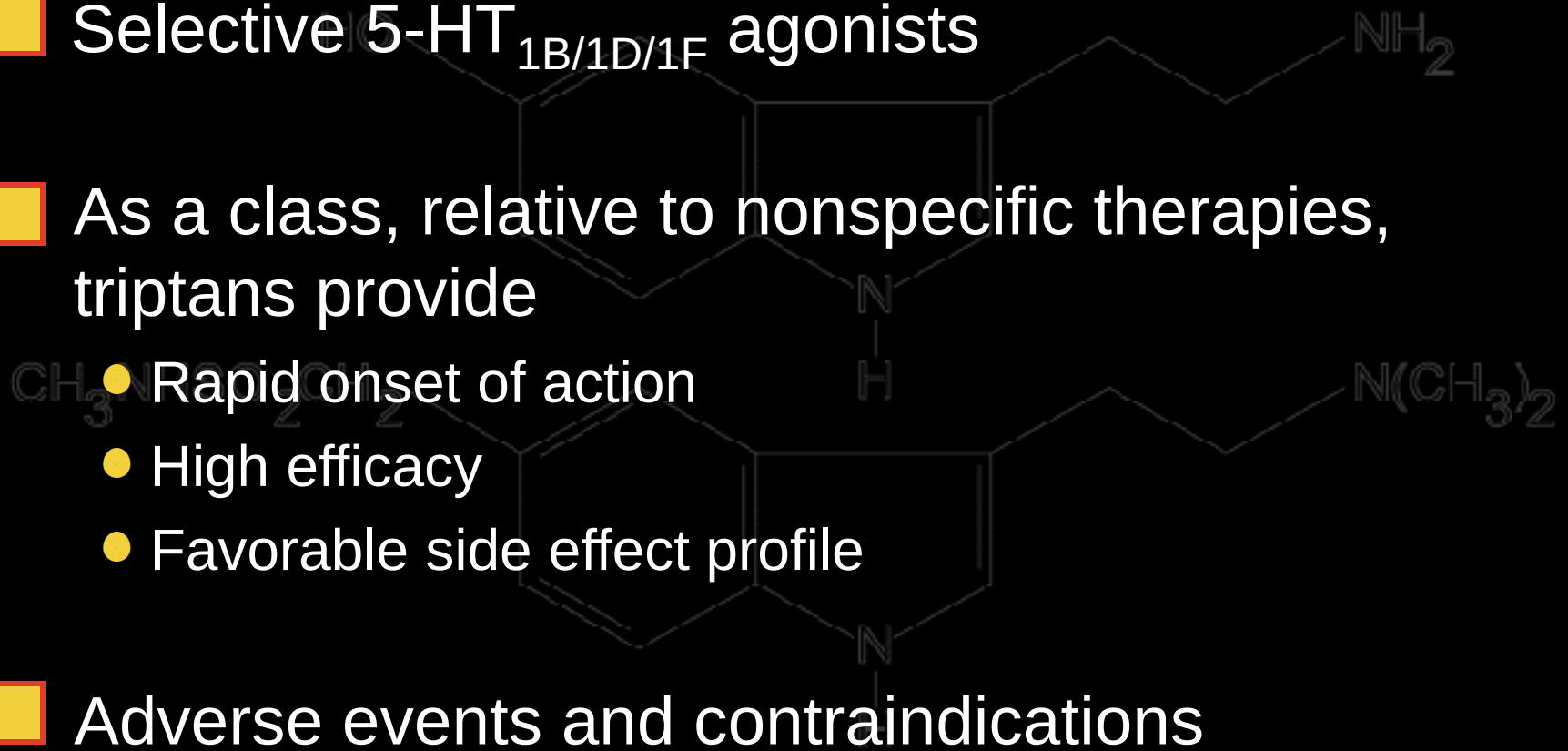
ACUTE TREATMENT PRINCIPLES

- Stratified care
- Early intervention
- Use correct dose and formulation
- Use a maximum of 2–3 days/week
- Use preventive therapy in selected patients

Silberstein SD. *Neurology*. 2000; Lipton RB, et al. *JAMA*. 2000.

TRIPTANS

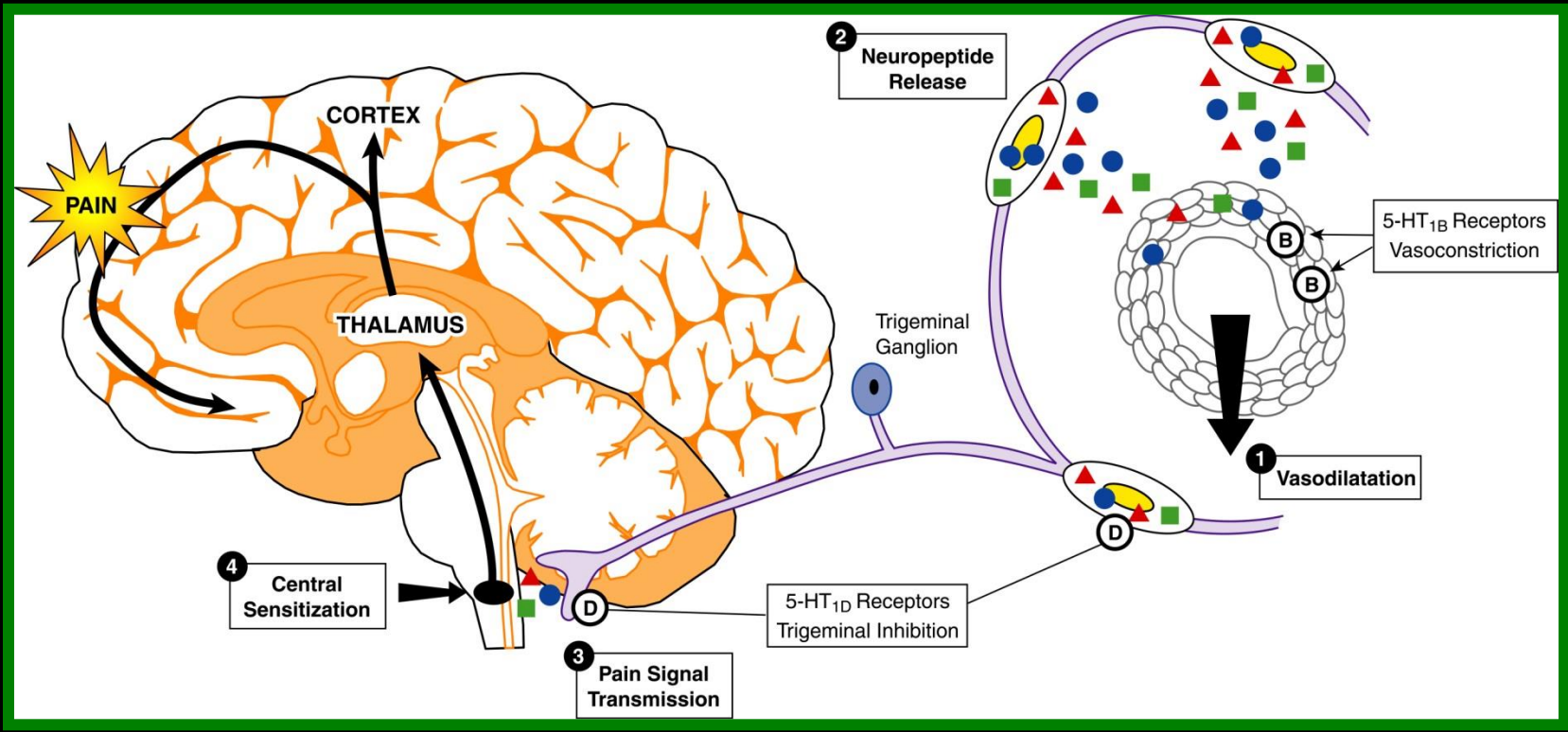
- Selective 5-HT$_{1B/1D/1F}$ agonists
- As a class, relative to nonspecific therapies, triptans provide
  - Rapid onset of action
  - High efficacy
  - Favorable side effect profile
- Adverse events and contraindications



Silberstein SD. *Neurology*. 2000.

HOW DO SPECIFIC MEDICATIONS WORK?

Trigeminovascular Antimigraine Targets



Hargreaves RJ et al. *Can J Neurol Sci*. 1999. (Modified)

TRIPTANS: TREATMENT CHOICES

- Sumatriptan
  - Tablet (25, 50, 100 mg)
  - Injection (3, 4, 6 mg)
  - Nasal spray (5, 20 mg)
  - Breath Powered Nasal
- Zolmitriptan
  - Tablet & melt (2.5, 5 mg)
  - Nasal spray (5 mg)
- Naratriptan
  - Tablet (1, 2.5 mg)
- Rizatriptan
  - Tablet & melt (5, 10 mg)
- Almotriptan
  - Tablet (6.25, 12.5 mg)
- Frovatriptan
  - Tablet (2.5 mg)
- Eletriptan
  - Tablet (20, 40 mg)

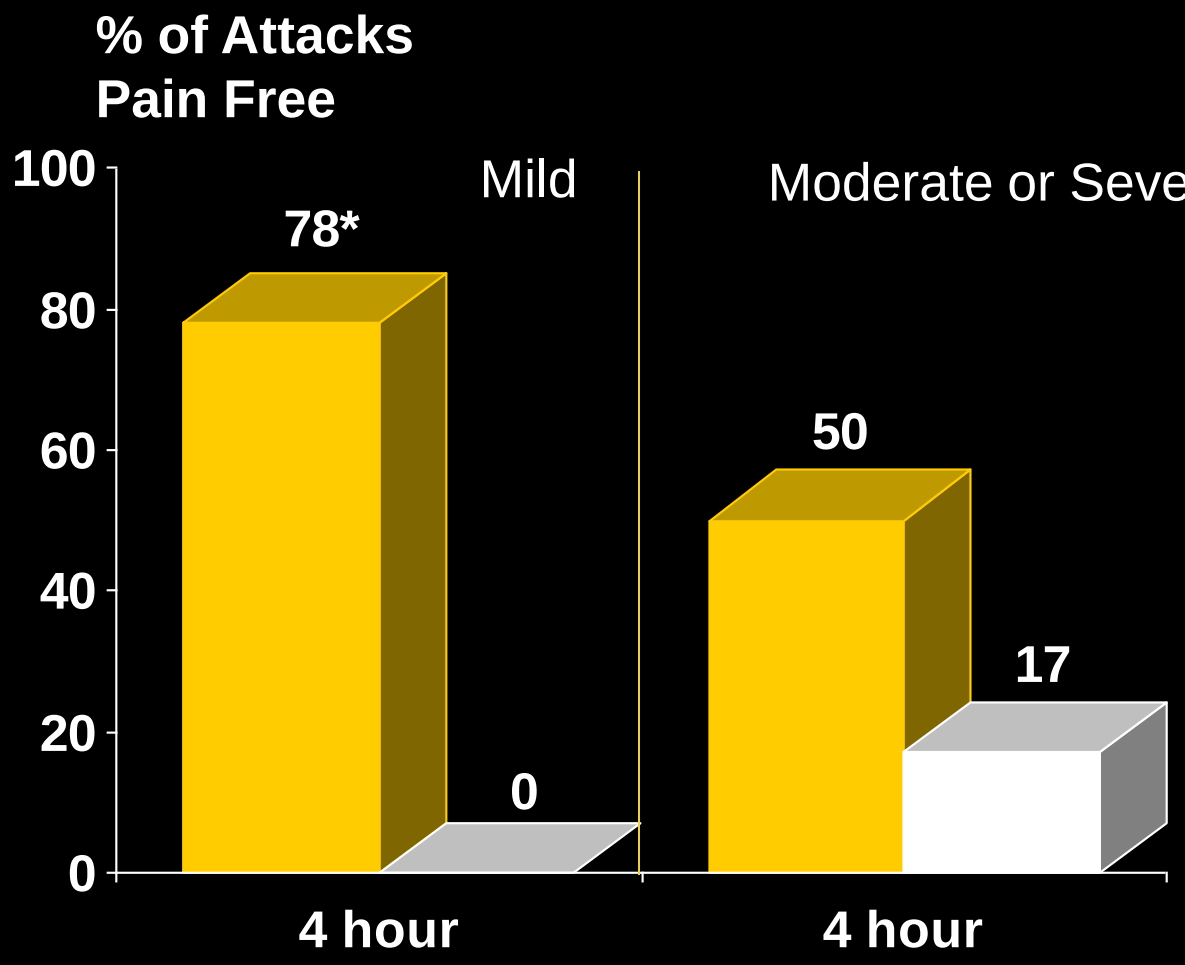
- Are there differences between the triptans?
- If one triptan fails, will another triptan work?

Ferrari MD et al. *Lancet*. 2001.

ROUTES OF ADMINISTRATION

- Oral therapies: most medications
- Nasal sprays: sumatriptan, DHE, zolmitriptan
- Injectable (SL, IM, IV) sumatriptan, DHE, injectable NSAIDs, neuroleptics
- Suppositories: antiemetics, ergots, opioids

TREAT MIGRAINE WHEN PAIN IS MILD



P<0.02* vs. placebo

Sumatriptan

Placebo

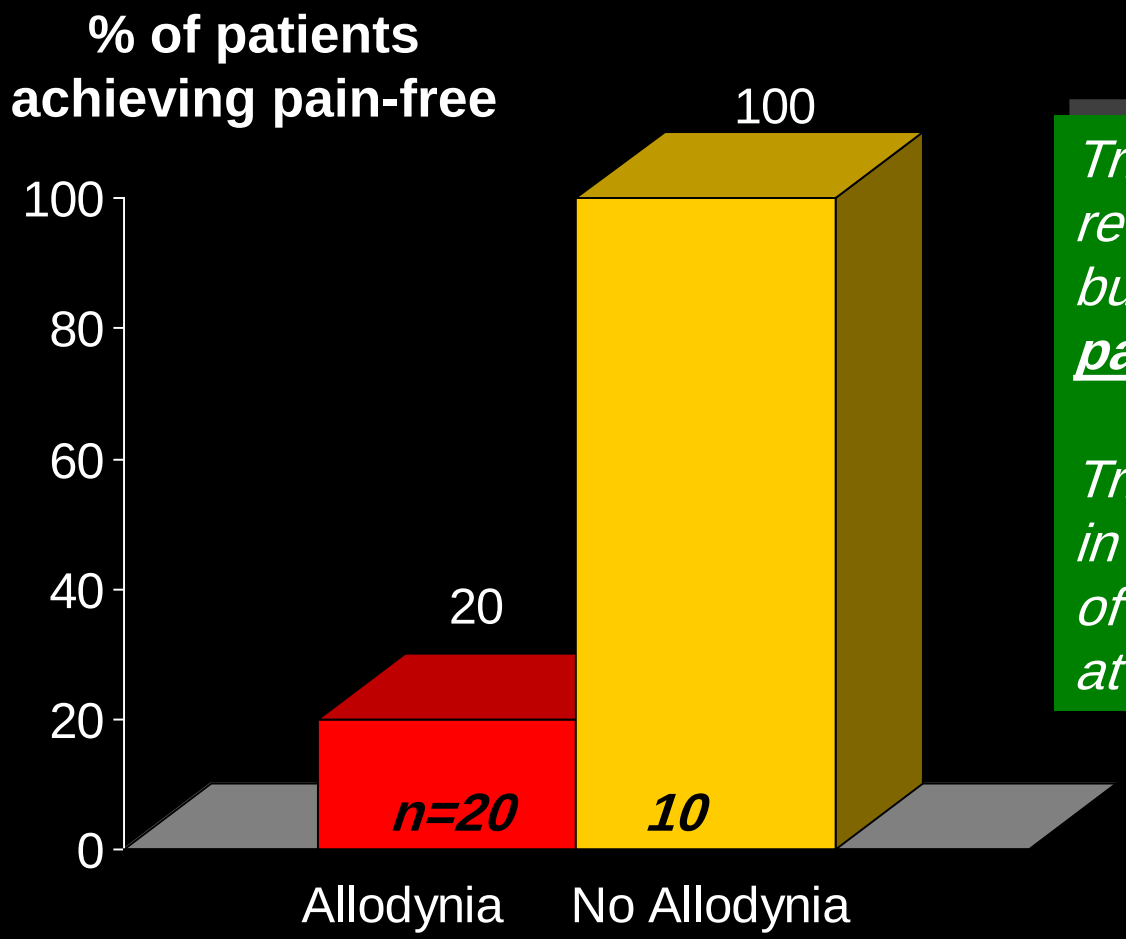
Mild headache:
N=40 sumatriptan;
N=6 placebo

Moderate/severe headache:
N=130 sumatriptan;
N=36 placebo

Cady RK et al. *Headache.* 2000

*post-hoc analysis

PRESENCE OF CUTANEOUS ALLODYNIA PREDICTS TRIPTAN EFFICACY

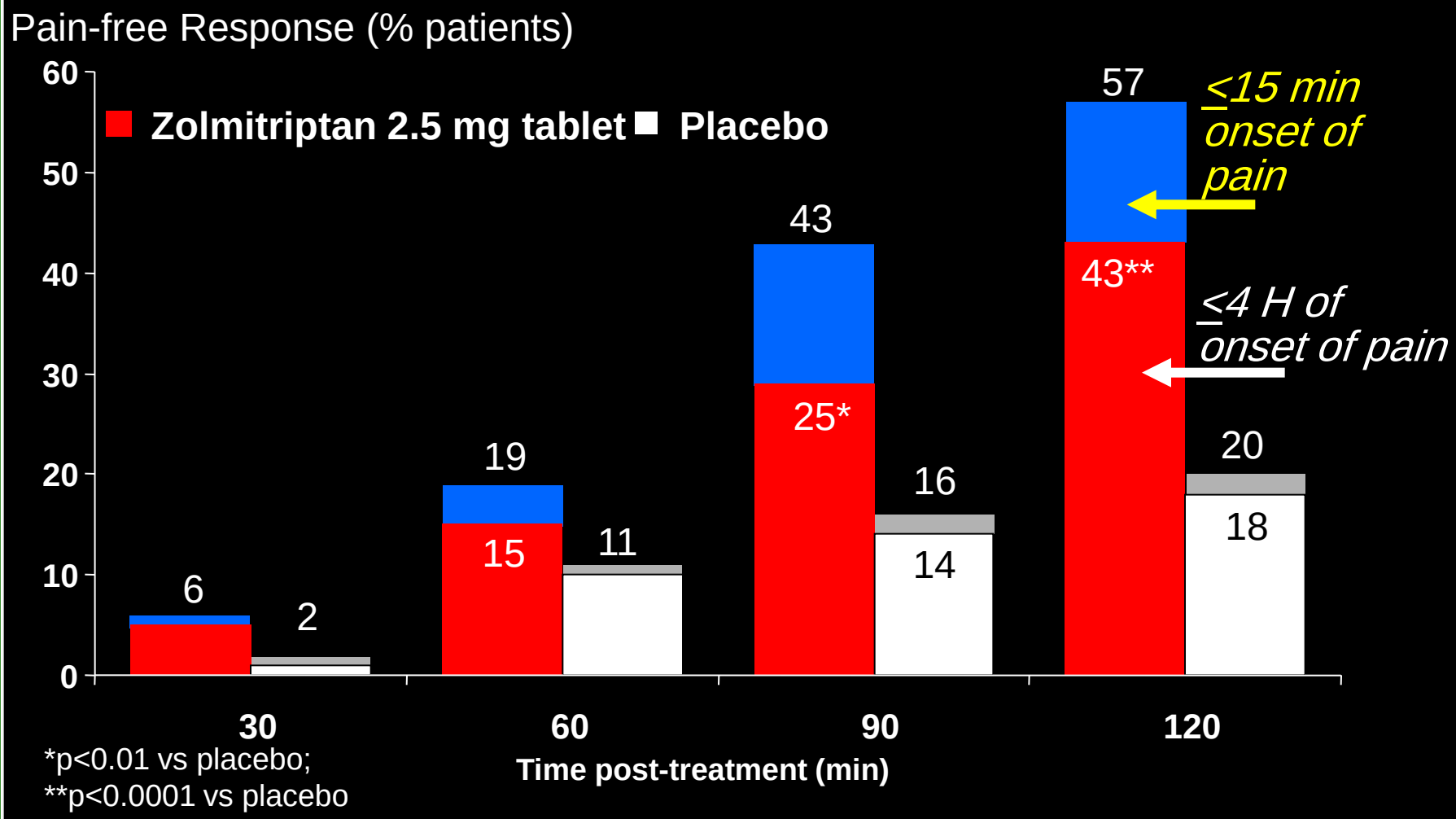


Triptans lead to a reduction in pain intensity, but only 20% achieved ***pain-free status***

Triptans relieve throbbing in all patients, regardless of presence of allodynia at time of treatment

Burstein R et al. *Headache.* 2002. (abstract; preliminary analysis)

TREATING WITHIN 15 MIN OF PAIN ONSET IMPROVES PAIN-FREE RATES



Klapper et al. *Neurology.* 2002. (abstract;)

REBOUND

- ***Rebound:*** Recurring headache induced by repetitive and chronic overuse of acute headache medication
  - Prevention: Limit frequency and dose of medications
  - Treatment: Withdrawal and washout of overused medication; consider using preventives

Capobianco DJ et al. *Headache*. 2001.

NON-DRUG SYMPTOM MANAGEMENT

- Quiet/White noise
- Dim Light (NO SCREENS!)
- Cool Temp
- Fluids
- Ignore?
- Setting Expectations – when will you return to class

HEADACHE TREATMENT: OPIOIDS AND BUTALBITAL

WHO USES THEM…?

Opioids

- Danger of abuse: restrict use

Butalbital Combination Analgesics

- No controlled studies have established their efficacy in migraine
- Major concerns are overuse, drug-induced headache, and withdrawal
- Use should be limited and carefully monitored

Silberstein SD et al. *Wolff's Headache And Other Head Pain*. 2001.

GUIDELINES: WHEN TO USE PREVENTIVE MANAGEMENT

- Migraine significantly interferes with patient's daily routine, despite acute R_x
- Acute medications contraindicated, ineffective, intolerable AEs, or overused
- Frequent headache (≥3 attacks per month?)
- Uncommon migraine conditions
- Patient preference

Silberstein SD et al. *Wolff's Headache And Other Head Pain*. 2001.

GOALS OF PREVENTIVE TREATMENT

- Decrease attack frequency (by 50%), intensity, and duration
- Improve responsiveness to acute R_x
- Improve function and decrease disability

Silberstein SD et al. *Headache in Clinical Practice*. 2nd ed. 2002.

PREVENTIVE MEDICATIONS: DRUG CLASSES

- Antiepileptics
- Antidepressants
- β-Blockers
- Ca^{2+}-Channel blockers
- NSAIDs
- 5-HT antagonists
- Neurotoxins
- Other
  - Vitamins
  - Minerals
  - Herbs
  - Angiotensin antagonists

Silberstein SD. *Cephalalgia*. 1997.

NONPHARMACOLOGIC TREATMENT: POTENTIAL INDICATIONS

- Patient preference
- Poor tolerance, response, or contraindications to drug therapy
- Pregnancy, planned pregnancy, or nursing
- History of overuse
- Significant life stress or deficient stress-coping skills

Goslin RE et al. *Behavioral and Physical Treatments for Migraine Headache*. 1999.

NONPHARMACOLOGIC TREATMENTS

Effective: **GRADE A**

- Relaxation training
- Thermal biofeedback with relaxation training
- EMG biofeedback
- Cognitive behavioral therapy

Insufficient evidence to recommend: **GRADE C**

- Acupuncture
- TENS
- Cervical manipulation
- Occlusal adjustment
- Hyperbaric oxygen
- Hypnosis

The benefits of behavioral therapy (eg, biofeedback, relaxation) are in addition to preventive drug therapy (eg, propranolol, amitriptyline): **GRADE B**

Goslin RE et al. *Behavioral and Physical Treatments for Migraine Headache*. 1999.

Questions?