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INSTITUTE FOR CLINICAL SYSTEMS IMPROVEMENT

Health Care Guideline:
Diagnosis and Treatment of Headache

Ninth Edition
March 2009

The information contained in this ICSI Health Care Guideline is intended primarily for health professionals and the following expert audiences:

- physicians, nurses, and other health care professional and provider organizations;
- health plans, health systems, health care organizations, hospitals and integrated health care delivery systems;
- health care teaching institutions;
- health care information technology departments;
- medical specialty and professional societies;
- researchers;
- federal, state and local government health care policy makers and specialists; and
- employee benefit managers.

This ICSI Health Care Guideline should not be construed as medical advice or medical opinion related to any specific facts or circumstances. If you are not one of the expert audiences listed above you are urged to consult a health care professional regarding your own situation and any specific medical questions you may have. In addition, you should seek assistance from a health care professional in interpreting this ICSI Health Care Guideline and applying it in your individual case.

This ICSI Health Care Guideline is designed to assist clinicians by providing an analytical framework for the evaluation and treatment of patients, and is not intended either to replace a clinician's judgment or to establish a protocol for all patients with a particular condition. An ICSI Health Care Guideline rarely will establish the only approach to a problem.

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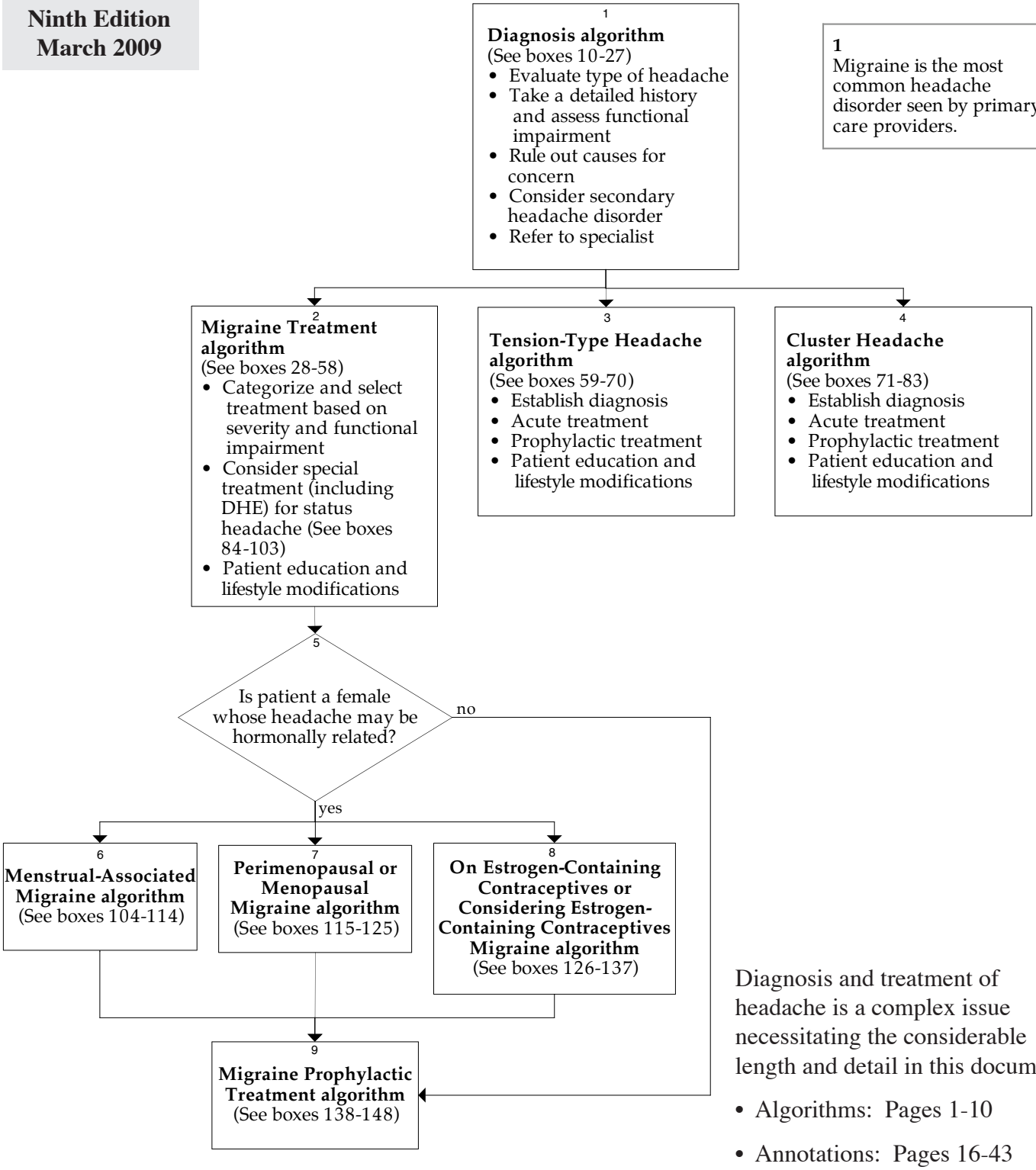
Health Care Guideline:
Diagnosis and Treatment of Headache

Main Algorithm

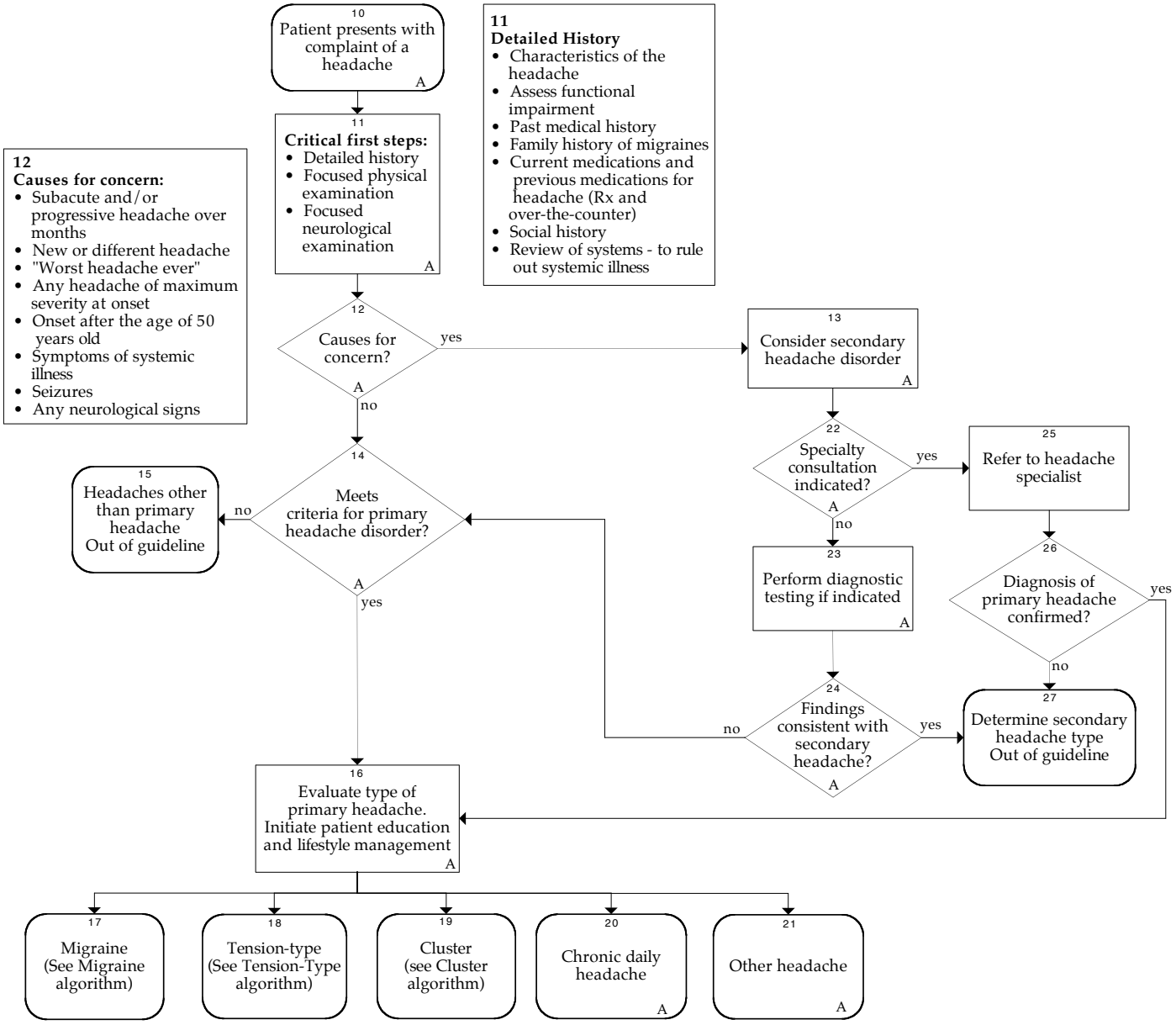
A = Annotation



1
Migraine is the most common headache disorder seen by primary care providers.

Diagnosis and treatment of headache is a complex issue necessitating the considerable length and detail in this document.

Diagnosis Algorithm



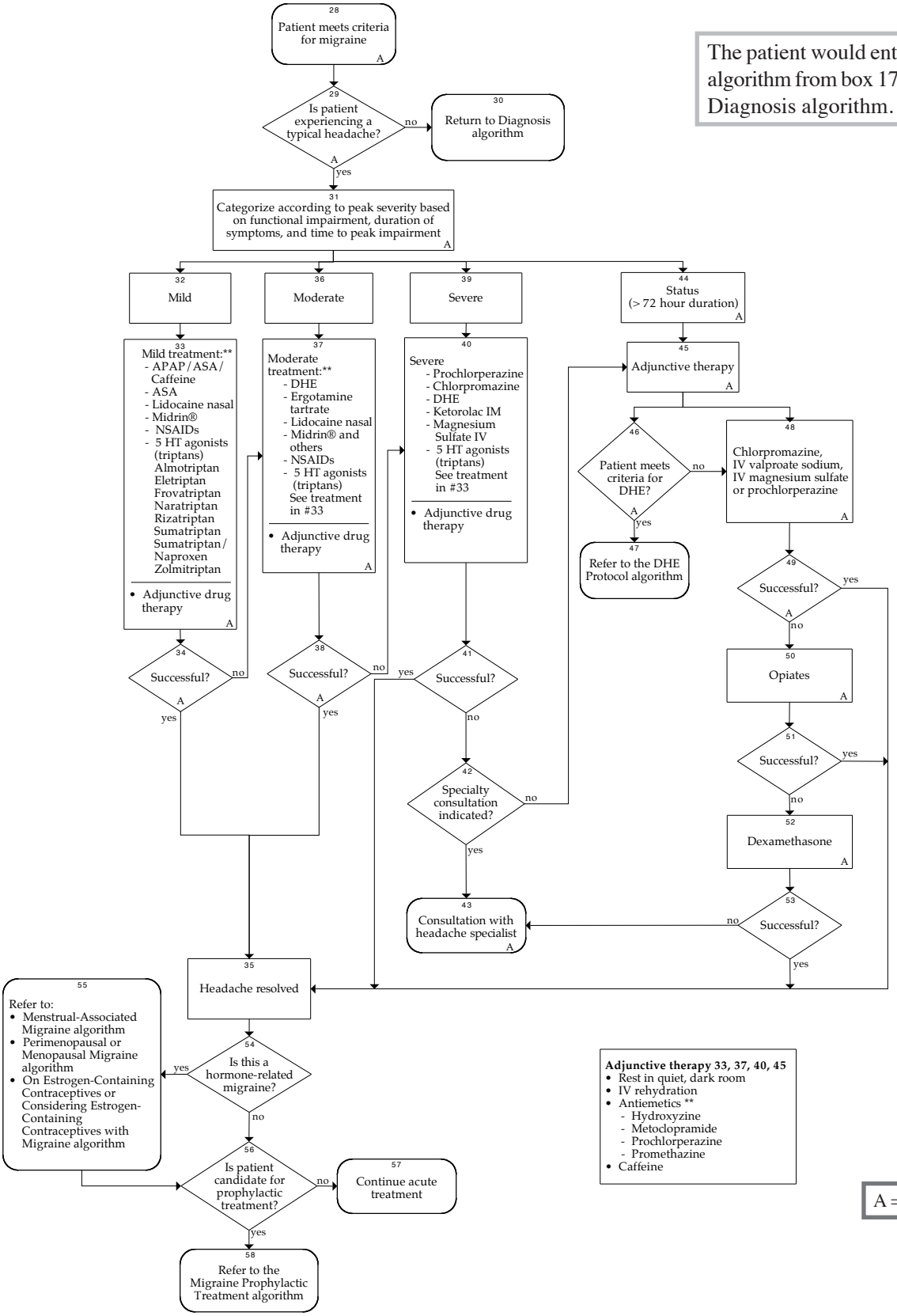
Sinus Headache **16**

Migraine-associated symptoms are often misdiagnosed as "sinus headache" by patients and providers. Most headaches characterized as "sinus headaches" are migraines.

The International Classifications of Headache Disorders (ICHD-II) defines sinus headache by purulent nasal discharge, pathologic sinus finding by imaging, simultaneous onset of headache and sinusitis, and headache localized to specific facial and cranial areas of the sinuses.

A = Annotation

Migraine Treatment Algorithm



The patient would enter this algorithm from box 17 of the Diagnosis algorithm.

A = Annotation

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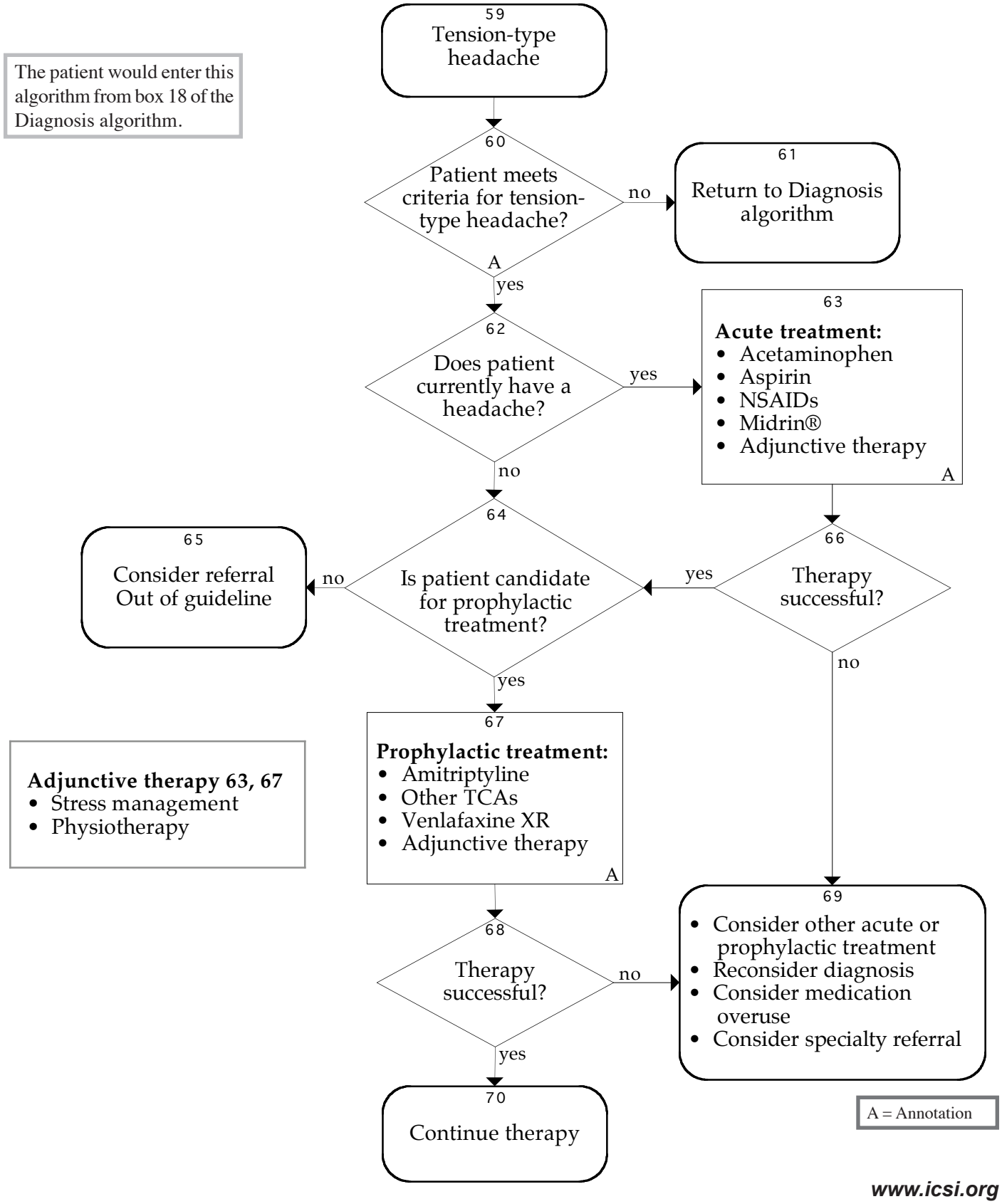
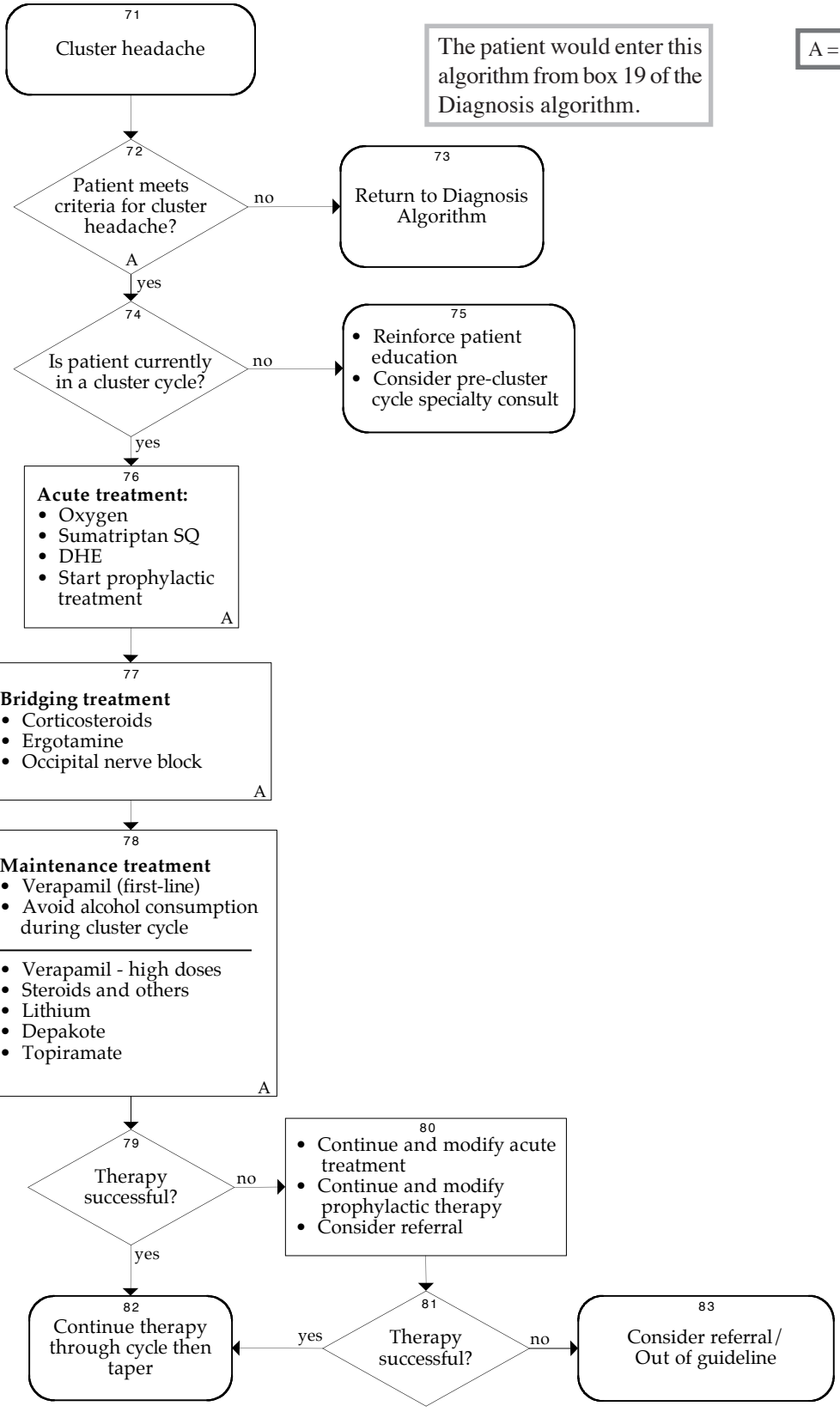
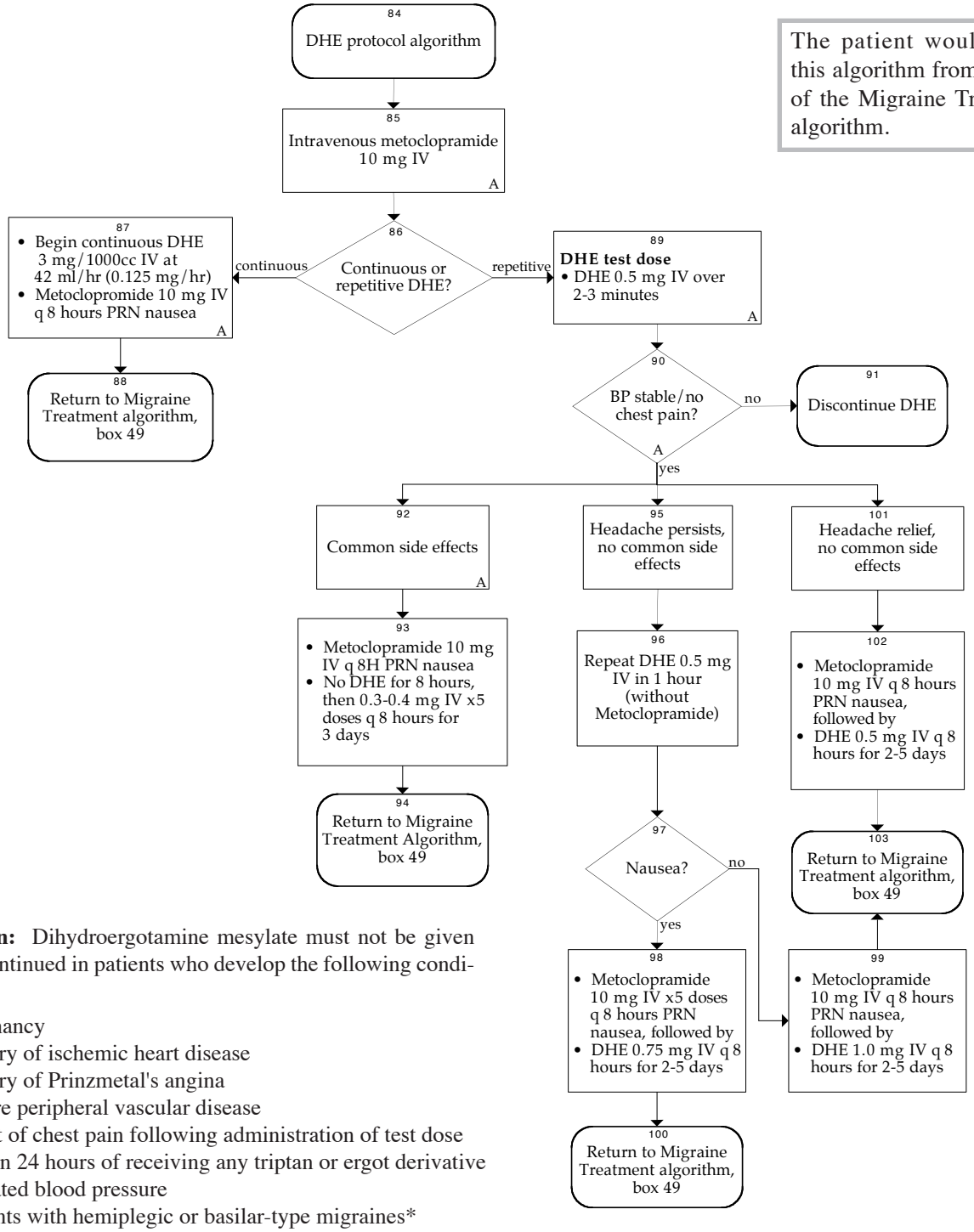
Tension-Type Headache Algorithm



Cluster Headache Algorithm



Dihydroergotamine Mesylate Algorithm



The patient would enter this algorithm from box 47 of the Migraine Treatment algorithm.

Caution: Dihydroergotamine mesylate must not be given to or continued in patients who develop the following conditions:

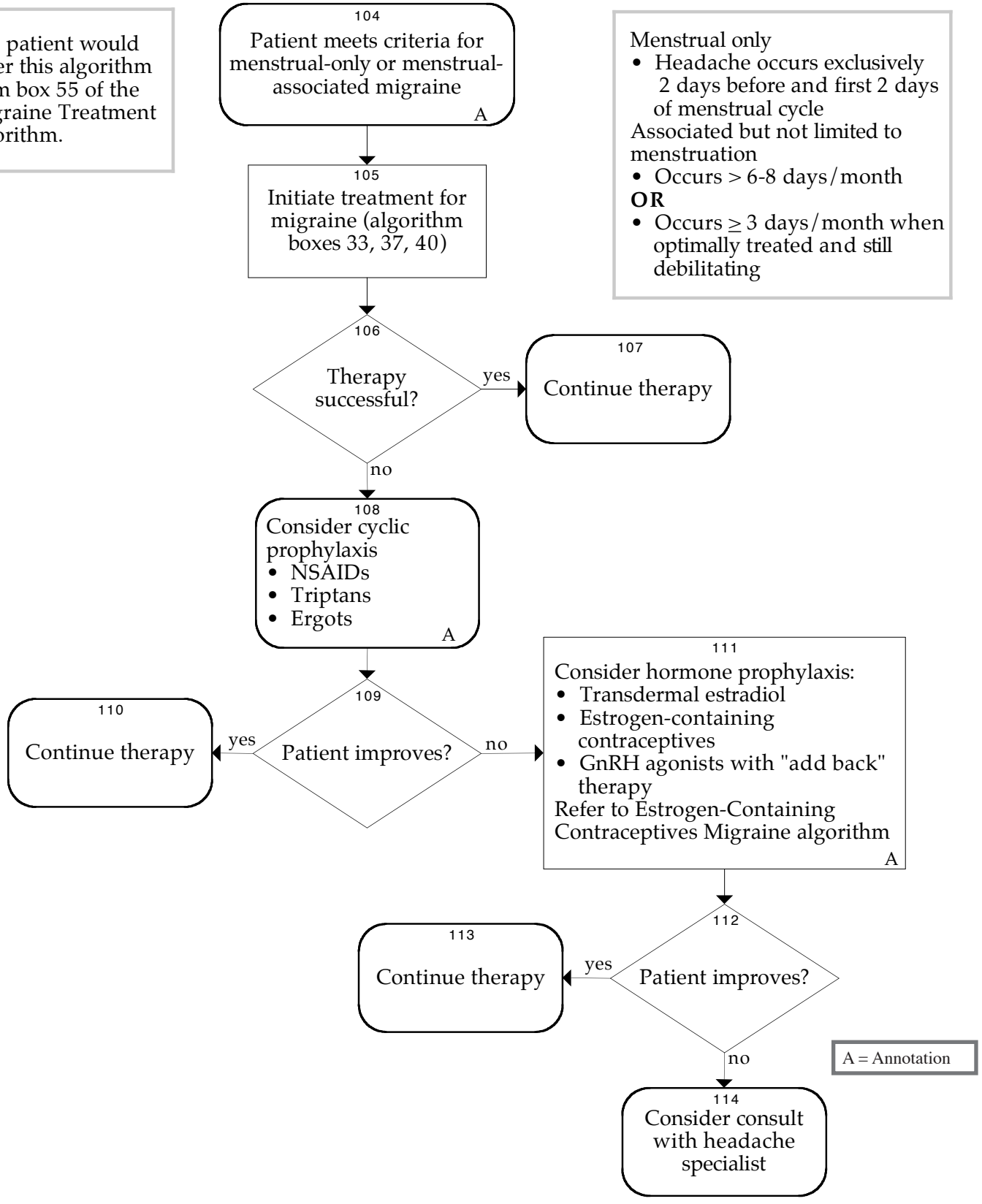
- Pregnancy
- History of ischemic heart disease
- History of Prinzmetal's angina
- Severe peripheral vascular disease
- Onset of chest pain following administration of test dose
- Within 24 hours of receiving any triptan or ergot derivative
- Elevated blood pressure
- Patients with hemiplegic or basilar-type migraines*
- Cerebrovascular disease

* Basilar-type migraine is defined as three of the following features: diplopia, dysarthria, tinnitus, vertigo, transient hearing loss or mental confusion *(Headache Classification Subcommittee of the International Headache Society, 2004)*.

A = Annotation

Menstrual-Associated Migraine Algorithm

The patient would enter this algorithm from box 55 of the Migraine Treatment algorithm.



Menstrual only
- Headache occurs exclusively 2 days before and first 2 days of menstrual cycle

Associated but not limited to menstruation
- Occurs > 6-8 days/month

OR
- Occurs ≥ 3 days/month when optimally treated and still debilitating

A = Annotation

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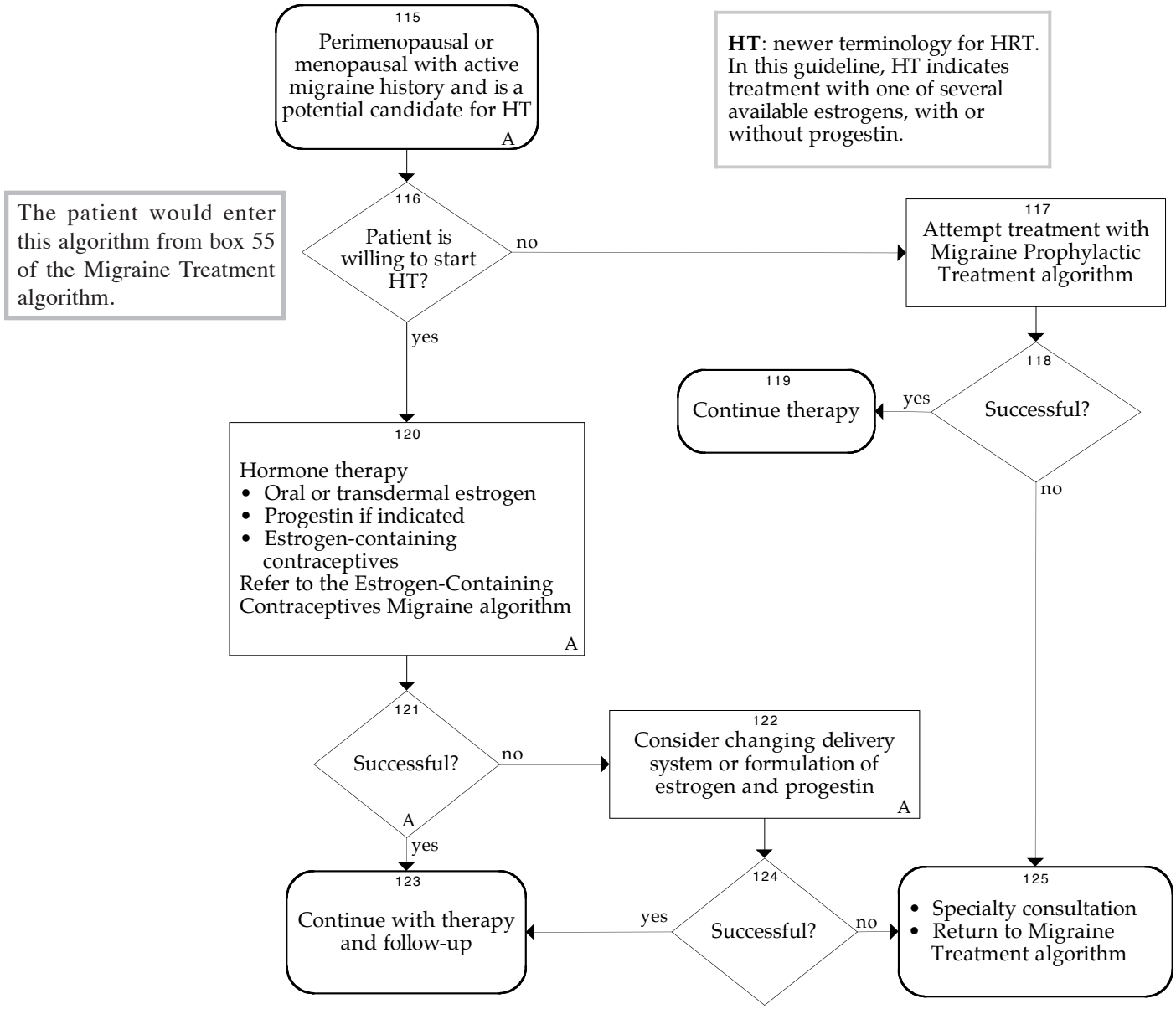
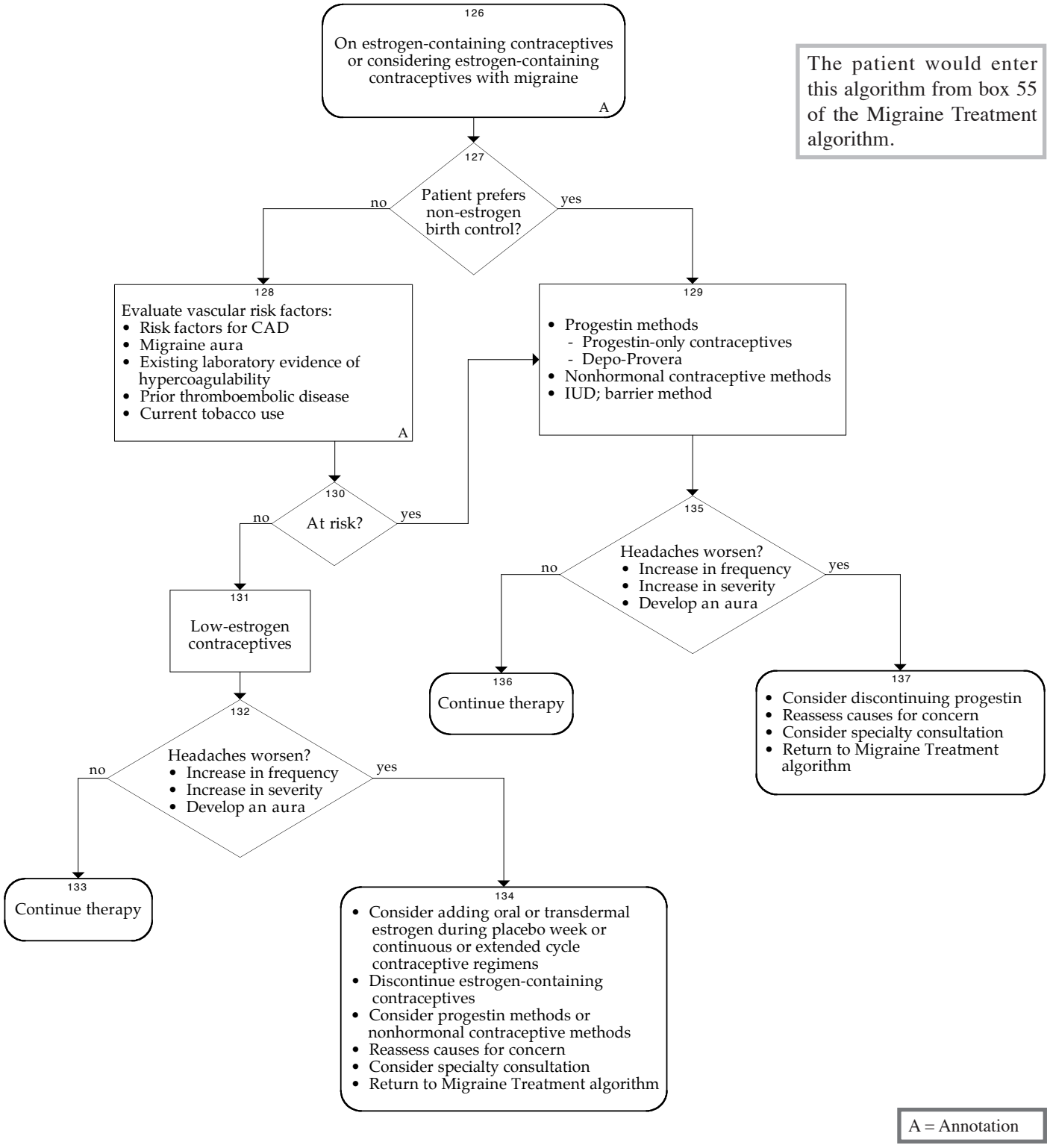
Perimenopausal or Menopausal Migraine Algorithm



A = Annotation

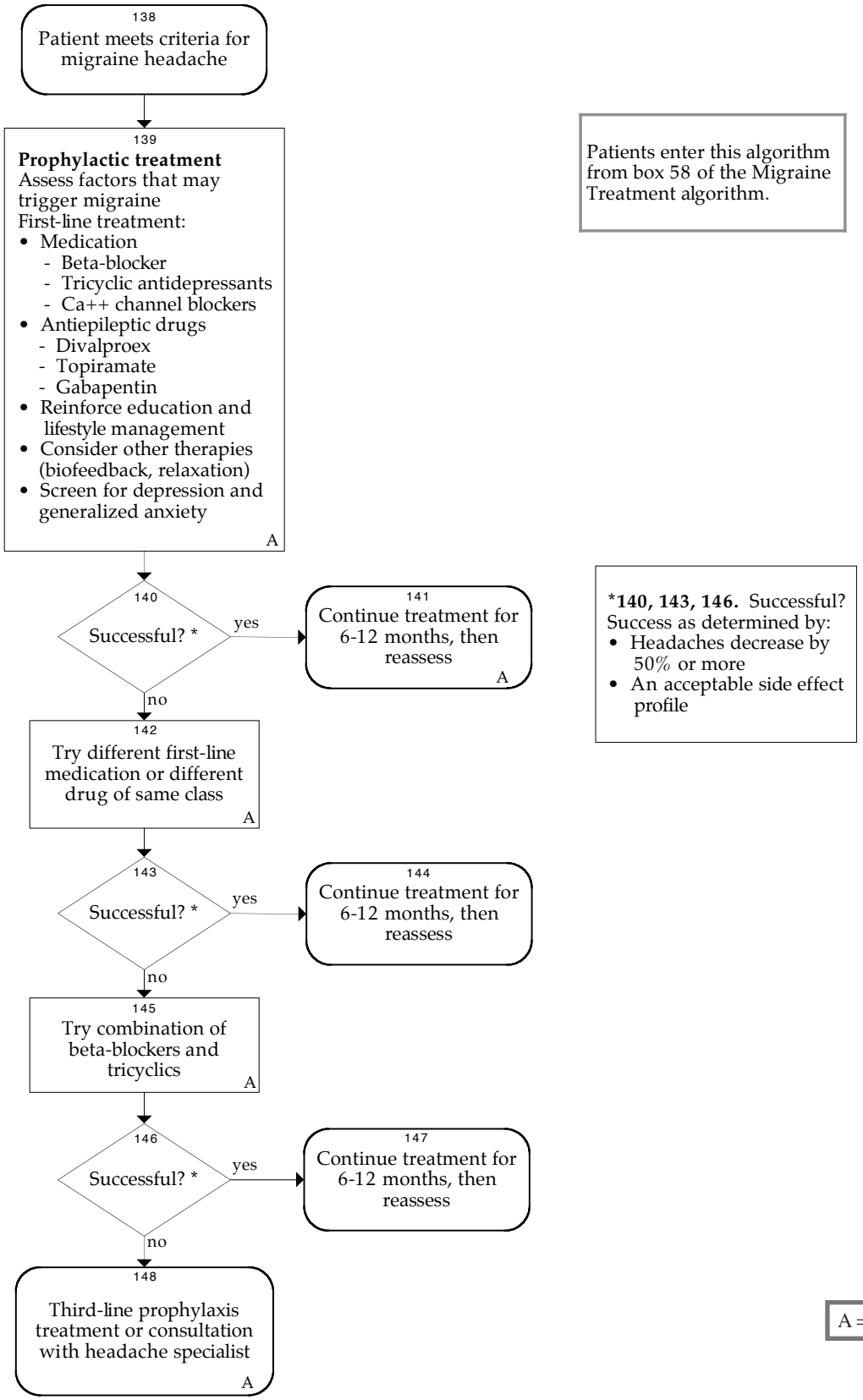
On Estrogen-Containing Contraceptives or Considering Estrogen-Containing Contraceptives with Migraine Algorithm



The patient would enter this algorithm from box 55 of the Migraine Treatment algorithm.

A = Annotation

Migraine Prophylactic Treatment Algorithm



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Foreword

Scope and Target Population

Patients age 12 years and older who present with headache.

Clinical Highlights and Recommendations

- Headache is diagnosed by history and physical examination with limited need for imaging or laboratory tests. *(Annotation #11; Aim #1)*
- Warning signs of possible disorder other than primary headache are *(Annotation #12; Aim #1)*:
  - Subacute and/or progressive headaches that worsen over time (months)
  - A new or different headache
  - Any headache of maximum severity at onset
  - Headache of new onset after age 50
  - Persistent headache precipitated by a Valsalva maneuver
  - Evidence such as fever, hypertension, myalgias, weight loss or scalp tenderness suggesting a systemic disorder
  - Presence of neurological signs that may suggest a secondary cause
  - Seizures
- Migraine-associated symptoms are often misdiagnosed as "sinus headache" by patients and providers. Most headaches characterized as "sinus headaches" are migraines. *(Annotation #16; Aim #1)*.
- Drug treatment of acute headache should generally not exceed more than two days per week on a regular basis. More frequent treatment other than this may result in medication-overuse chronic daily headaches. *(Annotation #33)*
- Inability to work or carry out usual activities during a headache is an important issue for migraineurs. *(Annotation #31; Aim #2)*
- Prophylactic therapy should be considered for all patients. *(Annotations #67, 78, 108, 111, 139, 148; Aim #6)*
- Migraines occurring in association with menses and not responsive to standard cyclic prophylaxis may respond to hormonal prophylaxis with the use of estradiol patches, creams or estrogen-containing contraceptives. (*Annotation #111)*
- Women who have migraines with aura have a substantially higher risk of stroke with the use of estrogen-containing contraceptive compared to those without migraines. Headaches occurring during perimenopause or after menopause may respond to hormonal therapy. *(Annotations #126, 128; Aim #6)*
- Most prophylactic medications should be started in a low dose and titrated to a therapeutic dose to minimize side effects and maintained at target dose for 8-12 weeks to obtain maximum efficacy. *(Annotation #139; Aims #6, 7)*

Priority Aims

1. Increase the accurate diagnosis of headaches. *(Annotation #11)*
2. Increase the functional status of those with migraine. *(Annotation #16)*
3. Increase the rate of treatment plans or adherence to plan for mild, moderate and severe headaches for migraineurs. *(Annotations #33, 34, 37, 43, 44, 45)*
4. Avoid the use of opiates and barbiturates for the treatment of primary headache. *(Annotations #37, 50)*
5. Increase education for patients with primary headache. *(Annotation #16)*
6. Increase appropriate prophylactic treatment based on headache type (i.e., migraine, tension-type, cluster, menstrual-associated migraine headache and chronic daily headache). *(Annotations #67, 78, 108, 111, 139, 148)*
7. Increase appropriate acute and prophylactic treatment for migraineurs based on level of severity (i.e., mild, moderate or severe migraine). *(Annotations #31, 33, 37)*

Key Implementation Recommendations

The following system changes were identified by the guideline work group as key strategies for health care systems to incorporate in support of the implementation of this guideline.

1. Develop a system for assessment of headache based on history and functional impairment.
2. Develop system for results of this assessment to be used for identification of treatment options/ recommendations.
3. Develop systems that allow for consistent documentation and montoring based on type of headache.
4. Develop a system for follow-up assessment that identifies success in management of headache in the primary care setting.
5. Develop a process that will remove barriers to referral to a specialist if indicated.
6. Develop a system for consistent documentation and monitoring of medication administration.

Related ICSI Scientific Documents

Guidelines

- Assessment and Management of Chronic Pain

Technology Assessment Reports

- Acupuncture for Chronic Osteoarthritic Pain, Headache, and Low Back Pain (#36, 2000)
- Percutaneous Radiofrequency Ablation for Facet-Mediated Neck and Back Pain (#88, 2005)

Disclosure of Potential Conflict of Interest

ICSI has adopted a policy of transparency, disclosing potential conflict and competing interests of all individuals who participate in the development, revision and approval of ICSI documents (guidelines, order sets and protocols). This applies to all work groups (guidelines, order sets and protocols) and committees (Committee on Evidence-Based Practice, Cardiovascular Steering Committee, Women's Health Steering Committee, Preventive & Health Maintenance Steering Committee and Respiratory Steering Committee).

Participants must disclose any potential conflict and competing interests they or their dependents (spouse, dependent children, or others claimed as dependents) may have with any organization with commercial, proprietary, or political interests relevant to the topics covered by ICSI documents. Such disclosures will be shared with all individuals who prepare, review and approve ICSI documents.

John Beithon, MD jointly owns stock through a family member's employee benefit option.

Frederick Taylor, MD has participated and received remuneration as an Advisory Board member for GlaxosmithKline and Merck. He received speakers fees and associated expense compensation for Speaker's Bureau participation for GlaxoSmithKline, Merck and Endo Pharmaceuticals. He has also received honorarium from Current Medicine for editorship of Current Pain and Headache Reports for 2008 and 2009. Additionally, he receives authorship content fees from Up to Date.

Jerry Swanson, MD has received royalties from Up To Date.

No other work group members have potential conflicts of interest to disclose.

Introduction to ICSI Document Development

This document was developed and/or revised by a multidisciplinary work group utilizing a defined process for literature search and review, document development and revision, as well as obtaining input from and responding to ICSI members.

For a description of ICSI's development and revision process, please see the Development and Revision Process for Guidelines, Order Sets and Protocols at http://www.icsi.org.

Evidence Grading System

A. Primary Reports of New Data Collection:

Class A: Randomized, controlled trial

Class B: Cohort study

Class C: Non-randomized trial with concurrent or historical controls
Case-control study
Study of sensitivity and specificity of a diagnostic test
Population-based descriptive study

Class D: Cross-sectional study
Case series
Case report

B. Reports that Synthesize or Reflect Upon Collections of Primary Reports:

Class M: Meta-analysis
Systematic review
Decision analysis
Cost-effectiveness analysis

Class R: Consensus statement
Consensus report
Narrative review

Class X: Medical opinion

Citations are listed in the guideline utilizing the format of *(Author, YYYY [report class])*. A full explanation of ICSI's Evidence Grading System can be found at http://www.icsi.org..

Algorithm Annotations

Diagnosis Algorithm Annotations

10. Patient Presents with Complaint of a Headache

Migraine is the most common headache disorder seen by primary care providers *(Tepper, 2004 [D])*.

A patient may present for care of headaches during an attack or during a headache-free period. If a patient presents during a headache, appropriate evaluation (history, examination, appropriate testing) needs to be in a timely fashion. Once the diagnosis of primary headache is established, acute treatment is instituted. If the patient has a history of recurrent headaches, a plan for treatment (acute and prophylactic) needs to be established.

11. Critical First Steps

Key Points:

- Headache is one of the most frequent diseases seen in clinics by health care providers.
- Minimal general physical examination is performed at the first consultation of patient presenting with a headache.

Headache can be diagnosed by symptoms and signs with the use of criteria. The International Classification of Headache Disorders, second edition (ICHD-II) system presently provides the gold standard. As empirical evidence and clinical experience accumulate criteria for diagnosing headaches will be revised *(National Headache Foundation, 1996 [NA])*.

Detailed History

Inquire about functional disabilities at work, school, housework or leisure activities during the past three months (informally or using well-validated disability questionnaire).

Assessment of the headache characteristics requires determination of the following:

Temporal profile:

- Time from onset to peak
- Usual time of onset (season, month, menstrual cycle, week, hour of day)
- Frequency and duration
- Stable or changing over past six months and lifetime

Autonomic features:

- Nasal stuffiness
- Rhinorrhea
- Tearing
- Eyelid ptosis or edema

Descriptive characteristics: pulsatile, throbbing, pressing, sharp, etc.

Location: uni- or bilateral, changing sides

Severity

Precipitating features and factors that aggravate and/or relieve the headache

Factors that relieve the headache

History of other medical problems

Pharmacological and non-pharmacological treatments that are effective or ineffective

Aura (present in approximately 15% of migraine patients)

Focused physical examination

Vital signs (blood pressure, pulse, respirations and temperature)

Extracranial structure evaluation such as carotid arteries, sinuses, scalp arteries, cervical paraspinal muscles

Examination of the neck in flexion versus lateral rotation for meningeal irritation. (Even a subtle limitation of neck flexion may be considered an abnormality.)

Focused neurological examination

A focused neurological examination may be capable of detecting most of the abnormal signs likely to occur in patients with headache due to acquired disease or a secondary headache.

This examination should include at least the following evaluations:

- Assessment of patient's awareness and consciousness, presence of confusion, and memory impairment.
- Ophthalmological examination to include pupillary symmetry and reactivity, optic fundi, visual fields, and ocular motility.
- Cranial nerve examination to include corneal reflexes, facial sensation and facial symmetry.
- Symmetry of muscle tone, strength (may be as subtle as arm or leg drift), or deep tendon reflexes.
- Sensation.
- Plantar response(s).
- Gait, arm and leg coordination.

12. Causes for Concern?

Headache features beyond that of International Classification of Headache Disorders, second edition (ICHD-II) system criteria should raise concern of a more sinister underlying cause *(Pryse-Phillips, 1997 [R])*.

Causes for concern in the diagnosis of headaches may alter a diagnosis of migraine to a secondary diagnosis of headache, which can be more serious and/or life-threatening *(Dalessio, 1994 [R]; Edmeads, 1988 [R])*.

Causes for concern must be evaluated irrespective of the patient's past history of headache. Warning signs of possible disorder other than primary headache are:

- Subacute and/or progressive headaches that worsen over time (months).

- A new or different headache or a statement by a headache patient that "this is the worst headache ever."
- Any headache of maximum severity at onset.
- Headaches of new onset after the age of 50 years old.
- Persistent headache precipitated by a Valsalva maneuver such as cough, sneeze, bending or with exertion (physical or sexual).
- Evidence such as fever, hypertension, myalgias, weight loss or scalp tenderness suggesting a systemic disorder.
- Neurological signs that may suggest a secondary cause. For example: meningismus, confusion, altered levels of consciousness, changes or impairment of memory, papilledema, visual field defect, cranial nerve asymmetry, extremity drifts or weaknesses, clear sensory deficits, reflex asymmetry, extensor plantar response, or gait disturbances.
- Seizures.

13. Consider Secondary Headache Disorder

The presence of the symptoms or signs listed above suggests a secondary cause for the headache and could be indicative of an underlying organic condition. Alternate diagnoses include subarachnoid hemorrhage, tumor, meningitis, encephalitis, temporal arteritis, idiopathic intracranial hypertension, and cerebral venous thrombosis, among others.

Secondary Headaches

- **Subacute and/or progressive, worsening headaches over weeks to months:**

  Headaches that worsen with time may be due to a progressive intracranial lesion such as tumor, subdural hematoma, or hydrocephalus. While the neurologic examination may reveal abnormalities that suggest a sinister process, this is not always the case. Accordingly, a history of a progressive headache is an indication for head imaging. For most processes, magnetic resonance imaging with and without gadolinium contrast will be more sensitive than a computed tomography head scan.

- **A new or different headache or a statement by a headache patient that "this is the worst headache of my life":**

  Primary headache disorders (mainly tension-type headache and migraine) are exceedingly common. A history of a primary headache disorder does not confer protection against a new, serious process that presents with headache. The acuteness of a headache will largely define the differential diagnosis. Headache that presents suddenly, "like a thunderclap," can be characteristic of several serious intracranial processes, including subarachnoid hemorrhage, venous sinus thrombosis, bacterial meningitis, spontaneous cerebral spinal fluid leak, carotid dissection, and rarely, pituitary apoplexy and hypertensive encephalopathy. The first investigation is a computed tomography head scan without contrast. If there is no evidence of a subarachnoid hemorrhage, a lumbar puncture should be performed. If both studies are normal and the suspicion of subarachnoid hemorrhage is still high, a magnetic resonance imaging with and without gadolinium should be obtained. Neurological consultation is indicated and further tests for consideration include magnetic resonance angiogram and magnetic resonance venogram.

  If the headache is more subacute in onset, chronic meningitis may need to be considered along with a space-occupying intracranial lesion or hydrocephalus. Again, neuroimaging should be performed. Whether a lumbar puncture is done will be guided by the index of suspicion regarding a meningeal process (e.g., meningitis).

- **Headache of sudden onset:**

  This refers mainly to thunderclap headache (see above). It should be treated as an emergency since the possible presence of aneurysmal subarachnoid hemorrhage needs to be assessed as outlined above. Other secondary causes of headache will be found less commonly.

- **Headache precipitated by a Valsalva maneuver such as cough, sneeze, bending or with exertion:**

  Valsalva headaches, while often representing primary cough headache, can signal an intracranial abnormality, usually of the posterior fossa. The most commonly found lesion is a Chiari malformation, although other posterior fossa lesions are sometimes found. Less commonly there are intracranial lesions located elsewhere. A magnetic resonance imaging needs to be obtained to appropriately investigate for these possibilities. Exertional headache, such as with exercise or during sexual activity, may represent a benign process such as migraine. However, if the headache is severe or thunderclap in onset, investigations will be necessary as already outlined above.

- **Headaches of new onset after the age of 50 years:**

  The large majority of individuals who are destined to develop a primary headache disorder do so prior to age 50 years. Of course, this is not universal and migraine or other primary headache disorders may begin even at an advanced age. Nevertheless, care should be taken before a diagnosis of a primary headache disorder is assigned. Many patients who do have the onset of a new headache disorder after age 50 years will merit brain imaging. In addition, after the age of 50 years, a new headache disorder should evoke suspicion of possible giant cell arteritis. Obviously, symptoms of polymyalgia rheumatica, jaw claudication, scalp tenderness or fever will increase the likelihood of this diagnosis. Findings of firm, nodular temporal arteries and decreased temporal pulses will increase the suspicion as will an elevated sedimentation rate.

- **Symptoms suggestive of a systemic disorder such as fever, myalgias, weight loss or scalp tenderness or a known systemic disorder such as cancer or immune deficiency:**

  Systemic disorders, while not incompatible with a coexistent primary headache disorder, should signal caution. Patients should be carefully evaluated. Obviously, the differential diagnosis will be long and the index of suspicion for any given process will largely depend on the clinical setting.

- **Presence of subtle neurological signs suggests a secondary cause for headache. For example, meningismus, confusion, altered level of consciousness, memory impairment, papilledema, visual field defect, cranial nerve abnormalities, pronator drift, extremity weakness, significant sensory deficits, reflex asymmetry, extensor plantar response, or gait disturbance when accompanying a headache should elicit caution:**

  While neurological signs may be unrelated to a headache, previously undocumented neurological findings that are presumably new need to be carefully considered. Usually cranial imaging will be the initial study. Depending on the index of suspicion, lumbar puncture and blood studies may be indicated.

- **Seizures:**

  While seizures can occasionally be a manifestation of a primary headache disorder such as migraine, this is the exception and not the rule; it is a diagnosis of exclusion. Other etiologies for seizures including space occupying lesions, infection, stroke and metabolic derangements will need to be considered. Again, magnetic resonance imaging is the imaging procedure of choice unless there is an issue of acute head trauma, in which case a computed tomography head scan should be obtained initially.

- **Diagnosis to be included in secondary headache:**
  - subdural hematoma
  - epidural hematoma
  - tumor
  - other metabolic disorders
  - craniocervical arterial dissection
  - giant cell arteritis
  - acute hydrocephalus
  - obstructive hydrocephalus
  - cerebral spinal fluid leaks
  - cerebral venous sinus thrombosis

This list is not intended to be all-inclusive but rather to represent the most commonly seen diagnosis for secondary headache by the primary care physician.

14. Meets Criteria for Primary Headache Disorder?

The International Classification of Headache Disorders, second edition (ICHD-II) system for migraine have been studied in a community population sample without consideration of treatment. Findings suggest that the best criteria differentiating migraine from other headache types are the presence of nausea and/or vomiting in combination with two of the following three symptoms: photophobia, phonophobia and osmophobia *(National Headache Foundation, 1996 [NA])*.

Modified Diagnostic Criteria

Migraine: with and without Aura

A. At least two of 1-4, plus one of 5 or 6:
   1. Unilateral location
   2. Pulsating/throbbing quality
   3. Moderate or severe intensity (inhibits or prohibits daily activities)
   4. Aggravation by routine activity
   5. Nausea and/or vomiting
   6. Photophobia and phonophobia

B. Aura criteria
   1. One or more fully reversible aura symptoms
   2. At least one aura symptom develops over more than 4 minutes or two or more symptoms occur in succession
   3. Symptoms do not last more than 60 minutes
   4. Attack follows within 60 minutes

C. Previous similar attacks

D. Organic disorder is ruled out by the initial evaluation or by diagnostic studies. If another disorder is present, the headaches should not have started in close temporal relationship to the disorder.

Episodic Tension-Type Headache

A. Headache less than 15 days per month.

B. Lasts 30 minutes to 7 days

C. At least two of the following characteristics:
   1. Pressing/tightening (non-pulsating) quality
   2. Mild to moderate intensity (may inhibit, but does not prohibit activities)
   3. Bilateral location
   4. Not aggravated by routine physical activity

D. Both of the following:
   1. No nausea or vomiting (anorexia may occur)
   2. Photophobia and phonophobia are absent, or only one of the two is present

E. Organic disorder is ruled out by the initial evaluation or by diagnostic studies. If another disorder is present, the headaches should not have started in close temporal relationship to the disorder.

Chronic Tension-Type Headache

A. Average frequency of greater than 15 attacks per month

B. At least two of the following pain characteristics:
   1. Pressing/tightening quality
   2. Mild to moderate intensity (may inhibit, but does not prohibit activities)
   3. Bilateral location
   4. Not aggravated by routine physical activity

C. Both of the following:
   1. No vomiting
   2. No more than one of the following: nausea, photophobia or phonophobia

D. Organic disorder is ruled out by the initial evaluation or by diagnostic studies. If another disorder is present, the headaches should not have started in close temporal relationship to the disorder.

Cluster Headache

A. Severe unilateral orbital, supraorbital and/or temporal pain lasting 15 to 180 minutes untreated

B. Attack is associated with at least one of the following signs on the side of the pain:
   1. Conjunctival injection
   2. Lacrimation
   3. Nasal congestion
   4. Rhinorrhea
   5. Forehead and facial swelling
   6. Miosis
   7. Ptosis
   8. Eyelid edema
   9. Agitation, unable to lie down

C. Frequency from one every other day to eight per day

D. Organic disorder is ruled out by the initial evaluation or by diagnostic studies. If another disorder is present, the headaches should not have started in close temporal relationship to the disorder.

The table "Modified Diagnostic Criteria" has been modified from the International Classification of Headache Disorders, second edition (ICHD-II) system criteria and describes the differentiating criteria applicable for the diagnosis of migraine and other primary headache disorders.

16. Evaluate Type of Primary Headache. Initiate Patient Education and Lifestyle Management

Migraine-associated symptoms are often misdiagnosed as "sinus headache" by patients and providers. This has led to the underdiagnosis and treatment of migraine.

While education is of paramount importance in managing any condition, it is especially important in the ongoing management of headache. Patients may have to make lifestyle changes, are often required to make self-management choices in the treatment of individual headaches, and should maintain a diary to clarify the frequency, severity, triggers and treatment responses. Related considerations are as follows:

- Headache is due to physiologic disorders, to which individuals may be genetically predisposed.
- Identifiable food or alcohol triggers are present in a minority of patients.
- Most patients will benefit from stress reduction, regular eating and sleeping schedules, and regular aerobic exercise.
- Chronic daily headache, including transformed migraine, is associated with overuse of analgesics or acute treatment drugs. Use of drugs for acute treatment of headache for more than nine days per month is associated with an increased risk of chronic daily headaches.
- Keeping a headache diary has the potential benefit of monitoring treatment effect upon severity, frequency and disability.
- Acute treatment has the goal of shortening individual headaches, while prophylaxis can reduce frequency and possibly severity.
- It is often not possible to eliminate primary headache completely.

The presentation of four clinical characteristics and duration can help providers determine if the migraine headache is likely, possible or unlikely by using the simple mnemonic POUNDing for the screening of migraine headache.

POUNDing Migraine Diagnosis Screening and Scoring System

P = **P**ulsating quality O = h**O**urs of duration (4-72) U = **U**nilateral location N = **N**ausea or vomiting D = **D**isabling intensity	Is it a pulsating headache? Does it last between 4 and 72 hours without medication? Is it unilateral? Is there nausea? Is the headache disabling? (Disabling headaches are those that disrupt the patient's daily activities.)
Number of "Yes" answers to the above questions: 5 Migraine Likely 3-4 Migraine Possible 1-2 Migraine Unlikely	

Detsky ME, McDonald DR, Baerlocher MO, et al. Does this patient with headache have a migraine or need neuroimaging? *JAMA* 2006;296:1274-83.

(Detsky, 2006 [M])

Sinus headache

The International Classification of Headache Disorders, second edition (ICHD-II) system criteria defines sinus headache by purulent nasal discharge, pathologic sinus finding by imaging, simultaneous onset of headache and sinusitis, and headache localized to specific facial and cranial areas of the sinuses.

Numerous non-pharmacological and pharmacological therapies are explored in the reference below. By understanding the pathophysiology, genetics, and receptor pharmacology of headaches, improvements and more effective therapies will likely evolve *(Lockett, 1992 [A]; Merikangas, 1994 [B]; Tepper, 2004 [D])*.

20. Chronic Daily Headache

Chronic daily headache refers to the presence of a headache more than 15 days per month for greater than three months. Chronic daily headache is not a diagnosis but a category that may be due to disorders representing primary and secondary headaches. Secondary headaches are typically excluded with appropriate neuroimaging and other tests. Chronic daily headache can be divided into those headaches that occur nearly daily that last four hours or less and those that last more than four hours, which is more common. The shorter-duration daily headache contains less common disorders such as chronic cluster headache and other trigeminal autonomic cephalgias. Only daily headaches of long duration are considered here.

Chronic daily headache has been estimated to occur in 2.5%-4% of the general population with surveys showing that chronic tension-type headache is a bit more common than chronic migraine (transformed migraine). In the clinic setting, chronic migraine is much more common than chronic tension-type headache. As with migraine, chronic daily headaches are more common in women than men. An associated factor for chronic daily headache is medication overuse. As outlined below, the Headache Classification Committee of the International Classification of Headache Disorders, second edition (ICHD-II) has provided revised guidelines for chronic migraine and medication overuse headache *(Olesen, 2006 [X])*.

In diary studies, patients who fulfill criteria for a diagnosis of the older definition of transformed migraine also fulfill criteria for a diagnosis of the revised definition of chronic migraine, which is presented below *(Bigal, 2006 [D]; Liebestein, 2007 [C])*.

Revised International Classification of Headache Disorders, second edition (ICHD II) criteria for chronic migraine:

Appendix 1.5.1 Chronic migraine

A. Headache (tension-type and/or migraine) on greater than or equal to 15 days per month for at least three months*

B. Occurring in a patient who has had at least five attacks fulfilling criteria for 1.1 Migraine without aura

C. On greater than or equal to eight days per month for at least three months headache has fulfilled C1 and/or C2 below, that is, has fulfilled criteria for pain and associated symptoms of migraine without aura

    1. Has at least two of a-d

        (a) unilateral location

        (b) pulsating quality

        (c) moderate or severe pain intensity

        (d) aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)

        and at least one of a or b

(a) nausea and/or vomiting

(b) photophobia and phonophobia

2. Treated and relieved by triptan(s) or ergot before the expected development of C1 above

D. No medication overuse and not attributed to another causative disorder

*Characterization of frequently recurring headache generally requires a headache diary to record information on pain and associated symptoms day by day for at least one month. Sample diaries are available at http://www.i-h-s.org.

Medication-overuse headache

History and physical and neurological examinations do not suggest any of the disorders listed in groups 5-12, or history and/or physical and/or neurological examinations do suggest such a disorder but it is ruled out by appropriate investigations, or such disorder is present but headache does not develop in close temporal relation to the disorder *(Olesen, 2006 [X]*.

International Classification of Headache Disorders, second edition (ICHD-II), system revised criteria for medication overuse headache:

Appendix 8.2 Medication overuse headache

Diagnostic criteria:

A. Headache greater than or equal to 15 days/month

B. Regular overuse for greater than three months of one or more acute/symptomatic treatment drugs as defined under subforms of 8.2.

1. Ergotamine, triptans, opioids or combination analgesic medications on greater than or equal to 10 days/month on a regular basis for greater than three months

2. Simple analgesics or any combination of ergotamine, triptans, analgesic opioids on greater than or equal to 15 days/month on a regular basis for greater than three months without overuse of any single class alone

C. Headache has developed or markedly worsened during medication overuse *(Olesen, 2006 [X])*.

Chronic Tension-Type Headache

As noted, chronic tension-type headache is the most common headache identified in epidemiologic surveys, but it is seen infrequently in headache clinics. The International Classification of Headache Disorders, second edition (ICHD-II) criteria for this disorder are:

Diagnostic criteria:

A. Headache occurring on 15 days or more per month on average for more than three months (180 days or more per year) and fulfilling criteria B-D

B. Headache lasts hours or may be continuous

C. Headache has at least two of the following characteristics:

- bilateral location
- pressing/tightening (non-pulsating) quality

- mild or moderate intensity
- not aggravated by routine physical activity such as walking or climbing stairs

D. Both of the following:

- no more than one of photophobia, phonophobia or mild nausea
- neither moderate or severe nausea nor vomiting

E. Not attributed to another disorder

(Headache Classification Subcommittee of the International Headache Society, 2004 [R])

Hemicrania Continua

A less common but not rare (and under recognized) cause for chronic daily headache is hemicrania continua. Hemicrania continua description is a persistent, strictly unilateral headache responsive to indomethacin.

Diagnostic criteria:

A. Headache for more than three months fulfilling criteria B-D

B. All of the following characteristics:

- unilateral pain without side-shift
- daily and continuous, without pain-free periods
- moderate intensity, but with exacerbations of severe pain

C. At least one of the following autonomic features occurs during exacerbations and ipsilateral to the side of pain:

- conjunctival injection and/or lacrimation
- nasal congestion and/or rhinorrhoea
- ptosis and/or miosis

D. Complete response to therapeutic doses of indomethacin

E. Not attributed to another disorder

A much rarer disorder is that known as new daily persistent headache. This disorder is characterized by its sudden onset with the patient often able to note the date and time it began. There is no history of prior significant headaches. It is typically bilateral and usually resembles migraine or tension-type headache. Some individuals report an antecedent viral infection.

21. Other Headache

Other headaches include cervicogenic and persistent daily headaches.

22. Specialty Consultation Indicated?

The decision to seek a specialty consultation will depend upon the practitioner's familiarity and comfort with headache and its management. Specialty consultation may be considered when:

- the diagnosis cannot be confirmed
- etiology cannot be diagnosed or warning signals are present

- headache attacks are occurring with a frequency or duration sufficient to impair the patient's quality of life despite treatment or the patient has failed to respond to the acute remedies, or is in status migrainosus

23. Perform Diagnostic Testing if Indicated

Key Points:

- The diagnosis of primary headache is dependent on the experience of the clinician. There are, as of yet, no tests that confirm the diagnosis of primary headache.
- A detailed headache history, including duration of attacks and the exclusion of secondary causes, is the primary means to diagnose primary headache.

There are, as yet, no tests that confirm the diagnosis of primary headache. The work group recommends careful consideration before proceeding with neuroimaging (computed tomography or magnetic resonance imaging). It is uncommon for neuroimaging to detect an abnormality in persistent headaches of longer duration versus new onset situations. Selective testing including neuroimaging or electroencephalogram, lumbar puncture, cerebrospinal fluid and blood studies may be indicated to evaluate for secondary headache if causes of concern have been identified in the patient history or physical examination. (See Annotation #12, "Causes for Concern?") Diagnosis may be complicated if several headache types coexist in the same patient *(Silberstein, 2000 [R])*.

Under the International Classification of Headache Disorders, second edition (ICHD-II) system, failure can occur in diagnosis, which is dependent on the experience of the clinician. Greater experience on the part of the clinician allows for a higher level of confidence in the diagnosis. In 750 patients questioned, 53% had throbbing quality of headaches, while 30% of 1,000 cases of tension patients had pulsatile quality, and 40% of patients with migraine had bilateral headaches. Duration of an attack is important. It is felt that pitfalls in interpreting diagnostic criteria may lie in how questions are asked *(Blau, 1993 [R])*.

There is difficulty in developing an operational system to diagnose headaches with the lack of objective diagnostic tests that identify various types of headache disorders absolutely. International Classification of Headache Disorders, second edition (ICHD-II) criteria depend largely on a detailed headache history and the exclusion of secondary cause for headache through a physical and neurological examination. Concern of a secondary cause for headache may necessitate testing or further evaluation *(Olesen, 1994 [R])*.

A total of 897 computed tomography scans or magnetic resonance images were done on migraine patients with findings of three tumors and two arteriovenous malformations. At this time, there is evidence to define the role of computed tomography and magnetic resonance imaging in the evaluation of headache patients. Of 1,825 computed tomographys and magnetic resonance imagings done on patients with headaches, including those that were acute, progressively worsening, and chronic, a yield of only 2.4% tumors, Arteriovenous malformation, aneurysms, subdural hematoma or hydrocephalus was found *(American Academy of Neurology Quality Standards Subcommittee, 1994 [R])*.

In a retrospective study, 592 patients with headaches and normal neurological exam were examined by computed tomography scanning between 1990 and 1993 at a cost of $1,000 per scan. None of the patients had any serious intracranial pathology identified. This technique is costly and unrewarding *(Akpek, 1995 [M])*.

In a case series study 52 migraineurs were evaluated by spinal taps, cerebral spinal fluid analysis and tap pressure. Pressures of cerebral spinal fluid and the chemistry evaluation of the same bore no direct relationship to the presence of headache diagnosis *(Kovács, 1989 [C])*.

A summary statement reviewed articles from 1941 to 1994 with no study of electroencephalograms improving diagnostic accuracy for the headache sufferer. Electroencephalography does not delineate subtypes or screen for structural causes of headache effectively *(American Academy of Neurology Quality Standards Subcommittee, 1994 [R])*. In the absence of studies showing improved diagnostics with electroencephalogram, there is no indication for routine use of electroencephalograms in the diagnosis of headache.

24. Findings Consistent with Secondary Headache?

If diagnostic evaluation leads to a diagnosis other than primary headache, subsequent care of the patient would fall beyond the scope of this guideline.

Migraine Treatment Algorithm Annotations

28. Patient Meets Criteria for Migraine

Migraine is the most common headache disorder seen by primary care providers.

It is expected that a patient with headache will undergo a diagnostic workup (see the Diagnosis Algorithm) establishing the diagnosis of migraine before initiating acute treatment.

29. Is Patient Experiencing a Typical Headache?

Key Points:

- The diagnosis of migraine does not exclude the presence of an underlying secondary cause of headache.

Each individual headache must be evaluated in the context of the patient's prior migraine headaches. The practitioner must always remain alert to the possibility of secondary causes for headache, particularly when there is a previously established history of a primary headache disorder such as migraine.

Migraine headache does not preclude the presence of underlying pathology (arterial dissection, intracranial aneurysm, venous sinus thrombosis, ischemic or hemorrhagic stroke, temporal arteritis, etc.) that may also present with "vascular headaches." If the history is scrutinized, ominous causes for headaches can often be identified and treated with the potential to avoid catastrophe.

31. Categorize According to Peak Severity Based on Functional Impairment, Duration of Symptoms, and Time to Peak Impairment

Accurate categorization and characterization by both providers and patients is important. The categorization of migraine influences choice of treatment method.

Severity levels:

Mild	Patient is aware of a headache but is able to continue daily routine with minimal alteration.
Moderate	The headache inhibits daily activities but is not incapacitating.
Severe	The headache is incapacitating.
Status	A severe headache that has lasted more than 72 hours.

There may be additional features that influence choice of treatment. For example, parenteral administration (subcutaneous, nasal) should strongly be considered for people whose time to peak disability is less than one hour, who awaken with headache, and for those with severe nausea and vomiting.

Determining functional limitations during migraine episodes is the key to determining the severity and therefore the best treatment for a patient. Physicians and patients should stratify treatment based on severity rather than using stepped care, though patients will often use stepped care within an attack. This algorithm uses a stratified-care model.

Factors That May Trigger Migraine

Certain influences can lead to a migraine attack. It is important to note that although a single trigger may provoke the onset of a migraine, a combination of factors is much more likely to set off an attack.

Environmental:

- Temperature (exposure to heat/cold)
- Bright lights or glare
- Noise
- Head or neck injury
- Weather changes
- Motion
- Odors (smoke, perfume)
- Flying/high altitude
- Physical strain

Lifestyle Habits:

- Chronic high levels of stress
- Skipping meals and/or poor diet
- Disturbed sleep patterns
- Smoking

Hormonal:

- Puberty
- Menopause
- Menstruation or ovulation
- Pregnancy
- Using oral contraceptives or estrogen therapy

Emotional:

- Anxiety
- Depression
- Anger (including repressed anger)
- Excitement or exhilaration
- "Let-down" response

Medications:

- Nitroglycerin
- Nifedipine
- Oral contraceptives
- Hormone therapy

The use of opiates and barbiturates should be avoided. Refer to discussion in Annotation # 37, "Moderate Treatment."

Dietary:

Dietary triggers vary considerably from patient to patient, are overall a minor and infrequent trigger for migraine headaches, and will not consistently precipitate a migraine headache in an individual for whom they have been a trigger in the past.

- Citrus fruit
- Aspartame
- Caffeine
- Aged cheese

- Chocolate
- Alcohol (red wine, beer)
- Foods containing nitrites
- Foods containing monosodium glutamate

33. Mild Treatment

Key Points:

- Mild migraines are usually managed by the patient, which implies an emphasis on over-the-counter medications.
- Triptans are more effective at halting migraine pain at mild levels than if the headache is more severe.

The guideline work group presumes most mild migraine headaches will be managed by self-care, which implies an emphasis on over-the-counter medications. However, since only 2%-12% of initially mild migraine episodes remain mild (with the remainder progressing), treatments effective for mild headaches may be useful for only a short time. Studies on treatment of migraine headache at the mild level show that triptans are more effective in abolishing pain at this stage than if the headache is more severe. It is acceptable to use other symptomatic headache relief drugs, as well as triptans, for mild headache. However, current retrospective analyses of mild pain treatment studies reveal triptan response to two-hour pain freedom to be superior to any other comparator drug. Please see Appendix A, "Drug Treatment for Headache" and "Drug Treatment for Adjunctive Therapy." See Appendix C, "Food and Drug Administration Risk Factors for Drug Treatment in Pregnant Women."

Use of drugs for acute treatment of headache for more than nine days per month is associated with an increased risk of chronic daily headache.

34. Successful?

Success for treatment of migraine is defined as complete pain relief and return to normal function within two hours of taking medication. In addition, patients should not have intolerable side effects and should find their medications reliable enough to plan daily activities despite migraine headache *(Dowson, 2004a [D]; Dowson, 2004b [D])*.

Consider reasons for treatment failure and change treatment plan.

Common reasons for migraine treatment failure:

- Acute medication or analgesic overuse
- Medication dose too little or used too late
- Inadequate medication for degree of disability. Medication not well matched with most disabling symptoms (e.g., using oral agents for a patient with vomiting) or inappropriate route of administration (e.g., using oral agents for a headache where maximum disability occurs quickly)
- Failure to use adjunctive medication (e.g., caffeine, antiemetics)
- Inaccurate diagnosis

Patient adherence to therapy contributes to reaching treatment goals. The clinician-patient relationship plays a key role in improving adherence. Clinicians should ask patients open-ended, non-threatening questions regularly to assess adherence. Questions that probe for factors that contribute to non-adherence could include those surrounding adverse reactions, misunderstandings of treatment, depression, cognitive impairment, complex regimens and financial constraints.

Interventions to improve adherence include simplification of the drug regimen (frequency and complexity); use of reminder systems; involvement of family or friends; a health care team approach including nurses, pharmacists, and educators in addition to physicians; written instructions; and educating the patient about potential adverse effects, importance of therapy, and realistic treatment goals.

For example:

A. Assess the patient's knowledge of the condition and expectations for treatment:

"What is/will be the most difficult task for you in reaching your treatment goal?"

B. Assess the patient's medication administration process:

"How do you remember to take your medication each day? Do you use a reminder device such as a pill box or alarm?"

C. Assess the patient's barriers to adherence:

"Do you have a difficult time opening medication bottles, swallowing pills or reading small print on labels?"

"Are you comfortable with your ability to follow the treatment plan that we have designed together?"

"Are you experiencing any unusual symptoms that you think may be due to your medication?"

(Nichols-English, 2000 [R])

37. Moderate Treatment

This guideline emphasizes the use of other agents over opiates and barbiturates, recognizing that many migraineurs are currently treated with drugs from the latter two classes. In general, opiates are characterized by having a short pain-relief window, release inflammatory neurochemicals, and increase vasodilation; none of these addresses the currently known treatment issues and pathophysiology of migraine.

Meperidine is commonly prescribed but its use should be avoided. The metabolite of meperidine, normeperidine, has a long half-life and produces less analgesic effect, and there is an increased risk of seizures that cannot be reversed by naloxone.

If an opiate must be used, meperidine should not be the opiate selected. We have specifically excluded butorphanol because of its high potential for abuse and adverse side-effect profile.

See Appendix A, "Drug Treatment for Headache" and "Drug Treatment for Adjunctive Therapy."

See Appendix C, "Food and Drug Administration Risk Factors for Drug Treatment in Pregnant Women."

38. Successful?

See Annotation #34 for information.

43. Consultation with Headache Specialist

A headache specialist is a practitioner, often a neurologist but not always, who has extensive experience, knowledge of, and demonstrated high standards of health care in the field of headache. There are advanced training programs in headache medicine.

The American Headache Society has a membership directory of practitioners interested in the field of headache and can be contacted if the name of a recommended specialist in a particular geographic location is

required. (American Headache Society can be reached by e-mail at AHSHQ@talley.com. The Web site: http://www.americanheadachesociety.org).

44. Status (Greater Than 72 Hour Duration)

It is recommended that the patient be hydrated prior to neuroleptic administration with 250-500 mL of 5% dextrose with 0.45% sodium chloride and advised of the potential for orthostatic hypotension and acute extrapyramidal side effects. The patient should be observed in a medical setting as clinically appropriate after administration of a neuroleptic and should not drive for 24 hours.

45. Adjunctive Therapy

See Appendix A, "Drug Treatment for Adjunctive Therapy." As adjunctive therapy, any of the listed medications can be used singularly or in compatible combination. For intermittent, infrequent headache, caffeine should be added as first choice when not contraindicated. The use of caffeine in patients with chronic daily headache is to be discouraged. The prokinetic agent metoclopramide could be considered next. This guideline has no other preferences.

46. Patient Meets Criteria for Dihydroergotamine Mesylate?

Key Points:

- Dihydroergotamine mesylate is effective in halting intractable migraine attacks or migraine status. Dihydroergotamine mesylate is also effective in halting the acute cycle of cluster headaches.

Dihydroergotamine mesylate must not be given to patients with the following conditions:

- Pregnancy
- History of ischemic heart disease
- History of variant angina
- Severe peripheral vascular disease
- Onset of chest pain following administration of test dose
- Within 24 hours of receiving any triptan or ergot derivative
- Patients with hemiplegic or basilar-type migraine
- Cerebrovascular disease

Intravenous dihydroergotamine mesylate is the method most frequently employed to terminate a truly intractable migraine attack or migraine status. The protocol outlined in the dihydroergotamine mesylate algorithm is effective in eliminating an intractable migraine headache in up to 90% of patients within 48 hours. This method of administration has also been found to be effective in terminating an acute cycle of cluster headaches, as well as chronic daily headaches with or without analgesic/ergotamine rebound.

48. Chlorpromazine, Intravenous Valproate Sodium, Intravenous Magnesium Sulfate or Prochlorperazine

See Appendix A, "Drug Treatment for Headaches" and "Drug Treatment for Adjunctive Therapy." Patients with a history of dystonic reaction should be premedicated with diphenhydramine or benztropine.

If chlorpromazine, valproate sodium or intravenous magnesium sulfate was used previously, one may not wish to repeat.

49. Successful?

See Annotation #34 for information.

50. Opiates

These are not drugs of first choice and headache practice recommends against the use of meperidine. Normeperidine, the active metabolite of meperidine, has a long half-life and is neuroexcitatory and neurotoxic. There is inconsistent absorption of opiates, at least with meperidine, when injected intramuscularly and they are less effective than when given intravenously. Opiates release inflammatory neurochemicals and increase vasodilation that are mechanistically counterproductive to currently known migraine pathophsiology and can exacerbate headaches. Studies have been done using meperidine, but the effects are likely due to class effect and other opiates are likely to be just as effective *(Duarte, 1992 [A])*. However, it should be noted that there are no studies to support opiate effectiveness.

See Appendix A, "Drug Treatment for Headache" and "Drug Treatment for Adjunctive Therapy."

52. Dexamethasone

See Appendix A, "Drug Treatment for Headache" and "Drug Treatment for Adjunctive Therapy."

Migraine Treatment – Annotations #33, 37, 40, 45, 48, 50, 52

The following references pertain to the medications included in the tables in Appendix A, "Drug Treatment for Headache."

Almotriptan:

(Ferrari, 2001 [X]; Spierings, 2001 [A])

Acetaminophen, aspirin, caffeine combination:

Because there is no good evidence to support the use of acetaminophen for treatment of mild migraine, the work group has replaced it with acetaminophen, aspirin and caffeine *(Lipton, 1998 [A]; Stang, 1994 [C])*.

Chlorpromazine – IM:
(McEwen, 1987 [A])

Chlorpromazine – IV:
(Lane, 1989 [A])

Depacon:
(Mathew, 2000 [D]; Norton, 2000 [D])

Dexamethasone – IM:
(Gallagher, 1986 [C])

Dichloralphenazone:
(Diamond, 1976 [A])

Dihydroergotamine:
(Callaham, 1986 [A])

Dihydroergotamine – nasal:
(Gallagher, 1996 [A])

Dihydroergotamine- IM:
(Weisz, 1994 [D])

Dihydroergotamine- SQ:
(Winner, 1996 [A])

Doxepin:
(Adelman, 1995 [A])

Eletriptan:
(Ferrari, 2002 [M]; Stark, 2002 [A])

Ergotamine:
(Dahlof, 1993 [R])

Hydroxyzine:
(Duarte, 1992 [A])

Ibuprofen:
(Kloster, 1992 [A])

Isometheptene:
(Diamond, 1976 [A])

Ketorolac:
(Duarte, 1992 [A])

Lidocaine – nasal:
(Maizels, 1992 [A])

Magnesium Sulfate:
(Demirkaya, 2001 [C])

Meperidine:
(Duarte, 1992 [A])

Metoprolol:
(Gerber, 1991 [A]; Sorensen, 1991 [A])

Nadolol:
(Ryan, 1983 [A]; Ryan, 1982 [A])

Naproxen:
(Krymchantowski, 2000 [C]; Nestvold, 1985 [A])

Naratriptan:
(Mathew, 1997 [A])

Nortriptyline:
(Adelman, 1995 [R])

Prochlorperazine – IV:
(Coppola, 1995 [A])

Prochlorperazine – rectal:
(Jones, 1994 [A])

Promethazine:
(Capobianco, 1996 [R])

Rizatriptan:
(Kramer, 1998 [A]; Teall, 1998 [A])

Sumatriptan – nasal:
(Ryan, 1997 [A])

Sumatriptan – oral:
(Cutler, 1995 [A]; Sargent, 1995 [A])

Sumatriptan – SQ:
(Ferrari, 2001 [M]; Subcutaneous Sumatriptan International Study Group, 1991 [A]; Visser, 1992 [A]; Wendt, 2006 [A])

Sumatriptan/Naproxen:
(Brandes, 2007 [A])

Zolmitriptan:
(Charlesworth, 2003 [A]; Dowson, 2003; Rapoport, 1997 [A]; Solomon, 1997 [A])

Tension-Type Headache Algorithm Annotations

60. Patient Meets Criteria for Tension-Type Headache?

Tension-type headache is one of the most common primary headaches. See Annotation #14, "Meets Criteria for Primary Headache Disorder?" for episodic and chronic tension-type headache.

It is important to evaluate the patient who comes to the office for tension-type headache for the possibility of migraine. While the International Classification of Headache Disorders, second edition (ICHD-II) system suggests migraine and tension-type headaches are distinct disorders, there is evidence to suggest that for the migraineur, tension-type headache is actually a low-intensity migraine.

(Ashina, 2003 [R]; Torelli, 2004 [A]; Zhao, 2003 [R])

63. Acute Treatment

Analgesics offer a simple and immediate relief for tension-type headache. Medication overuse is potentially a concern that can lead to chronic daily headache. Use of drugs for acute treatment of headache for more than nine days per month is associated with an increased risk of chronic daily headache.

See Appendix A, "Drug Treatment for Headache" and "Drug Treatment for Adjunctive Therapy."

(Ashina, 2003 [R]; Torelli, 2004 [A]; Zhao, 2003 [R])

67. Prophylactic Treatment

Prophylactic therapy is reserved for patients with frequent tension-type headache (more than 15 headaches per month).

Tricyclic antidepressants are effective in reducing the frequency and severity of tension-type headache.

See Appendix A, "Drug Treatment for Headache" and "Drug Treatment for Adjunctive Therapy."

(Ashina, 2003 [R]; Torelli, 2004 [A]; Zhao, 2003 [R])

Cluster Headache Algorithm Annotations

72. Patient Meets Criteria for Cluster Headache?

There is no more severe pain than that sustained by a cluster headache sufferer. This headache is often termed "suicide headache." Cluster headache is characterized by repeated short-lasting but excruciating intense attacks of strictly unilateral peri-orbital pain associated with local autonomic symptoms or signs. The most striking feature of cluster headache is the unmistakable circadian and circannual periodicity. Many patients typically suffer daily (or nightly) from one or more attacks over a period of weeks or months.

(Dodick, 2000 [R]; Goadsby, 1997 [R]; Lipton, 1997 [A])

76. Acute Treatment

Oxygen inhalation is highly effective when delivered at the beginning of an attack with a non-rebreathing facial mask (7-15 L/min). Most patients will obtain relief within 15 minutes.

Acute drugs may be difficult to obtain in adequate quantity.

Subcutaneous sumatriptan is the most effective self-administered medication for the relief of cluster headaches. Sumatriptan is not effective when used before the actual attack nor is it useful as a prophylactic medication.

Dihydroergotamine mesylate provides prompt and effective relief from cluster headaches in 15 minutes but due to the rapid peak intensity and short duration of cluster headaches, dihydroergotamine mesylate may be a less feasible option than sumatriptan.

See Appendix A, "Drug Treatment for Headache" and "Drug Treatment for Adjunctive Therapy."

(Dodick, 2000 [R]; Goadsby, 1997 [R]; Lipton, 1997 [A])

77. Bridging Treatment

Bridging treatment or transitional prophylaxis is initiated simultaneously with maintenance therapy after acute treatment has suppressed the initial attack. Bridging treatment allows for the rapid suppression of cluster attacks in the interim until the maintenance treatment reaches therapeutic levels.

Options for bridging treatment are:

- Corticosteroids
- Ergotamines

- Occipital nerve block

(Capobianco, 2006 [R]; Dodick, 2000 [R]; Husid, 2006 [R]; Peres, 2002 [D]; Sandrini, 2006 [R])

78. Maintenance Treatment

Effective prevention cannot be overemphasized in these patients. Maintenance prophylaxis is critically important since cluster headache sufferers typically experience one or more daily (or nightly) attacks for a period of weeks or months. The goal of transitional therapy is to induce rapid suppression of attacks while maintenance therapy is intended to provide sustained suppression over the expected cluster period.

If the patient has intractable headache or is unresponsive to prophylactic treatment, consider referral to a headache specialist.

See Appendix A, "Drug Treatment for Headache" and "Drug Treatment for Adjunctive Therapy."

(Dodick, 2000 [R]; Goadsby, 1997 [R]; Lipton, 1997 [A]; Olesen, 1999 [NA])

Dihydroergotamine Mesylate Algorithm Annotations

85. Intravenous Metoclopramide 10 mg Intravenous

Metoclopramide (10 mg) is given either by direct intavenous injection over two-three minutes, or infused intravenously in 50 mL of normal saline over 15 minutes. Each dose of metoclopramide should be administered 15 minutes prior to each dihydroergotamine mesylate injection. Although uncommon, acute extrapyramidal side effects such as dystonia, akathisia, and oculogyric crisis may occur after administration of metoclopramide. Benztropine mesylate is effective in terminating this unusual adverse event, given as a 1 mg injection (intravenous or intramuscular). Often after five doses of metoclopramide, it may be given as needed every eight hours for nausea *(Ellis, 1993 [A])*.

87. Begin Continuous Dihydroergotamine Mesylate

Begin dihydroergotamine mesylate 3 mg in 1,000 mL normal saline at 42 mL/hr.

Continue intravenous metoclopramide 10 mg IV every eight hours as needed for nausea.

Side effects:

- If significant nausea occurs at any time, reduce the rate of dihydroergotamine mesylate to 21 to 30 mL/hr.
- If diarrhea occurs, give diphenoxylate with atropine, one or two tablets, three times daily as needed.
- If excessive anxiety, jitteriness (akathisia) or dystonic reaction occurs, give intravenous benztropine 1 mg.

It may be continued up to seven days. Opioid analgesics should not be used with either protocol since these are likely to prolong the headache via analgesic rebound.

This approach is an alternative to the intermittent dosing of dihydroergotamine mesylate as outlined in the Raskin protocol and some practitioners may prefer it rather than the intermittent dihydroergotamine mesylate protocol. Continuous dihydroergotamine mesylate, like the intermittent administration, can be continued for seven days, although 72 hours is more typical. Opioid analgesics should not be used with either protocol since these are likely to prolong the headache via analgesic rebound.

Ford, et al. described results of an open trial comparison between intermittent intravenous dihydroergotamine mesylate and continuous infusion dihydroergotamine mesylate. Success in treating migraine status was virtually the same with each protocol. The Ford variation may be preferred by some physicians. This protocol should be used only with an intravenous pump *(Ford, 1997 [C])*.

89. Dihydroergotamine Mesylate Test Dose

A test dose of dihydroergotamine mesylate (0.5 mg) is given either as a direct intravenous push slowly over two-three minutes or as an infusion diluted in 50 mL of normal saline over 15-30 minutes *(Queiroz, 1996; Raskin, 1986)*.

90. Blood Pressure Stable/No Chest Pain?

Dihydroergotamine mesylate is relatively contraindicated if blood pressure is sustained greater than or equal to 165/95 mmHg. Discontinue dihydroergotamine mesylate if patient develops chest pain.

92. Common Side Effects

The most common side effects include nausea, vomiting, diarrhea, abdominal cramps, dizziness, paresthesia and leg pain. These side effects usually resolve by reducing the dose and coadministering metoclopramide as an antiemetic. Diarrhea can be managed with diphenoxylate with atropine, one or two tablets three times daily as needed. Although most patients who respond will do so within 48 hours, this protocol may be continued for up to seven days, although 72 hours is more typical.

Menstrual-Associated Migraine Algorithm Annotations

104. Patient Meets Criteria for Menstrual-Only or Menstrual-Associated Migraine

"Menstrual migraine," a term misused by both patients and providers, lacks precise definition. The International Classification of Headache Disorder, second edition (ICHS-II) system has proposed that menstrual-only migraine be defined as attacks exclusively starting two days before and first two days of the menstrual cycle *(Pringsheim, 2008 [M]; Headache Classification Subcommittee of the International Headache Society, 2004 [R])*. The woman should be free from attacks at all other times of the cycle.

Many women who do not have attacks exclusively with menses are considered to have menstrual-associated migraines *(MacGregor, 1996 [R])*.

The provider and patient need to discuss diary documentation. The patient should keep a continuous daily record for at least two months to include the following:

- Day/time of headache
- Duration
- Severity of headache
- Onset of menstrual flow

108. Consider Cyclic Prophylaxis

- Non-steroidal anti-inflammatory drugs

  Non-steroidal anti-inflammatory drugs should be considered approaches of first choice in the prophylactic treatment of migraine associated with menses. Many providers consider triptans to be equally effective, but there are no comparative studies. *[Conclusion Grade III: See Conclusion Grading Worksheet Appendix A – Annotation #108 (Non-Steroidal Anti-Inflammatory Drugs)]*

Naproxen sodium 550 mg twice daily has been used as a preventive agent, although other non-steroidal anti-inflammatory drugs may also be effective. Typically, the agent is initiated two to three days before anticipated onset of the headache and continued through the at-risk period.

Virtually every review paper supports the use of non-steroidal anti-inflammatory drugs for cyclic prophylaxis. There are almost no controlled studies in this setting, with two smaller studies supporting prophylaxis with naproxen sodium *(Boyle, 1999 [R]; Kornstein, 1997 [R]; Silberstein, 1999 [A])*.

- Triptans

  There are good placebo studies supporting the use of triptans (Sumatriptan, Naratriptan, Frovatriptan and Zolmitriptan) for cyclic prophylaxis *(Newman, 1998 [D]; Silberstein, 2000 [A]; Tuchman, 2008 [A]*.

- Ergots

  Very limited studies are available on the use of ergots for cyclic prophylaxis. While numerous review articles refer to their use, the current clinically available formulations do not correspond to those used in prior studies *(D'Alessandro, 1983 [D])*.

111. Consider Hormone Prophylaxis

- **Transdermal estradiol**

  Estrogen levels decrease during the late luteal phase of the menstrual cycle, likely triggering migraine. Estrogen replacement prior to menstruation has been used to prevent migraine.

  Estradiol patches, 50-100 mcg, are applied 48 hours prior to expected onset of migraine and used for one week.

  The 50 mcg estradiol patch, applied 48 hours before anticipated onset of menses and continuing for seven days, was effective in relieving headaches in a subgroup of women with menstrual migraines confirmed by neurophysiological testing. Others have shown a better clinical outcome with 100 mcg estradiol patches than with lower dose patches. Oral estrogen has been less effective than transdermal estrogen in prophylaxis of menstrual migraine.

  (Becker, 1999 [R]; Cupini, 1995 [C]; Larsson-Cohn, 1970 [D])

- **Estrogen-containing contraceptives**

  Estrogen-containing contraceptives have a variable effect on migraines, causing worsening of headaches in some patients, improvement of headaches in a small percentage of patients, and no change in migraines in other patients. We are not aware of any population-based studies on this topic.

  The effect of estrogen-containing contraceptives on migraines is unpredictable. In one study, migraines worsened in 39% of patients, improved in 3%, and remained unchanged in 39%. Another author reported improvement in migraines in 35% of patients when estrogen-containing contraceptives were started.

  (Becker, 1999 [R]; Cupini, 1995 [C]; Larsson-Cohn, 1970 [D])

- **GnRH agonists with "add back" therapy**

  For patients with severe menstrual migraine unrelieved by other therapies, suppression of the menstrual cycle with a gonadotropin-releasing hormone agonist and "add back" therapy may be effective. Lupron Depot 3.75 mg intramuscular is given monthly with "add back" therapy such as 0.1 mg transdermal estradiol patches and oral medroxyprogesterone acetate 2.5 mg daily, or micronized progesterone 100 mg daily.

Suppression of ovarian steroid production followed by a constant estrogen-progestin milieu was studied in five women with severe menstrual migraine. All patients reported dramatic improvement in functioning and quality of life and a decrease in analgesic medications used for headache relief. Two patients discontinued therapy and had increased headache frequency. The monthly cost of GnRH agonist therapy is about 10 times the cost of conventional hormone therapy. GnRH agonists and "add back" therapy may also be associated with erratic bleeding. This therapy should probably be managed by a gynecologist or endocrinologist in concert with a headache specialist.

Tamoxifen, danazol and bromocriptine have shown limited efficacy in treatment of menstrual migraine.

Whether oophorectomy is an effective treatment for refractory migraines is not settled at this time.

(Herzog, 1997 [D]; Lichten, 1991 [D]; Murray, 1997 [D]; O'Dea, 1990 [D])

Perimenopausal or Menopausal Migraine Algorithm Annotations

115. Perimenopausal or Menopausal with Active Migraine History and Is a Potential Candidate for Hormone Therapy

Menopause is the permanent cessation of menses.

Perimenopause is the span of time from the reproductive to the post-reproductive interval.

Hormone therapy may worsen, improve or leave migraines unchanged.

In a study of 112 women taking hormone therapy, 52 reported worsening of migraines, 50 reported improvement, and 10 reported no change in migraine headaches. More women improved with transdermal than oral estrogen *(MacGregor, 1997 [R]; Nappi, 2001 [A]; Wang, 2003 [C])*.

Women with these conditions are not candidates for hormone therapy:

- Pregnancy or unexplained bleeding: these are temporary but absolute contraindications to hormone therapy.
- Past history of breast cancer or endometrial cancer: while usually considered contraindications to hormone therapy, short-term use for severe menopausal symptoms may be considered with proper precautions.

120. Hormone Therapy

- Transdermal, transvaginal or oral estrogen
- Progestin if indicated
- Estrogen-containing contraceptives

(de Lignieres, 1996 [R]; Fettes, 1999 [R]; Silberstein, 1993 [R])

121. Successful?

Successful is commonly defined as a 50% reduction in frequency in headache days and/or severity of headaches.

122. Consider Changing Delivery System or Formulation of Estrogen and Progestin

Success is achieved through trial and error.

On Estrogen-Containing Contraceptives or Considering Estrogen-Containing Contraceptives with Migraine Algorithm

126. On Estrogen-Containing Contraceptives or Considering Estrogen-Containing Contraceptives with Migraine

Migraine patients who do not have absolute contraindications to estrogen-containing contraceptives should consider that estrogen-containing contraceptives may have unpredictable effects on the severity and/or frequency of headaches. In addition, evidence exists that the risk of ischemic stroke increases for migraineurs using estrogen-containing contraceptives *(Becker, 1999 [R]; Cupini, 1995 [C]; International Headache Society Task Force on Combined Oral Contraceptives & Hormone Replacement Therapy, The, 2000 [R])*.

128. Evaluate Vascular Risk Factors

- Risk factors for coronary artery disease
- Prior thromboembolic disease
- Migraine aura
- Smoking

Women who have migraine with an aura probably have significantly increased ischemic stroke risk if estrogen-containing contraceptives are used. This risk probably increases with age as baseline stroke rates increase, so that the increased risk may be acceptable to the younger patient (i.e., under age 30), but not to the older patient. It is probably too simplistic to say that no patient with migraine with aura should use estrogen-containing contraceptives. The decision should be individualized and should be made with the patient.

It appears reasonable that women who have prolonged migraine auras (certainly those beyond 60 minutes), multiple aura symptoms, or less common aura symptoms (i.e., dysphasia, hemiparesis) should be strongly discouraged from using estrogen-containing contraceptives.

Patients who develop a migraine aura for the first time while using estrogen-containing contraceptives, or whose previous typical migraine aura becomes more prolonged or complex should discontinue estrogen-containing contraceptives.

Use of oral contraceptives in patients with a history of migraine increases the risk of stroke. *[Conclusion Grade II: See Conclusion Grading Worksheet B – Annotation #128 (Risk of Stroke)]*

Women with migraine aura who smoke and are hypertensive further increase their risk. Additional risk is also noted if they are taking estrogen-containing contraceptives.

Migraine Prophylactic Treatment Algorithm Annotations

139. Prophylactic Treatment

- **Criteria for prophylactic treatment**
  - Three or more severe migraine attacks per month that fail to respond adequately to symptomatic therapy.
  - Less frequent but protracted attacks that impair the patient's quality of life.
  - Patient is interested in prophylactic treatment.
- **Prophylactic therapy**

  Prior to instituting prophylactic therapy for migraine, it is imperative that realistic goals and expectations be established. Patients should have a clear understanding that the goals of preventive therapy are to:
  - Decrease migraine attack frequency by more than 50%
  - Decrease pain and disability with each individual attack
  - Enhance response to acute, specific, anti-migraine therapy

  One or more of these goals may be achieved.
- **Medications**

  The choice of prophylactic agent depends upon:
  - Side-effect profile
  - Comorbid conditions
  - Medication interactions
  - Evidence-based efficacy
  - Patient preference (weight loss or gain)

  Patients should also understand that there is usually a latency of at least three to six weeks between the initiation of medication and recognizable efficacy. Often, an 8- to 12-week trial is necessary, allowing an adequate period for drug titration to a dosage likely to attain efficacy. It is also not uncommon for initial side effects to subside after continued therapy, and patients should be made aware of this so as to avoid premature discontinuation of a potentially effective medication.
- **First-line treatment**

  The choice of prophylactic medication should be individualized according to the side-effect profile, the presence of comorbid conditions and risk of medication interactions. For example, a tricyclic antidepressant may be especially useful with a migraineur with depression, while sodium valproate may be ideal for a patient with epilepsy. See Appendix B, "Prophylactic Treatment," and Appendix C, "Food and Drug Administration Risk Factors for Drug Treatment in Pregnant Women."

  There are additional medications other than the drugs recommended in the table in Appendix A, "Drug Treatment Tables," which may be of equal effectiveness. They are not included in the table, however, because of the infrequent use by primary care physicians.

  Reinforce education and lifestyle management.

  See Annotation #16 in the Diagnosis Algorithm.

Medications

The following references pertain to the medications included in the tables in Appendix B, "Prophylactic Treatment."

Amitriptyline
(Couch, 1979 [A])

Atenolol
(Johannsson, 1987 [C])

Gabapentin
(Mathew, 2002 [A])

Nebivolol
(Schellenberg, 2007 [A])

Propranolol
(Carroll, 1990 [A])

Valproate sodium
(Hering, 1992 [A]; Klapper, 1997 [A])

Verapamil
(Solomon, 1983 [A])

Topiramate
(Brandes, 2004 [A]; Silberstein, 2004 [A])

Other Therapies

The treatment therapies listed below are in alphabetical order and do not indicate work group preference or scientific support.

- **Acupuncture**

  This therapy has been found to be expensive and of variable availability. Controlled studies specifically applied to migraine have produced mixed findings *(Bausell, 2005 [A]; Vickers, 2004 [A]; Vincent, 1989 [A])*.

- **Biofeedback**

  Various methods of biofeedback have been used as adjunctive therapy for migraine. This treatment modality should be considered, particularly for pregnant patients and those not easily treated with pharmacological agents. Thermal control is frequently the preferred technique, wherein the patient learns to elevate finger temperature during therapy sessions using a digital temperature reading device *(Smith, 1987 [C])*.

  Biofeedback is time consuming and requires a commitment on the part of the patient.

- **Botulinum toxin A**

  There is one placebo-controlled, randomized trial and several observational studies that demonstrate the effectiveness of botulinum toxin A injections for the prophylaxis of migraine headaches. More recent studies lack strong evidence supporting botulinum toxin A as effective *(Mathew, 2007 [C]; Silverstein, 2005 [A])*. It should be considered when first-line prophylatic agents have failed or are contraindicated *(Ashkenazi, 2004 [R]; Silberstein, 2000 [A])*. For best results, therapy should be administered by a provider with experience using botulinum toxin A for headache.

- **Butterbur root (petasites hybridus)**

  An extract from the plant Petasites hybridus has been shown to have benefit for migraine prevention. Dosages were from 100 to 150 mg per day in these studies *(Grossman, 2000 [A])*.

- **Coenzyme Q10**

  In one randomized placebo-controlled trial, coenzyme Q10 was superior to placebo for attack frequency, headache days and days with nausea *(Sandor, 2005 [A])*.

- **Cognitive behavioral therapy**

  This therapy is based on the premise that anxiety and distress aggravate an evolving migraine, and it has the potential for helping the patient recognize maladaptive responses that may trigger a headache *(Andrasik, 1996 [R]; Campbell, 2003 [R]; Reid, 1996 [R])*.

- **Feverfew**

  This herbal therapy is made from crushed chrysanthemum leaves. 250 mcg of the active ingredient, parthenolide, is considered necessary for therapeutic effectiveness. Because these are herbal preparations, the quantity of active ingredient varies with the producer *(Johnson, 1985 [A]; Vogler, 1998 [M])*.

- **Magnesium**

  Daily oral dosages of 400 to 600 mg of this salt have been shown to be of benefit to migraineurs in European studies *(Peikert, 1996 [A])*.

- **Relaxation training**

  Relaxation training includes progressive muscular relaxation, breathing exercises and directed imagery. The goal is to develop long-term skills rather than to treat individual events. Repetitive sessions and practice by the patient increase the success of these therapies in reducing headache frequency *(Reich, 1989 [A])*.

- **Riboflavin**

  A randomized, placebo-controlled study has found daily supplements of 400 mg moderately effective in reducing the frequency and severity of migraine *(Schoenen, 1998 [A])*.

Several additional treatment modalities are available. The modalities listed below lack sufficient scientific support to be recommended as therapies of proven value.

- **Cervical manipulation**

  Previous studies suggested potentially high levels of risk associated with improper application of this modality. Although more recent studies report few complications, the scientific evidence of significant benefit is not convincing. There is well-documented evidence of cerebral infarction and death from cervical manipulation *(Haldeman, 2002 [D]; Krueger, 1980 [D]; Parker, 1980 [A])*.

- **Transcutaneous electrical stimulation units**

  Transcutaneous electrical stimulation units units for migraine or muscle contraction headache have not been found to be more beneficial than placebo when evaluated in a controlled study *(Solomon, 1985 [A])*.

141. Continue Treatment for 6-12 Months, Then Reassess

After 6-12 months, a gradual taper is recommended unless headaches become more frequent or more severe.

142. Try Different First-Line Medication or Different Drug of Same Class

Monotherapy is recommended with dose increasing until patient receives benefit, maximum recommended dose is reached or unacceptable side effects occur. If failure with one medication, try another from the same class.

145. Try Combination of Beta-Blockers and Tricyclics

A beta-blocker and tricyclic antidepressant may be more effective and produce fewer side effects in combination than a single drug at a higher dose from either class.

148. Third-Line Prophylaxis Treatment or Consultation with Headache Specialist

Please see Annotation #43, "Consultation with Headache Specialist."

Appendix A – Drug Treatment Tables

When viewing the following Drug Treatment tables, please consider the following key for the symbols used in each table:

*	Patient, lying down supine, head extended 45 degrees and rotated 30 degrees, drips 0.4 mL of 4% lidocaine solution in the nostril ipsilateral to headache when unilateral, or most clear nostril when headache is bilateral.
**	Effective headache treatment may require the manufacturer's recommended dosage limit to be exceeded in individual patients.
†	Combination products containing aspirin 250 mg, acetaminophen 250 mg, and caffeine 65 mg are sold over the counter under various trade names.
††	Headache response is delayed with Naratriptan when compared with other selective 5 hormone therapy receptor agonists. However, headache recurrence may be less frequent.
♈	Second doses have not been shown to improve efficacy.
♈♈	Please note use of parenteral corticosteroids should be considered as treatment of last resort and initiated only after careful consideration of the risks as they pertain to each individual. Their use is empiric and based upon anecdotal evidence. The rationale for the use of corticosteroids is uncertain, but they may reduce perivascular inflammation or sensitize the blood vessels to the vasoconstrictive effect of circulating catecholamines and specific anti-migraine agents.
♈♈♈	Opiates and barbiturates are not drugs of first choice and in general should not be used. Opiates have a short pain-relief window, release inflammatory products, and increase vasodialation that can complicate headache. If an opiate must be used, meperidine should be avoided.
♈♈♈♈	Recent studies show that sumatriptan and naproxen sodium in combination may be more effective than either drug alone. However, there are no studies that demonstrate that sumatriptan 85 mg/naproxen sodium 500 mg is more effective than sumatriptan and naproxen sodium taken together. Therefore, a dose of sumatriptan 100 mg and a dose of naproxen sodium 550 mg taken at the same time is recommended.
♈♈♈♈♈	Ergotamine is not commonly used and not recommended as a first-line treatment.
♈♈♈♈♈♈	Serotonin syndrome is a rare problem that can result from the use of a triptans in combination with selective serotonin reuptake inhibitors (SSRI) or serotonin and norepinephrine reuptake inhibitors (SNRI). This is a complex situation for the patient with migraines and comorbid conditions such as anxiety and depression requiring treatment with these medications simultaneously. Medication therapy needs to be thoroughly discussed with the patient.

Also, please keep in mind that all drugs are listed in alphabetical order, not in order of work group preference. The listings in each table include selected drugs of proven efficacy in each class and are not intended as inclusive of all possible treatment options. Lastly, we have listed drugs by their generic names and only included brand names in the situation where the generic name may not be well recognized.

These drug treatment tables have been compiled from package inserts, PDR.net and Micromedex.

Appendix A – Drug Treatment for Headache

Drug	Dose	Side Effects	Contraindications
Acetaminophen †	• 650-1,000 mg by mouth • Repeat every 4 hours as needed • Do not exceed 4,000 mg/day		Hypersensitivity to acetaminophen
Acetaminophen/Aspirin/ Caffeine †	500/500/130 mg every 4-6 hours x2 maximum	GI, nervousness, anxiety	Hypersensitive to acetaminophen, active peptic ulcer disease
Aspirin †	650-1300 mg by mouth every hr x 2	GI	Active peptic ulcer disease
Chlorpromazine (CPZ) Injection	• Dilute 1 ml CPZ (25 mg) with 4 ml normal saline (1 cc = 5 mg CPZ) • Inject into IV: 1 cc/5-10 min • Stop when headache relieved; not to exceed 25 mg/dose	Drowsiness, extrapyramidal symptoms	Hypotension, previous adverse reaction
Dexamethasone Injection♈♈	4-20 mg IM once per month	Cushingoid	
DHE (dihydroergotamine mesylate) **Injection**	0.5-1.0 mg subcutaneous, IM or IV, may repeat in 1 hr; not to exceed 3 mg in 24 hrs**	Chest tightness, tingling, nausea, vomiting	Ischemic heart disease, uncontrolled hypertension, vasospastic angina, advanced peripheral vascular disease, pregnancy, ischemic cerebrovascular disease
Nasal spray	0.5 mg in each nostril; repeat 0.5 mg in each nostril in 15 min; not to exceed 6 sprays (3 mg) in 24 hrs	Nasal congestion, throat discomfort, nasal irritation, nausea, chest tightness, tingling, vomiting	See DHE injection
Ergotamine♈♈♈♈♈ By mouth (1 mg ergot, 100 mg caffeine	Maximal subnauseating dose at onset; not to exceed 6 mg/day, 10 mg/week or 2 days/week of dosing	Chest tightness, tingling, nausea, vomiting	Ischemic heart disease, uncontrolled hypertension, vasospastic angina, advanced peripheral vascular disease, pregnancy, ischemic cerebrovascular disease
Rectal suppository (2 mg ergot, 100 mg caffeine)	1 suppository as needed at onset; not to exceed 2 suppositories/ attack or 3 suppositories/week	Chest tightness, tingling, nausea, vomiting	See Ergotamine by mouth
Sublinguil (2 mg ergot)	1 tablet at onset, 1 every 30 min PRN; not to exceed 6 mg/day, 10 mg/week or 2 days/week of dosing	Chest tightness, tingling, nausea, vomiting	See Ergotamine by mouth

Refer to the first page of Appendix A for the key explaining the symbols.

Many of the medications listed are available in a variety of formulations for different routes of administration (e.g., oral, IV, rectal suppository).

Drug	Dose	Side Effects	Contraindications
Hydrocortisone Injection♈♈	• 100-250 mg IM • Repeat parenteral or oral equivalent may be given within 24 hrs		
Isometheptene Mucate 65 mg Dichloralphenazone 100 mg/ Acetaminophen 325 mg Midrin® CIV	2 by mouth at onset; 1 every hr as needed; not to exceed 5 in 12 hrs; not to exceed 2 treatment days per week or 40 caps per month	Drowsiness, dizziness	Ischemic heart disease, severe renal disease, ischemic cerebrovascular disease
Ketorolac IM	30-60 mg IM; not to exceed 120 mg in 24 hrs.	Drowsiness, nausea, dyspepsia	Active peptic ulcer disease, renal insufficiency
Lidocaine 4% Solution*	0.4 ml-0.5 mL intranasally over 30 seconds	Burning or numbness in nose or pharynx	
Magnesium Sulfate Injection	1 gm IV	Flushing, hypotension, burning sensation in the face and neck	Heart block, severe renal impairment
NSAIDs			
Ibuprofen	400-800 mg by mouth every 4 hr x 2	GI	Active peptic ulcer disease, renal insufficiency
Ketoprofen	25-50 mg every 6 hr	GI	See Ibuprofen
Naproxen Sodium	550-825 mg by mouth every 6-8 hrs; Not to exceed 1,375 mg per day	GI	See Ibuprofen
Opiates♈♈♈			
Hydromorphone	1-2 mg IM or IV	Sedation, confusion, risk of habituation	
Morphine	5-15 mg IM or IV		
Meperidine CII Injection	50-150 mg IM/subcutaneous or 10 mg slowly IV		
Prochlorperazine IV	• Dilute 1 cc (10 mg) with 4 cc normal saline (1 cc = 2 mg) • Inject 1 cc/3-5 min; stop when headache relieved; not to exceed 10 mg/dose	Drowsiness, extrapyramidal symptoms	Hypotension
Valproate Sodium Injection	300-500 mg IV in normal saline at a rate of 20 mg/minute	Nausea, vomiting, tremor, dizziness	Liver disease, pregnancy

Refer to the first page of Appendix A for the key explaining the symbols.

Many of the medications listed are available in a variety of formulations for different routes of administration (e.g., oral, IV, rectal suppository).

Appendix A – Drug Treatment for Headache

Drug	Dose	Side Effects	Contraindications
5 HT Agonists (Triptans)♈♈♈♈♈♈			
Almotriptan♈	6.25-12.5 mg; may repeat in 2 hrs; not to exceed 2 tabs/24 hrs or 4 headaches/month	Tingling, nausea, dry mouth, drowsiness Chest tightness (26% time)	See Sumatriptan by mouth
Eletriptan	20-40 mg; may repeat after 2 hrs if headache returns; not to exceed 80 mg/24 hrs	Dizziness, drowsiness, nausea, dry mouth, paresthesia, chest/abdominal tightness, vomiting, dysphagia	Not to be used within 72 hrs of treatment with the following potent CYP3A4 inhibitors: ketoconazole, itraconazole, nefazodone, troleandomycin, clarithromycin, ritonavir and nelfinavir
Frovatriptan♈	2.5 mg; may repeat in 2 hrs; not to exceed 3 tabs/24 hrs or 4 headaches/month	Chest tightness, flushing, dizziness, tingling, fatigue	See Sumatriptan by mouth
Naratriptan ††	1-2.5 mg; may repeat once after 4 hrs; not to exceed 5 mg/24 hrs	Chest/throat tightness, tingling, flushing, dizziness, nausea	See Sumatriptan by mouth Hypertension, vasospastic angina, peripheral vascular disease, pregnancy, ischemic cerebrovascular disease, use of other 5-HT agonists or ergotamines if used within 24 hrs
Rizatriptan	5-10 mg: may repeat after 2 hrs; not to exceed 30 mg/24 hrs. Patients receiving propanolol use 5 mg dose; not to exceed 15 mg/24 hrs	Chest/throat tightness, dizziness, tingling	See Sumatriptan by mouth

Appendix A – Drug Treatment for Headache

Drug	Dose	Side Effects	Contraindications
Sumatriptan			
By mouth♈	25-100 mg; may repeat once after 2 hrs or more if headache reoccurs; not to exceed 200 mg/24 hrs	Chest tightness, tingling, flushing, dizziness, limb heaviness, nausea	Ischemic heart disease, uncontrolled hypertension, vasospastic angina, peripheral vascular disease, pregnancy, ischemic cerebrovascular disease, use of 5-HT agonists or ergotamines if used within 24 hrs, use of MAO inhibitors within two weeks.
Nasal Spray	5-20 mg in one nostril; may repeat once after 2 hrs.; not to exceed 40 mg/day, 2 treatment days/wk or 6 per mo	Chest tightness, tingling	See Sumatriptan by mouth
Subcutaneous♈	4 mg; many repeat x1 within 24 hrs if headache reoccurs 6 mg; may repeat x 1 within 24 hrs. If headache reoccurs; not to exceed 2 treatment days/wk or 6 per mo	Chest tightness, tingling	See Sumatriptan by mouth

Drug	Dose	Side Effects	Contraindications
Sumatriptan 85 mg/ Naproxen 500 mg♈♈♈♈♈	1 tablet at onset, may repeat once after 2 hrs, not to exceed 2 doses in 24 hrs	Chest tightness, tingling, flushing, dizziness, limb heaviness, nausea, GI. Also has a black box warning: Naproxen sodium/sumatriptan may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may be increased with extended duration of use or in patients with cardiovascular disease or risk factors for cardiovascular disease. Naproxen sodium/sumatriptan contains an NSAID. NSAID-containing products can also cause an increased risk of serious gastrointestinal adverse events especially in the elderly, including bleeding, ulceration and perforation of the stomach or intestines, which can be fatal.	
Zolmitriptan	2.5-5 mg, may repeat after 2 hrs; not to exceed 10 mg/24 hrs	Chest/throat tightness, tingling, flushing, dizziness, nausea	See Sumatriptan by mouth
By mouth	2.5-5 mg, may repeat after 2 hrs; not to exceed 10 mg/24 hrs		
Nasal Spray	5 mg into one nostril may repeat after 2 hrs not to exceed 10 mg/24 hrs		

Appendix A – Drug Treatment for Adjunctive Therapy

Drug	Dose	Side Effects
Caffeine	Minimum 65 mg by mouth	Tremors, nausea
Hydroxyzine	50-100 mg IM	Drowsiness, extrapyramidal symptoms
Metoclopramide	10 mg IV	Drowsiness, extrapyramidal symptoms
Prochlorperazine	5-10 mg IV, IM, or repeat suppository	Drowsiness, extrapyramidal symptoms
Promethazine	25 mg IV over 1 minute, IM, or rectal suppository	Drowsiness, extrapyramidal symptoms

Appendix B – Prophylactic Treatment

Prophylactic Drug Treatment: First-Line Treatment (Selected Listing)

Drug	Dose	Side Effects	Contraindications
Antiepileptics			
Divalproex Sodium (valproate sodium)	500-1,250 mg/day	Nausea, tremor, weight gain, alopecia, increased liver enzymes	Avoid in patients with liver disease, pregnancy
Gabapentin	900-2,400 mg/day, titrate from 300 mg	Dizziness, somnolence, peripheral edema, fatigue, ataxia, nervousness, tremor, weight gain	
Topiramate	50-200 mg/day, titrate slowly from 15-25 mg	Somnolence, nervousness, fatigue, dizziness, confusion, anorexia, ataxia, acute-angle closure of glaucoma, nausea, metabolic acidosis, paresthesias, kidney stones	Reduced renal or hepatic function
Beta-Blockers			
Atenolol	50-150 mg/day	Fatigue, bronchospasm, bradycardia, hypotension, CHF, depression, impotence, decreased libido, sleep disturbance	Sinus bradycardia, first-degree heart block, acute CHF
Metoprolol	50-200 mg/day		
Nadolol	40-240 mg/day		
Nebivolol	5 mg/day	Nausea, dizziness, headache, somnolence, angina, myocardial infarction, ventricular arrhythmia	Bradycardia, 2nd-, 3rd-degree heart block, sick sinus syndrome, cardiac failure, severe hepatic impairment
Propranolol	40-240 mg/day		
Timolol	5-30 mg/day		
Ca^{++} Channel Blockers			
Verapamil	120 mg/day, titrate up to 480 mg	Constipation, dizziness, edema, hypotension, nausea	Atrial fibrillation; CHF; sick sinus syndrome; hypotension; 2nd-, 3rd-degree heart block
Tricyclics			
Amitriptyline	10-150 mg/every bedtime	Dry mouth, constipation, weight gain, drowsiness	Urinary outlet obstruction complex, dysrhythmias; may precipitate acute glaucoma
Doxepin	25-100 mg/every bedtime		
Nortriptyline	10-150 mg/every bedtime		

Appendix C – Food and Drug Administration Risk Factors for Drug Treatment in Pregnant Women

When viewing the following Food and Drug Administration Risk Factors for Drug Treatment in Pregnant Women tables – as cited in Briggs G, Freeman R, Yaffe S; in Drugs in Pregnancy and Lactation; Baltimore: Williams & Wilkins; 1998 – please consider the following key for the letters used in each table:

A Controlled studies fail to demonstrate risk and possibility of fetal harm appears remote.

B Either animal-reproduction studies have not demonstrated a fetal risk, but there are no controlled studies in pregnant women

or

Animal-reproduction studies have shown an adverse effect that was not confirmed in controlled studies in women in the first trimester (and there is no evidence of a risk in later trimesters).

C Either studies in animals have revealed adverse effects on the fetus (teratogenic, embryocidal or other) and there are no controlled studies in women

or

Studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the fetus.

D There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (e.g., if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).

X Studies in animals or humans have demonstrated fetal abnormalities, or there is evidence of fetal risk based on human experience, or both. The risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.

Also, please keep in mind that all drugs are **not** listed in order of work group preference. The listings in the tables include risk factors in pregnant women for selected drugs of proven efficacy in each class, and are not intended as inclusive of all possible treatment options.

Drug	Trimester 1st	2nd	3rd	Lactation	Notes
ACUTE MEDICATIONS					
Acetaminophen (APAP)	B	B	B	The American Academy of Pediatrics considers this drug to be compatible with breast feeding	
ASA	C	C	D	Potential risk to infant platelet function; use with caution	Should be avoided at any time during pregnancy except for those patients on low daily dose (80 mg/day)
Ergots	X	X	X	Contraindicated	
Isometh/Dichlor/APAP	C	C	C	No data available, but is excreted into breast milk	
Ketorolac (IM)	C	C	D	The American Academy of Pediatrics considers this drug to be compatible with breast feeding	
Lidocaine (nasal)	B	B	B		Category B is inferred; no data for nasal use available
Meperidine	D	D	D	Not recommended; excreted into breast milk	May be considered Category B for **infrequent** use Neonatal addiction and respiratory depression are of concern
NSAIDs (by mouth)	B	B	D	The American Academy of Pediatrics considers this drug to be compatible with breast feeding	
Phenothiazines	C	C	C	Excreted into breast milk Possible sedation in infant is of concern	Category C is for psychiatric use Chlorpromazine and Prochlorpromazine are both considered safe and effective for treatment of N & V in pregnancy
Steroids					
Dexamethasone	C	C	C	No data available	Concern for neonatal adrenal hyperplasia or insufficiency
Hydrocortisone	D	D	D	No data available	
Triptans	C	C	C	Little data; best to discard milk for eight hours after dose	No adequate data or studies at this time; see pregnancy registries for specific agent manufacturer
Sumatriptan				American Academy of Pediatrics considers this drug compatible with lactation; best to discard milk for eight hours after dose	
ADJUNCTIVE MEDICATIONS					
Caffeine	B	B	B	The American Academy of Pediatrics considers this drug to be compatible with breast feeding	
Antihistamines	D	C	C	No data available; excretion into breast milk is expected	
Metoclopramide	B	B	B	Concern due to potential CNS effects	

Refer to first page of Appendix C, "Food and Drug Administration Risk Factors for Drug Treatment in Pregnant Women," for definition of risk category.

Drug	Trimester 1st	2nd	3rd	Lactation	Notes
PROPHYLACTIC MEDICATIONS					
Antiepileptics:	D	D	D	The American Academy of Pediatrics considers this drug to be compatible with breast feeding	
Divalproex Sodium					
Gabaperatin	C	C	C	Not recommended Excreted into breast milk	
Topiramate	C	C	C	Not recommended Excreted into breast milk	
Beta-Blockers:					
Atenolol	D	D	D	Not recommended	
Metoprolol	C	D	D	The American Academy of Pediatrics considers these drugs to be compatible with breast feeding	
Nadolol	C	D	D		
Propanolol	C	D	D		
Timolol	D	D	D		
Verapamil	C	C	C	The American Academy of Pediatrics considers this drug to be compatible with breast feeding	
Tricyclics:					
Amitriptyline	D	D	D	Not recommended	
Nortriptyline	D	D	D	Not recommended	
Doxepin	C	C	C	Not recommended	
OTHER DRUGS USED BY PRACTITIONERS *NOT* CONSIDERED IN THIS GUIDELINE					
Codeine	D	D	D	Not recommended; excreted into breast milk	May be considered Category C for **infrequent** use Neonatal addiction and respiratory depression are of concern
Barbiturates:					
Phenobarbital	D	D	D	Has caused major adverse effects	
Butalbital	D	D	D	No data available	May be considered Category C for **infrequent** use Neonatal addiction and respiratory depression are of concern

Refer to first page of Appendix C, "Food and Drug Administration Risk Factors for Drug Treatment in Pregnant Women," for definition of risk category.

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Brief Description of Evidence Grading

Individual research reports are assigned a letter indicating the class of report based on design type: A, B, C, D, M, R, X.

A full explanation of these designators is found in the Foreword of the guideline.

II. CONCLUSION GRADES

Key conclusions (as determined by the work group) are supported by a conclusion grading worksheet that summarizes the important studies pertaining to the conclusion. Individual studies are classed according to the system defined in the Foreword and are assigned a designator of +, -, or ø to reflect the study quality. Conclusion grades are determined by the work group based on the following definitions:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of any significant doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is some uncertainty attached to the conclusion because of inconsistencies among the results from the studies or because of minor doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from studies of strong design for answering the question addressed, but there is substantial uncertainty attached to the conclusion because of inconsistencies among the results from different studies or because of serious doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from a limited number of studies of weak design for answering the question addressed.

Grade Not Assignable: There is no evidence available that directly supports or refutes the conclusion.

The symbols **+**, **–**, **ø**, and **N/A** found on the conclusion grading worksheets are used to designate the quality of the primary research reports and systematic reviews:

+ indicates that the report or review has clearly addressed issues of inclusion/exclusion, bias, generalizability, and data collection and analysis;

– indicates that these issues have not been adequately addressed;

ø indicates that the report or review is neither exceptionally strong or exceptionally weak;

N/A indicates that the report is not a primary reference or a systematic review and therefore the quality has not been assessed.

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Conclusion Grading Worksheet A – Annotation #108 (Non-Steroidal Anti-Inflammatory Drugs)

Work Group's Conclusion: Non-steroidal anti-inflammatory drugs should be considered approaches of first choice in the prophylactic treatment of migraine associated with menses. Many providers consider triptans to be equally effective, but there are no comparative studies.

Conclusion Grade: III

Author/Year	Design Type	Class	Quality +,–,ø	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ *Work Group's Comments (italicized)*
Sargent, Solbach, Damasia, et al. (1985)	RCT	A	–	-Ages 18 to 65 years with confirmed diagnosis of common or classical migraine, or combination of migraine and muscle contraction headache (history of migraines for ≥1 yr, average of 12 migraine headache days over ≥6 migraine attacks in 3 months prior to entry) -Excluded: pregnant, major medical illness, active ulcers in previous year, bleeding problems, sensitivity to NSAIDs, rebound ergotamine migraine, contraindications to propranolol hydrochloride -Randomized to naproxen sodium (NS) (550 mg bid), propranolol hydrochloride (PH) (40 mg tid) or placebo (PL) -Patients could not take other NSAIDs, anticoagulants, or alpha-adrenergic antagonists during study period	-129 patients were included in the efficacy analysis (42 in NS group, 44 in PH group, and 43 in PL group); groups were comparable (demographic and clinical data) at baseline -Median outcomes (Patient daily improvement record): *No significant differences among groups -Data from 30 patients who reported at least 2 menstrual periods during the study period: frequency of migraine before start of menses was lower than after start of menses in both treatment groups (comparisons with placebo group were not significant, however); NS reduced severity of migraine before start of menses (relative to after start of menses) more than placebo (p=0.01) or PH (p=0.054) -More gastrointestinal complaints in NS group than PH group (p=0.02)	-NS and PH appeared to reduce headache frequency, headache severity, nausea and visual disturbances relative to placebo although the differences were not significant. PH was better tolerated than NS. Women treated with NS experienced the greatest decrease in headache severity during the premenstrual period. NOTES: 12-week full-dose phase (III) (all received PL) followed a 2-week washout phase (I) and 2 weeks where PH group received 40 mg bid (II) (NS group received full dose); 170 were enrolled, 161 entered washout (I), 149 entered phase II, and 129 completed phase III (efficacy data phase); excluded 20 who had entered phase III from analysis (14 with fewer than 4 wks of treatment, 6 with protocol violations) *Work Group's Comments: no explanation given for why 170 were enrolled but 149 entered active treatment phase; compliance with medication was not reported; little detail about measurement tools used*

	NS	PH	PL
Headache days per week	-0.05	0.33	-0.25*
Headache severity	0.83	1.00	0.66*
Nausea	1.42	1.66	1.37*
Vomiting	1.88	1.92	1.72*
Visual disturbances	1.80	1.30	1.18*

Author/Year	Design Type	Class	Quality +,–,ø	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ *Work Group's Comments (italicized)*
Sances, Martignoni, Fioroni, et al. (1990)	Non Random	C	–	-Ages 19 to 45 years; migraine without aura; menstrual-related periodicity of migraine for 2 to 30 years (headaches every cycle); free from endocrinological, metabolic or other organic abnormalities; no prophylactic treatment for migraine or no oral contraceptives for 6 months prior to study -2-month observation period -3-month (3 cycles) double-blind treatment with naproxen sodium (NS) or placebo (PL); treatment from 7th day before expected menses through 6th day of flow -3 additional cycles with all women treated with active drug -Calculated Pain Total Index (PTI) from daily diaries based on number of attacks, duration and severity	-35 completed the study (of 40 enrolled); 18 with NS for 6 mos, 17 with PL for 3 mos and NS for 3 mos; 2 groups comparable (age, history of disease, and migraine attack features); estradiol, progesterone and prolactin levels normal for all patients in each cycle in which they were tested -Percentage of response to treatment did not significantly differ between NS and PL groups in double-blind phase; response was almost equal in open phase; absence of migraine reported in 16.7% of NS group in 1st month of treatment and 33% in 2nd and 3rd months (compared to none in PL group) -NS group had significant change in PTI (relative to baseline) throughout study period (p=0.05 at month 2, others p≤0.01); PL group had significant change in PTI at 1st month (p<0.05) and at months 3-6 (all p<0.01); overall no difference between NS and PL -Days of headache: decreased throughout study period for NS group (all p<0.005) and at months 1, 2, 4, 5 & 6 for PL group (p=0.05 at month 2, others p≤0.005); NS group differed from PL group at month 3 (p<0.05) -Analgesic consumption: decreased throughout study period for NS group (all p≤0.01) and at months 1, 4, 5 & 6 for PL group (all p≤0.01); NS group significantly different from PL group at months 1 (p<0.02), 2 and 3 (both p<0.05) -Menstrual Distress Questionnaire: significant improvement (p<0.006) in premenstrual and menstrual pain during NS treatment but not PL treatment	-In comparison with placebo, NS is effective in reducing headache intensity and duration as well as days of headache and analgesic consumption. Good tolerability and few side effects were observed. NOTES: 3 dropped out for reasons unrelated to treatment; 2 dropped out due to severe gastralgia and nausea; non-significant differences in PTI between NS and PL were attributed to high variability of scores and high standard deviations

Conclusion Grading Worksheet B – Annotation #128 (Risk of Stroke)

Work Group's Conclusion: Use of oral contraceptives in patients with a history of migraine increases the risk of stroke.

Conclusion Grade: II

Author/Year	Design Type	Class	Quality +,–,Ø	Population Studied/Sample Size	Primary Outcome Measure(s)/Results (e.g., p-value, confidence interval, relative risk, odds ratio, likelihood ratio, number needed to treat)	Authors' Conclusions/ *Work Group's Comments (italicized)*
Tzourio, Tehindrazanarivelo, Iglésias, et al. (1995)	Case-Control	C	+	-Cases: 72 women under age 45 years hospitalized for first ischemic stroke -Controls: 173 women who agreed to participate from among 225 randomly selected patients hospitalized in same centers during same time for acute orthopedic or benign rheumatological illness -Interviewed (telephone) cases and controls about history of headaches and vascular risk factors; subjects were not aware of aim of study	-Baseline characteristics: no differences in age, BMI, history of diabetes, educational background, or hormonal content of oral contraceptives; smoking status, oral contraceptive use status, and history of hypercholesterolemia differed between groups -No association between migraine and present use of oral contraceptives in cases or controls -Migraine and ischemic stroke were strongly associated (60% of cases vs. 30% of controls; p<0.001); association persisted after controlling for age, history of hypertension, use of oral contraceptives, and smoking -In migrainous women using oral contraceptives (at time of stroke for cases, at time of interview for controls), risk of stroke was 13.9 (OR=13.9; 95%CI: 5.5-35.1) compared to those without migraine not using oral contraceptive	-Migraine is strongly associated with ischemic stroke in young women independent of main vascular risk factors. The risk of ischemic stroke was particularly increased for migrainous women who were currently using oral contraceptives. NOTE: used a group of 57 women under age 45 hospitalized for orthopedic conditions to determine expected prevalence of migraine in controls (since non-response in controls might be an issue); 73% of the stroke patients and 74% of the controls using oral contraceptives were taking 30-40 μg (micrograms) of estrogen. *Work Group's Comments: investigators used a structured interview to reduce potential for classification bias; recall bias is possible*
Becker (1999)	Review	R	**N/A**		-Assumptions: a. Women with migraine with aura have relative stroke risk of approximately 6 b. Low-dose oral contraceptives with estrogen content below 50 μg have increased ischemic stroke risk of approximately 2 c. If a patient with migraine with aura uses oral contraceptives and if the odds ratios are multiplicative, the expected relative ischemic stroke risk might be 6*2=12 -Expected incidence of ischemic stroke per 100,000 women per year: Age Without Migraine Migraine with Aura No OC use OC use No OC use OC use 15-19 0.4 0.8 2 5 20-24 1.4 3 8 16 25-29 1.9 4 11 23 30-34 2.4 5 14 29 35-39 3.4 7 20 41 40-44 11.6 23 70 139	-Risk for ischemic stroke associated with migraine without aura is probably low enough that it is not a major consideration in prescribing oral contraceptives unless the patient has other major risk factors or unless headaches become substantially exacerbated when oral contraceptives are started -For patients with migraine with aura or who develop migraine while taking oral contraceptives, the additional ischemic stroke risk should be considered in clinical practice

This section provides resources, strategies and measurement specifications for use in closing the gap between current clinical practice and the recommendations set forth in the guideline.

The subdivisions of this section are:

- Priority Aims and Suggested Measures
  - Measurement Specifications
- Key Implementation Recommendations
- Knowledge Resources
- Resources Available

Priority Aims and Suggested Measures

1. Increase the accurate diagnosis of headaches.

   Possible measures for accomplishing this aim:

   a. Percentage of patients with headache (migraine, tension-type, cluster, sinus or chronic daily headache) diagnosed using the appropriate diagnostic criteria. *(Annotation #11)*

2. Increase the functional status of those with migraine. *(Annotation #16)*

   Possible measures of accomplishing this aim:

   a. Number of days per month with migraine per migraineurs.

   b. Number of hours per month lost to migraine per migraineurs.

   c. Percentage of treated patients assessed for improved quality of life through the use of one of the following disease-specific tools/questionnaires (e.g., MIDAS, Headache Impact Test (HIT), Migraine Specific Quality of Life [MSQ])*.

   d. Percentage of migraineurs seen for migraine in the emergency department/urgent care.

   e. Percentage of migraineurs with headache calendar or diary.

* While general functional status/quality of life assessment tools are easier to administer, disease-specific measures may be easier to interpret for disease-specific disability.

3. Increase the rate of treatment plans or adherence to plan for mild, moderate and severe headaches for migraineurs. *(Annotations #33, 34, 37, 43, 44, 45)*

   Possible measures of accomplishing this aim:

   a. Percentage of migraineurs with treatment plans for mild, moderate and severe headaches.

   b. Percentage of migraineurs with a treatment plan who adherence to that plan for mild, moderate and severe headaches.

   c. Percentage of patients with documentation in the medical record that an assessment for success of treatment was administered.

4. Avoid the use of opiates and barbiturates for the treatment of migraines. *(Annotations #37, 50)*

   Possible measures of accomplishing this aim:

   a. Number of prescriptions for the treatment of migraine filled with opiates or barbiturates.

   b. Percentage of migraineurs with a prescription for opiates or barbiturates for the treatment of migraine.

5. Increase education for patients with primary headache. *(Annotation #16)*

   Possible measure of accomplishing this aim:

   a. Percentage of migraineurs who have documentation in the medical record that they have received written educational materials on migraine information at a clinic/office visit.

6. Increase appropriate prophylactic treatment based on headache type (i.e., migraine, tension-type, cluster, menstrual-associated migraine headache and chronic daily headache). *(Annotations #67, 78, 108, 111, 139, 148)*

   Possible measure of accomplishing this aim:

   a. Percent of patients with headache who are prescribed appropriate prophylactic treatment based on headache type.

7. Increase appropriate acute and prophylactic treatment for migraineurs based on level of severity (i.e., mild, moderate and severe headache). *(Annotations #33, 36)*

   Possible measures of accomplishing this aim:

   a. Percent of migraineurs prescribed appropriate acute treatment based on level of severity.

   b. Percent of migraineurs prescribed appropriate prophylactic treatment based on level of severity.

Measurement Specifications

Possible Success Measure #3a

Percentage of migraineurs with treatment plans for mild, moderate and severe headaches.

Population Definition

Patients age 12 years and older with diagnosis of migraine headache.

Data of Interest

$$\frac{\text{\# of medical records with treatment plans for mild, moderate and severe headaches}}{\text{total \# of patients with diagnosis of migraine whose medical records are reviewed}}$$

Numerator/Denominator Definitions

Numerator : Those medical records reviewed with evidence of treatment plans for mild, moderate and severe headaches to include:

- Pharmacological treatment
- Adjunctive therapy

Denominator: All patients age 12 and older who had an encounter with a primary care provider in the past month for migraine headache.

Method/Source of Data Collection

Each month, a sample of patients with migraine headache seen in the past month is identified. A chart abstraction is conducted to determine if there is evidence of a documented treatment plan defining medication and adjunctive therapy for treatment of mild, moderate and severe migraine.

Time Frame Pertaining to Data Collection

Suggested data collection time frame is monthly.

Notes

Designation of migraine as mild, moderate or severe is categorized according to peak severity based on functional impairment, duration of symptoms and time to peak impairment. This categorization influences the choice of treatment method.

Possible Success Measure #5a

Percentage of migraineurs who have documentation in the medical record that they have received written educational materials on migraines at a clinic/office visit.

Population Definition

Patients age 12 and older with diagnosis of migraine headache.

Data of Interest

$$\frac{\text{\# of medical records with documentation of receiving written education materials about migraine}}{\text{total \# of patients with diagnosis of migraine whose medical records are reviewed}}$$

Numerator/Denominator Definitions

Numerator : Documention is defined as any evidence in the medical record that written educational materials were provided to the patient about migraine and lifestyle management. This can include information about:

- Genetic predisposition to migraine
- Role of lifestyle changes
- Stress reduction, regular eating and sleeping schedules, and regular aerobic exercise
- Results of overuse of analgesics and acute migraine drugs
- Benefit of keeping a headache diary
- Treatment approaches

Denominator: All patients age 12 and older who had an encounter with a primary care provider in the past month for migraine headache.

Method/Source of Data Collection

A chart abstraction is conducted to determine if there is evidence that a clinician provided education about migraines.

Time Frame Pertaining to Data Collection

Suggested data collection time frame is monthly.

Notes

Providing education is of paramount importance in managing any chronic illness; it is especially important in the ongoing management of migraine. Patients may have to make lifestyle changes and are often required to make self-management choices in the treatment of individual headaches and to maintain a diary to clarify the frequency, severity, triggers and treatment responses to their headaches.

Key Implementation Resources

The guideline work group identified the following suggestions for systems changes as key strategies for health care systems to incorporate in support of the implementation of this guideline:

1. Develop a system for assessment of headache based on history and functional impairment.
2. Develop system for results of this assessment to be used for identification of treatment options/ recommendations.
3. Develop systems that allow for consistent documentation and montoring based on type of headache.
4. Develop a system for follow-up assessment that identifies success in management of headache in the primary care setting.
5. Develop a process that will remove barriers to referral to a specialist if indicated.
6. Develop a system for consistent documentation and monitoring of medication administration.

Knowledge Resources

Criteria for Selecting Resources

The following resources were selected by the Diagnosis and Treatment of Headache guideline work group as additional resources for providers and/or patients. The following criteria were considered in selecting these resources.

- The site contains information specific to the topic of the guideline.
- The content is supported by evidence-based research.
- The content includes the source/author and contact information.
- The content clearly states revision dates or the date the information was published.
- The content is clear about potential biases, noting conflict of interest and/or disclaimers as appropriate.

Resources Available to ICSI Members Only

ICSI has a wide variety of knowledge resources that are ***only*** available to ICSI members (these are indicated with an asterisk in far left-hand column of the Resources Available table). In addition to the resources listed in the table, ICSI members have access to a broad range of materials including tool kits on CQI processes and Rapid Cycling that can be helpful. To obtain copies of these or other Knowledge Resources, go to http://www.icsi.org/improvement_resources. To access these materials on the Web site, you must be logged in as an ICSI member.

The resources in the table on the next page that are not reserved for ICSI members are available to the public free-of-charge.

Resources Available

*	Author/Organization	Title/Description	Audience	Web Sites/Order Information
	American Academy of Family Physicians	General health information on various topics.	Patients and Families	http://familydoctor.org/127.xml
	American Headache Society® (AHS) Committee for Headache Education	This Web site is an excellent resource for patients and providers to learn more about headaches and resources to help manage them, including prevention and treatment. This site also has information on migraine assessments and headache diaries.	Health Care Providers; Patients and Families	http://www.americanheadachesociety.org
	Headache Care	This Web site is designed for viewers to educate themselves on types of headaches, treatment and prevention techniques. This site contains a complete migraineur's guide to migraine that will help patients understand migraines and how they can become an active participant in their care program to gain control over migraines.	Patients and Families	http://www.headachecare.com
	Healthfinder	General health information on various topics. Spanish link available.	Patients and Families	http://www.healthfinder.gov
	HealthPartners Medical Group	General overview on various topics and health information. (Need to register prior to accessing information.)	Patients and Families	http://www.healthpartners.com
	Mayo Clinic	General health information on various topics and interactive "Ask a Specialist" and Headache Center: A Complete Guide to Managing Headaches.	Patients and Families	http://www.mayoclinic.com
	National Library of Medicine's MEDLINE plus National Institutes of Health	Federal government source related to menopause. Updates on clinical trials, research, medication and treatment. Women's health related to menopause.	Health Care Providers; Patients and Families	http://www.nlm.nih.gov/medlineplus/menopause.html
	National Women's Health Information Center	Government resource for women's health information and referrals. Spanish language link.	Patients and Families	http://www.4woman.org
	North American Menopause Society	Focus on women's midlife and menopause, professional education, referrals and related links.	Health Care Providers; Patients and Families	http://www.menopause.org

* Available to ICSI members only.

*	Author/Organization	Title/Description	Audience	Web Sites/Order Information
	Primary Care Network	Patient-centered strategies for effective management of migraine headaches.	Health Care Providers	http://www.primarycarenet.org
	Quality Metric Incorporated	General health assessment tools including the Headache Impact Test (HIT). (Need to register prior to accessing information.)	Health Care Providers; Patients and Families	http://www.amihealthy.com

* Available to ICSI members only.