Headache

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Introduction

Headache is one of the more common symptoms that causes a patient to seek medical attention. It may accompany serious organic disease or result from a neurogenic vascular disorder or a psychological problem. Almost everyone has a severe headache at some time, but chronic recurrent headaches most often bring the patient to a physician. The pathogenesis of chronic recurrent headaches is incompletely understood; their categorization can suggest, however, therapies that may control the patient's symptoms. Treatment has been empiric, and continues to be so without full understanding of the mechanisms involved.

Mechanisms of headache

Pain perception depends on neural pathways. Information from peripheral pain receptors is processed in spinal cord, brainstem, thalamus, and cortex, and serotonin is probably an inhibitory transmitter in pain modulation (Basbaum and Fields, 1978). Pain may also result from injury to the central or peripheral nervous system and can occur without activation of peripheral receptors. It is not presently clear which types of headache originate centrally and which peripherally. In one study (Blau and Dexter, 1981), the majority of patients had an intracranial pain component during a migraine headache and both intra- and extra-cranial components were evident in only approximately half of other patients.

Headache may arise from dysfunction, displacement or encroachment on pain-sensitive intracranial structures that include the proximal portions of the cerebral arteries and the large veins and venous sinuses (Ray and Wolff, 1940). Other pain-sensitive structures are parts of the meninges, the cranial nerves containing sensory fibres, the upper cervical nerve roots, and scalp muscles. The brain itself, most of the meninges, the ventricular linings and the choroid plexuses are not pain sensitive.

Cranial blood vessels are innervated by branches

of the trigeminal, glossopharyngeal, and vagal nerves, and by the upper sensory roots of the spinal cord. Pulsation and stretching of arterial walls or contraction of skeletal muscle may stimulate peripheral receptors in these tissues to cause pain. However, people who habitually frown, clench their teeth, or are chronically anxious commonly contract head and neck muscles, but only a small number have headache. Similarly, vigorous physical exercise or a hot bath produces arterial vasodilatation but only rarely does headache occur in these circumstances. During a migraine attack, intracranial vasoconstriction and extracranial vasodilatation occur in sequence or concurrently. The neurological symptoms preceding the painful phase are caused by intracranial arterial constriction and cerebral ischaemia, and pain is related to dilatation of the extracranial and some intracranial arteries. Alteration of arteriolar tone is associated with liberation of vasoactive substances including catecholamines, histamines, serotonin, kinins, neuropeptides, and prostaglandins. The pounding headache is presumed to be related to neurogenic vasodilatation and a sterile inflammatory response generated by the interaction of these substances with blood vessels and nerves.

Migraine may be a genetic disorder of the brainstem pain modulation system in which neurotransmitter turnover, serotonin in particular, is defective (Sicuteri, Anselmi, and Fanciullacci, 1974). Proposed abnormalities in endorphin turnover could also explain many of the signs and symptoms of migraine (Sicuteri, 1978).

Headache classification permits an empiric plan of therapy. Severe recurrent headaches are usually not caused by organic disease. About 90% of all headaches of this type result from aspects of muscle contraction and vascular dilatation. A patient may suffer from more than one type of headache or have mixed muscle contraction-vascular headache. For convenience, headaches can be separated into non-organic (without a recognizable structural lesion) and organic. The non-organic variety comprises muscle

contraction, vascular and mixed varieties that have a humoral or neural basis. The organic headaches have a diagnosable underlying aetiology such as cerebrovascular disease, sinusitis, dental problems, post-endarterectomy headache, pheochromocytoma, acute febrile illness, or intracranial space-occupying lesions.

Muscle contraction headaches

Emotional factors play a significant role in the aetiology of muscle contraction headaches. These headaches often occur in persons who are tense and anxious and in whom somatization of anxiety causes skeletal muscle tension. Muscle contraction headache is often associated with depression, and the depressive signs and symptoms suggest its diagnosis. This type of headache may also result from cervical osteoarthritis, dental malocclusion, and temporomandibular joint dysfunction. They are also often associated with so-called myofascial syndromes, trigger-point tenderness, and pain in neck and shoulder muscles. Thus, muscle contraction headaches may occur in tense and anxious individuals, in those with depression, and in persons with structural abnormalities that trigger muscle contractions.

Vascular headaches

One classification of vascular headaches of the migrainous type includes common, hemiplegic, and ophthalmoplegic varieties. Cluster headache is usually considered vascular, and there are non-migrainous vascular headaches caused by factors such as acute febrile illnesses and hangover.

Common migraine is not preceded by a well-defined aura, though prodromal symptoms of several days duration may occur prior to an attack, such as fluid retention, or mood alterations including lethargy, fatigue, irritability and exhilaration. About 80% of all migraine patients have the common variety.

Classic migraine is preceded by a well-defined aura that consists of disturbances of cerebral function. Visual disorders are the commonest of these symptoms but other sensory or motor symptoms such as paraesthesiae, aphasia, and/or sensory hallucinations may occur. Fortification spectra or teichopsia or a transient visual sensation of bright, shimmering colours are pathognomonic of migraine. The visual symptoms often include the presence of flashing wavy lines or zigzag patterns or may occur as a blind spot with luminous borders that slowly enlarge and pass across the visual field. This slow progression has been termed 'build-up' and 'march' (Fisher, 1968), and is characteristic of migraine. It is not associated with the scintillations of calcarine region ischaemia in posterior cerebral artery thrombosis and embolism

or in transient hypo-perfusion for example after a stoop or sudden rise to the upright posture.

Visual displays are likely to be stereotyped for each person. In most patients, the visual hallucinations are present in both visual fields and are of unformed objects or shapes. Some patients have illusions of altered size, shape or position of structured objects, and in others, frank hallucinations of formed objects or persons occur. Still others describe a dazzling, bright, white light that obscures vision. The neurological abnormalities may be present before, during, or after the headache, and neurological symptoms may occur without the headache.

Diagnosis

The diagnosis of headache depends upon a carefully taken history and neurological examination. Since most headache patients have normal general physical and neurological examinations, a detailed history is most important for correct diagnosis. Some patients have more than one kind of headache. Necessary information includes duration of the problem, description of the aura or other prodromal symptoms, location of the pain at onset and its nature (throbbing, steady, piercing, knife-like). The length of time from onset to maximum severity of symptoms and the presence of associated symptoms, such as nausea and vomiting, are important in deciding the route of administration of medication. Most oral preparations require 25–30 min for absorption, whereas inhalation results in satisfactory blood levels almost immediately. Medication is most effective in migraine when taken at the first sign of an attack and is almost of no use if taken when the headache is well-established. Frequency and duration of attacks and efficacy of medication for individual attacks are important in the decision to use prophylactic or abortive therapy only. The time of onset of the headache may suggest the use of prophylactic medication, for example, if always well-developed on awakening.

A careful review of possible precipitating factors helps to eliminate some. The patient should be asked, 'Do you know of anything that always brings on a headache?' and, similarly, 'Do you know of anything that makes the headache go away?'. If the answer to the latter is alcohol, muscle contraction headache can be strongly suspected since alcohol ingestion usually aggravates migraine.

The sex of the headache patient provides a clue to the headache type. Seventy percent of migraine sufferers are female and 90% of cluster headache patients are male. Most patients with muscle contraction headache are female.

The age that headaches first began is important.

Those beginning in childhood and in the second or third decades are often vascular. Those beginning in later life suggest an organic aetiology or depression. If headaches appear for the first time after the age of 40 years, alertness to structural causes should be heightened.

In distinguishing migraine from cluster headache, one should remember that migraine may, but usually does not, awaken the patient from night-time sleep. Cluster headaches often awaken patients from sleep and may recur with a clock-like regularity during a 24-hr period. Muscle contraction headaches tend to begin late in the day and to increase in severity until the patient retires at night.

Migraine pain often begins unilaterally, but may be bilateral or switch sides during and between attacks. The pain usually starts frontally or temporally and generalizes. Recurrent pain localized in or behind an eye, always on the same side, and of excruciating severity suggests cluster headache. Generalized pain at onset or the 'hatband' distribution suggests the diagnosis of muscle contraction headache.

The frequency of occurrence varies widely with the headache type. Migraine occurs at regular or sporadic intervals throughout a patient's lifetime. In females, migraine may be strongly associated with the menstrual cycle. Migrainous headaches may be absent during vacations or occur in 'let down' periods such as weekends or vacations; it often disappears during pregnancy, particularly after the first trimester.

Cluster headache is occasionally chronic but most often occurs in bouts lasting from weeks to months during which time the patient has one or several headaches per 24 hr. Muscle contraction headaches often occur daily or persist for weeks, months or years.

Migraine can occur daily. Attacks usually last for hours but may go on for 1 to 2 days. Cluster headache pain characteristically lasts from 15 to 90 min and individual stabbing pains are of seconds duration. Muscle contraction headaches are present upon awakening only when the patient has gone to bed with a headache the previous evening. The pain usually intensifies as the day progresses and is somewhat relieved by sleep.

Migraine pain often begins as a mild, dull ache that intensifies to throbbing, incapacitating discomfort. The pulsating quality is characteristic of vascular headaches of both the migrainous and non-migrainous types. Pulsation of the pain is often aggravated by stooping. Nausea and vomiting, photophobia, sonophobia, and peripheral vascular changes causing cold hands and feet are frequent associated symptoms of migraine. Cluster headache pain is deep, burning, or stabbing. It is often

excruciating; and the patient may be suicidal. The associated symptoms of cluster headache are most often ipsilateral to the pain and include lacrimation, facial flushing and nasal discharge. The eye is often red; conjunctival vessels are dilated, and ptosis and pupillary constriction often occur. Muscle contraction headaches are dull, nagging, and persistent with periods of heightened pain and severe discomfort. The patient may describe a tight, pressing or squeezing sensation or say that his head feels locked in a vice. Intermittent piercing pain may also occur. Muscle contraction headaches may be episodic or chronic. The episodic variety occurs up to several times a month and is commonly relieved by non-narcotic analgesics. In contrast, chronic muscle contraction headache occurs daily and continuously for months or years, and is not controlled by non-narcotics. Patients with muscle contraction headache may also have neck and back pain and complain of difficulty in sleeping, depressed mood, fatigue and poor appetite.

Migraine is familial and 70% of patients have an affected parent. Among women with migraine, the incidence may be as high as 90% and the affected parent is usually the mother. If both parents are affected, offspring have a 70% chance of also having migraine. The depressive symptoms associated with muscle contraction headaches are thought to be learned behaviour and situational rather than genetic. Cluster headache is rarely familial.

Precipitating factors for migraine include physical and emotional stress, fatigue, loss of sleep, missing a meal, and hormonal changes at the time of menstruation. Ingestion of vasoactive substances such as alcohol or foods rich in tyramine (aged cheeses, etc) and phenylethylamine in chocolate may precipitate migraine in certain subjects. Cluster headaches are often precipitated in susceptible persons during a cluster period by use of vasodilators such as nitroglycerine or alcohol. These substances may not initiate a headache when the patient is not in a cluster period. Fatigue, stress and emotional crises exacerbate pain in muscle contraction and vascular headache patients.

Observations of patients with chronic, recurrent headaches have resulted in categorizing the personalities of those with various headache types. Migraine sufferers have been described as compulsive, rigid, and perfectionistic. Though seemingly true in anecdote, large studies have not substantiated this impression. Cluster patients often have peptic ulcers, are aggressive, frustrated and consume too much alcohol and tobacco. Muscle contraction headache patients have been said to be dependent with repressed hostility and many take large quantities of different drugs which they find difficult to relinquish.

Effort migraine can occur after exhaustive muscu-

lar activities of any kind, but is rare in well-trained athletes. It is usually associated with dehydration, excessive heat load and hypoglycaemia, and is more frequent at unaccustomed altitudes. Serious intracranial disease is often feared in this situation, but the condition is almost always benign and does not recur even with repeated exertion if physical fitness improves and dehydration, excessive heat load and high altitude are avoided. Headache is a prominent symptom of all forms of mountain sickness that is also associated with loss of appetite, nausea and vomiting. Migraine can be precipitated by relatively mild head trauma sustained by soccer players and 'goggle headache' has been described in swimmers whose goggles compress the supraorbital nerves and cause a neuropathy. So-called 'turtle headache' occurs in runners who cover their heads with their shirts after exercise and in others who sleep with their heads covered presumably from rebreathing expired air with consequent hypercapnic cerebral vasodilatation.

Management of the patient with chronic recurrent headache

The patient's decision to seek medical help and the physician's support, reassurance and concern usually diminish the frequency and severity of the headaches. Appropriate laboratory tests may establish the presence of symptomatic headaches that require treatment for an underlying condition. An explanation of the process causing the headaches should be given and the probability of reducing the frequency and severity of the attacks, but not 'curing' them, should be discussed. Precipitating factors should be identified and eliminated when possible. Most patients with long headache histories usually know their headaches' triggers. Patients with less than twice monthly attacks are unlikely to have unsuspected dietary triggers. On the other hand, patients with weekly attacks may need an elimination diet in order to identify the offending food.

Food allergy was studied (Egger *et al.*, 1983) in children, ages 3–16 years, who had had at least one headache per week for the previous 6 months. They were placed on an oligoantigenic diet typically consisting of one meat (lamb or chicken), one carbohydrate (rice or potato), one fruit (banana or apple), one vegetable (brassica), water, and vitamin supplements for 3 or 4 weeks, depending on the frequency of headaches. Other foods were reintroduced to those patients who had no headaches or only 1 during the past 2 weeks. Those who did not improve were offered a second oligoantigenic diet with no foods in common with the first diet. Normal daily helpings of excluded foods were reintroduced

singly, one a week. If no reaction occurred, the patient was advised to eat the food regularly. Foods that provoked symptoms were withdrawn at the end of the week. Foods were systematically reintroduced until the diet was nutritionally and socially acceptable. Of 88 children who completed the study, six did not improve, 78 recovered completely on the first or second oligoantigenic diet, and four improved greatly. An interesting associated finding was the failure of non-specific trigger factors to provoke migraine in responders when the patients were on appropriate diets.

It has long been contended that dietary precipitants of migraine are the result of idiosyncrasy or of metabolic rather than allergic factors, contrary to the implications of this study. Special diets may be dangerous and are socially disruptive. They should be tried only when symptoms are severe and only under experienced medical and dietetic supervision. If milk and milk products are omitted for any length of time, calcium supplements should be used, especially in children and postmenopausal women.

Anxiety and stress are probably the most frequent precipitating factors for migraine, cluster, and muscle contraction headaches. Relaxation techniques through biofeedback training, yoga, and/or physical endurance training are important adjunctive measures to help the patient relax.

The use of certain medications may cause exacerbation of vascular headaches of the migrainous type. The most common nowadays are oral contraceptives, or other exogenous oestrogens given for postmenopausal symptoms. Oestrogen use may increase the frequency and severity of existing vascular headaches or may produce daily non-vascular headaches that are refractory to treatment. In most patients with headaches of sufficient severity to warrant medical help, exogenous oestrogens should be discontinued as an initial step in therapy. Patients who are on oral contraceptives and also have a headache problem are at increased risk for stroke (Shafey and Scheinberg, 1966), and it may be that addition of antimigraine medication containing a vasoconstrictor increases this risk. After oestrogen therapy has been stopped, a marked decrease in frequency and severity of headaches occurs and the patient becomes more responsive to usual therapy. In very rare cases, migraine improves with oestrogen therapy.

Thyroid replacement therapy may aggravate vascular headaches, and reserpine (Curzon, Barrye and Wilkinson, 1969) and nitroglycerine (Schnitker and Schnitker, 1947) have been reported to trigger migraine. These drugs are important biological markers for migraine since they do not produce headaches in non-migrainous persons.

Pharmacotherapy of vascular and mixed headache

Abortive therapy

The ergot alkaloids used alone or combined with caffeine are the most effective agents for the early treatment of acute migraine attacks. The dramatic response of a headache to ergotamine therapy is almost conclusive evidence that it is vascular in origin. Ergotamine can be given orally, sublingually, by oral inhalation, parenterally or by rectal suppository. Parenteral and oral inhalation routes produce early effective blood levels. Ergotamine may cause nausea, vomiting and epigastric discomfort regardless of the route of administration, and other adverse side effects including rebound headaches if a patient uses the drug daily. If suppositories are prescribed, a small dose (1/2 suppository) may be used initially, followed by another half in 10 min and a whole one in 20 min if necessary to control the pain. The patient should cut the suppository lengthwise (not across) and take no more than 2 per day or 4 per week. One mechanism of action of ergotamine in migraine is extracranial vasoconstriction. Isometheptene mucate is another vasoconstrictor; it is less effective than ergotamine, but is usually better tolerated.

The combination of vasoconstrictors and antiemetic agents such as meclizine hydrochloride, 25 or 50 mg, metoclopramide 10 or 20 mg, promethazine hydrochloride 12.5–50 mg orally or rectally are often more efficient than either drug used singly. Non-narcotic analgesics such as paracetamol (acetaminophen) and, particularly, effervescent aspirin plus metoclopramide may be very effective when taken early.

Prophylactic therapy of migraine

Prophylactic daily medication to reduce the frequency and severity of migraine should be considered in patients with more than weekly attacks or when abortive therapy is ineffective. Methysergide, now rarely used, produced sustained improvement in over 50% of patients (Curran, Hinterberger and Lance, 1967). It is a peripheral serotonin antagonist but may be helpful in migraine because of its vasoconstrictor properties affecting the external carotid circulation. The dose is from 2 to 6 mg per day. It is usually not effective for treatment of an acute migraine attack. Strictly nocturnal headache may be controlled with bedtime medication only (Curran *et al.*, 1967). Continuous therapy with methysergide should not exceed 3 months. A drug-free interval of 3 to 4 weeks after each 3-month course of treatment must be used and the dose should be reduced gradually during the last 2 to 3 weeks of each treatment course to avoid 'headache rebound'. Side effects are frequent and its long-term, uninterrupted

use may result in retroperitoneal, pleuropulmonary and cardiac valve fibrosis. It should not be used in pregnancy, in patients with arterial or venous vascular problems, hypertension, infection or liver or renal failure.

Amitriptyline is useful in the prophylaxis of migraine, independent of its antidepressant action (Gomersall and Stuart, 1973; Couch, Ziegler and Hassanein, 1976). The effective dose varies from 10 to 150 mg given before bedtime. Amitriptyline is best introduced gradually to avoid excessive sedation. Doxepin in doses of 25 to 150 mg at night is often also useful and may cause fewer side effects than amitriptyline.

Cyproheptadine is a central serotonin-agonist (Haigler and Aghajanian, 1977) with platelet anti-aggregating properties (Ambrus, Ambrus and Thurber, 1977) that is sometimes useful in migraine prophylaxis. The dose varies from 8 to 24 mg a day. This is given once daily in the smaller doses and twice daily in the larger ones. Sedation and weight gain are the commonest side effects.

Propranolol 40 to 320 mg per day in three divided doses is of established value (Forssman *et al.*, 1976) in the prophylaxis of migraine. Its mechanism of action is uncertain, but may be related to central effects rather than peripheral beta-blockade (Stensrud and Sjaastad, 1976). The average effective dose is 120 mg daily. Congestive heart failure, asthma and renal insufficiency are absolute contraindications to propranolol therapy.

The slow calcium channel blockers have been shown to be effective prophylactic treatment for the prodromes and headache of classic migraine and for control of common migraine and cluster. There is no effect on muscle contraction headaches or on the muscle contraction component of combined headaches. Nimodipine (60 and 120 mg/day) was most effective with the fewest side effects. Beneficial effects were apparent 2–4 weeks after starting therapy in common and classic migraine. Relief from cluster headaches began after 4 weeks of treatment with nimodipine. Nifedipine (mean dose 60 mg/day) and verapamil (mean dose 240 mg/day) also reduced the monthly frequency of all three types of vascular headaches, but were less effective than nimodipine in controlling migraine. Comparable delays after initiation of therapy before onset of headache relief occurred with all three drugs. The most frequent side effects were peripheral vascular (oedema, flushing, dizziness) and skin rash. None were incapacitating and all promptly reversed when the medication was discontinued (Meyer and Hardenberg, 1983).

The treatment of cluster headache is essentially the same as the prophylactic treatment of migraine with a few additions. The daily use of ergotamine may be effective and warranted in this condition, keeping in

mind that the exposure should be relatively short. It is sometimes used 1–3 times daily, depending on headache frequency, for 5 days per week with 2 days off medication during which time the patient assesses whether or not he still needs the medication.

Oxygen inhaled at 7–10 litres per min is sometimes effective in aborting an acute cluster headache and may reduce frequency of headaches during a cluster period when used for 5 to 10 min 3 to 4 times a day. Vigorous physical exertion, such as running in place, at the first sign of a headache may decrease severity, or abort a cluster headache.

Prednisone in doses from 20 mg every other day to 40 mg/day suppressed cluster cycles in 75% of patients (Kudrow, 1978). The drug is usually given for 2 weeks, and then tapered and discontinued.

Lithium carbonate is often effective in treating cluster headaches, especially chronic non-cyclic attacks (Kudrow, 1977). The effective dose has ranged from 600 to 900 mg/day. Favourable responses occurred within the first week of therapy in the majority of patients. Its mechanism of action in cluster headache is not known, but the site is suspected to be central. Nausea, vomiting, diarrhoea, tremor, blurred vision and unsteady gait are the commonest side effects and these are dose related. The drug is often effective at plasma levels well below those required for psychiatric purposes.

The physician's attitude and communications of support and concern are most important in treating the patient with muscle contraction headache. Instruction in relaxation techniques and stress management, combined with tricyclic antidepressant drug therapy, are often useful to these patients.

Editor's note: A newer anti-serotonin agent, pizotifen, is available for anti-migraine prophylaxis in the U.K.

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