MIGRAINE AND ITS OCULAR MANIFESTATIONS*

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The syndrome called migraine has held the attention and interest not only of internists and neurologists for many years, but also of ophthalmologists because of the close association of ocular signs and symptoms with this disease. Solutions regarding etiology, pathology and treatment of this condition are yet far from reality, and especially is this true of many of the strange and bizarre ophthalmologic side-effects which occur; recent acquisitions to our knowledge regarding ocular involvement in this disease may be better evaluated if preceded by a review of the salient points of the disease itself.

Incidence and Etiology

Exhaustive investigation of the literature reveals that the etiology of this syndrome is still unknown and may probably be of multiple origin. It occurs in individuals commonly during adolescence, and although some investigators believe it limited to certain types, careful investigation reveals that no age or sex, economic, racial or social group is immune to this disease. It does appear that women are affected more frequently than men in a proportion of about 3 or 4 to 1. Allan, however, took 195 unselected persons and found identical proportions in the 2 sexes. Wilson cites the table on page 555 in regard to sex incidence.

More women are treated largely because their headaches are more severe, of longer duration, and they more frequently have nausea and vomiting. Usually the malady begins before the age of 20, the onset after 30 being exceptional. Balyeat and Rinkel studied a group of 202 adults and found that in

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almost 30% the disease occurred before the second decade; they also state that about 2% of all American children show symptoms before the age of 10. Gowers, however, has recorded the late appearance of this disease up to the age of 60. One must reach the conclusion then that the disorder is widespread among all social, economic and intellectual groups, with the onset usually manifest during the earlier years of life. Another rather conventional view states that the sufferer inherits a neuropathic legacy from his ancestors, and direct inheritance, according to Buchanan, Allan and Christiansen, is a very obvious feature, the disease being transmitted as a Mendelian dominant characteristic, not sex-linked.

SEX INCIDENCE

Author	*Males*	*Females*	*Total*
Bramwell	18	43	61
Ulrich	132	368	500
Bassoe	75	195	270
Möbius	52	78	130
Laing	29	116	145
Smith	200	533	733
Liveing	41	52	93
Symonds	14	76	90
Allan	200	478	678
Balyeat & Brittain	23	32	55
Hunt	17	43	60
Vaughan	15	48	63
Elliot	116	284	400
Total	932	2,346	3,278

Alvarez describes a definite type of personality which he believes to be an outstanding factor of this disease. He describes the typical migraine patient as one who has an hereditary disease of the brain and who is usually a tense, nervous, intelligent, socially attractive person, oftentimes a female. He believes that such a patient tends to become abnormally sensitive and reactive, striving toward perfection, quick, conscientious and easily fatigued. Many of these individuals have an added bad inheritance from some allergic or constitutionally inadequate or psychopathic or hypersensi-

tive ancestor, all of which may worsen the migraine tendency. He stresses knowledge of these facts as being most helpful in treatment.

Heredity plays an important part in the incidence of this malady. Allan's study of 500 cases showed that of 318 children from 56 families with both parents migrainous, 83.3% developed the malady; of 987 children from 240 families with 1 parent migrainous, the percentage was 62. On the other hand, a history of migraine in one or both parents was observed in 91.4% of 382 persons who suffered from migraine; and in families of 1,538 children originating from migrainous parents, 67.2% became affected.

The relationship of migraine to epilepsy has been a subject of investigation, and Ulrich reported 500 cases of migraine, 20% of whom were found to have epilepsy in the families, the 2 diseases affecting the same persons in 12% of the families. Flateau observed a history of familial epilepsy in 7.2%; Turner's figures are lower, 4.3%. Conversely, a history of migraine was observed by Bourneville in the ancestry of 24.5% of 250 epileptics, and comparison of the relative incidence of the 2 conditions in the ancestry of patients suffering from either was also made by Ely. Convulsive disorders were noted in the families of 5.7% of 104 migrainous subjects, and migraine in those of 60.8% of 170 persons suffering from idiopathic convulsive states. Among the relatives of 250 normal people, Cobb discovered that 15 per 1,000 were migrainous, the proportion increasing to 43 per 1,000 in those of epileptics. However, in analyzing such statistics, one reaches the conclusion that no definite or precise evidence has been offered in favor of the view that some sort of interdependence between the 2 diseases may occur.

From the point of view of allergy also, investigators have attempted to discover some sort of inherited disposition for migraine. Balyeat and Brittain found a family history of either hay fever or asthma in 35.4% of migrainous cases, and they put forth an idea of a specific sensitivity which may

become inherited and produces either hay fever, asthma or migraine. Bell also reported a series of 60 asthmatic patients in 251 families subject to migraine. This rather trite belief that sensitivity to foreign proteins or other substances is the cause of this disease is not borne out by case investigation.

Apart from the factor of direct inheritance, the problem of predisposition has been widely studied by various workers, and it is now believed that there occurs in many patients a vasomotor imbalance responsible for the predominant symptoms; this is thought to be a cerebrovascular lability with probably primary vasoconstriction and secondary vasodilatation, the latter producing the headache. Wolff and his coworkers have brought forward this most generally accepted idea of the underlying processes in migraine. These are that the production of the pre-headache visual symptoms is believed to be due to vasoconstriction of branches of the carotid artery with resultant anoxia and dysfunction of the occipital cortex. Special disorders, paresthesias, and so on, may also be due to cerebrovascular constriction. Observations have also shown that the headache is probably due to distention largely, but not exclusively, of the intracranial branches of the external carotid artery. This dilatation in turn may cause the production of an arterial wall which becomes unresponsive to vasoconstrictor drugs. The pain itself is transmitted to consciousness by way of the fifth, ninth, and tenth cranial nerves. An intimate relationship between migraine and Ménière's syndrome is claimed by other investigators, each entity being divided into primary vasodilator (histamine-sensitive) and primary vasoconstrictor (histamine-insensitive) types. This mechanism is closely related to underlying mental and systemic disorders such as fatigue, exhaustion of mind or body, anxiety, excitement, faulty diet, excess alcohol, tobacco, auto-intoxication, and so on.

To ascertain the role of the cerebral arteries in migraine headache, Schumacher, Cahan and Wolff performed lumbar punctures during severe headache in 5 patients. The spinal

fluid pressure was progressively increased to 800 mm. of water, such an increase in pressure being sufficient to abolish histamine headache; this procedure did not diminish the intensity of the headache, and the writers infer that it does not arise primarily from the cerebral arteries but chiefly from dilatation and stretch of the branches of the external carotid artery.

They also did perimetric studies of the pre-headache scotomata which were correlated with systemic arterial pressures during the action of amyl nitrite. They found that after inhalation of small amounts of this agent the scotomata diminished and disappeared within 10 seconds of the facial flush, remaining absent from 2 to 4 minutes. After inhalation of larger amounts of amyl nitrite, the scotomata again disappeared shortly after the flush, soon to be followed by confluent scotomata which merged to produce transient amaurosis; a fall in blood pressure followed, and then normal visual fields and scotomata reappeared. These investigators, therefore, infer that the pre-headache visual phenomena result from cerebral vasoconstriction, succeeded by dilatation. These findings of dilatation and stretch of the branches of the external carotid artery and then of the cerebral have a significance only in regard to the headache. The experiments would seem to show that visual disturbances arise from defects in function in the cortex possibly due to repeated angiospasm and anoxia. They observed no change in the retina during the course of the visual defect or afterward, and obviously such defects as homonymous hemianopsia may be more logically explained by cortical vasospasm than by retinal defects.

Foster Kennedy believes that the scotomata of migraine are cortical phenomena, cerebral rather than retinal. He believes that the various field defects and other neurologic symptoms such as anopsias are associated with edema (pericapillary transudation) localized in angulations of cerebral meninges and sulci.

It is evident then that the causative and pathologic features of migraine are so diffuse that the exact mechanism of the disease and of the ocular involvement is still unknown. The abnormal changes due to this disease may affect the lids, the extra-ocular muscles, the cornea, the iris, the pupil, the retina, optic nerve and the retinal blood vessel system. The remaining anatomic components of the eye are not affected, and the literature contains no example thereof. No particular relationship between this disease and glaucoma has been evolved, although its occurrence has been reported, possibly associated with psychic and emotional upsets which oftentimes accompany both diseases.

CLINICAL FEATURES

The disease is usually ushered in by certain prodromes which may be characterized as feelings of irritability, lassitude or malaise; auras are diverse, and of these the most typical are visual disorders encountered in over 50% of all cases. Möbius noted only 15 patients in a series of 130, but Liveing found 37 cases out of 60, and Allan found that 48% of males and 40% of females showed visual changes. Usually both positive and negative phenomena occurred, the former being composed of a spectrum and the latter of a scotoma or of a type of blindness. At some spot in the field of vision, oftentimes near the fixation point, vision becomes blurred, and the patient may see flashing or punctate lights which, in a typical case, enlarge to assume an expanding luminous spectrum. Elliot reported in 25% of 300 cases and in 35% of a second series of 100 cases that the aura took the form of a zigzag arc of flickering lights and colors moving toward the periphery of the field of vision and reminding the individual, by its shape, of the lines of a bastion, from which come the terms "fortification spectrum" or "teichopsia." These changes were reported by many of the older physicians, namely, Fothergill in 1778 and Airy in 1870; they described the spectrum as gleaming with brilliant red, blue and other colors, and inside

this an area of bright luminosity. Both parts appeared to be shimmering; as Airy described it, "the spectrum boils," and Charcot compared it to a display of fireworks. These scintillating scotomata may last for a period of several minutes, expanding, spiralling and contracting, and after reaching a climax, usually fade irregularly through a process of waxing and waning. Before one spectrum has completely vanished, the beginning of a second may appear; they are usually binocular and of similar pattern for each eye. Variations of the spectrum and scotoma commonly occur and assume many different forms. The spectrum may cross to the opposite field and may even enter the scotoma. The latter may even develop into a complete homonymous hemianopsia which at times may intercept the fixation point.

McMullen states that strictly central scotomas are uncommon and monocular types are rare. Casters and van Bogaert report a rare one-sided nasal hemianopsia. The scotoma can occur by itself, and the spectrum may consist merely of random flashes or sparks or a falling light curtain. In one case report the patient experienced a "thousand silver forks dancing up and down," while another saw everything through a "silver mist." These auras may not vary through a series of many attacks, although changes may occur indefinitely in the right or left fields of vision. Obviously, vision becomes distorted during the course of such spectra and scotoma, and following their gradual disappearance objects may appear to the patient to be tilted, and illusions of size and distance may occur; diplopia even may result. Some of these curious auras have been ascribed by Klien to entoptic visions of the retinal pigment epithelium.

Auras other than the visual disorders are rather infrequent, although a sensation of pins and needles occurring in the fingers of one side or both and ascending through the arm to the shoulder and face may occur. Schob reports sensory aphasia, apraxia, agraphia and word-deafness. Tingling of the lips or of the tongue has been reported; motor involvement is

rare, although cerebellar symptoms such as ataxia and nystagmus have been reported by Kennedy, Oppenheim, Phillips and Siebert. Dizziness is quite common and sometimes occurs before any of the signs, being very severe. Auras of smell and hearing and of the special senses have been reported. These various and multiple abnormalities may occur in puzzling forms and may even come after the onset of headache instead of before.

The main feature of the attack is the headache, usually occurring on the side opposite the peripheral symptoms but at times occurring on both sides or even all over the head or behind the eyes. Oftentimes it is at a particular place, radiating in a well-defined direction and of a type which has been described as throbbing, splitting, hammering, boring and unendurable; oftentimes it is accompanied by tenderness of the scalp and photophobia and, when extremely severe, usually with nausea and vomiting and even delirium and unconsciousness.

Investigation by Wolff of Cornell University in regard to the problem of causation of headache has been of extreme importance in revealing the probable mechanism of migraine headache. This worker ascertained the sensitivity to pain of various intracranial structures in a series of 45 patients who were undergoing surgical procedures upon the head. He found the entire parenchyma of the cerebrum and cerebellum including blood vessels to be insensitive to pain. The olfactory, the optic and auditory nerves were insensitive to pain, whereas the ninth and tenth cranial nerves were found to cause pain behind the homolateral ear and in the throat when stimulated; stimulation of the eleventh cranial nerve and of an inconstantly present posterior root of the first cervical nerve caused pain near the vertex of the head.

Wolff also investigated pain by distending the lateral ventricles with air; this procedure caused severe headache, although direct stimulation of the various parts of the ventricular walls and their blood vessels did not result in any pain.

Specifically it was found that coagulation, compression and faradic stimulation of the ependymal lining of the entire lateral ventricle wall produced no pain. The large terminal vein that passes along the floor of the body of the lateral ventricle was insensitive to compression, coagulation and faradic stimulation. The pain which accompanied distention of the third ventricle was proved to be due to traction and displacement of the large cranial arteries in the region of the circle of Willis.

Wolff drew the following inferences from his laboratory and clinical work concerning the mechanism of headache: inflammation, traction, displacement and distention of pain-sensitive structures are the primary disturbances responsible for headache. The cranial vascular structures far surpass all others as a source of pain, and it is to be expected, therefore, that vascular structures will often be involved. He summarized his observations as follows:

1. Traction on veins that pass to the large sinuses from the cerebral cortex results in a dull aching pain over the top of the head; brain tumors may produce such headache by displacement or direct traction upon these veins.

2. Traction upon the middle meningeal artery may produce pain as far forward as the eye and as far back as the ear; tumors causing traction upon these arteries in any part of their course may cause headache.

3. Traction on the large arteries at the base of the brain causes headache, and tumors in the region of the sella turcica may cause pain by traction upon the branches of the circle of Willis. Distention of the third ventricle causes traction upon numerous arteries at the base of the brain and causes pain over the entire head.

4. Distention and dilatation of intracranial arteries result in headache; this is believed to be the mechanism producing migraine headache.

5. Inflammation involving the pain-sensitive structures at the brain base causes severe headache. Examples of this are

headaches produced by meningitis, subarachnoid hemorrhage or meningeal invasion by tumors.

6. Direct pressure by tumors upon nerves possessing pain-conducting fibers, such as compression of a portion of the fifth cranial nerve, can produce pain in various parts of the head.

This monumental clinical investigation has shed much light, not only upon the probable mechanism of migraine headache, but also upon various other forms of head pain. It demonstrated that the great intracranial venous sinuses and their tributaries from the brain surface, parts of the basal dura, the dural arteries and the cerebral arteries at the brain base, are sensitive to pain; that the cranium (including the diploic emissary and veins), the parenchyma of the brain, most of the dura and pia-arachnoid, the ependymal lining of the ventricles and the choroid plexuses are not sensitive to pain.

Allan noted the occurrence of nausea in 63% of men and 70% of women in a series of 402 cases of which 122 were men and 280 were women; vomiting occurred in 53% and 61% respectively. Ranzou, Mosher and Mingazzini have reported visual and auditory types of hallucinosis, usually affecting males and lasting from a few hours to 1 or 2 days. Moersch reported these psychotic changes as occurring in 22 of 1,000 cases of migraine from the Mayo Clinic. Impulsiveness, anger, anxiety, terror and temporary changes in personality have all been observed during the attack. The headache oftentimes changes from one attack to another occurring on either side indiscriminatingly and varying in severity and duration. Coughing, vomiting, straining and other actions increasing intracranial pressure worsen the pain. Usually the duration of the headache is 24 hours or less, at times only a few minutes. Allan reported that the headache is usually of longer duration in women than in men, occurring in 8 per cent of men for 2 days and in 4 per cent for 3, while the corresponding figures for women were 19 per cent and 10 per cent respectively.

Various features of neurosympathetic origin such as excess secretion of tears and saliva may occur. Christiansen stated the belief that it is possible to differentiate between a "white migraine" with pallor, coldness and dry skin and "red migraine" with hot flushed facies, small pupils and excess lacrimation. These assumptions have led to much confusion, and both paling and flushing may occur in the course of a single attack. These and other cervical sympathetic involvements were reported many years ago by Eulenburg. Usually the pulse rate increases with the headache, and vascular dilatation may be accompanied by capillary effusion or punctate hemorrhage in the conjunctiva. Goldflam, Adie, Critchley and Ferguson have noted the probability that subarachnoid bleeding may take place at this stage. Disorders such as erythema and angioneurotic edema may occur, while constipation, diarrhea, palpitation, yawning and dyspnea have been noted. Schroder has reported that metabolism is not basically modified during the attack. Many observers have examined the optic discs at the time of both the headache and scotoma, usually without any change being noted. Patton has stated that retinal veins have been engorged during the headache, while the retinal arterioles were constricted during the scotoma. Higgins and de Lapersonne have reported that as vision returned, the retinal vessels also returned to normal size.

Usually the attack ends in a flush, gradually waning and oftentimes ending in sleep; sequelae are rarely very marked. The patient may feel rather exhausted following a bad attack and not regain a normal state for several days. Very rarely cases have been reported, such as by Thomas, Gowers and Holmes, in which hemianopsia has lasted for an abnormally long time; continuance of such signs should cause further study for a possibly different etiology. To recapitulate the symptoms and characteristics of this disease:

1. A family history of migraine occurring in about 70 per cent of patients; in 10 per cent a family history of epilepsy;

and in 30 per cent a family history, especially in children, of allergy.

2. A personality structure consisting of considerable drive and ambition together with tensional, meticulous tendencies.

3. Temporary visual disorders preceding the headache such as spectrum, scintillating scotomata, blurred vision and sometimes hemianopsia.

4. Recurrent throbbing, oftentimes unendurable and incapacitating headache occurring in a relatively well person. It is usually unilateral, frequently temporal or frontal, although not exclusively so.

5. The occurrence of nausea, vomiting or retching, usually occurring during the height of the attack, and less frequently vertigo, tinnitus, paresthesias, flushing or paling, tremor, speech disorders, hallucinations and disorders of taste or smell.

CLINICAL TYPES

In addition to the classic type there are subtypes which have special features and present particular variations which must be considered.

Abdominal migraine: This term is employed to describe a condition occurring largely in children of migrainous parents in which abdominal pain occurs, associated with migraine or a substitution for the headache. Curschmann in 1922 reported this condition, and Brams collected 22 examples of it. Buchanan, Pollock and Barborka also reported such cases. Woltman told of a woman aged 28 whose headache and visual symptoms were promptly succeeded by intense abdominal pain followed by vomiting. Bassoe reported 2 cases that had undergone futile laparotomy. This type of periodic abdominal pain may persist after the migraine has vanished, while at times cerebral and abdominal syndromes alternate. Kinnier Wilson believes that should abdominal symptoms alternately occur without a history of any cerebral migraine, the diagnosis of abdominal migraine is

extremely difficult and may well be wrong. Some of these so-called visceral equivalents may be epileptic and not migrainous, whereas others might simulate a tabetic crisis.

Ophthalmoplegic migraine: This condition may be a form of recurrent oculomotor paralysis with headache and not a form of migraine. Gubler as long ago as 1860, Saundly in 1882 and Möbius in 1884 reported cases of ocular palsy associated with migraine headache; Charcot, however, originally proposed the name given this condition. This type of headache is oftentimes severe; it may be felt behind the eye or over the temple and is usually confined to one side. As this headache wanes, ocular palsy may develop and may attain maximum effect in a few hours or less; at times the third nerve is affected, usually on the same side as the headache, and rarely the fourth or sixth nerves may be involved. Convergence had been affected, and in one case a completely unilateral ophthalmoplegia had been observed. Such paralysis usually lasts for 2 or 3 days, but it may persist for weeks or months. It is usually followed by complete return of function, although after attacks become more frequent recovery is less complete and may go on to permanent paralysis; diplopia, mydriasis, ptosis and strabismus have been observed to persist during the entire period between attacks. Such findings provide suspicion that the cause of the ocular palsy is not of the same etiology as migraine. Of the findings which lend suspicion to this belief, first is the fact that the heredity factor is not so marked in this type as in simple migraine; secondly, and of more valid proof, is the finding of localized lesions in many oculomotor nerves in the few cases that have come to autopsy. Aneurysms may at times be responsible, and Riley has reported the demonstration of brain-stem lesions; repeated angiospasm could conceivably, however, produce such a permanent ocular muscle weakness.

Ophthalmic migraine: This is a term used to describe cases with the ocular manifestations of migraine such as recurrent scintillating scotomata and hemianopsia without headache.

Such forms may occur or be preceded or followed by the usual classic type of migraine; ocular migraine is the term reserved for headache of ocular origin which resembles migraine. However, it has none of the characteristics of migraine and should not be termed such, as it usually results from such factors as errors of refraction, extra-ocular muscle imbalance, aniseikonia.

Claims have been made for including certain recurrent facial palsies with headache in this general class such as the so-called facioplegic migraine; Bernhardt, Neumann, Flateau and Riley have reported such cases, but most of these are in the older literature, and all seem quite doubtful. It would appear that such a syndrome would probably involve other types of organic lesions such as aneurysm, tumor or infection.

Precordial migraine is characterized by intense pain around the heart without evidence of disease which might produce such pain. This condition has been reported by Fitz-Hugh as occurring in 27% of 880 patients with migraine. It may occur as a "substitute" for headache and has been confused with angina pectoris.

Atkinson has stressed the fact that Ménière's syndrome may sometimes substitute for an attack of migraine and occasionally even replace the disease. He pointed out the similarity of the two conditions.

OCULAR COMPLICATIONS

During all phases of migraine, ocular complications may be observed affecting the lids, conjunctiva, iris, pupil, media, optic nerve, retina, retinal blood vessels and extra-ocular muscles. During the prodromal stages, as well as during the actual attack, various components of the eye may be affected either singularly or in definite combinations.

Eyelids: The eyelids have been reported as being swollen and edematous with little redness and no induration or tenderness. These cases have occurred naturally enough in those

individuals in whom an allergic etiology was proposed; relief of the condition by allergic therapy was promptly obtained.

Ptosis of the lid has been reported rather extensively and may recur during various attacks. Townsend, Konstam, Drell and Kennedy have observed such ptosis, and in one case the ptosis remained indefinitely. This may occur early in the disease and in conjunction with paralysis of other extra-ocular muscles. It has been suggested that the ptosis may be the result of aneurysm, tumor or localized edema, occurring upon an allergic basis and accumulating within the skull in those areas best adapted by formation and the exercise of gravity to permit it. This is the theory held by Foster Kennedy, and he cited such a case in 1947. As a rule, such types of eyelid abnormalities are recurrent and transient.

Complications involving the conjunctiva in this disease are not common and not particularly serious. Occasionally, there may occur some congestion of the conjunctival vessels, and Kinnier Wilson describes capillary hemorrhages in the conjunctiva; corneal sensitivity is unchanged during the course of migraine, but edema of the cornea occurring in a patchy distribution has been described.

Iris: The anterior uveal tract is rarely involved in migraine with the exception of various pupillary changes; organic disturbances of the iris stroma have been described, and stromal hemorrhage and focal areas of hyperemia have been reported as occurring in this disease. Pupillary changes, however, are common. Chambers states that the pupils are usually dilated but react well to light and accommodation; dilatation and fixation of the pupil both unilaterally and bilaterally have been reported, and in some cases the pupils may be in a state of hippus, contracting and dilating rhythmically quite apart from any change in the light intensity. Rowbotham considers such changes as being related to disturbances of the autonomic nervous system. Daily described pupillary dilatation and constriction in association with extra-ocular muscle paralysis, ptosis and auditory disturbances. A dilated fixed

pupil occurring homolaterally with the head pain has been reported; no example of the Argyll Robertson pupil was found in the literature. In cases having a dilated pupil, Weber and Runge have noted absence of the hemianoptic pupillary reaction, inferring therefrom a cortical site for pre-headache visual scotoma.

PARALYSIS OF OCULAR MUSCLES

Ocular muscle paralysis is not infrequent in migraine and occurs in the so-called ophthalmoplegic migraine. This term indicates a paralysis of an extra-ocular or intra-ocular muscle occurring in conjunction with classic migraine syndrome. Such paralyses have long been recognized, and there is an extensive literature upon this phase of the disease. The third nerve is commonly affected, rarely the fourth or the sixth, and infrequently complete unilateral ophthalmoplegia may be encountered. Marlow, Mackay, Susman and Reese have reported at various intervals cases exemplifying such paralyses. In a case reported by Herman and Hall, a sphenoidal mucocele was thought to be the cause. Foster Kennedy believes that localized edema occurring in the neighborhood of the sphenoidal ridge can compress the nerves passing through the superior orbital fissure and impair their function; severe compression in such a bone-surrounded area can produce such anatomic changes as to abrogate function temporarily. He feels that it is quite usual to find the paralysis of ophthalmoplegic migraine lasting for several weeks and even months, and that it is to be expected that if headaches producing compression of these nerves occur regularly and frequently throughout a greater part of life that paralysis may ensue. Other neurologists disagree with this theory, believing that the disease entity called migraine does not produce any ocular paralysis, but that such changes are due to organic lesions in the brain such as aneurysm, tumor or arterio-sclerosis.

Marion Amat described a case in 1921 in which there was a complete third nerve paralysis which became permanent.

Susman stated the belief that unilateral hydrocephalus on the side corresponding to the headache might be related to the ocular palsy. Reese suggests roentgenography of the optic canals and orbit as a means of explaining these cases. Kamstam observes that the palsy may be due to a neuritis of the third or sixth nerve and rejects vascular pathology as the possible cause, because of the occurrence of relapses with identical symptoms. Daily sets forth that emotional disturbances are the exciting factor in precipitating the paralysis, and that psychotherapy is the therapeutic procedure of choice. Verhoeff records a case in which there occurred recurring attacks of concomitant exotropia, each followed by transient esotropia; each phase persisted about 1 week.

The author expressed the belief that such muscular anomalies may be explained on the basis of a vasomotor disturbance, first producing a reduction of tonus, and secondly an increase of tonus in the region of Perlia's nucleus. Sometimes the paralysis involves several nerves simultaneously, each of which must be individually involved, and the question has been raised as to whether these paralyses are actually complications of migraine or merely individual disorders which are occurring coincidentally. As the problem of determining the exact pathology of migraine is still unsolved, it is difficult to associate such paralysis with it. Aneurysms may probably be responsible for the syndrome of anoxia due to angiospasm; it may be postulated that recurrent angiospasm could produce such a degree of permanent vascular change or damage that resultant permanent dysfunction of a nerve or muscle might ensue, as occurs in blood vessel walls in hypertensive retinopathy.

THIRD CRANIAL NERVE

The most common ocular muscle paralysis occurring in conjunction with migraine is a total or partial paralysis of the muscles supplied by the third nerve with or without involvement of the pupil. Of 126 articles referring to cases of ophthalmoplegic migraine, paralysis of the third nerve was re-

ported in 78. Such paralysis usually occurs either during the acute attack or shortly thereafter and is of a transitory nature in most cases. Townsend describes a case in which the paralysis disappeared after 2 months' duration, while other cases involving either partial or complete paralysis of the third cranial nerve were reported by Möbius, Bussola and Amat. Cases of internal ophthalmoplegia are infrequent, although they are encountered in this disease. In such cases a paralysis of accommodation and paralysis of the pupil may persist for several weeks.

Only one branch of the third nerve may become affected, that which supplies the levator palpebrae muscle producing ptosis of the upper lid. A number of such cases which are usually unilateral and most frequently homolateral with the head pain have been cited by Kennedy, Townsend, Komstam, Daily, Drell and others. Marlow and Lawford reported cases of convergence paralysis.

THIRD, FOURTH AND SIXTH CRANIAL NERVES

Numerous cases of involvement of the third, fourth and sixth nerves have been reported, and an isolated paralysis of the fourth nerve represents a rather rare finding in the course of migraine. A. Fuchs, however, reported such a case in 1920 in connection with other cases showing involvement of the third and fourth nerves. Bramwell described the relationship of the third and sixth nerves to the arteries at the base of the skull. He demonstrated that the third nerve lies immediately posterior to the posterior cerebral artery, and that the sixth nerve lies in a similar position in relation to the transverse artery to the pons. He believed that recurring points of pressure upon the nerve might well occur due to arterial dilatation; he further stated that ocular muscle paralysis is also of the peripheral type, and although always occurring in a sudden manner, usually regressed slowly. In summation, one gets the impression after reading many case histories that it is usual to expect complete return of function in the majority

of cases demonstrating ocular muscle paralysis in migraine; however, in the event that the attacks persist, even in wide intervals, recovery may be retarded, or paralysis may become permanent. This finding, as has been stated, lends support to the view that the cause of the ocular muscle paralysis may exist as an organic abnormality quite apart from the causative factor of migraine or may possibly be the end result of long-continued periods of angiospasm, edema or possible pressure due to vascular dilatation.

INVOLVEMENT OF THE RETINA AND OPTIC NERVE

The conducting system of the eye is affected in many cases of migraine. This occurs in the form of changes in the caliber of retinal vessels which have been observed prior to and during the acute attack. Such observations lend evidence in support of the theory of vascular lability which is now a widely recognized mechanism responsible for the chief symptoms of migraine. Other peripheral vessels showing alteration in function due to emotional stimuli as well as during migraine have been reported by A. Hauptmann. Temporary dilatations of the retinal vessels as well as superficial retinal hemorrhages have been demonstrated. These alterations are of a temporary character and are reversible. Papillitis, visual papilledema and separation of the retina have been described. Visual field changes are extensively described. Such phenomena as fleeting scotomata, flashes of light, fortification spectra, "pinwheels" and "black spots" have been variously interpreted; Horrax stated that while operating on a patient under local anesthesia, manipulation of the visual cortex produced visual phenomena. Some of the older observers noted the relationship of the visual phenomena of migraine and spasm of the cerebral vessels.

Schumacher and Wolff concluded that the scotomata and scintillation are largely due to vasoconstriction of cortical vessels with resulting anoxia and disturbance in cortical function. Dynes reports 3 cases in which typical migraine

occurred associated with an elevated blood pressure and in which were noted quadrantic field defects; in these cases the author believes the changes to be due to vascular disease with cerebral hemorrhage or thrombosis which occurred in conjunction with migraine. T. H. Butler describes a case in which the right field of vision showed a uniform peripheral constriction together with a relative scotoma; he postulated aneurysm as the cause of this field defect. He also cited the case of a woman 45 years of age who had had typical migraine headaches for 30 years and who showed a hemianoptic crescentic scotoma. The blindspots were normal, and 5 months following this observation no trace of the scotomata was noticeable, fields of vision being normal. He believes this to be a pure case of migraine. Pinard relates that a course of treatment for lues may cure migraine accompanied by visual field defects, thus revealing a latent syphilitic arteritis as responsible for the disorder. B. Daniels reports a case in which homonymous hemianopsia occurred in a 34-year-old man with migraine. In the beginning there was a left lower quadrantanopsia protruding slightly into the upper left visual field; 5 hours after observation, the residual defect started to clear up slowly and concentrically from the periphery. In the course of the next several weeks, there were temporary changes in the size of the scotomata, it finally being reduced to a narrow arc-shaped defect. He assumes that the above climactic symptoms were caused by functional changes (spasms) of the vessels of the brain, and in view of the absence of the hemianoptic reaction of the pupils, the disturbance must have been behind the genu. Poos also reported a case of chronic right homonymous hemianopsia which followed various attacks of scotoma scintillans extending over a period of years. Similar cases have been reported by Sidler, Frederick Schultze, Möbius, Pandelescu and Dumitrescu. In many of these cases, it was apparent that the abnormal field defects might be accounted for by pathologic processes co-existing with migraine.

INVOLVEMENT OF OTHER NERVES

The involvement of the facial nerve in the form of a recurrent facial paralysis occurring with migraine is frequently merely a coincidence and probably would indicate some additional pathology which could explain the symptoms. Certainly one should view such cases with caution. Hemiplegic attacks in migrainous individuals have been reported by Clarke, Oppenheim, Jelliffe and Ferguson. Monoplegias have also been described. As previously stated Kennedy stated the belief that transient hemiplegias are due to localized cerebral edema.

There is no evidence in the literature of any causative association between migraine and glaucoma, although 2 cases have been recorded.

PATHOLOGIC FEATURES

As Wilson has stated, "Mere recurrence of an evanescent neural disorder even in long cases can hardly by itself induce visible lesions." In accordance with this statement, migraine at the present time may be said to have no well-defined pathology. To ascribe anatomic changes found at autopsy in cerebral tissue as productive of migrainous symptoms is not possible scientifically in most instances; cases reported by Morenas, Dechaume and Hilpert described individuals who spent a lifetime suffering from migraine with complicated neurologic disorders and in which degenerative vascular disease was present upon post-mortem examination. It is difficult to correlate such findings with the individual symptoms. Some examples of the ophthalmoplegic type have been autopsied, namely, cases described by Richter, Karplus, Shinoya and Dassen. In all of these, various types of lesions such as neurofibroma, aneurysm and fibrochondroma affecting the third nerve were found, obviously unrelated to the pathology of migraine.

LABORATORY FINDINGS

BLOOD AND CEREBROSPINAL FLUID

Studies of the body fluids either during or between migrainous attacks do not add to knowledge of the disease. Hahn and Bonn have reported transient increase of blood pressure during the course of the attack, but other observers have found the pressure to be normal. Vallery-Radot particularly examined 5 patients at the beginning of an attack for eosinophilia and found no increase in these cells. He was also unable to find an excess of eosinophiles in 15 out of 18 patients between attacks. Reymond Rouzard, and Moehlig found an increased value for blood cholesterin, but McLure and Huntsinger were unable to confirm this. Hartung extensively studied the blood chemistry in migrainous patients and found no noticeable variation from normal. The acid-base equilibrium is not changed to any extent; Weismann-Netter reported that a preceding alkalosis seemed to foretell some attacks of migraine. Diamond stated that the bilirubin and urobilinogen contents of the blood were high in a series of about 35 migrainous patients; however, hepatic and other intestinal symptoms were pronounced. Van Leeuwen discovered toxic substances in the blood having vasoconstrictor effects, probably amines, and a similar finding was noted by Kammerer, but further study is required.

Von Storch and Merritt published the following results in regard to their findings related to the spinal fluid pressures:

SPINAL FLUID PRESSURES

Time	*Number of Cases*	*Number with High Readings*	*Number with Low Readings*	*Average Reading mm.*
During attack.....	15	1 (190*)	3 (40, 60, 80)	123
Between attacks....	29	2 (185, 190)	3 (90, 90, 95)	139

* Figures in mm. of water.

Other investigations by Critchley, Ferguson, Quincke, Sicard and Claude reveal conflicting evidence in this regard. Von

Storch and Merritt in 43 cases, found the cell count, the colloidal gold curve, the reactions for globulin and the total protein content to be essentially normal. In brief, the composition of spinal fluid does not deviate to any degree from normal.

URINE

Transient acetonuria has been reported by Fawkes, while diminished excretion of chlorides and of urea was also described by Gerson, and Reymond and Rouzard. Riley stated that Prolan appears in the urine a few days before the onset of migraine and apparently disappears soon after, while on the other hand, estrone was usually below the normal level, unrelated to the headache. In the female, Prolan from the anterior lobe of the pituitary is taken up by the ovaries; therefore, when found in the urine of migrainous patients it would indicate either overactivity of the pituitary or underactivity of the ovary. The occurrence of the above abnormalities does not seem oversignificant, and the urine is not greatly affected by the migrainous attack.

PATHOGENESIS

In regard to the pathogenesis of the ocular symptoms arising in migraine, it would seem that the fairly common visual field defects are due to pathologic changes along the visual path between the optic chiasm and occipital cortex, most probably being the result of cerebral vascular spasm and anoxia, with possible edema. Visual hallucinations, so far as is known, do not arise from lesions of the optic tracts, but usually from disturbances in the cortex; aphasia and other sensory symptoms are also evidence in favor of a cortical site. Altitudinal hemianopsia may be produced by involvement of the calcarine cortex above or below the fissure. Visual auras confirm the cortical theory, and even scotomas might have a central origin, the maculae having extensive representation in the occipital areas; occasionally one sees a case in which

monocular scotoma may be present. All these findings force one to believe that different sections of the visual pathway are affected at different times and in different attacks of the disease; and, although most of our knowledge would impel one to accept a cortical theory, other facts indicate abnormalities in a more peripheral position. Unilateral paralysis of oculomotor muscles cannot be due to lesions higher than the mesencephalopontine nuclei and may possibly be lower. Wilson believes that the varied neurosympathetic features of the disease must be largely hypothalamic, or better, periventricular; he states that the characteristic headache cannot depend upon cortical malfunction, that it must be related to meningeal and meningo-vascular derangement, that is, an intracranial neuralgia. This possibility was inferred by Hasse 85 years ago, and now it seems proved that cranial arteries are potential sites of pain as demonstrated by Ray and Wolff, Penfield and others. Such pain may be elicited through stretch of relaxed dilated arterial walls, and this mechanism has been demonstrated in 4 types of headache: first, that induced by histamine; second, that produced by fever; third, that produced by migraine; and fourth, that produced by vascular hypertension.

In all of these, the amplitude of the pulse wave is an important factor in causing the headache as shown by its diminution with compression of the temporal and internal carotid arteries. It has also been demonstrated that the headache caused by drainage of the spinal fluid, as in lumbar puncture, and from lesions that produce change in intracranial pressure including tumors results from traction on or displacement of pain-sensitive intracranial anchoring structures, chiefly the large venous blood sinuses and the circle of Willis. These facts have been demonstrated by the above investigators. Hughlings Jackson believed that discharging lesions of the sensory cortex began the attack but could not account for the entire syndrome.

The reviewer is forced to the conclusion, then, that the very

complicated symptoms of migraine indicate changes localized in the cranial arteries, in the cerebral cortex, in the meninges, around ventricles and perhaps also in cranial nerves. No solitary site is conceivable. Some of the theories regarding pathogenesis follow:

1. The hypothesis of vascular spasm has been ascribed by duBois-Reymond as the cause more than 70 years ago. Brunton reported a case in which the temporal artery dilated proximally in the course of an attack, while its smaller branches were harder and more sclerosed, feeling like wire twigs upon palpation. As the heart propelled impulses through the dilated vessel into the constricted distal branches, there resulted acute pain. Hare brought forth evidence to demonstrate that migrainous pain is relieved by any procedure producing constriction of dilated vessels. Schumacher and Wolff have reported the most generally accepted theory of the basic pathologic processes. They stated the belief that the preheadache scotomata are due to vasoconstriction of branches of the internal carotid artery with resulting anoxia and distortion of function of the occipital cortex. The headache has been shown to be due to dilatation of the intracranial branches of the external carotid artery, the pain itself being transmitted to actual consciousness by way of the fifth, ninth and tenth cranial nerves. This idea had also been investigated by Ray and Wolff in 1940, who suggested that the upper 3 cervical nerves may also play a part in conduction of pain. This entire mechanism of vasomotor change is associated with temporary body changes underlying physical disorders, and probably allergic conditions. Some neurologists, however, doubt as to whether the beginning vascular constriction could be the cause of a luminous, expanding spectrum, believing that local ischaemia produces loss of function, rather than irritation of function. Nevertheless, the negative aspect of the aura, that is, the blindness and scotoma, could be accounted for by angiospasm; and re-establishment of blood flow through such vessels might produce the pains of vascular

distention. Little study has been given to the manner in which the vascular disturbance begins, and it is not yet known if the vasoconstriction starts locally in the tiny branches of the posterior cerebral vessels from changes in the bulbar area or vasomotor centers, or how such vasoconstriction extends, or whether it conforms to a nerve or blood vessel distribution. Vasoconstriction itself probably is induced by a neural factor, in which case migraine could be chiefly neurogenic. Moreover, the theory of vascular spasm does not fully explain the events that occur in ophthalmoplegic migraine. First of all, it is obvious that angiospasm ought to produce a temporary muscle paralysis by inhibiting the blood flow to the nerve, and yet not account for prolonged paralysis. Ehlers showed that the third nerve and the posterior cerebral artery lie together near the interpeduncular fossa and stated that when this vessel becomes distended it will exert pressure upon the nerve trunk and produce interference with function. The effect of such dilatation producing rather long-drawn-out paralysis of nerve tissue and briefer effects upon other tissue is not explained; of course, it would not apply to the fourth nerve and some other forms of ocular palsy. It is still also unexplained why permanent symptoms are not more common and why the oculomotor nerves should be particularly selected to become affected in migraine. The belief that the longer vascular spasm persists, and the more frequently attacks occur in the same locality the more likely is degeneration to be induced, is still conjectural. Another perplexing feature is that after many recurring attacks of angiospasm in the visual area permanent visual field defects are extraordinarily rare, especially as experiments have proved that nerve cells are more readily distorted by anoxia than are nerve fibers.

2. A second hypothesis is somewhat related to the theory of vascular spasm. This is the belief brought forward by Kennedy, Schüller, Quincke, Otto and Holmes that fluid edema results from increased vascular permeability, which, in

turn, produces arterial constriction and is followed by areas of cerebral or meningeal edema; these localized areas form quickly and by their presence induce various symptoms such as visual phenomena due to irritation of the calcarine tissue. Distention of sensitive tissues in the meninges due to such accumulation of fluid could produce severe pain. Cases were described by the above writers in which there occurred localized swellings in the eyelids, face, lips, breast, arms and back in conjunction with the typical migraine syndrome. Some inferred that migraine is merely a form of angioneurotic edema occurring in brain tissue. Even the most enthusiastic of believers must admit that other contributing causes may be present, since in any group of individuals suffering from a particular disability one may obtain a number who may be considered significantly allergic.

Before accepting this theory, more study is necessary, as there are various unsettled points requiring elucidation. It is difficult to understand why typical hemicrania accounted for by meningeal edema should not soon become diffused, and if edema produces visual illusions in the calcarine area, it would have to be assumed to elicit other cerebral symptoms indicating an almost total hemispheric edema. In simpler terms, such an edema could not be quite so selective as proposed. Spinal fluid readings also lend no support to the assumption that intracranial pressure is increased. The belief that the rare finding of subarachnoid hemorrhage during the course of an attack confirms the etiologic significance of edema is not necessarily true because vascular spasm alone may produce hemorrhages in the retina and conjunctiva and may also do so within the brain; the proponents of the allergic theory can only say that possibly some exudative process resulting in edema accumulation may occur in migraine and may be responsible for some symptoms.

3. A further hypothesis ascribes the disturbance to changes occurring in the autonomic nervous system, attempting to explain the intracranial vascular change by perverted cervical

sympathetic function; such a view has been proposed by Dandy, Penfield, Hartenberg and others. Whether such a vascular change—that is, constriction followed by dilatation—is due to a central abnormality, or whether it may be caused locally by action upon the vessels by circulating toxins is still undisclosed. Experimental stimulation and even extirpation of the cervical sympathetic ganglia or nerve trunk have been contradictory, and whether or not the pain of migraine is of trigeminal or sympathetic origin is still in doubt. Experimental studies on sympathetic nerve tissue have not reproduced the same degree of vascular spasm that is supposed to occur clinically. In regard to the causation of pain, Dandy states that migraine pain is "meningeal and therefore sympathetic," but anatomically the fifth nerve supplies the coverings of the brain. The problem as to the initial origin of the pain has been the subject of a great variety of clinical and experimental work. Recapitulation of such study tends to demonstrate that sympathetic fibers on the intracranial vessels carry impulses which produce pain from these arteries to the cerebrospinal neurons; according to the theory of the autonomic origin, migrainous pain is caused by "stretch" of the vascular tree and such impulses would pass over the trigeminal field to reach the cortex (an assumption in accordance with the findings of Harold Wolff). At the present time, however, one cannot state definitely that vascular spasm itself is caused by sympathetic stimulation, either from a central origin or by local reaction to various toxins. Ray and Wolff stated the belief that the pain itself is transmitted to the thalamus and cortex—that is, to consciousness —by means of the fifth, ninth and tenth cranial nerves and the upper 3 cervical nerves.

4. There are other ideas which have been put forward to explain the pathogenesis of this disease. Thomson attempted to show hypophyseal malfunction as a cause of the syndrome. He reported 17 cases in a series of 25 in which roentgenograms showed changes in the sella turcica. This theory is

that some endocrine change causes pituitary enlargement which then produces headache by pressure upon the sella, visual symptoms also being due to pressure upon the nearby optic chiasm and *bandelette* and ocular palsy to pressure upon the nerves as they traverse the cavernous sinus; such a theory has been proposed by Deyl and Plavec. This hypothesis does not seem to be free from criticism, as symptoms of tumors of the pituitary gland do not particularly resemble the characteristics of migraine. These tumors do not usually present the typical unilateral headache nor the visual auras which are consistent with migraine, and many pituitary headaches depending upon transitory enlargement of the gland have been successfully treated with theelin and other hormones. These facts were reported by Thomson, Riley and others. It is true that in the female, migraine has been frequently associated with puberty, the menopause and the menstrual cycle, and Price and von Storch investigated this situation in analyzing a series of 200 women with migraine. They concluded that in only 10% was there a definite relationship between the migraine attacks and the menstrual cycle, although they found that estrogenic therapy was most effective in this group. Alvarez in discussing the induction of the menopause as a means of treatment of migraine was vigorous in his nonrecommendation. Endocrine therapy of this disease has been largely disappointing, while the psychogenic aspects of puberty, the menopause and the menses have been widely neglected. Any attempt, therefore, to ascribe migraine to glandular derangement would seem incompatible with present-day evidence.

It is obvious then that not one of the several theories advanced to explain the pathogenesis of this condition is entirely satisfactory. The migrainous disposition would seem to be one consisting of a sensitive reaction on the part of the intracranial neurovascular system to diversified stimuli; production of symptoms would seem to be brought about by changes occurring in the vasomotor control of extracranial

and intracranial blood vessels, either from central sympathetic changes or local abnormalities. The cerebral cortex, the hypothalamus and the meninges all are involved in a complete attack, but exactly what transpires in regard to the sequence of symptoms is still unknown.

DIAGNOSIS

The classic type of migraine with a preceding family history and the previous record of sick headache in early life together with intermittent unilateral pain, visual aura and vascular imbalance usually are sufficient for diagnosis. Various minor forms and incomplete varieties of the disease, however, sometimes cause difficulty. Of the several other conditions which may produce confusion are cerebral tumors, especially those of the lateral ventricles; occasionally the typical hemicranial type of headache will occur with a neoplasm. Extremely important is examination of the ocular fundi to rule out papilledema. Cerebral aneurysm may simulate migraine for many years, as may the so-called histamine headache. This is characterized by sudden onset with unilateral parietal pain increased by vasodilators and reproduced by the injection of histamine; it is accompanied by lacrimation and congestion of the eyes and nose on the same side and does not usually cause gastric symptoms. It usually occurs in patients over the age of 40 and may be treated by histamine desensitization. Hypertensive headache, facial neuralgia, temporomandibular neuralgia, sinus headache and temporal arteritis must be considered in differential diagnosis. Tic douloureux should not be confused with migraine. Usually the most difficult problems in diagnosis occur in individuals who possess neurotic personalities or who may be undergoing other organic disease when first observed.

As a further aid to diagnosis, Dow and Whitty report 51 cases of migraine studied by electroencephalography. Of these, abnormalities were found in 30; generalized dysrhythmia was found in 14; symmetric bilateral episodic activity in

12, and a persistent focal abnormality in 4. They concluded from their studies that the use of electroencephalography in investigating cases of migraine is always advisable, even though a persistent focal abnormality is only rarely demonstrated. In cases in which ocular signs were present during the aura, generalized dysrhythmia was the rule. Further study, especially in the investigation of cases of migraine over a period of years, is necessary, but this should be a valuable adjunct in diagnosis.

COMPLICATIONS

There are a few complications reported in the literature which may be considered due to migraine itself, most of the so-called complications having been due presumably to ruptured aneurysms, unrecognized tumors or to vascular thromboses. Such events would explain the few instances in which hemianopsia or other ocular changes have become permanent. The occurrence of glaucoma, brain abscess or sinus complications, although reported, should undergo careful scrutiny; migraine has never, per se, resulted in fatality.

PROGNOSIS

In consideration of the possibility of recovery from the ocular complications of migraine, the prognosis should be reserved, as in the present state of knowledge the actual cause of many of the complications depends upon rather intangible factors. Obviously, a reserved prognosis is necessary, as ophthalmoplegic symptoms occur which do not recede completely. The muscular complications may be divided into 2 classifications, those which tend toward complete recovery and those in which a certain tendency to paresis remains permanent. The prognosis in the disease itself would appear to vary, although chances of complete recovery are good in many cases. In general, migraine is a self-limited disorder, gradually ameliorating in the course of time and oftentimes disappearing completely with the climacteric. This disease is

never fatal unless due to suicide; in those cases in which there is a strong element of heredity, improvement is slower, and proper therapy is the means of obtaining earlier improvement and elimination of the disease. Unquestionably, the prospect of permanent cure in many cases is remote, but in all cases aid may be given by proper treatment.

TREATMENT

The course of treatment of this disease consists of 2 main divisions, the treatment of predisposing factors and the treatment of the disease itself. It is obvious that in order to prevent a disorder which is inherited in a large percentage of cases, intermarriage among individuals with migraine is inadvisable. The occurrence of migraine, epilepsy and an extensive or strong tendency toward allergy in both partners would be strong reasons to avoid marriage. Other forms of preventive treatment are to be found in the field of psychiatry, where psychoanalysis and personality treatment are methods now recommended for many patients. In attempting to advise the patient in regard to his habits, reactions and environmental situations, the physician may relieve the patient of many situations involving tension and emotional conflict. Whitehorn and Wolff have described a method of treating such patients by means of bringing to the fore the relationship between emotion and physical state; such therapy was of definite benefit. The belief that auto-intoxication is a prominent factor in leading to migraine should result in a regime of suitable intestinal hygiene; tests for sensitivity to the various proteins should be made in those cases in which allergy is suspected, but results from allergic therapy have been varied. Naturally if blameworthy protein substances are found, relief may be obtained by desensitization or avoidance of them. Errors of refraction and eye muscle imbalance, according to Elliot, are predisposing factors in many cases. He obtained a definite cure in 37 out of 100 cases by suitable correction of the error of refraction; this obviously was in cases of "ocular

migraine." Endocrine treatment has been reported as being effective, some physicians employing thyroid extract, some using intramuscular injections of pituitrin. Sajitz advocated the use of progynon, obtaining relief in 7 cases in a series of 11. Theelin and emmeninS have been used by Blakie and Hossack with some success in women who underwent attacks of migraine during the menstrual period. Alvarez strongly protests against the induction of menopause as a means of treating migraine. Further methods of preventive treatment include the use of histamine infusions which attempt to alter the vascular tendency toward constriction, and dilatation which occurs in migraine. Histamine seems to be effective when given in the form of intravenous infusions of 1 mg. of histamine base in 1,000 cc. of normal saline solution; such infusions are administered slowly to prevent severe flushing, headache, tachycardia or drop in blood pressure. During such treatment, 2 ounces of amphogelS in 400 cc. of milk should be taken slowly by mouth to relieve gastric irritation. As stated previously, this type of treatment probably increases the individual's tolerance to histamine, thereby changing an underlying vascular imbalance. Pelner and Aibel attempted to treat migraine headaches with desensitizing doses of neostigmine and reported fairly impressive results in a rather small series of cases. Atkinson, Goldzieher and Popkin described successful preventive therapy from the use of intravenous injections of nicotinic acid starting with 20 to 30 mg. and slowly increasing the dosage to 50 mg. daily in the form of 6 to 8 injections. Palmer described preventive therapy in the form of intramuscular injections of 30 to 100 mg. of thiamine hydrochloride daily for 4 weeks; he admits that the action of this vitamin in migraine is obscure, but states that improvement has resulted in more than 65% in a large series of cases following treatment for 4 weeks as described. Thirty milligrams is given three times a week for two weeks, the amount being diminished or increased as necessary. In addition to thiamine,

riboflavin and nicotinic acid are given daily with large doses of the vitamin B complex; treatment should be observed from three to six months before being considered ineffective.

Various types of diet have been proposed to prevent the attacks; high calcium, low carbohydrate, ketogenic diets and lowered fluid intake have been employed. Pfeiffer, *et al.*, described a type of treatment which attempts by the use of calcium lactate and potassium chloride to compensate for changes in the arterial blood volume, to prevent diuresis and to attempt to withdraw extracellular fluid. They report successful results in a series of 150 patients who were maintained upon this therapy for several weeks.

Surgical treatment of migraine, especially arterial ligation and sympathetic surgery, has been recommended. It should be a method of last resort, except in a well-localized and properly diagnosed unilateral headache. Arterial ligation has been done upon the temporal, middle meningeal and external carotid artery with good results. Improvement, however, from this method of treatment does not last usually for more than 1 year. G. F. Rowbotham described 4 cases in which sympathetic surgery was performed. He stated the belief that the pain of migraine is probably due to excessive expansion or dilatation of the arteries of the scalp and the dura, and that painful impulses are conveyed to the brain through the upper half of the posterior root of the fifth nerve. The trigeminal pathways may, therefore, be regarded as the sensory arc of the migraine cycle. It is not known why the arteries concerned occasionally dilate or contract excessively. One theory is that a migrainous person is born with an unstable mechanism in the hypothalamus, which reacts excessively to the stimuli reaching it through the higher centers of the brain and causes explosive or dysrhythmic messages to be sent to the larger blood vessels of the head. These large blood vessels are supplied with motor fibers of the efferent side of the autonomic system; therefore, since disordered messages from the hypothalamus are transmitted by the motor autonomic

pathways to the vessels concerned, sections of those pathways should give relief in cases of migraine. Therefore, in 4 cases he exposed the sympathetic chain between the middle and anterior cervical ganglion and removed the lower half of the upper cervical ganglion; the outer coats of the internal and external carotid arteries were stripped and removed in the manner of Leriche's periarterial sympathectomy. Finally, the external carotid artery was ligated. In all 4 cases, the pathologic report revealed the tissue to be sympathetic ganglia and sympathetic chain; in all cases, the patient was left with a Horner's syndrome. The author then discusses the rationale of such treatment, stating that the pain is transmitted to the brain through the upper part of the posterior root of the trigeminal nerve as arterial spasm is aroused by stimuli passing along vasomotor pathways; therefore, a neural mechanism acting for it can be constructed. He claims that since the fibers of the first division of the fifth nerve represent the pain pathways in migraine peripheral sympathectomy as described above should be a means of relief from the pain. In all 4 cases reported, complete relief from pain was obtained, but the author does not state how permanent such results were and whether or not complications ensued. Sympathetic surgery for migraine in the hands of other investigators has not resulted in any consistent amount of improvement.

Engle and Evanson have employed potassium thiocyanate in treating headache and in preventing migraine. It would appear to be of value as a preventive measure but is handicapped in universal use because of its dangerous systemic reactions. It must be used under careful observation and with frequent blood analyses.

Unceasing efforts have been made to relieve symptoms of the attack itself. Brunton long ago advocated the immediate use of potassium bromide and sodium salicylate. Fantus employed sodium bicarbonate with tartaric acid. Bigland believed that calcium lactate should be administered at the

very first sign of a visual aura. In a series of 16 to 20 patients prevention of paroxysm was accomplished. Hunt treated patients with intradermal injections of 1 cc. of a 1:1,000 solution of epinephrine hydrochloride; the results were inconclusive. Ephedrine has also been tried. Intravenous injections of 3 to 30 mg. of benzedrine sulfate were used successfully by Gottlieb in a small series of cases; relief of 6 to 7% of 18 patients in a period varying from 7 to 45 minutes was reported by this investigator. Other substances which have been employed to produce vasoconstriction are intravenous 10% solution of sodium chloride, combined with a 20% solution of glucose and intravenous injection of caffeine and sodium benzoate U.S.P. in a dosage of 4½ gr. (0.29 gm.). The method of treating the predominant symptoms varies according to the severity of the attack. In mild attacks, 10 gr. (0.65 gm.) of acetylsalicylic acid with 5 gr. (0.3 gm.) of caffeine may be sufficient to relieve the headache. Wolff, Hardy and Goodell have shown that aspirin is equally effective as similar doses of acetanilid, acetophenetidin and amidopyrine either singly or combined in combating the headache; therefore, they do not recommend the use of the latter. Moderate attacks have been relieved by demerolS in a dosage of 100 mg. usually combined with acetylsalicylic acid. Occasionally, intravenous injections of 5 cc. of 50% magnesium sulfate are of benefit. In severe episodes the pain usually responds to dilaudidS in a dosage of 1/32 to 1/20 gr. (2 to 3 mg.) or 1/6 to ¼ gr. (10–15 mg.) of morphine sulphate. The number of such treatments is constantly being increased by new synthetic preparations combined in different forms; the opiates and morphine derivatives are never desirable to use because of their habit-forming tendencies. Specific nonalgesics are better employed, especially those drugs producing vasoconstriction. The first of these is ergotamine tartrate (gynergenS). Ergot was in use many years ago in the treatment of migraine, as reported by Eulenberg and Campbell in 1894. Its employment, therefore, is not of recent origin as some imagine;

Lennox, O'Sullivan, Logan and Allen, Meyer, Tzanck, Brock and von Storch all report successful results in a high percentage of cases, reaching nearly 90% in a large series of cases reported by von Storch. Its action inhibits or retards the pulsations of the large cranial arteries by direct action upon the vessel wall; it produces better results when given early in the attack and does not possess any preventive value. It may be given parenterally in an effective manner in a dosage of .25 mg.; subcutaneous or intramuscular injections are most commonly employed, and such a dosage is .5 mg. Intravenous injections merely produce more rapid relief and should be used only under the supervision of a physician. Results from the intramuscular injection may be evident within 45 minutes to 90 minutes and are more effective when the injection is given early. If given orally, about 10 times the parenteral dosage is necessary, and this form of treatment is effective in about 40 to 60% of cases. Slower and less effective absorption requires crushing of the entire dosage in the mouth, and if allowed to dissolve under the tongue the effect is more rapid; however, because of the unpleasant taste and the occurrence of severe vomiting during the course of many attacks oral administration is of doubtful value.

The continued use of parenteral injections of ergotamine tartrate is not advisable in dosages of more than .25 mg. given twice a day, and such treatment should not be continued. Nausea or vomiting may occur after administration of the drug, as may "cramps" along the arms and legs after parenteral injections. Persistent numbness and tingling of the fingers and toes should suggest ergotism and indicate immediate cessation of the drug. Von Storch states that the main contraindications to the use of ergotamine are "septic states, especially when associated with intravascular foci, and obliterative vascular disease, especially when coronary."

Another ergot derivative in which the oxytocic effect has been removed is dihydro-ergotamine methanesulfonate (D.H.E.-45, Sandoz). This drug has proved to be very effec-

tive but requires twice the amount in dosage as gynergen; it may be given intramuscularly and intravenously in dosages of 1 mg. It has already proved to be harmless when given to patients in early pregnancy. Horton, Peters and Blumenthal have stated that good results were obtained in approximately 80% of 150 cases.

Ergonovine (Ergotrate, Lilly; Ergotasine, Sandoz; Ergometrine, Burroughs and Wellcome) is another ergot compound which produces considerable improvement and causes less nausea than ergotamine. It is contraindicated in pregnancy.

Alvarez and Mason have treated a series of cases by inhalation of 100% oxygen with good results. Other forms of therapy include the use of vasodilating drugs such as amyl nitrite, nitroglycerin, trichlorethylene, intravenous magnesium sulfate and intramuscular acetylcholine. Histamine has been given intravenously by Thomas and Butler. All such dilating drugs have been reported as beneficial in terminating some migraine episodes, probably by becoming effective in the primary vasoconstrictor phase by inhibiting or lowering the blood pressure sufficiently to avert the second stage. Patton describes the highly effective use of prostigmine bromide given orally which acts as a parasympathetic stimulant producing vasodilatation.

While most of the medications described above are of advantage during the crisis itself, others may be given systematically with advantage in the treatment of migraine. The migrainous individual should pay careful attention to diet, digestion, eye conditions, menstrual cycle, and whatever else may be in need of attention, including the removal of any focus of infection. In addition to such measures, of great importance is supervision along more general lines. Relaxation and freedom from irritability, worry, unhappiness, excitement, overwork and a lessening of the daily stress and strain of modern living should be instituted. Sedation may be necessary to produce relaxation. The proper amount of sleep

should be carefully observed, and any articles of food which may produce distress should be avoided. If dehydration occurs, fluids should be replenished; whatever may be the best treatment for each individual patient must be carefully evolved and selected and should offer the best prospect for alleviation, and in some cases, termination of this disabling disease.

CONCLUSIONS

In migraine, which is really a symptom-complex, there occurs a morbid condition of the brain, the pathologic processes of which are still a source of considerable disagreement. Specific mechanisms which produce the predominating symptoms, however, are well recognized and are due to some form of cerebrovascular imbalance, resulting in vasoconstriction and probably secondary vasodilatation of cranial blood vessels. In the vast majority of cases, the headache is due to distention largely of the intracranial branches of the external carotid artery, while the various visual auras seem to be largely due to anoxia and disturbances of cortical function resulting from angiospasm, possibly abetted by edema. The causes and the type of the basic disturbance vary and are largely in the realm of conjecture. According to some investigators, toxic, hepatic, duodenal or intestinal disorders may be the offending agents which instigate the attack. Various ocular disturbances, endocrine irregularities of the thyroid, pituitary or adrenal glands may be considered as productive of migraine, but all lack confirmation by worth-while evidence. Heredity plays an important part in migraine, and there appears also to be a definite hereditary relationship between migraine and epilepsy. Many authorities agree that another important factor is the so-called "migraine personality," which embraces factors which may not alone produce migraine or become associated solely with migraine but seem to call forth emotional reactions at times which allow the onset of a migrainous attack. Such personal characteristics may be described as ambitiousness, efficiency, tension,

perfectionism, meticulousness and stubbornness; in such persons there is present a great part of the time considerable tension with tendencies toward vasomotor imbalance and the occurrence of migraine. Ocular symptoms which occur during the course of migraine are prevalent, although their frequency is variously estimated by different investigators. With the aid of 3 translators, I have completed a comprehensive review of over 1,600 cases of migraine and have concluded, as a result of such investigation, that ocular symptoms occurring during the course of migraine are extremely common. Many case reports were lacking in detail and accuracy, and in many instances much important information was omitted. Many investigators have repeated previously known facts in the disease, while others have made only brief reports containing little essential data; there was much in the literature of migraine irrelevant to this study, and one encountered an astonishing amount of repetition.

The incidence of visual disorders in migraine with scintillating scotomata and fortification spectra occurred in 34% of cases; such auras have been previously described and are supposedly due to cortical malfunction produced by cerebral anoxia. Hemianopsia, both transverse and vertical, occurred in 4%, but central scotomata were found to be rare; such scotomata are possibly due to cerebral angiospasm and edema.

Various ocular paralyses which supervene during migraine have been analyzed and occurred in 17% of cases; angiospasm, aneurysm and cerebral anoxia, together with other cerebral lesions may produce such factors of the disease, and in many of the inadequately reported cases oculomotor palsies of a recurrent type probably occurred coincidental with migraine and not due to it. Especially is this true in the cases in which oculomotor palsies had become permanent. In most instances the paralysis lasted for a period of 3 to 4 days, slowly passing away, but occasionally it persisted for weeks or more. Usually complete return of function may be ex-

pected, although in some recorded cases recovery became less perfect as the attacks persisted, and then the paralysis became permanent (in one case, in the absence of any further headache).

Diplopia occurred in 14% of cases; involvement of the third nerve occurred in 88% of those having muscle palsies. Isolated cases of a sixth-nerve paralysis have been reported by 7 observers, and in no case was there a complete bilateral paralysis of the ocular muscles. I discovered 296 cases of paralysis of the ocular muscles in the available literature. Other ocular factors relevant to the disease are as follows: conjunctival hemorrhage occurred in 4 cases; unilateral ptosis occurred in 6% of cases; in no case was there a bilateral ptosis. The corneal sensitivity was unchanged in any case, and irregularly distributed areas of corneal edema were described twice. Pupillary disturbances have been reported in many forms; a unilateral fixed dilated pupil was reported in 76 cases. A unilateral dilated pupil reacting to light with varying degrees of rapidity occurred in 49 cases. The occurrence of an Argyll-Robertson pupil was not noted; hippus was reported in 3 cases, and inequality in pupils was noted in 423 cases. Hyperemia of the iris vessels with stromal hemorrhages was noted in 3 cases. During the course of an attack spasm of the retinal arterioles has been observed by some, whereas others have found no abnormal change in the vessels. Unilateral blindness, transient amaurosis and obstruction or thrombosis of the retinal vessels have been described. There seems to be no association between this disease and vascular hypertension. Edema of the retina and retinal hemorrhage have been recorded in numerous cases, being reversible in all. Glaucoma has been reported in 2 cases. Exophthalmos and separation of the retina were described in 1 case. The average age of the onset of migraine was found to be 22. Females were affected in 65% of the cases, whereas males were involved in 35%. No information regarding the location of the disease upon the right or left side of the head was of value. The

ocular muscles were involved in 17% of cases, whereas scotomata and other visual disorders occurred in 34%. Retinal degeneration and optic atrophy were recorded in 6 cases, and in 1 case endophthalmitis was described. In numerous cases varying permanent residua were reported as being due to defects in the visual field which occurred in conjunction with migraine.

In consequence of the observations and experiments made by many investigators, one must conclude that ocular abnormalities of diverse types are very common findings in the course of migraine and play an important role in the symptomatology of this disease. In common with our lack of precise knowledge in regard to much of the underlying disease process itself, however, explanation of many of the ophthalmologic features which occur is still far from clear. No gross or histologic pathology has yet been demonstrated in migraine; studies in endocrine pathology and vascular pathology have not brought forward any genuine evidence and have not demonstrated any actual changes other than transient abnormalities which are of value in explaining symptoms, but have produced no basic facts in explaining the etiology and pathology of migraine.

In conclusion, it may be said that although the recent years have shed much light upon many of the symptoms of migraine, one must agree with Von Storch that "no true responsible organism nor toxin nor definite histologic pathology has as yet been demonstrated."

CASE REPORTS

CASE 1.—A. C., a 27-year-old white American housewife, complained of severe periodic head pain which occurred in and around the right eye and radiated to the right temporal region. These headaches had been present since the age of 14 and were unrelated to any particular food or drug. They occurred at intervals varying from 2 weeks to 2 months. The patient usually experienced a sensation of dull frontal pain during the late afternoon or evening preceding the attack, and a few hours prior to the onset of a

torturing, boring episode of pain she would experience visual disorders which consisted of shimmering, flickering bright spots which oscillated rapidly throughout the fields of vision. The usual sequence was then to be awakened after 2 or 3 hours of sleep by such pain as described. There followed an attack of severe vomiting and retching which usually continued for 12 to 15 hours. During this period, excess lacrimation and salivation occurred at intervals.

This patient had always been of a striving, ambitious temperament who had earlier in life studied for a graduate degree, but this plan had not met with the approval of her husband. In her student days she had been unusually successful and had been asked by the institution which she had attended to continue on as a teacher. She became occasionally frustrated and irritated and dissatisfied. To compensate for this dissatisfaction, she plunged into her work at home, and during these periods her headaches became more frequent and intense. Her situation in life seemed to precipitate definitely the attacks of migraine. The past history was noncontributory, and vision in each eye was 20/20.

Examination revealed no ocular pathology, and extra-ocular muscles were normal. There was a very inconsequential error of refraction. Physical examination revealed nothing organically abnormal with the exception of a slight degree of undernutrition. The heart, blood pressure, lungs, abdomen and urine were normal.

This condition obviously seemed to be a typical case of migraine with prodromal scintillating scotomata, and the patient was referred to an internist for treatment. After almost daily visits to investigate this patient's condition, it was found that the subject's attitude toward her life situation could be altered. An attempt was made to cause her to become more realistic and less sensitive and detached from the actualities of her existence. Following such advice the frequency and intensity of her attacks became less, and upon the advent of an attack she was advised to use ergotamine tartrate in a dosage of 0.5 gm. to be administered intramuscularly during the first phase of the episode. Since adoption of this procedure, patient has been able to experience 18 months of freedom from the tormenting head pain; attacks have been slightly less frequent.

CASE 2.—B. F., a 44-year-old white male American office worker, complained of frequent left-sided frontal headaches. These attacks of headache usually occurred during the late morning or afternoon hours and appeared at intervals 2 or 3 weeks apart. Patient suffered no prodromal symptoms, and the head pain usually increased in

degree and severity over a period of 6 to 7 hours. No visual disorders were present, and no teichopsia or anopsias were experienced.

This individual was an extremely hard-working, driving, perfectionistic and ambitious type of man who was interested in and able to keep a number of different activities in operation at the same time. In order to accomplish this, he was required to make quick decisions and to be constantly alert and attentive; if he encountered any delay, or if for some reason he became unable to maintain his high standard of efficiency, he became exceedingly tense and resentful. It was during these periods that his migraine attacks took place.

After careful observation over a period of 6 months (during which time the patient was seen during periods of extreme tension, irritability and dejection), certain psychotherapeutic measures were instituted which gradually lessened the frequency of these attacks. It seemed that this patient's temperament, which permitted no compromise with excellence and effectiveness in his work, would play a great part in the onset of his attacks of migraine. In addition to this form of therapy, however, there was introduced a correction for a marked error of refraction and eye muscle imbalance, which was the only abnormality found upon physical examination. The relationship of personality features, emotions of a distressing nature, and attitude toward life of this patient demonstrate quite clearly what can be accomplished by careful investigation and proper treatment of migraine through psychotherapy.

CASE 3.—E. P., a 31-year-old white female American hotel worker, complained of recurrent attacks of "bright spots before the eyes." These occurred during periods in which the patient felt perfectly healthy and usually were present at 2 to 3 week intervals. They assumed the appearance of flickering, dazzling, white, red and yellowish spots assuming starlike zigzag formations, changing to what the patient described as resembling "a huge diamond brooch." During the period of such attacks, patient would be afflicted by some throbbing in the right parietal region, but no true pain was ever present; there also occurred blurring of vision with occasional photophobia. Frequently prior to the attack the patient experienced periods of depression and irritability.

Further inquiry into her history revealed that because of her husband's inability to support her properly she had been obliged to obtain a position as a hotel clerk. This in itself produced in her a feeling of resentment, and although she accepted it at first with complacence, it later involved limitations upon her social life which caused her to become increasingly restless most of the time. The

routine and restrictions of her life became extremely boring, and during the periods when she was most dissatisfied with her lot the frequency and intensity of her headache were most severe. She felt insecure and hopeless about her future and cried when she was asked concerning life in her own home and bringing up a family. Such a failure to adjust to economic and social situations was thus shown to be definitely related to her migrainous attacks.

Examination revealed a well-developed and well-nourished female who showed nothing abnormal after a complete and thorough physical examination; the vision was 20/20 in each eye, and the eyes were entirely normal. There was no ptosis, nystagmus or strabismus; fields of vision were normal.

She was referred to an internist who, having been given certain facts in regard to her history, was able through patient, intensive personal interviews and psychotherapy to reduce the frequency of the attacks by means of improving this patient's attitude toward her life situation. He also prescribed the intramuscular use of dihydro-ergotamine methanesulfonate upon the first premonition of an attack. Since employing this type of therapy, the patient has been greatly relieved of the previously almost incapacitating episodes of discomfort and occasional head pain.

This case also demonstrates what can be accomplished in the treatment of migraine by carefully analyzing the personal reactions, the life situation and the emotional features of each patient affected with this disease. Such evidence indicates that there are many features of this character which are of extreme importance in migraine.

CASE 4.—F. S., a 20-year-old white female American college student, complained of extremely sharp boring pain localized in and around the right eye and recurring approximately every 3 weeks. Usually such an attack would be preceded by a period of blurred vision, and often this patient noted portions in her visual field which were momentarily obscure. She also would experience luminous flashes which appeared before her eyes. Such symptoms preceded the headache by periods varying from a few minutes to 3 to 4 hours. The past history revealed that this patient had been subject to "sick headache" since the age of 10. When younger she stated that she would oftentimes undergo severe headache upon returning from school. This would be in some instances accompanied by nausea and vomiting; no specific treatment was ever given to her for such a condition. The mother of this girl had had typical migraine for a period of 20 years.

Questioning concerning her past history revealed that as a child her relations with her mother were bad. Upon occasions she had temper tantrums, was extremely obstinate and seriously distressed her mother. She had been the youngest of 5 children and had been considered a bashful and disobedient child. She had always been a fussy person, wanting things done just right and easily irritated and enraged when things went wrong. She was also under the influence of a dominating father and oftentimes was extremely unhappy in her home life. Such a background could easily produce a fertile field for migrainous attacks.

Examination revealed a well-developed and well-nourished female whose physical examination was declared to be entirely normal by her physician. Ocular examination revealed the pupils, media and fundi to be normal; the ocular muscles and fields of vision were normal. After correction of a moderate error of refraction consisting of myopia with astigmatism, vision was corrected to 20/20 in each eye. As her eye abnormalities did not explain her severe head pain, and as her history seemed typical of migraine with visual disorders consisting of scotomata and amaurosis, she was referred to an internist for treatment. Therapy consisting of an attempt to regulate and remove the reasons for personal dissatisfaction and tension and resentment was instituted; attainment of genuine relaxation was emphasized and advice as to achieving satisfaction in her school work was given. Regulation of general hygiene and periods of relaxation and rest, together with the use of one of the ergot derivatives, have gradually improved this patient's condition and lessened to some degree the frequency of the attacks. The ergot medication when given early during the prodromal symptoms has prevented all but 3 attacks of head pain during the past 14 months.

CASE 5.—O. K., a 34-year-old white American businessman, had experienced intermittent attacks of excruciating neuralgic pain, which was localized to the left frontal and parietal region. These episodes of tormenting pain usually occurred in the early hours of the morning, awakening the patient from a sound sleep. They seemed to occur most commonly following days on which his occupation entailed periods of tension and more than average emotional strain. The pain was described by the patient as being almost unendurable, and upon many occasions he had been obliged to call a neighborhood physician, who had in rare instances ameliorated the symptoms with sedatives. He had undergone various laboratory tests and x-ray studies without benefit and was becoming somewhat

apprehensive and frightened at the prospect of future attacks. The episodes usually occurred on an average of every 8 to 10 weeks and were not accompanied by any type of visual disorder. There was no history of observing luminous spectra or scintillating scotomata; nor had the patient experienced any diplopia or any sensory disorders.

He was seen by me 2 days following the experiencing of a particularly severe headache. Examination revealed a well-developed, well-nourished, healthy-appearing man; vision was 20/40 in each eye, and when an error of refraction consisting of hyperopic astigmatism was corrected in each eye, vision was brought to 20/20. The lids, conjunctiva, cornea, pupil, iris, media, fundus and tension of each eye were normal. It seemed obvious that such severe, tormenting pain could not result from any eye abnormality, and the patient was referred to an internist with the suggestion that this case presented symptoms that could well be those of migraine. The physical examination reported by the internist was entirely normal; investigation, however, revealed that this man had formulated a very rigid attitude toward his work, imposing standards of performance which he frequently failed to reach. As a result, his work fell short of his ideals and caused him great disappointment. Repeated attempts to improve his work were unsuccessful, causing him more and more frustration; as a result he had more frequent and severe headaches. Upon a regime which included abandonment of his previous system and standards his efficiency increased, and his headaches became decidedly fewer. He was also placed upon a regime of general hygienic improvement, and instruction in methods to lessen mental conflict and strain were given. In addition to this type of therapy, patient was instructed to employ dihydroergotamine methanesulfonate intramuscularly at the earliest possible instant of the attack. Since such measures have been employed, patient has informed me that he has not suffered one episode of the torturing headache previously experienced, and that the frequency of such attacks has become somewhat diminished.

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