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Migraine

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MIGRAINE

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CHAPTER I

The purpose of this paper is to present a review of the recent current literature in relation to migraine. Since a comprehensive review (46) of literature on the subject had been made up to the year 1932, the present paper summarizes the findings and continues with a resumé of the more recent material. The scope of this discussion is intended to include the whole of the syndrome-complex known as migraine.

The term, hemicrania, which means pain or aching on one-half of the skull, was first introduced by Galen about the middle of the second century A.D. This term was taken by the Romans and after it was translated into Latin it appeared as hemicranium. Following that, it became corrupted into the low Latin form of hemigranea. Abbreviations caused it to become successively emigranea, migranea and migrana. Upon adoption into various European languages many alterations in terminology took place. In 1398 the English used the term as mygrame which became myegrym in 1460, migrim in 1579 and megrim in 1713. As late as 1873 Liveing used the latter term but all English

speaking people now use the French version, migraine.

The "Father of Medicine", Hippocrates, made no special study of the types of headache. Celsus was the first in history to deal with headaches but this was merely a description which designated the symptom as an acute and dangerous distemper. This was early in the first century A.D. Later in that same century Aretaeus of Cappadocia made the first description of migraine, calling it heterocrania. However, he made no attempt to determine the cause of the disease nor the location of the symptoms. During the latter part of the second century A.D. Galen became interested in this problem and attempted to determine the cause of the malady and the anatomical site of the disturbance which caused the pain. He came to the conclusion that disturbances in various parts of the body sent liquids or vapors containing harmful qualities to the brain. In 400 A.D. Caelius Aurelianus believed that chilling, exposure to the sun or prolonged vigilance, caused the pain of this disease. He called attention to the fact that the Greeks named headache, cephalea. The Arabian contributions consisted of nothing more than transcriptions from Galen. In 1070 A.D. Serapin transcribed

from Galen the theory of movement of fluids to the head. He described headache and stated that the harmful hot or cold effluvia formed in the intestine was transported to the head, thereby causing the pain. In 980-1037 A.D., Avicenna, another Arabian Physcian similarily showed the influence of Galen in his description of headache.

The Dark Ages contributed nothing to the study of migraine. Alexander Trallianus, the Byzantine, who lived from 525-605 A.D., made one of the first attempts at independent thinking. He subdivided headache into three groups according to an ascending scale of severity - cephalalgia, cephalea and hemicrania. These he then attributed to the action of the bile. Albucasis who lived from 936-1013 A.D. described a treatment for migraine which is in itself not only complicated but very heroic. He advocated, as the first mode of treatment the application of a hot iron. When the proper relief was not given by this method an incision was made over the temple with an excavation of a cavity of great size under the skin. Into this hole was placed a piece of garlic which had previously been cleaned and pointed at both ends. After this procedure, tight compresses were applied

for about fifteen hours. At the expiration of this time the dressing was removed and the wound left open for three days. The wound was then dressed with cotton soaked in butter until it suppurated, after which it was treated with unguents until it healed.

At the beginning of the Renaissance, Valesco de Taranta, who lived from 1382-1417 advanced the idea that the cerebral ventricles were the site of the pain. This he explained as the result of the action of noxious vapors produced by disorders of an unknown origin. However, the period of the Renaissance was really productive of nothing of importance in regard to this disease. Between the years 1497 and 1558 Fernal classified the disease systematically and described its symptoms with clarity. In 1618 Charles Lepois presented in his autobiography a detail of his attacks of frontoparietal headache which terminated with vomiting. He then went on to formulate a theory as to causation which was based on winds from the west and the approach of rain-storms. He stated that these phenomena of nature provoked serous effusions which caused the headache. In 1724, Anhalt made a vague approach to the present day vaso-motor theory of causation by suggesting that the vessels were affected by a chyle of

poor quality which altered their form and made them dilate or contract. At least he came close to one of the popular modern theories when he stated that this alteration of the vessels gave rise to the pain. The ideas of Lepois were carried on by Wepfer in 1726. He explained the hemicranial irritation by a condition of stasis of the blood, relaxation of the vessels and impeded resorption of the fluid. This was a closer approach to modern ideas than Anhalt had made although no demonstrable structure basis for this theory was present since no vaso-motor apparatus had been recognized at that time.

The foregoing statements indicate that no real advancement was made during the Dark Ages and the Renaissance. However, during this period the symptomφatology was rather well worked out and adequate descriptions of the disease were made.

In 1784 Tissot began the scientific study of migraine. He can really be credited with first diverging from the ancient method of thinking. He made a reasonable hypothesis and supported it by logical arguments. Instead of reiterating the statements already made about migraine he tried to investigate facts. He emphasized the role of the stomach

and digestion in the causation of the disease and supported his belief by a number of observations. Among these were the conclusion of an attack by vomiting, the aggravation of an attack by dyspepsia and frequent relief by the use of stomachics. He went even further and explained many symptomatic manifestations of the disease as due to irritation of the nerves. Although in many ways Tissot's work was not as important as that of Wepfer, Lepois and Fernel ~~but~~ it did have great value in that it classified the ideas of the disorder current at that time and built up a more precise conception of the malady in its various manifestations.

This contribution by Tissot may be said to mark the beginning of the modern era in regard to the study of migraine. Dating from the work of Tissot the various conditions which were confused with migraine by the older writers have been differentiated one by one and recognized as distinct and separate entities.

With the advent of discoveries in neuroanatomy and neurophysiology application has been made in an attempt to solve the problems of causation and mechanism of attacks. When Claude Bernard, in the

middle of the nineteenth century, published his report of the investigation of the sympathetic nervous system and the results of stimulation of the superior cervical ganglion an impetus was given to the study of migraine. This report led Dubois-Reymond, who himself suffered from migraine, to advance the theory that migraine was caused by an irritation of the cervical sympathetic nerves which produced an angiospasm. Therefore he termed the disorder a vasomotor neurosis. In 1867 Mollendorf stated that he believed the vasomotor disturbances to be angioneurotic in origin. At the same time two other men, Jaccoud and Eulenburg, advanced the idea that the symptoms of migraine were either due to overaction or paralysis of the blood vessels. One type they called the angioparaly-tic and the other the angiospastic.

Six years after Mollendorf published his work Liveing published an extensive monograph on the malady. He regarded the symptoms as being due to a "nerve storm" relating the disorder to a convulsive state in which one disturbance might pass over into the other. From this time on up to the present the syndrome-complex of migraine has continued to attract a great amount of attention.

CHAPTER II

Migraine, or "sick headache" which is a common synonym, especially among the laity, is defined in the Dictionary (16) as; "A nervous affection marked by a periodic headache, often one sided, and accompanied by nausea, vomiting, and various sensory disturbances". Various definitions have been given by many writers but one in particular seems best suited to the scope of this paper. "Migraine ------ may be defined as a recurrent headache, usually unilateral, often incapacitating in severity, culminating in nausea or vomiting, frequently accompanied by evidences of disturbances in various parts of the brain, occurring against a background of relatively good health and associated with a familial history of headache, convulsions or other paroxysmal disorders." (47) This definition, while being entirely adequate, requires some interpretation. Inasmuch as the concept of migraine has broadened considerably during the past twenty years too rigid an adherence to the foregoing definition is not advisable. Also it must be pointed out that no case of migraine is apt to present all of the symptoms and signs of the syndrome. Even the

cardinal symptom, headache, may be absent. Hyslop (27) believes that the concept of migraine is now extended to include various other manifestations of a transitory, paroxysmal nature such as some varieties of tachycardia, atypical Meniere attacks and psuedo-appendicitis. He also states that transient mental disturbances or psychic equivalents have been described.

For the purpose of clarity it is advisable to make some attempt to classify the syndrome-complex into types. Due to the lack of knowledge of etiology no classification can be made on this basis. This is true also for a physiological, pathological or therapeutic basis. Therefore the designation into types will have to be made on clinical criteria. Because the disorder occurs in many individuals and is characterized by a definite and often stereotyped appearance it is possible to determine a certain number of well recognized types.

Simple migraine, which is the disorder indicated when the term hemicrania is now used, is the most frequent and the simplest. Unilateral headache which is usually followed by nausea and if the attack is severe, by vomiting, is a brief description of

this type. There may be prodromal symptoms but usually there are no sequelae.

Ophthalmic migraine occurs in about 7.2 per cent of the cases. Its chief characteristic, as is indicated by the term, is the scintillating scotoma that accompanies the attack. It is more irregular than simple migraine and its association with other distinctly paroxysmal and convulsive disorders is also closer. The visual disturbances may vary considerably in character and in degree. There may be part of a field of vision affected, one eye only, just a fine cloud or a single colored shimmering effect or there may be total loss of vision in both eyes. Many patients describe a black, dull, colored or shining spot which appears motionless or moving about, gradually increasing in size until it occupies a definite part of or the whole of a visual field. A simple, transitory amblyopia may also appear. As the irritative or paralytic manifestations of this type fade away headache usually appears and is followed by nausea and vomiting. The scotoma which is so characteristic of ophthalmic migraine may become fixed and result in a permanent loss of vision if the frequency of attacks is great enough.

Psychic migraine is a type which is not common but may be very serious in its results. The psychic involvement usually appears as a twilight state in which the patient is confused, disoriented as to place and time and has occassional hallucinations of sight and hearing. These hallucinations may become very clear and acts of violence, including suicide and murder have been perpetrated in the migrainous psychotic state. Emotional disturbances with changes in mood, and a feeling of depression quite commonly accompany or follow the headache. Manic-depressive types of disturbances may also appear. Many writers have described psychic equivalents in which temporary disturbances of the psychic sphere may alternate with definite attacks of migraine. There is some doubt, however, whether these and other similar manifestations can be attributed to the same type of disturbance which underlies the other features of migraine.

Abdominal migraine is evidenced by pain of a cutting, boring or grinding nature situated anywhere within the abdomen but usually in the epigastrium. The outstanding symptoms are nausea, vomiting and diarrhea. Headache may be entirely absent.

Facioplegic migraine presents symptoms relative to paralysis of the face. There may be weakness of the entire face with paralysis of the tongue or there may be paralysis of the entire face. A metallic taste in the mouth and a roaring or clicking noise in the ears is not uncommon. Sometimes there is edema of the various parts of the face. This type is really open to more objection than any other type.

The abortive type appears with prodromal symptoms and then fails to develop. Whether any patient ever suffered from this type exclusively is problematical. The literature examined reported no such case. However, the abortive type interspersed with other types is not uncommon.

CHAPTER III

The incidence of migraine in this country is somewhat startling. It is stated (5) that eight per cent of the people in the United States have the malady at some time in their life. At the present time it is estimated that there are about five million actual sufferers. Of these about one million are children under ten years of age. More women seek relief from migraine than do men and it was formerly thought that the incidence was greater among women than men. However, the opinion of present day writers (5) (46) (47) seems to favor an equal distribution of cases between the two sexes.

Balyeat (5) states that about ten per cent of patients obtain relief from symptoms without treatment before forty years of age; fifty-five per cent between the ages of forty and fifty; twenty-five per cent between fifty and sixty; and ten per cent continue to have migraine after sixty years of age.

In a family where migraine is present ninety to one hundred per cent of all descendents will show some sort of inherited tendency to the malady. Unless migraine is associated with the menses the recurrence

of attacks tends to be irregular. They may occur as often as once or twice a day or only appear two or three times during a lifetime. The age incidence may be anytime during a lifetime but most frequently the attacks come between the ages of eighteen and thirty-five years. In about eighty-two per cent of the cases attacks occur about once a month and in about fifty-two per cent every two weeks or more frequently. The relation of the incidence of migraine to the menstrual cycle cannot be overlooked as it is very obvious in certain individuals. Social position and occupation apparently have no relationship to the incidence of migraine as the disease is found in all walks of life and in all social strata.

The literature on the etiology of migraine is very extensive. Sluder (50) states, '"Headache, whether it be seldom, or frequently recurrent and bear the names "Megrim", "Bilious Headache", "Blind" or "Sick Headache" or "Hemicrania" like all other pain, according to present thought, must be a symptom of a lesion of some kind, whether a pathological-histological change, or a toxemia, be (at present) recognized as its cause."' If this statement is taken as true then the etiology of migraine can be

said to be unknown. However, a number of observations have been made in regard to predisposing factors and various theories of causation have been presented.

That heredity is the most potent factor in the production of migraine seems not to be questioned by any of the writers on this subject. In fact this characteristic of the disease was predicated in the definition given as the guide for this paper. However, it does not necessarily follow that migraine itself may be transmitted. It may be that only the ability to become sensitive and not the specific state is passed on. Apparently the type of sensitivity the antecedents suffered from has no relation to the type the descendants may have. Of course this latter statement would apply only to the cases where the etiology is thought to be on an allergic basis.

Steiglitz (52) reasons that if migraine is familial then there may be constituitional types. He took one hundred, unselected, consecutive, private cases and compared them as to various constituitional characteristics. The heights and weights he found not to be unusual. The hair is usually brunette,

slender, straight and rather oily. It is also almost always fine and soft. The pupils are large in proportion to the amount of light striking them. This dilatation is exaggerated with fatigue. Normal reaction is present, however. The facies are of the finely chisled, classical type. The nostrils are narrow and the nasal alae are small. Extremities of these patients were found to be habitually cold and frequently moist and clammy. Less obvious characteristics were; arterial hypertension, apokamnosis and habitual fatigue, and a peculiar immunity to upper respiratory and chronic infections. The patient was in almost all cases thermostable and if a fever did appear it was usually very slight.

Knopf (32) is making a study of the personality traits of migraine patients but inasmuch as only the preliminary report has been made no conclusions can as yet be drawn.

The following is a discussion of the most recent theories of the causation of migraine. The Reflex Theory is based on the assumption that migraine results from the presence of a source of irritation somewhere within the body. This is rather vague and not very well supported and can therefore be disregarded

without much discussion. About the only reflex that is accepted is the one of eye strain.

The Central Theory assumes that there are direct, general, or local changes in pressure or abnormal conditions of pressure within the cranial cavity. This, like the preceding theory is poor as none of the symptoms, not even headache, can be explained on this basis.

The Allergic Theory presents a great mass of clinical evidence but explains in no way the essential mechanism of migraine. Allergy of one kind or another may set in motion certain trains of events but allergy does not cause migraine.

The Duodenal Stasis Theory has very little direct evidence in its support. It may be taken as typical of the group of so called toxic causes. It is possible that the absorption of toxic products from a disordered liver may cause migraine but as yet it is not understood. The absorption of materials may set in motion certain processes which may eventuate in migraine but this still leaves untouched the central nucleus of migraine and its mechanism.

The Endocrine Theory has a great amount of evidence in its support and is therefore worthy of

careful consideration. The glands that have received the greatest attention are the gonads and hypophysis. The association between the female gonad and migraine has long been recognized. It has also been shown that radiation of the testes in the male has in some cases caused a cessation of attacks. It is argued that an enlargement of the hypophysis would give rise to an increased pressure within the cranial cavity in addition to the hormonal changes resultant of this hypertrophy. A number of general considerations such as craving for sweets, a low blood sugar, polyuria, and the occasional appearance of acromegaly seem to link the hypophysis with migraine. The observation has been made that the activities which call forth an unusual hypophyseal activity are indentical with those which may precipitate an attack , such as overexertion, hunger and fatigue. It has been found that theelin, the ovarian follicular hormone is either markedly reduced or absent whereas prolan, the hypophyseal hormone is almost regularily present in the urine of patients suffering from migraine. This is a condition found heretofore only in pregnancy, after the menopause and with certain neoplasms of the genital tract. In following the excretion of these hormones,

it was found that the amount of prolan was regularly increased a day or so before the onset of the migrainous attack. This is, of course, the first factual evidence connecting the hypophsis, ovary and migraine and needs further investigation. The possibility of the artificial production of typical migrainous attacks in susceptible individuals by the injection of the various hormones must be investigated. By administrating hormones to patients suffering from migraine it would be possible to demonstrate the causal relation of these hormones to the malady. This, however, would not solve the problem of actual mechanism. However, it would indicate a trend of investigation that might ultimately lead to the solution of the mechanism.

The Vasomotor Theory of causation of migraine is the best one and is based on the activity of the vegetative nervous system in the production of local constriction of blood vessels. The character and the appearance of the symptoms, the very evident disturbances of circulation in the head and other parts of the body, the demonstration of a disturbed circulatory reaction to scratching the skin, the transient character of the attack and the development of sequelae can all provide evidence which closely associates

the disorder with a disturbed vasomotor control. In the words of Riley, (47) "The participation of the vegetative nervous system and its vasomotor control while not in itself sufficient to explain the entire picture is probably one of the links in the pathophysiological process which results in migraine". This is supported in the cases where surgical intervention has relieved the attacks. They all introduce the factor of the removal of the efferent vasomotor impulses or the interruption of the inward flow of afferent stimuli.

A combination of the vasomotor and endocrine theories would probably come very near to the best basis available to account for the syndrome-complex. This combined hypothesis would presuppose an irritability of the vasomotor system which is at times aroused into abnormal activity by a change in the relation between the circulating hormones.

CHAPTER IV

The physiology involved in migraine is a barren subject due to the paucity of known facts. The hydrodynamics of the cerebrospinal fluid has received some consideration. Von Storch and Merritt (58) investigated not only the dynamics of the spinal fluid but the protein content, cytology and serology as well. They state, "WE observed no significant abnormality of, nor consistent deviation from the normal cerebrospinal fluid pressure in forty-four cases of migraine. The total protein content, cytology and serology of the cerebrospinal fluid were normal. Any significant abnormality of the cerebrospinal fluid renders doubtful a diagnosis of migraine". The study of the efferent and afferent nerve supply to the cranium is still far from being thoroughly understood. Before a definite foundation can be made the pathways of the pain must be thoroughly understood. In addition, an understanding of the possible sensory innervation of the ventricles and associated structures of the brain must be obtained.

Recently the presence of hypoglycemia in migrainous patients has been definitly proved. Gray

and Burtness (22) examined a group of thirty-eight patients and made some interesting notes on their blood sugar level. They found that when these patients suffered headache, twenty-two of which were true migraine, their blood sugar level was between sixty and ninety milligrams per cent. They also reported complete relief or amelioration of headache following frequent feedings of carbohydrates. In addition they state that a characteristic headache has been reproduced by induced hypoglycemia. The glucose tolerance curve of these patients is of the flat type. If these findings are borne out by other investigators a step forward has really been made toward the solution of the riddle of migraine.

Another writer, Norman, (41) feels that a study of blood calcium has revealed important facts. A number of cases were studied and found to be relieved when means were taken to raise the values of calcium to normal. He states that symptoms of migraine and tetany are maintained dormant in the migrainous patient by the calcium regulating mechanism.

In a study of the hydrogen ion concentration and the alkalai reserve of migrainous patients it was found that they were normal in the periods of

freedom from attacks but that a tendency toward alkalosis develops forty-eight hours prior to an attack. It was also noted that hyperventilation may result in an attack of migraine, probably through an excessive loss of carbon dioxide. This work was done by R. Weissmann and S. Nelter and Myers et al (39) checked their results. Todate they have tabulated ten cases. The blood was taken during and early in an attack. The pH, carbon dioxide content, chloride and total base remained normal. However, they did find a fairly definite elevation of blood cholesteral in fifty per cent of the cases.

Beazell and Crandall (7) report that experimentation shows no abnormality of purine metabolism in migraine.

The conflicting results and the small number of cases studied shows that nothing reliable has been done, but the way has been opened for further study along the lines of blood chemistry.

The study of the pathological changes in migraine is even more barren than that of the physiological changes. Very few autopsies have been performed on migrainous patients and in those cases that have been reported the character of the examinations

is very superficial. If a careful, detailed examination were made of the relation of the hypophsis to the surrounding structures some light might be thrown on the connection between this gland and migraine. Also the exact condition of the vascular apparatus in relation to the areas which may be presupposed to have a direct association with the clinical symptoms of the cellular and fiber topography in these affected areas themselves might be determined.

CHAPTER V

A great amount of material has appeared in the literature concerning the symptomatology of this disorder. Apparently all of the subdivisions of the central nervous system may be involved in the underlying abnormal process.

The symptoms may be divided into four groups, each representing a definite stage. The first is the prodromal stage in which there may be depression, hyperactivity, bulimia, abdominal distress or profound sleep. Only one of these symptoms may occur or there may be a combination of two or more. True migraine may occur without the prodromal stage. The second stage is the aura which is evidenced by dizziness, visual disturbance, hallucinations of smell or hearing, paresthesias, motor disturbances, photophobia or psychic manifestations. Not all of these symptoms are found in the aura of any one patient but one or more is almost always present. The aura is a very constant stage in true migraine. The third stage constitutes the attack which varies a great amount with the patient. It may begin at any time of the day or night but the larger number of cases have their onset between eight

and twelve in the morning. The pain may last only fifteen minutes to one hour or it may last for several days. Most patients suffer pain from two hours to two days. There is a feeling of pressure in the cranium which many describe as a throbbing pain or a feeling of expansion. Nausea and vomiting are also quite common. The fourth stage is accompanied by exhaustion and depression, sleepiness, polyuria, and generalized body soreness. This period is called the post migrainous stage and may contain one or more of the foregoing symptoms.

Headache is the most constant and outstanding symptom and may be generalized or develop in one part of the head and radiate to other regions of the head, face, neck, shoulders or even upper extremities. This symptoms is commonly limited to one side of the head with no migration or radiation. The pain ranges in severity from a mild form to an unbearable, terrific pain.

Nausea and vomiting are very common and usually occur near the termination of the attack. The nausea may occur without the vomiting and the attack may terminate without either symptom.

There may be vasomotor alterations in the

face and head. This symptom may extend so far as to produce actual retinal hemorrhages or bleeding from mucous membranes or parts of the skin. There is coldness in the extremities, goose flesh and excessive perspiration. Again, these symptoms are not all present in any one particular case and a great amount of variation takes place in different attacks.

The motor symptoms which present themselves are either of an irritative or paralytic character. There may be paresis or actual paralysis of one or more limbs. Aphasia or agraphia may be in evidence as may vertigo, tinnitus or diminution of hearing. Hallucinatory disturbances of sight or hearing may take place while alterations in smell have occassionally been described. The termination of an attack may be sudden but it is usually prolonged. The attacks are never febrile but the pulse is often slow.

In order to make a diagnosis of migraine it is first essential that other disorders be ruled out. Epilepsy is often mentioned in the literature as being somewhat akin to migraine but so far no one has definitly shown that they are related. However, the two maladies may co-exist. Cortical features must be present and this provides a criterion on which

to base a differential diagnosis. Headache is a very common ailment and if it is caused by brain tumor, menigitis, neuralgia, epilepsy, or other various disturbances care must be taken not to confuse it with migrainous headache.

The diagnosis of migraine requires a thorough physical examination and in many instances, comprehensive study by all available means of laboratory diagnosis. Such an examination often demonstrates a physical basis for the symptoms and in such instances, the diagnosis of a symptomatic migraine may be made.

This type of the disorder may be found to depend upon uncorrected refractive errors, sinus diseases, severe scondary anemia, nephritis, serious disease of the gastro-intestinal tract and its appendages, particularily the liver, intoxications - such as lead, gout or other exogenous and endogenous poisons and many miscellaneous conditions. A careful neurological examination may demonstrate the presence of a neoplasm of the brain affecting specialized areas or structures, internal hydrocephalus, tabes, cerebral arteriosclerosis or cerebral edema. Psychogenic factors must also be taken into consideration. The patient may be trying, subconciously, to accomplish

something by having an illness.

The laboratory is not of great aid in the diagnosis of migraine. In fact most of the laboratory procedures are negative in this malady. The urine is negative save for a diminution in chloride excretion during the premigrainous period. The blood, spinal fluid and metabolic rate are negative. X rays of the skull have revealed abnormal ossification or calcification in the interclinoid ligaments and also other evidences of abnormal bone formation in the region of the sella turcica but these conditions have also been found in non-migrainous patients.

Gordon, (21) has listed eight features that he considers important clinically in the diagnosis of migraine. They are as follows:

1. Periodicity.
2. A return to normal between attacks.
3. Headache.
4. Nausea and vomiting.
5. Prodromata.
6. Ocular manifestations.
7. Time of onset.
8. Group of unilateral sensory and sometimes motor symptoms.

CHAPTER VI

The prognosis in migraine is entirely hopeful in regard to mortality but not so where morbidity is concerned. These headaches are probably never the primary cause of death. However, all who suffer have their lives incapacitated to some degree. The migrainous period of their life is usually during the most active years. The cases seen during infancy are probably confused with cyclic vomiting. (51) It is generally believed by the laity and the medical profession that patients, both men and women, suffering from familial periodic headaches lose them during their forties. As has been stated in the foregoing most of the patients do lose their headaches in the forties but at least thirty-five per cent continue after fifty years to suffer from migraine. There is also a tendency in a small percentage of the cases to develop chronic headaches in the late thirties. Many patients also suffer from other allergic diseases, such as asthma, hay fever, hives, eczema or gastro-intestinal symptoms which complicate their headache problem to some extent. It is not so uncommon for a patient to have his life very seriously

interfered with due either to the frequency or the severity of the migrainous attacks.

"A multiplicity of remedies advocated for the treatment of one disease indicates poverty rather than wealth in therapy." (29) This statement most certainly applies to migraine and considering the fact that the malady has been recognized since 20 A.D. it can justly be called a riddle. Every known form of treatment has been used both to remove the causative factors and to relieve the symptoms.

However, there are a number of general principles which can be considered in the management of migraine even if a cure cannot be effected. First, a differential diagnosis should be made in which eye strain, sinusitis and other migraine simulating diseases are ruled out. This would involve, of course, a complete physical and neurological examination with supporting laboratory and X ray investigations. Second, the life of the patient should be made as rational as possible and include such factors as rest, exercise and the curbing of excesses. Third, the acute attack should be treated with known instruments of relief such as ice packs, a dark room, rest and sedatives. Fourth, some therapy should be used during the interval

between attacks such as control of the diet and keeping the bowels open.

A number of symptomatic treatments have been used during an acute attack and with varying amounts of success. If there is vomiting and retching relief is frequently obtained by a glucose enema. This is done by introducing into the rectum every two hours or so five to ten ounces of a warmed ten per cent glucose solution. To this enema may be added twenty to forty grains of bromide or ten to twenty grains of chloral hydrate for sedation. Sodium luminal by hypodermic also has a tendency to reduce the nausea and vomiting. No foods or liquids should be given during an acute emesis but cracked ice may be allowed to melt in the mouth. Caffein, in the form of black coffee, or in doses of one quarter to two grains has been used for relief. Acetanalid in doses of two to three grains, three to five grain doses of phenacitin, one to five grain doses of sodium salicylate, one half to two grain doses of monobromated camphor, one-eighth grain doses of the extract of hyoscyamus and four minim doses of tincture of gelsemium have all been used in varying combinations with some success. In some instances opiates must

be used where the pain is too great to tolerate and the coal tar analgesics and other drugs give no relief. Either codeine or morphine can be given and although adequate doses should be used care should be taken that addiction does not follow. The real therapy during the attack must await the identification of the mechanism for the attacks.

The therapy used during the interval between attacks has received more attention than symptomatic treatment. Again the real therapy during the interval must await the solution of the problem of causation. As there are a number of divergent theories of causation so there are a number of different methods of treatment, each based on the particular theory of causation in which the therapist believes.

If the malady is thought to be caused by a sensitivity on the part of the patient the method of treatment is to remove the substances causing the reaction. Migraine has interested Allergists to a great extent as evidenced by the prolific writings on the relationship between the disease and allergy. Andresen (3) feels that migraine is an allergic phenomenon and certainly this view must receive consideration. He states that the term migraine should

not be used to designate a group of symptoms referable to an organic cuase and that the malady is an allergic phenomenon, probably caused by a transient edema of the cerebral meninges. His treatment consists of rest, sedation, rapid elimination, or neutralization of offending factors and the use of adrenalin or pituitary extract. For prophylaxis he recommends avoiding offending foods, desensitization where removal is impossible, the obliteration of foci of infections and the restoration of a normal endocrine balance.

Nickum (40) believes that in the light of the clincal evidence of excessive call on the endocrine system which results in an hypoglycemia that therapy should be stimulative and supportive rather than sedative.

If there are gastro-intestinal or biliary disorders the diet must be controlled. An intraduodenal lavage with two to four ounce infusions of thirty three and one third per cent magnesium sulfate may be used. If the symptoms warrant it, and the case is severe enough a duodenojejunostomy may be performed. Among the diets recommended are the non-specific diet, the non-allergic diet and the ketogenic diet. A non-

specific protein therapy has been used, the purpose of which is to produce a hyperthermia which has been said by some mysterious alterative effect to influence the underlying basis for migraine. Autogenous whole blood has been used. About twenty c.c. of blood is withdrawn and immediately reinjected either subcutaneously or intramuscularily. Tuberculin and peptone have also been used.

Glandular therapy has always been more or less popular. The pituitary and ovarian extracts have been used with varying amounts of success. Many investigators have recommended a destructive radiation of the gonads by X ray or radium. Some even suggest surgical removal of testicles or ovaries. Whitehead and Mc Niel (60) report a series of twelve selected cases of migraine in which estrogenic substances such as emmenin, theelin, theelol and amniotin were used. They state that six of these cases were markedly relieved, three were partially benefited and three showed no response.

The drugs used for interval therapy are numerous and some are of recent discovery. Ergot in the form of ergotamine tartrate or "gynergin" is at the present time enjoying some popularity since its

revival in use. Lenox and von Storch (34) report an expierience with this drug in one hundred and twenty patients suffering from migraine. The dose used was about 1/120 grains and was administered by intravenous or subcutaneous injection two or three times a day. Oral administration was considered ineffective. The initial trial resulted in abrupt and complete relief from headache in one hundred and seven of the patients. Nineteen patients have used ergotamine tartrate for more than one year, and all but one have obtained relief on each of the repeated occassions in which the drug has been used. In some patients a tendency for the headaches to recur at more frequent intervals or the appearance of unpleasant accompanying symptoms limited the use of the drug. The writers further state that the mechanism by which relief is given is unknown as yet. Pool and Nason, (44) after their experiments on cats with ergotamine tartrate, come to the conclusion that the clinical relief by this drug might be related to dural vasoconstriction.

Luminal has been used for a number of years and is given in one-half to three-fourths grain doses three times a day. In some cases relief is obtained and in others not. However, it has the advantage of

being able to be used over long periods of time if it is successful. Elixir of ephedrin hydrochloride in doses of one to two teaspoonfuls two or three times a day has been used. Daily, intravenous injections of ten per cent calcium chloride has also been used. The usual results of sometimes failure and sometimes whole or partial success have been obtained. Nitroglycerine to reduce the blood pressure during the interval has been tried and again the results are vague and indefinite.

One of the most recent drugs to be used is chondroitin sulfuric acid. This drug has been used for the treatment of peptic ulcer and it was noted that ulcer patients who also suffered from migraine were relieved from symptoms of the latter disease when they took chondroitin sulfuric acid. Crandall (10) has used this drug in forty-two cases of idiopathic headache. The period of treatment was from two to twelve months and fifty per cent were reported markedly benefited with thirty per cent only partially relieved.

Surgical therapy may follow one of three lines. The first is the removal of certain sympathetic ganglia. The second is the ablation of some

of the vascular plexuses of the sympathetics. The third is the occlusion of the middle meningeal artery. Craig (9) reports two cases where surgical therapy was performed with success. Both of these patients suffered severe, excruciating pain of the type where heroic measures must be undertaken when other methods fail. In the first one a ligation of the middle meningeal artery had no effect. A left cervicothoracic sympathetic ganglionectomy was then done and complete recovery ensued. Fifteen months after the last operation the patient showed no recurrence of the attacks. The second case had a right cervicothoracic sympathetic ganglionectomy with complete recovery. However, these are only two cases and the surgical method of therapy has yet to be proved efficacious.

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In conclusion it may be stated that migraine is a disease which has been recognized for almost two thousand years; it affects a great number of people of all walks of life and both sexes; it is definitly familial but the etiology is unknown; the pathology and physiology of the disease have not been determined satisfactorly as yet but the symptomatology is well worked out; the prognosis as to mortality is good but as to

morbidity poor; and lastly, the treatment is not adequate wither during or in the interval between attacks.

BIBLIOGRAPHY

1. Allan, W., Relationship of allergy to migraine, Internat. Clin. 3:78-88, Sep't. '35.

2. Alvarez, W.C., Present day treatment of migraine, Proc. Staff Meet., Mayo Clin. 9:22-27, Jan. 10, '34.

3. Andreson, A.F.R., Allergic phenomenon, Am. J. Digest. Dis. & Nutrition. 1:14-17, March '34.

4. Auerbach, Siegmund, Headache. 1913.

5. Balyeat, R.M., Diagnosis & Differential diagnosis of migraine, Northwest Med. 33;343-351, Oct.'34.

6. Bassoe, P., Migraine, J.A.M.A. 101:599-605, Aug. 19, '33.

7. Beazell, J. & Crandall, L.A. Jr., Blood purine derivatives in migraine, Proc. Soc. Exper. Biol. & Med. 32:1450-1451, June '35.

8. Cecil, Russel L., A Text Book of Medicine. Pp. 1528-1531.

9. Craig, W.M., Hemicrania of migraine, Proc. Staff Meet. Mayo Clin. 10:362-364, June 5, '35.

10. Crandall, L.H.Jr. & Roberts, G.M., Treatment of periodic headache with chrondroitin sulphuric acid, Illinois M.J. 63:513-519, June'33.

11. Critchley, M., Mechanics of migraine, Practitioner. 133:54-61, July '34.

12. Critchley, M. & Ferguson, F.R., Lancet. 1:123, Jan. 21, '33.

13. Critchley, M. & Ferguson, F.R., Migraine, Lancet. Jan. 28, 1933.

14. Day, Wm. H., On Headaches. 1883. Pp.75.

15. Dickerson, D.G., Surgical relief in migraine, J. Nerv. & Ment. Dis. 77:42-52, Jan. '33.

16. Dorland, W.A.Newman, The American Illustrated Medical Dictionary. Sixteenth Edition. P.790.

17. Forman, J., Migraine-like headache due to allergy, Ohio State M.J. 29:28-31, Jan. '33.

18. Gainsborough, H., Ketogenic diet in migraine, Practitioner. 132:45-53, Jan. '34.

19. Gittins, T.R., Differential diagnosis in headaches of periodic type, Am. Otol., Rhin. & Laryng. 42:463-475, June '33.

20. Gordon, A.H., Migraine, Northwest Med. 33:151-156, May '34.

21. Gordon, A.H., Migraine - clinical lecture, New England J. Med. 213:1017-1021, Nov. 21, '35.

22. Gray, P.A. & Burtness, H.I., Hypoglycemic headache, Endocrinology. 19:549-560, Sep't. - Oct. '35.

23. Hamilton, Allan McLane, M.D., Modern Treatment of Headaches. 1880. P. 21.

24. Holt, L. Emmett & Howland, John, Diseases of Infancy and Childhood. P. 579.

25. Holzman, M.B., Value of diet in treatment of migraine and arthritis, Delaware State M.J. 5:212-213, Sep't. '33.

26. Hunt, T.C., Bilious migraine: Its treatment with bile salt preparations, Lancet. 2:279- Aug. 5, 1933.

27. Hyslop, G.H., Therapy in Migraine, M. Clin. North America. 18:827-830, Nov. '34.

28. Inskeep, L.D., Etiology and treatment of migraine, Northwest Med. 32:67-68, Feb. '33.

29. Journal of A.M.A., Editorial on migraine, Vol. 102, P. 2188, June 30, 1934.

30. Kampmeier, R.H., Ephedrine in allergic migraine, J. Allergy. 5:74-75, Nov. '33.

31. Kennedy, F., Migraine, a symptom of focal brain edema, New York State J. Med. 33:1254-1258, Nov. 1, '33.

32. Knopf, O., Personality studies in thirty patients, J. Nerv. & Ment. Dis. 82:270-285, Sep't. '35.

33. Konstam, G., Opthalmoplegic migraine, Roy. Soc. Med. 26:277, Jan. '33.

34. Lenox, W.G. & von Storch, T.J.C., Experience with Ergotamine Tartrate in 120 patients with migraine, J.A.M.A. 105:169, July 20, '35.

35. Leonard, S.L. & Smith, P.E., Hypophseal-like qualities of gonadotropic principle found in urine of certain individuals, Am.J. Physiol. 108:22-32, April '34.

36. Lewis, W.W., Migraine - baffling commonplace, Journal-Lancet. 54:659-663, Oct. 15, '34.

37. Mc Carthy, D.J.,& Keyes, B.L., Migraine without headache, Tr. Am. Neurol. A. 60:209-210, '34.

38. Murray, R.V., Migraine, Texas State J. Med. 29: 514-517, Dec. '33.

39. Myers, V.C. Muntuyler, E. Way, C.T. & Danielson, W.H., Blood in migraine, acid base balance, Proc. Soc. Exper. Biol. & Med. 31:622-623, Feb. '34.

40. Nickum, O.C., Migraine, Nebraska M.J. 19:26-27, Jan. '34.

41. Norman, G.F., Hypoglycemia: Relationship to migraine, J.A.M.A. 102:529-532, Feb. 17, '34.

42. Patek, A.J., Headaches of toxic and metabolic origin, Wisconsin J.J. 33:403-405, June '34.

43. Podolsky, E., Migraine, a new approach, West Virginia M.J. 29:173-175, April '33.

44. Pool, J.L., & Nason, G.F., Cerebral circulation in migraine, Arch. Neurol. & Psychiat. 33:276-282, Feb. '35.

45. Pulsifier, L., Common - sense approach of migraine, Am. J. Digest. Dis. & Nutrition. 2:397-401, Sep't. '35.

46. Riley, H.A., Migraine, Bull. Neurol. Inst. New York. 2:429, 1932.

47. Riley, H.A., Migraine and its treatment, Bull. New York Acad. Med. 8, 717, 1932.

48. Rinkel, H.J., Considerations of allergy as factor in familial recurrent headache, J. Allergy. 4:303-314, May '33.

49. Sheldon, J.M. & Randolph, T.G., Etiology and pathogenesis of migraine, Am.J.M.Sc. 190:232-237, Aug. '35.

50. Sluder, Greenfield, Nasal Neurology & Eye Disorders. 1927. Pp. 27,29,173.

51. Smith, P.S., Cyclic vomiting and migraine in children, Virginia M. Monthly. 60:591-595, Jan. '34.

52. Stieglitz, E.J., Migraine physique, Am.J.M. Sc. 189: 359-364, March '35.

53. Sweetser, H.B.Jr., Allergic factor in migraine, Minnesota Med. 17:31-32, Jan. '34.

54. Todd, L.C., Food allergy in migraine, South. Med. & Surg. 95:587-592, Nov. '33.

55. Traut, E.F., State of hypersensitivity to ingests, Clin. North. America. 18:1241-1243, March '35.

56. Vaughn, W.T., Allergic migraine; analysis of follow up after five years, Am. J. Sc. 185: 821-832, June '33.

57. Vaughn, W.T., Analysis of allergic factor in recurrent paroxysmal headaches, J.Allergy. 6: 365-382, May '35.

58. Von Storch, T.J.C. & Merritt, H.H., Cerebrospinal fluid during and between attacks of migraine headaches, Am.J.M.Sc. 190:226-231, Aug. '35.

59. Weber, F.P., Erythemia with migraine, Lancet. 2: 808:809, Oct. 13,'34.

60. Whitehead, R.W. & Mc Niel, E.E., Effects of estrogenic hormone preparations in certain cases of migraine, Am. J. Psychiat. 91:1275-1288, May'35.