Migraine

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MIGRAINE

by

WARREN H. ALDEN

SENIOR THESIS

THE UNIVERSITY OF NEBRASKA COLLEGE OF MEDICINE
OMAHA, NEBRASKA
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INTRODUCTION

When I chose this subject, I must admit it was from a purely personal point of view. Perhaps the reasons may be listed as being interest, inquisitiveness and vindictiveness, all subservient to the end of gaining as much knowledge about this subject as one can attain from the writing of such a compendium.

This apparently selfish attitude has been prompted by the fact that all of the members of my family and myself are subject to migrainous attacks. I have been unable to trace the occurrence of these any further back than two generations, in the paternal ancestry. But from this hereditary evidence, which was forcibly brought to my attention years ago in the nature of my initiation into the throbbing ranks of the migraines, I received my first opinion of the disease; and when I subsequently undertook the study of Medicine I resolved to make a thorough study of migraine.

The following pages will consider this subject from all practical standpoints, from the history down to and including the modern methods of treatment, with special emphasis on the diagnosis of migraine, and the latest and most effective procedures and drugs used in the treatment of it. Any and all material taken from the articles of authors who have written on
this subject or subjects associated with it will be so designated, and the proper source given credit for the same.

Warren H. Alden
Every writer who touches or dwells upon the History of Headache, assigns to that malady, one of the oldest niches in the annals of Medicine. Although they did not know, perhaps, just what all was in the head, anatomically speaking, they could localize the pain, and the students and recorders of the time could definitely put their finger on one spot and describe it. Description from the patient's standpoint, it is true, with the doctor's own guess as to the probable pathology and treatment. But, nevertheless, it could be limited to one circumscribed region, and the disciples of Apollo could, and have, recorded it with some degree of accuracy, thus differing from the floundering diagnoses often made in explanation of various remote body pains of man. These early headaches were thought to arise from widely differing sources, depending upon the then prevalent theories concerning the anatomy and physiology of the body. Classification of headaches was relatively slow in evolving, yet we find remarkably clear and conscientious attempts at this in the records of men who lived before Christ.

Migraine (pronounced me-grān') was recognized as a definite symptom-complex and registered as such near the end of the first century in the Christian era. Riley (45) gives us the most complete historical account of the ailment from that time...
forward. The results of his efforts, as well as a few contributions from several other modern writers, are set forth in the following paragraphs.

Aretaeus of Cappadocia (AD 30-90) first writes about this severest of all headaches. He described the paroxysmal severity, the one-sidedness, association with nausea and vomiting, and the periods of intense pain and freedom from pain. His term for the condition was "heterocrania". But his interest seemed to lapse with description, for he made no attempt to discover the cause of the abnormality nor the definite site of it.

Galen (AD 131-201) was more interested in these two latter problems and tried to determine the etiology and anatomical site of the pain producing the disturbance. His conception of the pathogenesis of migraine was based upon the humoral hypothesis and the influence of black bile upon the brain. His conclusion was that the source of the head pains lay in disturbances in various parts of the body which dispatched liquids or vapors containing harmful qualities to the brain. Galen, in his treatment, wrote that the sufferer "must have sleep, happiness, and quiet, and avoid noise, strife and wine bibbing". Spriggs (55).

Galen changed the name of the headache to "hemicrania". From this it has been progressively altered to today. The Romans translated it in Latin to "hemicranium", which was later corrupted to "hemigranea" in low Latin. By abbreviations it eventually

... 5 ...
became successively "emigranea", "migranea" and "migrana". At present the English usage includes "migrim", "megrim" and "migraine", the latter being accepted as standard.

Caelius Aurelianus (AD 400) offered no further description of the headache, but he believed the cause to be chilling, exposure to the sun, or prolonged vigilance. He also recorded that the Greeks had called headache by the name "cephalea".

Following him, during the Dark Ages, there was little achieved in Medicine, as in the other arts and professions. The writers showed little initiative, copying the theories and advances made by their predecessors.

Arabian contributions on migraine were confined chiefly to transcriptions from Galenic writings.

Alexander Trallianus, the Byzantine (AD 525-605) was one of the first to show indications of independent thought on the subject. He subdivided headache into three groups, and named them according to their severity, from lesser to greater, "cephalalgia", "cephalea" and "hemicrania". He, like Galen, thought the cause was some disturbance related to bile.

Albucasis (AD 936-1013) prescribed a very radical treatment for migraine which is as follows: First, apply a hot iron over the area of pain. If this is unsuccessful, make an incision over the temple and excavate a cavity of considerable size under...
the skin. Put within this cavity a piece of cleaned garlic which has been pointed at both ends. Apply tight compresses for fifteen hours, then take them off and leave the wound alone for two or three days. It is then dressed with cotton soaked in butter. When suppuration takes place, the wound is treated with unguents until it becomes healed. The efficacy of this remedy is not recorded, but we may suppose that the majority preferred to have their headaches.

Avicenna (AD 980-1037) showed the influence of Galen in his description of headaches.

Serapion (AD 1070) wrote a Galenic compendium in which he stated that the cause of migraine was various harmful hot or cold effluvia formed in the digestive tract and transported to the brain.

Valesco de Taranta (1382-1417) believed the site of the pain in migraine was the cerebral ventricles, and that the cause was the action of noxious vapors produced by unknown disorders.

During the period of the Renaissance, a few men did work on the subject of migraine, chiefly in the field of symptomatology. But there was no definite advance in scientific study of the condition. Since that period, however, many theories have been advanced. Sluder (51).

Fernel (1497-1558) whose work may be referred to as having perhaps the greatest influence during the above period,
described the symptoms and classified the disorder systematically. He opined that it wasn't a disease, but more truly a symptom. The site, he said, was the cerebral substance and its canals and passageways. He did not believe in the humoral theory of vapors and gases, but rather that the bile caused the symptoms, and the organs of the epigastrium were blamed for the disorder of the bile.

Charles Lepois, whose autobiography appeared in 1618, was the outstanding contributor of the seventeenth century. He described in detail his own attacks of fronto-parietal headache which terminated in vomiting. He formed a theory as to the cause of the disorder, based upon serous effusions provoked by winds from the west and the approach of rain storms. The chief value of his work is the very detailed description and the logical order it possesses.

Anhalt, in 1724, wrote that the cerebral vessels were affected by a chyle of poor quality which caused them to dilate or contract, which in turn gave rise to the pain.

Wepfer, 1726, believed there was a stasis of blood, a relaxation of the vessels, and an impeded resorption of the body fluids. This theory seems to be the first which somewhat approaches the more modern ideas.

Tissot (1728-1797) left a contribution which may be credited as marking the beginning of the modern era as applied to the conception and study of migraine. Instead of writing
parrot-like, he offered some reasonable hypotheses which were supported by logical arguments. He investigated former and new facts which presented themselves, and emphasized the role of the stomach and digestion as the underlying cause of migraine. Tissot believed that the many symptomatic manifestations of the disorder were due to irritation of the nerves.

Since that time, there have been many discoveries in neuroanatomy and neurophysiology, and these have been associated in one way or another with migraine. Many well known men have studied the symptom-complex and left their mark in history, among them Claude Bernard, Dubois-Reymond (who was himself a sufferer, and theorized that migraine was caused by an irritation of the cervical sympathetic nerves which produced a vasomotor neurosis), Mollendorf, Jaccoud, Auzias-Turenne (who, in 1849, stated that "migraine was a pain in the head resulting from compression of the trigeminal nerve, particularly its ophthalmic branch, this compression being produced by an accumulation of blood in the sinuses at the base of the brain, especially the cavernous sinus"), (quoted by Goltman 21), Eulenburg, and Liveling, 1873, who ascribed the symptoms of migraine to a "nerve-storm", related to a convulsive state, into which it might pass or from which it might develop.

The subject migraine, indéfinte as it still is, now attracts the interests of neurologists, biologists, chemists, allergists, endocrinologists and others, as evidenced by the voluminous literature on all aspects of the disorder.

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DEFINITION AND ETIOLOGY

Migraine may be defined as "a periodic, incapacitating headache, culminating in nausea or vomiting, often preceded and accompanied by visual disturbances, followed by sleep and occurring against a background of relatively perfect health". Smrha (52). Rudolph (48) further complicates the definition by stating it is a "paroxysmal disease characterized by hemicrania (also bilateral headache) and symptomatic evidence of cortical involvement". Migraine is characterized usually by the absence of any local lesions which might occasion headache. Every case of migraine, with the exception of the abdominal type, we may consider as headache, but all headache is not migraine. Davis (16). There are several restricting definitions of the different types of migraine which will be taken up in the chapter on diagnosis. Synonyms and lay terms for the disorder include "sick headache", "bilious headache" and "blind headache".

The above definitions must not be regarded as absolute in diagnosing migraine. As is seen so often by observers, any of the criteria may be lacking, perhaps just one or two being evident, and indeed, even new ones are not infrequently encountered. Riley (43). Also, in our diagnosis, we must be cautious not to use the term migraine to designate a group of ...

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symptoms definitely referable to an organic cause. Sheldon (49).

According to Bassoe (7) we may regard migraine as a warning to the patient that something is wrong with his hygiene, occupation, food, habits or the like. He explains it as being Nature's protest at the speedy readjustments which have taken place in the past several generations to give the right of way to the forebrain.

In discussing the etiology of migraine, it is probably best to consider it under the various predisposing causes, enumerated below and in the order of importance which seems most evident.

1. **HEREDITY:**

   Regarding the heredity of this disorder, Riley (43) states that it may be "attributed to an inborn predisposition to pathologic neurometabolic processes which have been described rather loosely and unsatisfactorily as an inherent neurotoxic diathesis".

   A disease is to be considered hereditary when it is transmitted as an integral part of the male or female germinal cells to the product of these two cells. It may not be so considered just because the parent or parents and the child both have it. Only through the medium of chromatin and the cytoplasmic structures of the germinal cells can heredity occur. Buchanan (11) has carefully worked out this phase of migraine in 127 families, members of which were first seen at the Mayo Clinic, 1919. In
three cases where both parents had migraine fifteen children were born, and the fifteen children had migraine. In the cases where one or the other parent had migraine, a total of 148 children were studied. Of these, 138 had migraine and 610 did not. This gives a ratio of 3.08 to 1, which definitely places migraine in the Mendelian Ratio and establishes the hereditary nature of the affection. Looking at it from this standpoint, he makes the rather hopeless assertion that "there is no medication known that will alter its course. It is a distinct part of the patient's economy, and it will have no harmful influence on longevity".

We find that several authors give as one of the criteria for diagnosing migraine, the presence of migraine in the family history. These men are careful to make account of the occurrence of migraine equivalents (to be discussed later) when there is no history of migraine as such. Slight (50).

Both Pulsifer (42) and Tuft (59) aver that the migraine inheritance behaves like a dominant in Mendel's Law, being passed down, mainly through the female, as this dominant Mendelian characteristic, but not as a sex-linked characteristic.

Present material leaves little doubt that migraine is passed down from one generation to the next. We find this most true in nervous people, or members of neurotic families. Davis (16). In regard to transmission, the maternal side seems to be the worst offender. Riley (43) quotes Flatau as having
found the ratio to be 4 to 1 for maternal as against paternal transmission. Various other authors have reached determinations quite similar to this one.

2. EMOTIONAL IMBALANCE:

Pulsifer (42) considers migraine from a strictly nervous approach. Far more than we suppose, the underlying cause for the patient's attacks may be directly traced to some nervous upset which perhaps has seemed negligible to the patient, if noticed at all, or to which the patient knowingly attributes his trouble. This nervous type of person, because of being in "high gear" continually, as the habitual migraine is, is thus rendered more likely to have attacks of hemicrania.

Slight (50) also deals exclusively with the part played by emotions in the production of migraine, and his conclusions are based on a study of fifty unselected cases. In his explanation of migraine, he considers it a process of nervous discharge which affects both the autonomic and sensory centers, and blocks the pathways leading to co-ordinated expressive action, motor, mental, or emotional. The preceding phase of increased tension involves two factors: (a) The excitation of centers subserving emotion; (b) The blocking of discharge pathways until the tension reaches an overflow point.

An emotional organization based upon the experiences of early or adult life which have befallen the individual with certain necessary constitutional tendencies determines this
imbalance. Detailed history taking is important in these cases. In migrainous children we get a history of early emotional difficulties, which may be sought out once we detect their sense of severe frustration and resentment to authority. Slight finds that these children develop an equally strong social sense or conscience which prevents outward expression of anger and resentment.

Vital changes in life and the defeat of important plans or desires may quite frequently be determined as the cause of a migrainous onset after adult life is reached. Examples of such difficulties might be --- after a disappointment in love; after marriage in accordance with parents' wishes instead of to the person of own choice; after the death of the mother in the case of a spinster aged 38; after a marriage wherein the wife was sexually frigid.

3. ENVIRONMENT AND OCCUPATION:

Riley (43) states that the disorder is encountered less frequently in the rural sections and in outdoor workers than in the city, and especially in mental workers. Critchley (13) finds that European victims of migraine are quite adversely affected by the tropical climates. He also states that the disorder, when in Jewish or colored people, is especially resistant to treatment. Migraine is rare among the uneducated poor, according to Block (10).

4. TIME OF LIFE AND TIME OF DAY:

Migraine is quite frequently seen in children. Older patients applying for treatment often use the expression "as long as I can remember". We may be safe in saying that the vast majority...
of cases begin before the age of twenty. It often begins at puberty, especially in girls. Women frequently become subject to migrainous attacks after the menopause. Occasionally, we see migraine beginning as late as at the age of 50 or 60 years. Block (10).

Another report states the estimation that three fourths of all cases of migraine commence before the age of 25 years, and that one half of these give history of at least one other case in the same or the previous generation. Gordon (23).

The attack may make its appearance at any time of day, but is most often reported as starting early in the morning on waking, or soon after rising. Although one may be awakened in the middle of the night by the splitting, pounding migraine in full bloom, it is only encountered at that time about one fourth as often as during the day. Block (10).

Researchers Critchley and Ferguson (15) noted a decided frequency of the headache in the mornings. This is seen also after exercise and in starvation, which suggests glucose insufficiency and will be discussed later.

5. VARIOUS PREDISPOSING CAUSES:

Any disturbance or strain may precipitate an attack in a liable person, and therefore these factors are as numerous and variable as the circumstances in daily life. A few are enumerated here as examples: fatigue, not especially mental; food, especially rich or creamy; alcohol; excessive smoking; constipation; riding; east winds and cold weather; reading at night; sleeping too long...
in the morning, or lying abed after waking; anticipating an event, especially seen in cases in children; working in overheated rooms; possibly onanism, and sometimes coitus. Spriggs (55) and Block (10).

6. THE MIGRAINE PHYSIQUE:

Stieglitz (56), from study and tabulation of one hundred cases, has evolved what he terms the "migraine physique". Of course, all migrainous persons do not conform exactly to this pattern, just as all cases of cholecystitis are not found in short, stout people, nor pulmonary tuberculosis in those of the Stiellar physique. However, the incidence seems high enough to justify the correlation. Below, are the physical characteristics most often seen in the migrainous:

1. SEX -- Female 86%, male 14%.

2. AGE -- Varies from 16-60. Average 31.

3. HEIGHT AND WEIGHT -- Not unusual, but frequently the extremes in either.

4. HAIR -- Almost invariably (96) fine, slender and straight. Oily. Moderate amount. Brunette - 93%, blonde - 7%.

5. EYES -- Unusually large pupils in proportion to the exposure to light - 90%. This is more marked with fatigue or just before an attack. React normally to light and accommodation.

6. SKIN -- Thin, fine, and usually smooth as a child's. Pallor more common than ruddy facies.

7. FEATURES -- Most commonly finely chiseled and classical, with delicate molding, narrow nostrils and small nasal alae.

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8. EXTREMITIES -- Habitually cold and frequently moist and clammy - 01%.
Although statistics conclusively show that migraine is the most frequently encountered type of headache (Spriggs, 55, treated 103 migraines in a total of 500 cases of all varieties of headaches), we cannot be positive as to the relative frequency of the disorder in the total population. Because, as in the other branches of Medicine, there is an unknown percentage which never comes to the attention of the profession. Basso (7) states that "it is safe to say that much less than half of all migraine victims ever consult a physician for it". There are various other estimations of the prevalence of this most agonizing disorder, and though there is no method at present of securing this data with the utmost of accuracy, we are probably on the safe side if we take Sheldon's (49) computation that 7 per cent of the total population is subject to migrainous attacks.

Relative to the comparison between male and female sufferers, we find that here, as in heredity, the latter take the leading role. As the number of researchers showing interest in this baffling malady increases, more and more figures from groups of test cases are brought to light. Several of these showing the widest deviations are herewith presented. These are all of the ratio female to male. Riley (43) places the relative frequency from 1.3:1 to 5.4:1. Stieghitz (56)
finds it to be 4:1. Andresen (4) had sixty percent females among his cases, and found that forty-eight percent of the cases developed at the onset of puberty. Bassoe (7), studied 270 cases, 195 of which were female and 75 male patients. He further states that 161 of these had the onset of attacks before the age of sixteen years, and that there was a history of migraine in one or both parents in 153 of the cases. Lennox and von Storch (32) had 97 women and 23 men as their patients. O'Sullivan (39) conducted an extensive experiment on the efficiency of ergotamine tartrate in treating migraine and her patients numbered 78 females as against 19 males. The average duration of the attacks over a period of years was found to be sixteen years. Frequency of the disturbance varied from twice a week to once or twice a year among her cases. Gray and Burtness (24), who made a study of hypoglycemic headaches, estimated that migrainous attacks occur about twenty times as often among people with a high carbohydrate tolerance than in those with a low one.
SYMPOTOMATOLOGY

CLINICAL HISTORY:

The symptomatology of migraine covers, or at least touches upon so many of the myriad of pathologic indications experienced by man that at first glance it may appear impossible to catalogue it with any semblance to precision. However, if we consider it from the standpoint of majority, disregarding the relatively infrequent hybrid and atypical cases, it becomes more apparent that the subject may be discussed with more or less definiteness under the following three heads.

1. PRODROMATA — A few hours or even a day before the attack hits, the patient, if he is intelligent and observant, may notice his characteristic warning. This may take any one of various forms. In some there is an unusual sense of well-being, a spiritedness which is not so marked on other, normal days. His elated feeling is dampened only by the realization of what is to befall him, and if he is wise and one of the too few fortunate ones for whom a simple remedy taken early enough will abort an attack, or at least alleviate the agony, he may do so at this time.

A usual sign is an abnormally morbid appetite on the day before. In these cases, if he eats correctly as experience has taught him, he may lessen the severity of the attack to come.
But whether he satisfies his appetite or not, the headache comes the next day. Constipation, mental depression, drowsiness and languor often precede an episode. On the other hand, many patients report that there are no warnings whatsoever - that they just awaken in the night with the headache, or it comes on gradually during the day, preceded by all of the unmistakable signs so well known to them.

One of the most universal prodromata is that which affects the sight. Block (10) gives such a splendid description of this phase, with which I am personally well acquainted, that I wish to present it here. "The prodromata of sight may consist of dark spots, or bright lights which may assume varying shapes, such as zigzags or fortification figures, changing in color, shape, position, or size as they develop. They do not occur in the center of vision, but to one side of the fixing point, and are on the side opposite to the headache; or in cases where the headache is bilateral or medial, they are on both sides. These may always be the same in a patient or may vary in different attacks. The lights may be white or colored, yellow, blue, or red. The visual hallucinations are spoken of as teichopsia. In some cases the lights occupy a segment of the field of vision, (scintillating scotomata) in which bright spots, balls of light or colors are seen (irritation), or the vision may be blurred or dim, or dark spots may occur (inhibition). Sometimes there is a shimmering appearance similar to that from the glare of sunlight on water".

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The cause of visual scotomata is not completely explained to the satisfaction of all observers, but a quite likely theory has been advanced by Timme (58) who discusses migraine from the hypophyseal standpoint. He believes it is due to traction plus pressure on the chiasm, exerted by swelling of the entire hypophysis which lies beneath it. The cause of the variability of the scotomata in different patients is the great individuality in the arrangement of the chiasmatic fibers.

Besides the visual aura mentioned above, there are various non-visual auras involving different parts of the body. The latter includes hot or sore eyes, dizziness, pressure or tenderness on one side of the head, aphasia, soreness of the scalp, "pins and needles" in arms and legs, stiffness, numbness, and abdominal discomfort. Spriggs (55).

Cutaneous manifestations are common before an attack. These do not include pain or temperature sensations, but are confined to numbness and tingling. The sensation starts usually in the fingers of one hand, passes up the arm, leaving decreased sensitivity behind, and may advance up the neck and involve the cheek, temple, gums and tongue on one side, or both. The lower limbs and trunk are rarely affected. The entire advancing process may last a half hour or more, never less than five minutes.

Cortical phenomena are in the nature of hallucinations and are referable to the cerebral cortex on the side of the headache. Aphasia is a common forerunner when the headache is
on the left. Visual hallucinations or homonymous hemianopsia are encountered when the cuneus is involved. Hemiparesia and hemianesthesia may occur and may be permanent.

Psychical disturbances, excitement, confusion or depression, or mental attacks rarely occur. Block (10).

2. LOCATION OF THE PAIN IN MIGRAINE HEADACHE -- This is variable in different persons, but is usually the same in one patient’s successive attacks. Statistics have been compiled from the groups of cases and Allan (1) reports 75 percent frontal and 60 percent unilateral. Keith (28), who studied menstrual headaches which may not have been strictly of migrainous character, found the pain most frequently in the occipital region. Spriggs (55) gives these figures from his group of 103 cases - frontal 25, eye 24, temporal 24, diffuse 13, vertical 10, occipital or neck 4, and parietal 3.

3. SUBJECTIVE SYMPTOMS -- The patient need not be told to go to bed in a dark, quiet room. Light and noise aggravate the condition beyond description, and movements of the head or eyes seem to start up new pains of doubled intensity. These pains are of a deep, sharp, boring, throbbing, head-splitting nature and must really be experienced before the full significance of the term "migraine headache" can be comprehended.

Loss of appetite is commonly seen in these cases. We may consider this one of Nature’s methods of remedying the situation, because in many people, eating will increase the
severity of the attack. In others, however, eating makes no difference. In fact, it is the simple and effective treatment for migraine employed by some.

Nausea begins from one to five hours after the attack makes its appearance. Following this we may find retching, quite persistent and exhausting. Vomiting then occurs, which always gives relief and may even terminate the attack. Block (10).

Cutaneous hyperesthesia may be elicited, especially of the scalp, temples, and cheeks. This may be best compared with the general body soreness felt by a patient with the grippe when clothes or bed clothing touch him.

The crisis of the attack usually ends in a deep, undisturbed sleep. The patient has become thoroughly exhausted and once he has succeeded in dropping off, he is quite liable to sleep for eight or ten hours. Upon waking, the headache is usually gone and the patient feels immeasurably relieved, though weakened and a little "jittery", and his eyes seem to pain him somewhat when he moves them. Some patients require medication to bring about sleep after which the sequence is the same except for possible after effects of the drug.

PHYSICAL FINDINGS:

Physically, the migraine patient is usually found to be perfectly sound. Indeed, it is the rule that between attacks he enjoys the best of health and happiness. Even during an attack he may not show many signs upon examination. But such as
are mentioned below are quite positive and quite significant, and are seen when the patient is in the throes of a violent seizure.

There may be a cold, clammy sweat, pallor, polyuria, diarrhea, flushing, salivation, a throbbing and a fullness in the temporal artery. The symptoms may come on arising in the morning and may last but a few hours, or for a day or two, sometimes longer. Besides the visual symptoms mentioned, there may be lachrymation and even an iritis. The sensory symptoms may be followed by motor ones, such as weakness in the extrinsic eye muscles, especially the internal recti, or of those of an arm or a leg, or of the muscles of the face. There may be a slight aphasia, and a staggering gait. Smrha (52).

Grayness or localized alopecia may develop on the side habitually attacked. Unilateral hyperhidrosis may occur from sympathetic irritation, and the pupils may be either dilated or contracted, depending upon the state of the sympathetics. Sometimes the pupil on the affected side shows alternating dilatation and contraction (hippus). The eye on the side which is attacked may be sunken, and the upper lid droops. Frequently, we notice a corrugation between the eyebrows. Block (10).

If any gastro-intestinal symptoms are present, they are probably referable to the sympathetic nervous system. As a rule, in these cases we find them associated with a comparatively mild attack of headache. However, the visual and vertiginous
disturbances are present, with a localization of the severe 
pain in the abdomen.

The attack is never febrile although the patient may 
appear to be with fever due to the extreme flushing and sweating. The pulse may be noticeably slowed. Davis (16).

Stieglitz (56), in addition to his "migraine 
physique", has listed what he believes to be the physiologic 
characteristics of these people. 1) There is marked apokam-
nosis (sense of exhaustion and fatigue) and therefore a 
lessened ambition. This was present in 82 percent of his 
cases. 2) The intellectual level of the person is usually 
very high. 3) There is frequently a hypotension present 
(see in 38 percent of his group), which would account for 
the pallor and cool skin, and the paroxysmal tachycardia which 
was noted in 49 percent. 4) Thermostability. He believes 
that migraine subjects are relatively resistant to acute in-
fecitions, except rheumatism. Upper respiratory infections 
are rare. Even though they do become infected, he maintains 
that as a general rule they will run a relatively afebrile 
course. However, a patient may have an infection or an intox-
ication due to chronic migrainous debility and a low blood 
pressure which reduces resistance.

LABORATORY FINDINGS:

There has been a comparatively large amount of 
scientific research carried on by those interested in migraine
in heroic effort to determine the underlying causes and to evolve the most efficient remedies. Believers in different theories of causation have carried out laboratory examinations along the trend of their theory and many of these men have seemingly derived some conclusive results. Others have only negative results to report concerning their experiments, which may appear discouraging in the eyes of both sufferer and therapeutist, yet it is narrowing the field of possibilities and bringing the goal closer.

1. SKIN TESTS -- Although cutaneous tests, by the dermal or intradermal method, are rarely necessary or desirable in the case where migraine is the only allergic phenomenon (Rudolph 48), it is often employed in the more baffling cases, yielding varied results. Sheldon and Randolph (49) report on 127 patients who were tested with 96 food extracts and 25 epidermals which were prepared by the method of Coca. Testing was done by the intradermal method on the skin of the back, and the dosage was 0.03 c.c. of a 1:1000 dilution for each test. All injections were made in one afternoon and the results read in 30 minutes and again in 18 hours. The percentage of positive reactions is not given, but upon the determination of the causative agents and instigation of proper treatment, relief was either complete or partial in two-thirds of the cases. A great many negative results are obtained in skin tests and Vaughan (60) believes that these are

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due to failure to pay attention to delayed reactions, 6 to 24 hours after the scratch.

2. BLOOD -- Gray and Burtness (24) in studying migraines' relation to carbohydrate tolerance found that attacks were most frequent when the blood sugar was low. Rudolph (48) and Andresen (4) both report that the finding of an eosinophilia of 3 to 20 percent, is a very suggestive finding. Davis (16) places the increase in eosinophiles at 5 to 16 percent, and states that there is never a leucocytosis. Riley, Soltz, Brickner and Hare (46) in reporting their routine laboratory examinations of migrainous persons report no consistent deviation from the normal, not only in the blood picture, but also in the urine and spinal fluid. Kast (27) found his patients had a low blood calcium, associated in most cases with an enlargement of one or both lobes of the pituitary.

3. URINE -- Glass (20) studied ten cases of menstrual migraine and made quantitative assays of the estrin (female sex hormone) and prolan A (follicle-stimulating hormone of the pituitary) in their urine. He found that practically all cases yielded at least twice as much prolan A as normal, and that estrin was subnormal or absent.

4. SPINAL FLUID -- The cerebrospinal fluid has been tested during and between attacks by von Storch and Merritt (63) and although they were able to detect slight
variations from normalcy, they conclude that migraine cannot be diagnosed on the basis of the spinal fluid picture.

5. DETERMINATION OF THE ACTIVITY OF THE SYMPATHETIC NERVOUS SYSTEM -- The method employed by Solomon (53) was measurement of the electrical resistance of the skin, which he calculated with the aid of a portable apparatus. The measurements were made during the relief obtained after the administration of ergotamine tartrate to determine whether or not it acted as an inhibitor or a stimulant to the sympathetic nervous system in bringing relief. Stimulation of the latter causes a decrease in electrical resistance of the skin, and inhibition a rise. Results showed no specific change in cutaneous electrical resistance in any case, thus indicating that relief from migraine was not accompanied by a change in the sympathetic nervous system as a whole.

6. LEUCOPENIC INDEX -- This is a procedure originated by Vaughan in testing patients for food allergy. It is based upon the principle of hemolytic crisis. In normal persons the ingestion of foods produces a mild leucocytosis. In cases where a person is allergic to a certain food, the ingestion of that particular food produces a marked leucopenia. This test is believed to be 90 percent accurate.

7. X-RAY -- Results from radiographic study in suspected cases of hypophyseal dysfunction have been found positive in many cases of menstrual migraine. Moffat (37) reports
that in only 4 of 11 cases X-rayed, a normal sella turcica was found. Thomson (57) tells of 17 of his 25 cases having abnormally small sellae or calcified diaphragma sellae. Facetting and erosions of the retaining sellar walls were seen in the many X-rays by Timme (58).
DIAGNOSIS

Diagnosis of migraine may in one instance be a comparatively simple matter yet, on the other hand, may resolve into a most difficult and trying procedure. In many cases the term "migraine" has been used where the term "headache" alone should be employed. Recurring one-sided headaches caused by sinusitis or eye-strain are quite commonly and erroneously termed migraine. We must ever keep in mind that headache is only a symptom, while migraine is a disease.

The clinically important features to be taken into consideration in the diagnosis of migraine are many, but definite and are enumerated below.

1. Periodicity - May be long or short, regular or of wide variance.

2. Return to normal between attacks.

3. Headache which in its character of one-sidedness has given the disease its name of hemicrania or migraine. Always severe, the attacks are often prostrating.

4. Nausea and vomiting occur in three-fourths of the cases and give to the attack its name of sick headache. Vomiting as a rule does not end the headache.

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5. To be classed with nausea and vomiting are a group of other symptoms involving the vegetative nervous system: coldness, giddiness, collapse, pallor, sweating, polyuria, and diarrhea which are of a general character. Unilateral sweating and flushing and fullness and throbbing of one temporal vessel point toward a sympathetic involvement on one side.

6. Prodromata are not invariable but are frequent. Languor and malaise, followed by giddiness and coldness, often precede the headache.

7. Ocular manifestations, such as zigzags, spectra and scotomata, are found in about half the cases and in the form of hemianopia in one fourth of them.

8. Time of onset. It is quite striking in how many instances the attack commences in the morning on rising. Another feature difficult to explain is that, if the attack continues into the second day, the sufferer's sleep may be undisturbed in the night. Ordinarily when sleep occurs, the storm has blown over.

9. Undoubtedly a feature of true migraine but approaching the borderline of diagnostic error is the group...
of unilateral sensory and sometimes motor symptoms. These are numbness of the face, arms and hands, slight weakness and aphasia, and certainly hemianopia. Gordon (23).

10. Heredity. A definite history of migrainous or migraine equivalents is more often than not found to have been present in former generations or in the same generation.

11. Age of onset. The greater majority have the beginning of attacks before the age of 20. Often the patient has had them "as long as he can remember".

Because of the multiplicity of seeming causes, the diagnosis of migraine must be arrived at cautiously. A complete physical examination must be made, if not advisable right during an attack, then as soon as the patient can be gone over thoroughly. This should be done to make sure that some other and more grave trouble may not be overlooked.

The eyes should always be refracted and the necessary glasses properly fitted. The eye grounds should be examined ophthalmoscopically, the head should be X-rayed if it is thought to be necessary to exclude tumor of the brain, or a narrow sella turcica. A metabolic test, a sugar tolerance test, and a protein tolerance test should all be made and evaluated. The patient should be examined for mental disease and the usual physical
examinations made routinely to exclude organic disease.

The history should be thoroughly taken. The onset, the periodicity, the state of health between the attacks, and the time of day must be determined. The nature of the headache, whether frontal, temporal, occipital, in the back of the nose, whether severe and prostrating, whether aggravated by noises, light, motion; whether nausea and vomiting occur, and when; whether sleep follows after an attack and whether the migraine repeats after sleep; whether the headache comes on gradually or suddenly, and whether there are prodromata of listlessness, languor and malaise; whether they are followed by giddiness and coldness, or else by a feeling of exhaustion—all of these must be carefully recorded in the history.

Smrtha (52).

CLINICAL VARIETIES:

Most cases of the disease which the practitioner will encounter will fall into one or the other of the following categories.

1. BILIOUS TYPE -- In this type vomiting dominates the picture, and ocular disturbance is slight or absent. Headache is present but not severe. The patient refuses food, and collapse, loss of weight, and acidosis are most often present towards the end of the attack. An icteroid tinge may be noticed in the conjunctivae in some cases. Abdominal discomfort or pain are complained of at times. In these cases there may be
a slight rise in temperature.

2. OCULAR TYPE -- Visual symptoms here dominate the picture. The attack commences with a series of visual experiences of a positive nature, such as fortification figures and zigzags, or of a negative character, such as scotomata and hemianopia. An illusory distortion of vision may accompany or follow the above. These may take the form of diplopia, megalopsia or micropsia, or optical alloaesthesia. A state of ocular vertigo follows, often accompanied by pain in the head or in the eyeball. In this type we do not ordinarily see vomiting. The visual symptoms persist throughout the attack, dominating the picture. Examination usually reveals some slight and uncorrected refractive errors, often heteronomous in type. Full correction of these errors often leads to marked relief. This type is also called Ophthalmic migraine.

3. MENSTRUAL MIGRAINE: -- This is a very common type, starting at the time of the first period, and regularly recurring with each succeeding menstruation, which it may accompany, or closely precede or follow. In these cases, should the patient miss a period, no migraine occurs. During pregnancy, the migraine usually ceases, though vomiting may be excessive. Usually the symptoms are aggravated at the menopause, but they cease with the complete cessation of the climacteric. Whether any structural peculiarities exist in these cases, as, for example, in the region of the sella turcica, is debatable.

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Theoretical as well as practical data both seem to indicate that special endocrine therapy is necessary and effective in these cases.

4. CEREBRAL TYPE — In this type there is intense headache without the visual or bilious accompaniments. Because of the severity of the pain, we may suspect a focal intracranial lesion. Also, because of the dramatic type of onset in some cases, the frequent localization of the pain to one particular region of the cranium, the severe giddiness, restlessness, irritability, and photophobia suggestive of meningeal irritation. Sudden physical exertion, such as running up a station incline with a suitcase, may precipitate attacks of this kind. Exposure of the bare head to sunlight may be responsible. Often there is some degree of hyperpiesis with or without arterial change.

5. ALLERGIC MIGRAINE — This type, occurring in families in which there are other allied affections, is quite familiar. Unquestionably there are patients in whom migraine occurs in alternation with attacks of asthma, of angioneurotic edema, or of urticaria. It is also an established fact (Balyeat 6) that migraine may develop during adolescence after a childhood of cyclical vomiting. For these and other reasons it appears clear that a type of migraine exists which bears a close association with disorders of an allergic character. These cases are, however, considered to be in the minority.
6. MIGRAINE MAJOR -- This is so named because of its severity, and at times almost dramatic characters. In this category can be placed the particularly severe examples of the bilious and of the cerebral types, where the intensity and protraction of the symptoms may arouse doubt as to the original diagnosis. Differentiation will have to be made in such cases from acute abdominal emergencies and from gross intracranial disease. These examples of migraine are taken out of the category of a minor malady because of the accompanying prostration and loss of weight. In this group also belong those cases where neurologic symptoms are present in striking degree. These include mental confusion, the paraphasic speech defects and the feelings of numbness in the face or extremities, any of which may be so marked as to suggest cerebral tumor or thrombosis.

Status hemicranicus also belongs in this group. In these cases the patient may emerge from one attack only to commence again immediately with another. This may keep up for a month at a time. During this time the patient is never free from the headache, though it may fluctuate in degree. Extreme physical and mental prostration may result and the patient may lose considerable weight. Objective sensory impairment of a hemiplegic distribution may be demonstrable.

7. OPTHALMOPLEAGIC MIGRAINE -- This type is quite characteristic, a recurrent ocular paresis eventually becoming
permanent. The third nerve is the one implicated in most of the
cases, but occasionally the fourth or the sixth nerves may be con-
cerned. The paralysis is on the same side as the pain. Following
the first few attacks of this type of migraine the paralysis passes
away in a few days. But it remains longer on succeeding attacks,
finally becoming a permanent disability. Ophthalmoplegic migraine
attacks usually last for three or four days. It occurs in women
twice as frequently as in men. The pain always precedes the
paralysis. Critchley and Ferguson (15).

8. FACIOPLEGIC MIGRAINE — This type is questioned by
some observers. Sluder (51) maintains there is no facial nerve
involvement because there is no earache. In isolated cases,
however, we may see spasm of one eyebrow and eyeball, and a
permanent elevation of an eyebrow.

9. ABDOMINAL MIGRAINE — Blitzen and Brams (9) have
reported on several of this type. In these cases the abdominal
pains were associated with the headache, and when the latter
was relieved, the abdominal discomfort was also. The pain may
be in just one of the two sites, and alternate in each attack.
Gordon (23) says that this subject is a dangerous one to venture
upon, for the physician and especially the surgeon. An attack
of epigastric pain and vomiting without fever, with or without
diarrhea, periodical in its appearance, either replacing a
cephalic migrainous attack, or appearing in a person who has
such attacks, should be carefully weighed and measured before
its victim is submitted to abdominal section.

10.IDIOPATHIC MIGRAINE--Into this group fall all those cases for which no cause can be found. These are usually the hereditary familial type. Block (10).

"Migraine equivalents" is a term which may be applied to those episodic events which occasionally seem to replace a true attack of migraine. Their nature is varied. They may comprise a period of mental confusion and a sense of unreality lasting for a few hours, or a spell of giddiness or of nausea, paroxysmal tachycardia, or tinnitus. The transient psychoses are the common equivalents. Critchley and Ferguson (15).

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THEORIES OF CAUSATION

At the present writing there are several views as to what the underlying causes of migraine are. Each has its group of supporters with the proof that their theory is more nearly the correct one. Below are listed the prevailing explanations.

1. That migraine is a toxemia. But no group of cases has yet given evidence of significant alteration in the blood or urinary chemistry to substantially uphold this theory. True, such things as infected teeth may serve as an exciting cause, but the wise physician will not promise great things as a reward for their removal. He has seen too many toothless patients with the headaches still as bad as ever. The nose must be ruled out by an examination for sinusitis.

2. That it is an allergic disease. There have been occasional instances in which certain foods, strangely enough some of the more common ones as bread, chocolate, milk, eggs, nuts, meat, and some vegetables, would bring on an attack when ingested. But the evidence of production of migraine by allergens has still a long way to go to be convincing.

3. That it is due to dysfunction of the pituitary gland. More and more data is becoming available each year on this theory, and as yet no one can deny this theory's soundness. But the type of evidence put forth to support it is considered somewhat bewildering... 40...
to the ordinary mind. Gordon (23).

4. That it is due to eyestrain. This is the most important single factor in the production of migraine (that is, errors in refraction), and without over-emphasizing the role of ocular defects in the etiology of migraine it must be laid down that the first step in treatment is to secure expert ophthalmic assistance. Critchley (14).

5. That it is associated with disturbance of the genital glands. In connection here are its appearance at puberty, its exacerbations about the menstrual period and frequent disappearance at the menopause, and its similarly frequent disappearance during pregnancy, which all are very suggestive. Of course, just what one would do about male patients on this basis raises a difficulty. Recent studies by Riley, Brickner, and Kurzrok (44) indicate that, in most women, and in some men, an attack comes when there accumulates in the blood an excess of prolactin A, one of the internal secretions of the pituitary gland. Normally, this substance may perhaps be absorbed by the ovary or neutralized by some of the secretions of the ovary. Many puzzles still remain, but it seems logical that the eventual control of the disease, at least in women, will come through an understanding of the interrelated functions of hypophysis and ovary.

6. That it is due to some disturbance of the vegetative nervous system. This statement is a sort of revelation of the
obvious. The almost constant association of sympathetic phenomena with all cases and their predominance in some is well known and set forth elsewhere in this paper.

7. That it is of a vascular nature. The headache and vomiting remind one of a temporary cerebral tumor and the occasional hemianopia and other visual aberrations point to local swelling of the occipital cortex and regions more anterior. All of these symptoms would indicate some process causing temporary swelling of regions of the cortex, whether of vascular or lymphatic origin being still a question. Gordon (23). Histologists have demonstrated not only an efferent nerve supply to the arteries of the brain and meninges, but also an afferent system. Neurologists and neurological surgeons report that among the few structures within the skull which are sensitive to mechanical stimulation, are the larger cerebral arteries. The engorgement and tenderness of the temporal blood vessels, together with the changes in the retinal and conjunctival arteries, the lacrimation and rhinorrhea, the throbbing character of the pain, are all suggestive of a vascular origin to the headache. Critchley (14).

8. The most likely of all theories, and most indefinite, is that migraine is due to some innate peculiarity, liable to be excited or aggravated by accessory causes. Gordon (23).
ASSOCIATION WITH OTHER DISEASES

Although migraine is usually an independent hereditary disease, we frequently find it in more or less close association with various other diseases. The most common of these are listed below, but a detailed discussion will not be attempted.

Arnbrecht (5) states that several of the early nineteenth century writers on the migraine syndrome recognized a similarity between the other allergic diseases, such as hay fever and asthma, and migraine. Many of the modern writers continue to bear this out. Rowe (47), in his book on allergy, states that food allergy is the most probable type of sensitization operative in migraine and these associated diseases, and concludes that allergy explains best all the migrainous symptoms.

Evidence is presented that migraine is associated with epilepsy rather closely and that they are both of a very similar physiologic order. Perhaps migraine is a protracted form of epilepsy. Frequently one disease alternates with the other, or one replaces the other in the same individual.

Wilson (65). Epilepsy occurring at menstrual time is often linked closely with water retention, and it is known that the female sex hormones, which have been shown to aid the migrainous, influences water balance and aids in the control of epilepsy.

Whitehead and McNeil (64).
Migrainous neuralgia is an anterior substituted migraine, probably due to a vasomotor neurosis of the meningeal vessels. There are never any of the cerebral symptoms as seen in true migraine. It is a recurrent neuralgia affecting the temple or side of the forehead, and often both jaws, but usually strictly unilateral. Harris (25).

Although we do not call it a disease, migraine is often associated with pregnancy. The correlation here is the fact that pregnancy headaches are most often due to hypertrophy of the pituitary gland, as we have shown many migraines to be, and this swelling subsides after delivery with no treatment being necessary. Gellhorn (19).

Riley, Brickner, and Soltz (45), in studying a group of cases from the Migraine Clinic of New York, have listed a number of types of unusual migraine, in which migraine can be closely simulated. These are: intracranial neoplasms; cerebral aneurysms; progressive paralysis; epidemic encephalitis; arteriosclerosis; mediastinal tumors; cerebral vascular insults; any interference with cerebrospinal fluid; and sinusitis.
COMPLICATIONS AND SEQUELAE

This subject is still a trifle uncertain because of the absolute uncertainty with which migraine itself is still viewed. But several conditions are mentioned in literature which are thought to have arisen from or in some way be connected with migraine, and these are set forth here. Detailed discussion of the association will be omitted, however.

Critchley (13) states that cerebro-vascular degeneration is the most common of the complications of lifelong migraine. He also mentions premature ageing, and cerebral arterio-sclerosis with all its attendant manifestations. Gordon (22) likewise finds that hypertensive vascular disease is common in the later life of the migrainous. Critchley further notes that thrombosis of a retinal vessel is sometimes seen in a severe attack; and that permanent hemiplegia or aphasia may occur which is much more grave.

Migrainous neuralgia may be again mentioned here as quite often following an attack of migraine. Critchley and Ferguson (15). Persistent hemianopia is another well-known sequel of chronic migraine. This defect may appear insidiously as a permanent feature, but more often it is ushered in abruptly at the height of an attack by an epileptiform seizure.
PATHOLOGY

In considering the pathology present in a migrainous individual we find that we are untimely cut short in the discussion by the utter lack of material at hand. Of course, we may take account of the obvious superficial abnormalities which have been told of in previous paragraphs, but when it comes to true deep-seated findings, especially at autopsy, there is not much literature concerning them.

Riley (43) has observed several autopsies and states that there is very limited material found, and that much study of the pituitary gland and its neighboring structures is needed. Macroscopically the brain appears to be slightly atrophied, with internal hydrocephalus and a granular appearance in the ependyma of the lateral ventricles. He tells of various microscopic findings, but declares that there are no discriminating points and that observations were practically valueless.

Kennedy (29) writes that "it is in no way probable that the headache comes direct from brain involvement for the cerebral tissue would seem to lack sensitiveness; needling the brain under local anesthesia is painless but pinching or stretching the meninges or meningeal vessels is agonizing". Edema of the brain, seen in alcoholic or uremic poisoning, causes fits,
and edema of the cerebral meninges with especial pressure in the meningeal crevices produces the localized headache and the local cerebral symptoms of migraine.

Sluder (51), who studied migraine from the standpoint of nasal and accessory sinus involvements, states that in every one of his many cases, except one, he observed that there were post-nasal lesions present.
TREATMENT AND PROGNOSIS

There have been so many different drugs and procedures tried in the prevention and treatment of migraine that it would be impracticable as well as unnecessary to review them all in this paper. Practically every drug in the pharmacopeia has at some time or other been employed. Suffice it to mention the most important ones in the different groups as practiced at present.

The treatment of migraine consists of the treatment of the attack, and of the prevention of future attacks, or treatment between attacks. In treating the attack, it is important to eliminate the causative factor as rapidly as possible. In the case of food allergy, prompt catharsis is indicated, and the drinking of large quantities of water is distinctly of advantage. The latter, when vomited, often producing an advantageous autolavage of the stomach. Emesis can be produced by other methods also, and often will greatly relieve an attack.

The patient must go to bed in a dark room and be quiet. Often a laxative taken early in the seizure will give relief. He should take a hypnotic, such as phenobarbital or amytal in order to induce sleep, after which the attack will quite frequently be gone. If vomiting is a persistent symptom, we may give

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rectal injections of potassium bromide (20 to 40 grains) and chloral hydrate (10 to 20 grains). Morphine should, of course, be strictly avoided, as addiction is easily formed in these cases.

Anything which increases the irritability of the brain tends to bring on an attack in the susceptible. Hence it is that worry, excitement, overwork, insomnia, or loss of temper must be avoided. The most important measures in preventing an attack in many cases are: better mental and physical hygiene, more rest and more play, more physical work and less mental work, plenty of good sleep, even with the aid of drugs.

Both in the relief of attacks and the prevention of future ones, the relatively new drug "ergotamine tartrate" has been found by many experiments to be of value. This drug is the most recently isolated active principle of ergot (isolated by Stoll in 1918). It is a specific alkaloid similar to, but not identical with ergotoxine. The chemical formula is $C_{33}H_{35}N_5O_5$.

Pool, von Storch, and Lennox (41).

Lennox, von Storch, and Solomon (33) carried out an experiment to determine whether or not ergotamine tartrate (gynergen) was a specific for migraine, or if it could be classed as a headache panacea. The results were as follows:

1. No. of patients Stopped Unchanged Worse
   Non-migrainous 48 15% 63% 22%
   Migrainous 120 89% 9% 3%

2. Of 38 persons without headache, given gynergen, 16% developed headache.

... 49 ...
3. Conclusion -- Gynergen has a specific action on migraine type headaches. The present evidence is that the action is not directly on the sensory nerve endings in the dura or skull, but that there is an intermediate systemic action.

Koppanyi and Evans (30) studied the emetic and anti-emetic action of gynergen, and concluded that the drug acts directly on the vomiting center. They used dogs and cats as subjects, and performed such operations as removal of the stomach and vago-sympathectomy, and still got vomiting and retching with gynergen intravenously.

Hinnant (26) used ergotamine tartrate in a few of his cases and gives it a creditable standing. Soltz, Brickner, Riley, and Salmon (54) experimented in the oral administration of the drug, and report that they encountered no cases of ergotism by that route.

O'Sullivan (39) has done perhaps the most work with this drug during the past two years. She reports that all but eight of her ninety-seven patients were benefited by this medicament. It completely checked 1,042 episodes in eighty-nine persons. It is calculated that the subjects in her series were freed from approximately 39,000 hours of suffering.

It was realized early that gynergen could not be used as a cure for migraine, even though it seemed to be of unquestionable value in aborting attacks. The drug has no effect on the
frequency of the attacks, but once it has abolished an attack, it has never failed to check again a migraine headache in that individual if given in adequate dosage. The amount required is very important, and the minimum is directly proportional to the severity of the attack, which varies widely.

The method of administering the drug subcutaneously is to inject a trial dose of 0.25 mg., and the effectiveness of this is used as an index to future medication. If the headache persists, repeat the dose in two hours. In more severe cases, or where the episode has reached its peak, the dose may be 0.5 mg., and rarely more than that is needed. When nausea and vomiting follow the injection, these may be relieved by the injection of atropine 1/100 grain with the alkaloid or any time after its use.

Ergotamine tartrate produces uncomfortable concomitant symptoms in many individuals. These include nausea, vomiting, weakness of the legs, stiffness of the joints, a sense of constriction in the throat, a heaviness of the chest, and a burning and tingling of the fingers and toes. But these are not severe, and are usually borne by the patient much more readily than the headache.

The alkaloid is also dispensed in tablet form, each tablet containing 1 mg. If the required amount is taken at once, rather than in divided doses, a more efficient relief will be obtained. Naturally, if vomiting is occurring, this route is useless. The tablets have not been found to be as effective as... 51...
the intravenous administration.

Blackie and Hossack (8) used emmenin (contains the ovarian-stimulating hormone of the placenta) in twenty cases of menstrual migraine, in doses of \( \frac{1}{2} \) drachm twice a day between the menstrual periods. They conclude: 1. It gave relief to the point of complete freedom; 2. In addition the patients experienced improvement of menstrual disorders, loss of excessive weight, and a new sense of well-being.

Moffat (37) tested a group of seventeen cases of menstrual migraines for a period of over three years, using gonadotropic factor from female urine as the medicament. This substance is normally found in a certain percent in healthy female urine. When given in cases of menstrual migraine it restores the balance between the pituitary and the ovaries, upset of which is given as the cause of menstrual migraine by many observers, and thus removes the cause for an attack.

Several experimenters have used theelin and amniotin (ovarian follicular hormones) in treatment of the headache, with degrees of success. Allen and Diddle (2) made tests to see if the use of these was injurious to the ovaries. The results of the tests have all been negative.

Chondroitin sulphuric acid has been used successfully by Crandall, Roberts, and Snorf (12). They treated 151 patients over a period of three years, and report 50 per cent of the cases had marked reduction in the number of attacks, while 20 percent
had only half as many and as severe attacks. There is little known concerning the action of this drug, but it is thought that the active part is the glucuronic fraction, and that the liver is concerned in whatever metabolic changes are brought about by its administration.

Sodium thiosulphate has been used to advantage in some cases, the dosage being 15 grains intravenously. Fluid extract of cannabis indica given in the largest doses tolerated, starting with two minims every four hours, depresses the spinal sensory pathways and has been found to relieve. Also, inhaling the contents of a pearl of amyl nitrite may bring some relief. Etteson (18).

Hypoglycemia has been given as one of the causes for migraine and in treatment of these cases Gray and Burtinss (24) have found that frequent feedings of high carbohydrate food is of aid in preventing or curing the headache. If the headache is continually present in the mornings upon waking, the patient is told to take orange juice or gingerale or some other carbohydrate at four in the morning.

It was noticed long ago that an attack of typhoid fever can give relief from migraine for a year or more. Perhaps for this reason injections of peptone or foreign protein are sometimes helpful. In a few cases, good results have followed intravenous injections of peptone, beginning with 0.5 cc. of 5 percent solution, and running rapidly up to 2 cc. twice a week. Good results have been reported also from the use of
tuberculin, typhoid vaccine, and sterile milk. Alvarez (3).

Radiation therapy has been used by some men in correcting ovarian function and in producing artificial menopause in the treatment of migraine. The dose of radium is 1300 to 1800 milligram hours, intrauterine. Keith (23). Small doses of roentgen rays to the ovaries has in many cases re-established normal flow in cases of functional amenorrhea. Likewise large doses has a paralyzing action on the gonads. Menopause artificially produced by irradiation is of very doubtful value, and should not be thought of in women under forty, as in these cases it may even accentuate the symptoms. Past forty it may partially or completely relieve some women. Martin (34) and Martin (35).

Psychotherapy is advocated by Slight (50) and Pulsifer (42) as being the only treatment needed in some cases. Always endeavor to maintain the patient's nervous and emotional equilibrium and tranquility. Because being in "high gear", as the habitual migraine is, renders them more likely to have attacks of hemicrania. Tell the patient in some detail the nature of his affliction, since, as Alvarez has quoted, "the successful conquest of fate is not by struggling against it, nor by trying to escape from it, but by acquiescence". Such peace of mind instilled may indeed even lessen the frequency and severity of attacks. Try to make alterations in the life-habits of the person with such restrictions and limitations as will avoid emotional conflict.

Finally, in those cases in which life has become a burden,

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relief by surgery may be sought. Surgical procedures have been fairly successful in a few instances, and the operations include subtemporal decompression, ligation of the middle meningeal artery, or section of the posterior cervical sympathetics. Cutting the inner fibers of the fifth nerve just after they leave the gasserian ganglion has in instances given complete relief. Smrha (52) and Gordon (23).

PROGNOSIS. There are several types or classes of migraine patients which are relatively intractable, and treatment is very discouraging. These include:

1. Where all the relatives of the patient have migraine, and where no certain precipitating factors can be determined.

2. "Insanity equivalents", so poorly equipped mentally that they are beyond much help.

3. Patient insists on believing the cause for his migraine is some abdominal organic condition, is unco-operative, and even has needless operations with no relief.

4. Intolerance to luminal -- it is a good axiom that when a patient cannot tolerate luminal, medicinal cure will be difficult.

5. Morphine addiction. If they have relied on morphine, they will respond badly to all other attempted treatment.

6. Hypotension, debility and asthenia -- Chronic migraines with this condition have exaggerated attacks. It is hard
and slow to relieve these three.

7. Adverse psychological factors -- as of environment, occupation, social condition, etc.

However, the general outlook for the migraine patient is usually quite favorable. The headaches and other symptoms as a rule grow less frequent and less severe as age advances, and the disease usually ceases in old age, especially after fifty years of age. Therapy is undoubtedly difficult in such a polymorphic disease, but we must not allow ourselves to become despondent, despite the importance of the hereditary factor and the migraine constitution. Knowing that the malady grows less severe as old age advances, we may at least hold that out to those so afflicted and thus hold out a ray of hope. Though we cannot always cure, we can at least relieve, and migraine can be made more bearable.
CASE REPORT I

Minor Migraine

Female, age 20

Patient of simple ability, but great ambitions, attending a business college, and having migrainous attacks occurring following days of particular difficulty at school. Other reactions were noted at these times as narcolepsy and weeping. Also, an attack of migraine would terminate immediately if she had a fit of weeping. This case illustrates migraine as a special form of emotional reaction, where the attack followed directly on situations arousing emotion and it is worthy of note that attacks would terminate if free emotional expression took place, as by weeping.

Treatment in this case was psychotherapy.
CASE REPORT II

Chronic Migraine
Female, age 26

Patient has had migraine all of life. Has an opening over left frontal region of skull through which her brain has been explored. Present Illness -- Has a languid feeling for twenty-four hours before attack. Pain over right eye which goes back. At height has nausea and vomiting. Pain lasts twenty four to seventy two hours. No relief from drugs. Wheat causes attack. Family History -- One brother with hay fever, one with asthma.

Past History -- Patient otherwise normal and always well except for tonsillectomy in 1927. Physical Examination -- Negative except for the hole, 1" in diameter.

Laboratory -- All normal. X-ray negative. Allergic to cereals and milk products and sea foods. Operation done because she had entered a hospital with symptoms suggesting a brain tumor. On operation no tumor found. Found increased fluid under pressure beneath the dura and in lateral ventricle. Dura tight and blood vessels dilated. Post Operative Diagnosis -- Edema of brain and idiopathic migraine.

Attack -- languid, sallow complexion changing to

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pallor. Skull hole is definitely depressed. Eyes stare. Pain over right eye spreads back. Avoids light and noises. Hole begins to show bulge, looking like a tumor. Not tender, does not pulsate. Does not feel like brain tissue. Feels definitely tense and with fluctuation. As pain grows, patient vomits. Pallor goes over to flush. Goes on seventy two hours, then subsides. Goes into deep sleep exhausted. The swelling goes down until it is a depression again.

Conclusions from above:

1. Vasomotor spasm (blanching and depression).
2. Vascular dilatation with edema of brain.
3. The hypersecretion of fluid is followed by a just as rapid absorption.
CASE REPORT III

(Author's note: This interesting case report was given to me by a personal friend who is a victim of migraine attacks, and who has some knowledge of medical terms and procedures. It is written in her own words and describes quite clearly the prodromata, symptoms, and effects of medication.)

Patient V.R., age 24.

"No warning that headaches are coming on and they are not correlated with any special activity, form of diet etc. (apparently). This particular attack came on at night and I awoke on a Saturday feeling slightly dizzy and upset. The first part of the first phase was a 'jittery feeling - 'all falling apart'. Difficulty in focusing the eyes and sometimes nausea. Lasted about 2 to 4 hours and then there came a slight pain in the right temple, about one inch from the right eye and about two inches above the right ear. Continued to feel 'jittery' with the headache. When reading or trying to read or using the eyes for any close work, the pain intensified and involved the eye itself. Felt as though it could be relieved by pushing on it. Pressure did relieve it momentarily. The headache was not bad enough to force going to bed for one afternoon. Went to sleep at night with no difficulty but sleep was restless. In the morning awoke

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and headache was more intense. Very uncomfortable to read and in fact so noticeable as to interfere with any activity. Went to bed lying flat on the back and tried to use hot water packs on the pain, alternating with cold water for about one hour. Temporary relief, but both these remedies wore out and the headache was not better. Headache grew more and more intense, involving the larger portion of head and going into the back of the ear on the right side and the cord back of the ear and the neck and felt as though pain could be relieved by pressing on this cord. Heart action seemed to be speeded up causing more and more nervousness and feeling of being 'jittery'. Impossible to sleep at this point and this continued until about 5 P.M. of the second day (Sunday). Doctor called at this time, who administered 2 c.c. gynergen (ergotamine tartrate) preparation intra-dermally.

Symptoms following gynergen -- Immediate effect was quickened heart action. Sense of 'all falling to pieces'. Feeling of the whole body action speeding up, accompanied by strong muscular contractions and extreme nausea and regurgitation. As the drug reaches the lungs, great difficulty in breathing. Felt as though there were several people sitting on the chest and the world seemed very far away. Then the feeling of not breathing at all. The effects of the gynergen lasted about two hours; and then, having taken two sedatives,
fell into a sound sleep from about 7 P.M. till 8:30 A.M. It seemed as though the headache left as soon as the gynergen was administered, but this may have been an illusion due to the fact that the action of the gynergen was so intense that the headache was no longer noticed.

Next Day:— Extremely weak. Stiffness and soreness of all the muscles as though they had been over-worked the previous day. Dizziness, etc. This gradually subsides over a period of about a half day after which there is a gradual return to normal condition.
SUMMARY

In the second century A.D. Galen wrote of migraine -- "Cephalaea is a diurnal headache with vehement occasions from small causes. The sufferer cannot endure noise, raising of the voice, the brilliance of light, or movement; but seeks quiet and a dark chamber on account of the severity of the pain. Some are as under the blows of a hammer, some as if crushed and distended; and in not a few there is pain to the roots of the eyes. There are, as in epilepsy, remissions when there is complete freedom".

In the twentieth century A.D. doctors write of migraine, using the very same words. Patients who suffer from the disease frequently come to us and say their head feels "as if it had been hit with a hammer".

Much has been accomplished in the study of migraine during the intervening eighteen centuries it is true. Modernized methods have aided in establishing the many theories which we have to choose from in establishing the etiology of this disease. But like so many other of the age old maladies of man, we must consider migraine as still requiring a considerable amount of research and application of existing theories and proffered treatments before we may start to consider it a completed chapter.

This thesis, of course, is a mere scratch on the surface of the subject, and there are so many conflicting and
widely variant ideas expressed on it by those with the authority to do so that I do not wish to draw any conclusions at this time. However, in its scope I have found enough of value to reward my original interest and perhaps to someday prompt further study.
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