

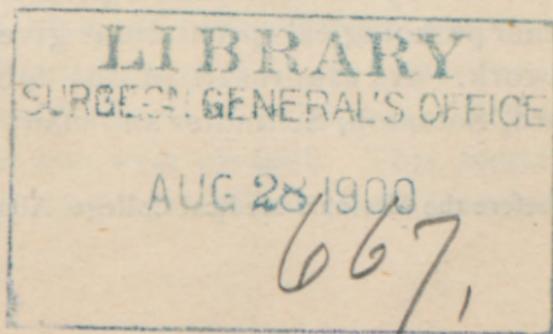
Zahorsky (John)

A STUDY OF MIGRAINE.

BY JOHN ZAHORSKY, A.M., M.D.,

OF ST. LOUIS, MO.

Reprint from the MEDICAL REVIEW, St. Louis, Mo., March 5, 1898.



A Study of Migraine.¹

BY JOHN ZAHORSKY, A B, M.D., ST. LOUIS, MO.

House Physician to the Bethesda Foundling Home; Clinician to Childrens' Department, Missouri Medical College, Etc.

The classical description of migraine by Eulenberg* can no longer bear the test of modern investigation, for the symptomatology as given is incomplete and his theoretical conclusions untenable. Neither can we allow the pathogenesis to be set aside by the fanciful designation of "nerve-storm," as Liveing^b would have us do, for such a metaphor lacks all analogy and is certainly not a scientific expression. Moreover, we must admit that the appellation, "sensory neurosis," is merely a term to conceal our ignorance.

It will, therefore, be conceded that a study of migraine is working in a field where much labor is needed and, consequently, even small gains are valuable.

The most recent view which deserves our consideration is the theory of leucomaine poisoning, and, unlike the former pathological speculations gives some tangible groundwork. As the result of the labors of Gautier, Bouchard, Solomon, Schindler and many others, already

Read before the Missouri Medical College Alumni Association.

the way in this direction has been made passable, and it is to be hoped that soon this dreadful malady may be somewhat understood.

It is unfortunate that we have as yet no term to designate all toxic products of metabolism; the name, leucomaine, being restricted to the alkaloidal substances; but it is not by any means certain that all offending substances are basic in character. On the contrary, we have good reason to suppose that toxic products, other than alkaloids, may be formed in the body, *e.g.*, toxalbumins, glucosides, acids, etc. Still, until some one coins a new word, we shall be compelled to apply the word leucomaine to all deleterious substances which are the result of katabolism, even when their chemical constitutions are unknown.

Recently, I have had occasion to study several cases of migraine, and these form the basis of my study.

A phenomenon, which first drew my attention to the possible pathology of this affection, was the occurrence of polyuria immediately preceding and during the first part of the paroxysm. The specific gravity of the urine was very low, and in two cases particularly, I demonstrated, in the presence of increased flow of urine, a subnormal excretion of urinary solids. In one instance the quantity of urine passed was less than the normal daily average of 1500 cc., the specific gravity being 1006, with only $\frac{1}{4}$ per cent of urea, no trace of earthy phosphates, and only a trace of sulphates. But neither albumin nor casts was ever present. This secretion of pale urine, mostly in large quantities, is mentioned by

various writers, but few attach any significance to it. Haig,* for instance, mentions the lessened excretion of uric acid before, and a greater discharge after, the paroxysm.

Following this stage of polyuria, usually at the height of the attack, the urine becomes suddenly highly colored, having a specific gravity of about 1030, or even more, showing more than 3 per cent of urea, an enormous sediment of amorphous urates, all other solids increased, and the xanthin compounds in larger quantities. Following this discharge, the symptoms rapidly mitigate.

It occurred to me to make a comparison of the disease under consideration with the symptom complex of normal urinary poisoning. Bouchard^a has formulated the toxic principles of normal urine as follows:

1. A diuretic, probably urea.
2. A narcotic.
3. A sialagogue.
4. An organic convulsivant (probably heteroxanthin and paraxanthin).
5. A mineral convulsivant, (potassium salts).
6. A myotic.
7. An antithermic.

These toxic principles being retained explain only partially the symptom complex of uremia, where we suppose these substances are great factors, but the absence of the internal secretion of the kidneys must also be considered.

The most characteristic symptom of migraine is the

agonizing cephalalgia. The pain, however, is not necessarily limited to the head, for frequently we find intense rachialgia. Very commonly pain is felt along the course of the lumbar nerves. Gastric pains are very common, so, also, are uterine and ovarian pains.

While we can not place pain as the direct result of the toxic principles mentioned, nevertheless, its usual occurrence in uremia, and its frequent premonition in puerperal eclampsia suggest that all these headaches depend on the same toxic substances.

The symptoms of migraine which show urotoxemia are hypothermia, myosis and salivation. In every case, even when the internal temperature is not below normal, we find cold extremities. This, no doubt, is due to arterio-spasm, but the deficient radiation of heat from the surface of the body, without a corresponding rise of internal heat, proves that thermogenesis is decreased. In two cases a subnormal temperature in the mouth was observed; the thermometer registered 97° and in another 97.6° . I excluded all errors that might possibly make these figures erroneous.

Contraction of the pupil is almost an invariable phenomenon, until the discharge of leucomains takes place, when it rapidly dilates.

Salivation is one of the classical symptoms, although its severity varies in different cases.

Bouchard has shown that normal urine does not cause convulsions, for the simple reason that the narcotic principle is antagonistic to the action of the convulsivants.

Retardation of the pulse rate is a common symptom

during the height of the attack. The blood pressure is very much augmented, and the whole cardiac phenomena resemble the symptoms of poisoning by digitalis. For, as in the action of this drug, we find a slow pulse, frequently a *pulsus intermittens* or a *pulsus intercedens*. In two cases, seeing the patient for the first time, I had to exclude grave disease of the myocardium. Acute dilatation of the heart was also noted once, as shown by a systolic murmur and enlarged area of cardiac dulness. These physical signs disappeared soon after the paroxysm.

We find this same increased blood pressure in a less degree in interstitial nephritis, in both cases depending on some powerful vaso-constrictor; let us suggest either the xanthin bases or adrenal secretion. Haig refers this increased blood pressure to an excess of uric acid in the blood.

Vaso motor disturbances are very prominent. For, while the arterioles, as a whole, are contracted, various areas of relaxation occur. The face may be flushed, but often it is pale. This peculiar symptom has formed the basis for a great deal of speculation, and even a division into classes has been made: the sympathetico-paralytic and the sympathetico tonic, making the malady essentially one of the splanchnic nervous system.

How easy it is to select a single symptom and make it stand in a causative relation to all other symptoms. This is being continually done. The ophthalmologist, finding derangements of vision, frequently discovers errors of refraction, and he regards all other symptoms as

the result of the ocular derangement. The gynecologist in nearly all cases finds a retroflexed uterus, a slight tear in the cervix, or other pelvic lesion; all other symptoms are, therefore, caused reflexly from this irritation. The rhinologist finds a nasal deformity or disease in most cases, and it consequently becomes an important etiological factor. The neurologist finds a disease of the neuron; the splanchnologist, a gastric lesion; the genito-urinary surgeon, a sexual derangement; other specialists follow in the series, each clamoring that his field of practice contains the offending *materies morbi*.

The gastric symptoms are very frequent, simulating the digestive disturbances of uremia. The leucomaine gastric neuroses, as Rachford* calls them, are sometimes met and are very distressing and persistent. The recital of the following case illustrates this.

A widow, aged 34 years, has suffered from paroxysms of migraine since a little girl, but in the last four years these have become fortnightly and very severe. She gave a history of having what was diagnosed as gastritis some time before coming under my care. I had the opportunity to study several paroxysms of hemicrania. But thrice in the last two years she has suffered from a severe gastric neurosis. The headache would commence as usual, but would reach only a moderate severity; gradually the gastric symptoms developed. There was nausea, vomiting, pain, and tenderness in the epigastrium, and an utter inability to retain anything on the stomach. Twice a slight diarrhea was associated with this. In correspondence to the aggravation of the

gastric disorder the headache lessened in severity, and other sensory symptoms disappeared. The gastric attacks are not self-limited like the headache, as Rachford has pointed out. Twice these attacks lasted more than two weeks, and the patient recovered very slowly. During all this time the urine had a low specific gravity, ranging from 1006 to 1012; polyuria, however, was conspicuous; yet, every time the total daily solids was diminished. As soon as the renal secretion became normal in composition, the gastric disorder rapidly disappeared. This was a very striking feature and corroborated the view that renal insufficiency and gastric excretion of metabolic products were the existing pathogenic factors. The irritating action of urea and other urinary constituents on the gastric mucous membrane has been demonstrated by Hirschler.^f Smith^g has also shown such action of creatinin.

Another group of phenomena occurring so frequently in uremia and forming such interesting feature of migraine, are the visual disturbances: Amaurosis, hemianopia, scintillating scotomata, and ophthalmoplegia are frequently noted. In fact, Claus^h has made a classification based on ophthalmic symptoms, but he admits their production by auto-intoxication.

It is unnecessary to mention all the motor and sensory symptoms that have been cited. One of the most interesting is aphasia. But this has been observed in uremia also. A peculiar sense of burning in the throat is often found. An offensive odor from the mouth is also characteristic of the two diseases.

Dysmenorrhea and menorrhagia frequently accompany or even take the place of a paroxysm. The pain and excessive flow produced by the injection of diphtheria antitoxin, as pointed out by Prof. Saunders,¹ are analogous, in each case depending on leucomaines.

Adopting the nomenclature of von Jaksch,² we would, therefore, provisionally at least, regard migraine as a retention toxicosis plus an auto-toxicosis, basing this theory on the following evidences:

1. The normal excretory products are retained immediately before the paroxysm.

2. The symptoms of migraine show a great similarity to those diseases known to be due to uro-toxemia.

3. There is great evidence that the gastro-intestinal mucous membrane acts as an excretory organ.

4. The malady persists until a great discharge of urinary solids takes place, when the symptoms rapidly disappear.

5. The more or less continuation of the symptoms, when there is no great discharge by the kidneys.

6. The implication of the whole nervous system, sensory, secretory, and psychological functions.

7. The presence in increased quantities of normal poisonous leucomaines in the urine after the paroxysm, I refer to heteroxanthin and paraxanthin.

But while the xanthin bases are present in increased quantities, we are unable to say that their retention causes pain. Being allied in chemical constitution to caffeine, we are compelled to doubt this. It can not be doubted that many symptoms are due to leucomaines,

still the paroxysmal character of the renal insufficiency is inexplicable. Haig considered the possibility of the renal capillaries or tubules being plugged with uric acid.

All cyclical phenomena, from menstruation to pathological painful paroxysms, have as yet received no explanation. In physiological actions an inherent automatism, working rhythmically, might be considered sufficiently explicit; but even here gradually several cyclic functions are being scientifically explained by leucomaine formation—*e. g.*, sleep and waking.^k From a pathologic standpoint, it is difficult to conceive the formation of an automatism, cyclical in function, and not having a physiological basis. Moreover, the rapid disappearance of this paroxysmal malady speaks at times against such automatism.

To the logical mind it is reasonable to suppose a disproportion between the activities of various organs and the formation of poisons, which gradually accumulating produce a change in renal activity with the subsequent toxic stage. The paroxysmal attack probably excites accessory organs to greater activity and thus the symptoms are removed—*e. g.*, the adrenals, which as we know secrete a substance that enormously increases blood pressure. Who will say that this great blood pressure during the paroxysm is not due to increased secretion of the adrenals?

Increased internal secretion of the kidneys must also be considered. In our study the possibility must be considered that antitoxins are formed under the stimu-

lation of leucomaines and thus rapidly curing the disease; just as antitoxin following poisons formed by bacteria rapidly cure this infection. As an example the crisis in pneumonia may be cited. Antivenenes are formed after the poisoning by snake venom, why not after leucomaine poisoning? Brown-Sequard¹ and D'Arsonval have shown that animals whose kidneys are extirpated live much longer if extract of healthy kidneys are injected.

A rapid cure in migraine is only affected by the great accumulation of the toxic material; for when other organs, as the stomach, take up the excretion, the toxicosis becomes indefinite in length, not being so self-limited, as when the cerebral symptoms are pronounced.

The occurrence of unilateral symptoms presents some difficulty in the above explanation, but in uremia unilateral pains and motor symptoms are common enough, instanced by cases reported by Brennet,^m Bunet,ⁿ and Westphal.* Unilateral symptoms in gout and rheumatism present the same difficulty.

Recently Herter^p has advanced the hypothesis that the absorption of albumoses from the stomach may cause the disease; but this as yet lacks all proof. The theory of auto-intoxication from intestinal putrefaction is denied by the absence of any excess of ethereal sulphates in the urine, as I have repeatedly demonstrated.

Haig's theory of the greater or less alkalinity of the blood and the consequent precipitation of uric acid, or its presence or absence in the blood, is not borne out by clinical experience. Thus the administration of alkalies

does not hasten the great discharge of urates and other solids; in one case this was accomplished by the administration of sulphuric acid.

The causes producing or accompanied by an excessive formation of leucomaines are: fatigue, prolonged mental application, psychological depression, irritation of afferent nerves, and dietetic errors. These with a hereditary predisposition are the most important conditions connected with the causative perverted cell action.

TREATMENT.—If the pathogenesis of migraine is admitted to be obscure, we must also admit that the treatment is very unsatisfactory. Not only in severe cases are the paroxysms unyielding to mitigating measures, but also their prevention is a thankless undertaking. Each specialist finds evidence that these cases are very much benefited, if the organ of their practice is properly adjusted to a normal physiological activity. The best proofs of benefit have been shown by the oculists. I need only refer to the statistics of Mittendorf,⁴ who reports 4000 cases of headache relieved by the correction of various forms of ametropia, principally hyperopic astigmatism. But the truth is that nearly all cases of headache due to eye-strain are not migrainous in character, and if so, only the milder cases are relieved. Often the relief obtained is only temporary, but this short relief is sufficient to swell the statistics of the oculists.

The rhinologist can show nearly equally surprising figures, as evidenced by the study of an article recently published by Snow,⁵ who gives statistics to support the

view that 70 to 80 per cent of migrainous paroxysms are due to the presence of diseases of the nasal passages or the adjacent air passages. The gynecologist also can give similar figures.

One is convinced after a study of these reports that the benefit is derived—first, by removal of peripheral irritation, and second, by changes in neural activity incidental to severe operations. For it seems that the more severe the operation the more lasting are the results. It is well, therefore, to remove peripheral irritation, even if the result is not permanent.

Dietary regulations are important. Care should be taken to exclude those foods containing xanthin compounds in excess. Changes in occupation, habits, and climate also act well in producing changes in neural activity. Still any change advised is only an experiment, since rules to guide us in this change have as yet not been formulated.

In regard to medication, there is nothing new to offer. The analgesic coal tar products soon lose their efficacy. It is the trial of one's life to choose an anodyne at each attack. The Rachford salts have been only of slight benefit in my hands. Sulphuric acid has acted better than the sulphates. But the administration of potassium permanganate, in view of its beneficial action in other alkaloidal poisoning, as morphina, deserves an extended trial.

Gowers* recommends nitro-glycerine in increasing doses three times a day after meals. I can not say that I have had any marked results from this. Gowers ad-

vocates the treatment especially in those cases where distinct pallor supervenes in the early stage, while Herter fears to give it except when there is distinct flushing of the face.

Charcot's treatment, recently emphasized by La Tourette,⁴ seems very rational and has given the best results. But the mixed bromides should be used, or bromide of soda, and not bromide of potassium; for potassium being one of the toxic products of urine its administration should be limited. The patient takes 2 grammes of bromides daily the first week, 3 grammes the second, 4 grammes the third, and so on, until the paroxysms become retarded, when the dose is gradually reduced. The rationale of its efficacy is easily found in the diminished metabolism, and the lessened excitability and activity of the nervous system induced.

In view of the pathology as outlined above, stimulating diuretics were tried, but with negative results. I tried urea and thyroid extract, but failed to see any retardation. Theobromin salicylate failed to increase the urinary constituents very much, although the urinary flow was increased. Strychnia acts very well in the milder forms in retarding the paroxysm. When the urine seems to be lacking in the solids I have found the administration of ergot to decrease the solids; possibly by the increased blood pressure it induces. Potassium salts act unfavorably as a rule.

For the relief of the paroxysms the coal-tar anodynes frequently produce amelioration of the symptoms; when tolerance to them is established it is useless to increase

the dose very much. Sixty grains of antipyrine has failed to give relief. Morphine has to be resorted to in many patients, but it should not be given in large doses, on account of its checking the renal secretion, and I am convinced that it prolongs the paroxysm; frequently the administration of morphine produces almost complete anuria. Small doses lessen the sensibility of the sensorium without impairing renal function, and can be given.

A powerful measure to abort an attack is a steam bath. Under its influence the integumentary capillaries dilate, and the overstimulated heart, finding diminished blood pressure, beats tumultuously. A weak patient can not stand this powerful procedure, for during the bath the headache is very much aggravated.

Acids administered frequently do good, even if the explanation offered by Haig is not correct.

In conclusion, we must admit that often we stand at the bedside of a suffering woman, powerless to do very much, and fearing that what remedies might be used would probably only prolong the paroxysm.

REFERENCES.

- ^a Eulenberg—Ziemen's Cyclopedia.
- ^b Liveing—Quoted by Gowers.
- ^c Haig—Uric Acid in the Causation of Disease.
- ^d Bouchard—Auto-Intoxication in Disease.
- ^e Rachford—Medical Record, 1892.
- ^f Hirschler—Wien. Med. Wochenschrift, March 2, 1893.
- ^g Smith—Gaillard's Medical Journal, March, 1893.
- ^h Claus—Year-Book of Treatment, 1895.
- ⁱ Saunders—Medical Mirror, August, 1897.
- ^j Von Jaksch—Pathologie.
- ^k Brown—Universal Medical Annual.
- ^l Brown-Sequard—Universal Medical Annual.
- ^m Brennet—Jour. de Med. de Bordeaux, March 2, 1893.
- ⁿ Brunet—Rev. de Med., December, 1892.
- ^o Westphal—Medical Week.
- ^p Herter—Medical Week, November 20, 1896.
- ^q Mittendorf—Trans. Amer. Ophthalmological Society, 1895.
- ^r Snow—Medical News, July 10, 1897.
- ^s Gowers—Diseases of the Nervous System.
- ^t La Tourette—Medical Week, July 17, 1896.

[1635 South Grand Avenue]