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by

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Of the whole group of nervous diseases there is no other so widely spread in time and space as epilepsy. During the early stages of civilization the disease was connected with many superstitions. The first statement that epilepsy was not a "sacred disease" but rather a disorder which was due to natural causes, was made by Hippocrates. The universal incidence of this disease is shown by the reports of the present time. Davenport,[22] in 1923, estimated that almost 500,000 individuals in this country alone were subject to epilepsy.

Perhaps the most promising progress since the time of Hippocrates concerns the conception, now well established, that the term epilepsy does not describe a disease entity but rather a syndrome of symptoms, the chief phenomenon being the convulsion. In the past, many attempts have been made to explain epilepsy as the result of intoxications, infections, functional disturbances, irritations, injuries and other irregularities. As knowledge increases, however, it gradually becomes evident that no single one of these conditions is universally responsible for the production of epileptic seizures, but that any one of them may play some part in a given case. The therapeutic measures which have proved of value up to the present are few. Those which stand out are: diet, drugs, principally sedatives, brain surgery in a few cases, and the establishment of suitable physical, social and mental hygiene.

Fay,[1] in working out a rational means of treatment, utilized many important observations of the physiologist, biochemist and neuropathologist. He found that one of the most common factors or findings was the accumulation of subarachnoid fluid and cortical edema. In his experience as a neurosurgeon, he has noted the milky appearance of the arachnoid in convulsive states. Alexander, in

a treatise on epilepsy in 1889, called attention to the glossy appearance of the arachnoid and collections of subarachnoid fluid. Dandy[3] has emphasized these collections of fluid and the edematous milky appearance of the arachnoid. Dandy[4] has also shown, in his work on introduction of air into the ventricles and subarachnoid spaces, that a large number of so called "essential" epileptics were found to show an increase above the normal in the subarachnoid spaces especially over the fronto-parietal area. In Fay's [5] experience covering 59 cases of encephalography, a characteristic picture was obtained in patients showing convulsive seizures. Air is seen in greater amounts especially over the frontal and parietal areas; the convolutions appear small, the sulci deep, and the distance between the brain surface and the skull is distinct and may approach one centimeter in some cases. The frontal pole is shrunken and much air is seen between the brain and frontal bone shadow. A fairly large collection of air is usually present around the pacchionian bodies, especially the middle pair situated at the vertex and directly over the upper motor area. Fay believes that the dilatation of the lateral ventricles depends somewhat on the duration of the symptoms, and show more definite enlargement if the attacks began early in life or have persisted for some time.

According to Fay there is a possibility that a chronic form of cerebrospinal fluid pressure due to excessive accumulation of fluid over the cortex (external hydrocephalus), finally by back-pressure along the subarachnoid spaces and pathways may eventually produce pressure to an equal degree upon the ventricles. It seems probable that the soft tissues of the brain, caught between long standing attacks of such pressure, might undergo atrophy as noted above, either due to the direct influence of the pressure or the

secondary effects of this pressure upon the small capillaries whose resistance to the slight compressing force would be less than that of the larger vessels.

According to the above, it would be expected that the recorded spinal fluid pressure of epileptics would be higher than normal. Patterson and Levi[6] have shown an average pressure of 13.9 mm of mercury in a series of 50 epileptics (8 mm of mercury being normal). In a few cases in which the seizures were severe in character, they were able to perform lumbar punctures during the convulsions. In these cases the pressure was increased. In one, the pressure rose from 25 to 50 mm of mercury. Fay's observations give an average of 11.2 mm of mercury.

Fay believes that the basis for this increased pressure is in the dysfunction of the pacchionian bodies. He bases his opinion to a large extent on the observations of Weed and Winkelman. Weed[7] describes his method of demonstrating cerebrospinal fluid pathways after the injection of particles of matter and the mechanism of absorption of spinal fluid as follows: "These granules, representing the foreign solution, were found within the mesothelial cells covering the villi (subarachnoid) and the endothelial cells lining the venous sinuses, as well as within the lumen of the venous sinus, thus demonstrating the essential pathway of the absorption. In no other place was there evidence of direct passage thru a cell membrane, as in the villi. The mechanism of passage of this fluid seemed to be a process of filtration from a point of higher pressure (subarachnoid space) to a point of lower pressure ( venous sinus) though factors of osmosis and diffusion were not excluded." The villi to which he refers are defined by him: "The arachnoid villi are normal structures; the great enlargement of these in adult life results in the formation of the well known pacchionian

granulations." In summing up the question of absorption of spinal fluid, Weed states: "Thus it seems fair to assume that the absorption of the cerebro-spinal fluid is a two fold process, being chiefly a rapid drainage into the great dural sinuses, and in small part a slow indirect escape into the true lymphatic vessels."

Winkelman[8] made a study of 150 brains of normal as well as of arteriosclerotic and senile patients. Brains from chronic epileptics, traumatic, and eclamptic patients were studied histopathologically. He has demonstrated acute changes associated with infections or toxic processes; subacute and chronic manifestations have also been found. Arachnoid villi were demonstrated filled with debris from a former cerebral insult, or loaded with blood pigment following subarachnoid hemorrhage ( the source of it being either adjacent of distant) and in various stages of sclerosis and calcification. In some chronic cases of epilepsy, there has been a failure to develop these pacchionian granules and a search for other subarachnoid villi has shown extremely few, small and poorly developed cell clusters to take over the function in the absence of the normal major outlets for cerebrospinal fluid. It has been shown that red blood cells floating free in the subarachnoid fluid spaces, apparently gravitate to the vertex about the pacchionian bodies even though the source of hemorrhage be at a distance. The sections of Winkelman have shown their presence within the bodies themselves and Fay brings out the point that numbers of these cells, blocking the filters, with the subsequent cell reaction to their presence, might be the actual mechanism of the acute pressure symptoms seen so frequently following intracranial injuries, or post-operatively where hemorrhage has occured into the subarachnoid space. The reaction to hemorrhage and the abnormal presence of red blood cells in the tissues throughout the body,

is followed by organization with fibrous tissue formation, and later, sclerosis with contracture and scar formation. He believes that the sclerosis noted within the subarachnoid villi under pathological conditions may well be the result of this factor, and mentions the fact that the mechanism of labor itself presents the first possibility of cerebral trauma in the new born. Sharpe[9] holds the view that this unrecognized hemorrhage at birth may be responsible for the occurrence of the so-called "idiopathic" epilepsies in later life. Concerning the involvement of these pacchionian bodies and the possibility of compensation Fay says: "It is my opinion that in the many possible degrees of involvement of these arachnoid structures by pathological processes may lie the reason for the great variability in frequency of attacks, period of onset and types of cases presenting the major form of the convulsive state. The disappearance of attacks in some cases occuring in early life (adolescent period) may be ascribed to further development of these structures with later compensation. As these pacchionian bodies are multiple (usually three pairs) the threshhold of compensation would vary, depending upon whether one or more of the system was involved in the process, or whether the function of all was slightly, moderately or seriously distrubed. Thus compensation by the remaining intact cells might be great or very slight and the latitude for fluid intake in the individual, without producing symptoms, would vary accordingly."

In expounding his theory, Fay next points out the results of excessive fluid intake; the observations of numerous physiologists. Rowntree[10] introduced water by stomach tube into dogs in large quantities ( 50 c.c., per kilogram of body weight) every half hour. Within four to eight hours there occured, in these animals, nausea, vomiting, convulsions of a cortical type and coma. This procedure was associated with a rise of intra-cranial pressure

and distinct edema of the brain at necropsy. Weed and McKibben[11] demonstrated marked alterations of the brains' bulk in animals in which from 35 to 100 c.c., of distilled water had been introduced intravenously. Marked swelling of the brain was demonstrated in from 36 to 81 minutes. Kubie[12] has found by introducing large quantities of fluid by stomach tube, that convulsions occured and has demonstrated marked changes in the brain bulk in those animals where no relief of pressure was undertaken. If, however, a puncture of the subarachnoid space was made on the animal during the period of fluid administration and continuous free drainage of the spinal fluid permitted, no convulsive seizures resulted and there was no alteration in brain bulk.

Fay calls the dysfunction of the pacchionian bodies with the consequent subarachnoid edema the predisposing factor in epilepsy. In going further into the theory, he considers the vascular disturbances. He mentions the clinical evidence noted in the onset of an attack; pallor, loss of consciousness, and sweating similar to syncope as showing distinct signs of circulatory disturbance.

Kennedy and others have noted the appearance of cerebral anemia followed by intense venous engorgement occuring in the exposed motor area of an epileptic. Lennox and Cobb[14] give the following changes as a possible factor: "We might assume in the induction of a fit some physiological mechanism as the following. Contraction of cerebral vessels might lead to a decrease in oxygen supply to the brain. Because of the anoxemia there would be dilatation of the capillaries with passage of fluids outward through their walls. One or more of these factors, decreased oxygen tension, edema, increased intracranial pressure, might lead to abnormalities in the activity of cortical neurones and a fit."

Landis[15] pointed out that in the presence of anoxemia fluid passes through the capillary walls at four times the normal rate.

This circulatory disturbance Fay calls the Precipitating factor. In summary he says, "It seems reasonable to accept, therefore, a disturbance of circulatory function occuring just prior to an attack. It may be considered as the precipitating factor. That cerebral anemia and anoxemia are insufficient in themselves to bring about a convulsive response is evident, else we would find this symptom associated with almost every case of death by natural causes. If,however, we combine what I have termed the predisposing factor (subarachnoid edema) with the precipitating factor (circulatory disturbance, cerebral anemia and anoxemai), we may reasonably assume that certain conditions will result."

Based on the above conception of the factors concerned in epilepsy a program of dehydration was devised for the patient with chronic epilepsy and a series of observations was begun in June, 1927. Fay says, "The application of the principle of this theory is therefore possible throughout the convulsive state and results should be obtained, if this theory is tenable, in proportion as it is possible to regulate cerebrospinal fluid production to a point equal to or below the threshhold for compensation of the absorptive mechanism."

The method employed requires from three to six weeks or longer to establish a basis for fluid balance and to accomplish the desired dehydration. This necessitates hospitalization under careful check and observation, as the accurate determination of the intake and output as well as supervision of the diet cannot at once be left to the patient, no matter, how co-operative he is. The patients are first observed for a number of days to determine the

quantity of liquids consumed normally in their routine life. Water, tea, coffee, milk, soup, fruit juices, soft drinks, ice cream, ices, etc., are carefully measured, charted and totaled each day. The total urinary output is also carefully collected and measured. During this period the usual diet is continued. The average water represented in the diet can be computed using the estimations of Sodestrom and Dubois[16]. The character, duration and frequency of the attacks are, of course, recorded.

An encephalogram is then made, or if previously obtained, the patient is given an initial start on dehydration by administering one and one-half ounces of magnesium sulphate crystals in water by mouth. This dose is repeated every other motning for three consecutive doses. At the same time the patient is placed on a carefully measured liquid intake, eight ounces (240 c.c.,) to twenty ounces (600 c.c.,) per 24 hours. The urine is collected and measured as usual. The variety of liquids given may be apportioned in any way that the patient desires as long as the total fluid intake does not exceed eight to twenty ounces in 24 hours. In selecting the water intake level, one must be guided by the severity of the case and frequency of attacks. Later in the treatment, the intake may be increased or diminished as the patients symptoms indicate and their true level of fluid tolerance determined.

This degree of fluid limitation is followed by some discomfort on the part of the patient for the first ten days, but in all cases where this initial period has been assomplished, they have maintained the restriction of fluids without difficulty and with no ill effects. It must be born in mind that: unless absolute fluid regulation is maintained, little or no results can be expected.

During the first few days of fluid limitation at this low level it is interesting to note the high output of urine in contrast

to the intake. The accumulation of body fluids in excess, from former free intake of fluids, persists for about six days. Following this, there may be a drop in volume of urine passed to below the intake level; again a sharp rise above the intake point with fluctuations for several weeks may occur. It will be found after several weeks, the diet content remaining constant, that a level is reached which so closely corresponds between liquid intake and urinary output that it may not vary more than 20 c.c., The patients are, of course, on a low salt diet and the control of the carbohydrates is limited to sweets. Starches are permitted to avoid acidosis. The patients are taught to measure their own intake and output but are checked by the nurse until they show that they are capable and co-operative. It is of interest to note that there hase never been any pathological urinary findings due to the dehydration except, of course, high specific gravity.

As early as September, 1927, Fay was able to demonstrate that severe dehydration caused disappearance of the grand mal phase of the attacks leaving focal attacks without the loss of consciousness and relieving the postepileptic manifestations of stupor, sleep and mental torpor. With the forcing of fluids, the grand mal phase was promptly reinstated, and the frequency and severity of the attacks was as great as formerly; the dehydration again bringing forth only the petit mal manifestations.

The reports of two and one-half years of dehydration on various types of epileptics, 22 in number, indicates that the results have been obtained in proportion to the co-operation and efforts of the patient. In all except the mentally defective group or those with gross organic lesions, control or great modification of the major seizures has been possible. This has not been true entirely of the petit mal seizures, which in some patients persisted in spite

of the most rigorous dehydration and demonstrated co-operation.

The following chart gives an idea of the results obtained in the 22 cases of this series:

| Patient Number | Co-operation | Period of dehydration | Average Grand Mal Seizures per Month | |
|---|---|---|---|---|
| | | | Before treatment | After treatment |
| 1 | Excellent | 30 Months | 19-25 | .1 |
| 2 | Fair | 30 " | 1-4 | .3 |
| 3 | Good | 27 " | 12-20 | .14 |
| 4 | Excellent | 26 " | 18-20 | 0 |
| 5 | Fair | 24 " | 2-3 | .25 |
| 6 | Excellent | 22 " | 1 | 0 |
| 7 M. Def. | None | 21 " | 200-800 Petit | 10-100 Petit |
| 8 | Good | 15 " | 7-9 | .07 |
| 9 | ?? | 16 " ? | 30-60 | ? |
| 10 | Excellent | 15 " | 1 | .6 |
| 11 | Fair | 13 " | 1-4 | .5 |
| 12 | Poor | 12 " | 100-150 | 9-15 |
| 13 M.Def. | Poor | 12 " | 10-12 | 1-3 |
| 14 | Excellent | 9 " | 1-4 | .6 |
| 15 | Excellent | 7 " | 4 Grand 150 Petit | 4 Grand 20-30 Petit |
| 16 | Good | 7 " | .18 | 0 |
| 17 | Good | 6 " | .5 | 0 |
| 18 | Good | 6 " | 10-30 | .3 |
| 19 | Good | 6 " | 15-20 Petit | 1 Grand |
| 20 M.Def. | Poor | 6 " | 2 | 1 |
| 21 M.Def. | None | 1½ " | 20-30 | 10-20 |
| 22 M.Def. | None | 1 " | 3-7 | 3-7 |

The clinical confirmation of this method or treatment has been done mostly with children. Bauer[17] pointed out that of 25 infants maintained on a ketogenic diet, he had obtained symptomatic relief in approximately 35 %. When these same infants were placed on fluid limitation and dehydration for one year he was able to establish 100% symptomatic relief in his group. His series included 50 cases in all, ranging from the very severe to the milder types. Only the severe cases, those having three or more seizures a day, were put on a starvation period. These were given a fluid intake of 40 ounces the first day, including milk and water, aside from what was contained in two plates of

cereal administered daily. Bran bread and butter, zweiback and Holland rusks were permitted. Salad and lemon were given once daily. The fluid intake was cut down the second day to 32 ounces, the third day to 24 ounces, the fourth day to 16 ounces. Cascara kept the bowels open and fairly loose. When the attacks were reduced, additional food was given in the form of green vegetables and potato, with a further reduction in the fluid intake that more than compensated for the fluids in the articles of diet that had been added.

In twenty cases of children that had been having from three to sixteen attacks daily, the attacks disappeared completely in from five to twelve days. The highest amount of fluid allowed daily upon cessation of symptoms was twenty-four ounces and the lowest, six ounces. These children rapidly lost weight. They were more mentally alert, however, and played more good-naturedly and wholeheartedly than they did before treatment was instituted. Bauer has found that by keeping these children from 6 to 8 % underweight, they gett all the food necessary to satisfy their hunger, they are sufficiently well fed to be active and alert, and are free from attacks.

Of the entire 50 cases, 25 were still under observation after one full year and still free from attacks. The other 25 have passed from observation after a period of from 3 to 9 months of freedom from attacks. In a later report[18] he mentions that he had observed 86-88 cases, with similar results. He says in conclusion, "I am convinced that the use of the ketogenic diet is incomplete, both in its hypothesis and in its execution as a relief for epilepsy. The ketogenic diet is cumbersome, burdensome and necessitates altogether too much discomfort for the amount of good that follows its use. The limitation of the diet and fluid intake at the same

time affords the easiest and most complete relief from unhappy symptoms and attacks".

Some very interesting results were also reported by McQuarrie[19] who observed frequency and severity of convulsions and the occurence of other symptoms in epileptic children when they were placed on different levels of water intake. He says concerning this treatment, "The method which we have found go be most suitable for the routine management of the epileptic child differs from the ketogenic dietary regimen already in vogue in that emphasis is placed primarily on the establishment of water balance at a much reduced level. We believe that the effectiveness of fasting and the ketogenic diet is due not so much to the presence of ketosis per se as to the associated dehydrating effect".

Palmer[20] reports a case of traumatic epilepsy which responded well to dehydration and ketogenic diet. His case indicates that the control of convulsions rests largely on the variation of fluid intake. Eight hundred cubic centimeters was set as a maximum total fluid intake and in the weeks in which there were no convulsions it was considerably below this figure. The days in which two convulsions occurred are those in which the maximum fluid allowances was consumed. Palmer says in commenting, "The method described here has been of value in treating a group of severe traumatic epilepsies in the neurologic clinic of the Pennsylvania Hospital. These cases have shown comparable results, but detailed records are not available".

----SUMMARY----

The theory of the dehydration treatment as presented is based upon sound physiology, chemistry, physics, and the observations of a large number of men who are outstanding in their fields. The results obtained to date have been very encouraging. In the series.

of cases studied, where definite co-operation was obtained and a fluid balance effected 94% have shown definite improvement. Bauer[18] believes that the best result will occur in children. He points out that we are apt, then, to have results that will perhaps save these individuals from a certain degree of mental deterioration and gross brain pathology.

It must be remembered that there has been a return of the major seizures whenever indiscretions or storage of fluid has occured indicating that no permanent benefit can be expected from this method. At best it is a rational control of the major attacks and many place epilepsy in the same category as diabetes mellitus in which symptomatic relief is possible as long as the patient adheres to the proper routine.

Spiller[18] in discussing this work says, "Doctor Fay has been a pioneer on this question of dehydration and regulation of the balance between intake and output and in a recent J.A.M.A.[23], he has received merited praise in an editorial that represents suitably the credit that is due him."

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