KETOSIS AND EPILEPSY

A Thesis For The Degree of M.D. of Glasgow University

Presented by

Samuel Miller Allan M.B., Ch.B., D.P.M.

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

Introduction

Therapeutics has made many advances in recent years but the treatment of epilepsy to a great extent has remained stationary. Few conditions are treated in so many ways, a sure sign that cure is as far off as ever. Yet epilepsy is so distressing and so incapacitating that one wonders why it has been neglected so long. Most textbooks stop short at citing a number of sedative drugs, that have proved useful. Little attempt has been made to enrol the patients' own help in curtailing the seizures and ameliorating the subsequent debility. That much can be done by judicious advice and interest is evident to anyone who has studied the results of investigators. The patients are always eager to embrace new remedies and try out even the most heroic measures, and in this disease success or failure is at once revealed. No doubt faith in cure is of great importance and the physician should never neglect his function of healer, but to prove to a patient that salvation may lie in his own efforts is to solve half the problem in epilepsy. In recent years new avenues of approach to this subject have been opened up, investigation and experiment have been stimulated and especially in young patients definite hopes of cure have been held out. The most recent work has been in metabolism, where experiment has shown that a condition of acidosis is antagonistic to epilep-

tic seizures. The Ketogenic diet is one designed to produce acidosis artificially, this being achieved by reducing the carbohydrates and greatly increasing the fats.

This thesis is an investigation into the effects of Ketosis in epileptic patients. For hundreds of years it had been known that fasting had a beneficial influence on epileptics, reducing the number of convulsions and ameliorating the mental depression and anguish. This effect of fasting was attributed to so many things that not till recent years was a careful enquiry made. In 1921 wilder (1) maintained that the ketosis invariably associated with fasting was the factor responsible for the good results in epilepsy. However, since many diseases are favourably influenced by fasting much more was needed than a mere statement to prove that the ketosis was responsible. This led to patients being treated theapeutically in order to produce an artificial ketosis, a ketosis not dependent on the amount of food consumed. Consequently workers in the Mayo Clinic started a system of dieting in epileptic adults that had the production of ketosis as its object. The results were indifferent but in 1922 Helmholtz (2) treated children in this manner and found that 31% were free from attacks and 23% benefited. The remaining 46% were not improved. Later on, in 1924, the Mayo Clinic again started the treatment of 'selected' cases in adults with more encouraging results than the first trial.

The present investigation is on twenty cases of idiopathic epilepsy, that is, epilepsy in which there is no apparent organic lesion. The patients have not been selected because of preconceived ideas of their likelihood to react well, but with the view of testing the diet on all types of major epilepsy. Care has been taken to have representative cases. Thus some have many fits, others few, some are bright and cheery, others are dull & demented. Many of the cases have violent bouts of excitement.

History

Epilepsy was one of the earliest diseases described, no doubt on account of its dramatic effects and the violence of its visitation. In early historic times epileptic patients were said to be possessed of devils and spirits. They were exorcised and shunned, and at times led terrible lives. Hippocrates, almost alone, recognised that this disease was of the brain and not of the 'spirit'. He described it accurately and pronounced opinions on prognosis that read like the dicta of present day alienists. After Hippocrates, medical science was not advanced much, so great was superstition and so dreadful the visitation on the agnostic and the unbeliever. The Middle Ages were the dark ages, and the insane and epileptic were regarded either as saints or demons. There was much speculation on the nature of disease, little genuine work. Facts were not recorded so consistently and so accurately as today, with the result that modern times were reached before true investigations were made into the subject of epilepsy.

In 1870 Fritsch & Hitzig (3) stimulated the cortex. This led to the cortical theory strongly held by Hughlings Jackson (4) & Gowers, who maintained that the convulsion was due to over excitement of the motor area. This excitement might begin in a 'sensory' area (resulting in the aura) and become so intense

that it spreads in all directions, reaches the motor area, and so causes a generalised convulsion. Today however the conception of cortical function is far removed from the simplicity of Jackson's time, although that neurologist also suggested that convulsions might be release phenomena. Recent work has tended more and more to show that the nervous system is made up of masses of co-ordinating centres where excitation and inhibition go on side by side; these centres corelate but cannot be said to initiate, impulses. Thus it is held today by leading neurologists that the mapping of the cortex into motor, sensory, visual and auditory areas is a quite arbitrary arrangement, and that no collection of neurones can be said to be the "centre" for one particular function. Thus, whether the physiological mechanism of the fit is due to over excitation or the removal of inhibition is still an open question.

There have been many theories on the other hand as to the pathology and pathogenesis of epilepsy. To say that a fit is the result of over excitation of the motor cortical cells is not to explain the reason for the over excitation. Therefore a great deal of speculation and as much research has been directed to this problem. It is clear that three factors must be considered; first organic abnormalities of the brain, second functional abnormalities of motor cells increasing convulsions, third abnormalities elsewhere.

No two investigators agree on the pathological findings in epilepsy. According to Munson (5) the brain weight in epileptics is less than normal, except in those surviving beyond 25 years. Others notably Ganler (1922) (6) & Lind (1926) (7) reported that epileptic brains were on the average heavier than brains from idiots and feeble-minded, which seems to suggest that but for the convulsive habit the unfortunate victim of fits would have a fairly normal brain capacity. The gross lesions found post mortem are legion with regard to numbers. Thom & Southend (8) (1915) found brain lesions in 63%, Munson 34%, Gregory 89%. The lesions found are numerous but no one type has a decided predominance. At the Craig Colony post mortem observations were carried out on 718 epileptics, when the following were the findings.

Table I.

Dura - evidence of inflammation	12%
Arachnoid - evidence of inflammation	10%
Subarachnoid hydrops	13%
Brain - cerebral sclerosis	14%
Hemiatrophy	10%
Softening	13%
Tumors	2%
Porencephaly	2%
Arteriosclerosis	6%
Hemorrhage	8%
Edema	27%
Gumma	0.3%
Ventricles - assymetry	3%
Dilatation	12%
Choroid plexus - cystic	3%
Sella turcica - abnormality	9%

Lind (9) in Australia on 259 cases had somewhat similar findings, except that in 52% he discovered dilatation of the ventricles. Dandy (10), at operation, confirmed this, with the addition that the subarachnoid spaces were dilated and overlay small soft convolutions. These facts are interesting since in uraemia there is oedema of brain tissue accompanied by convulsions. The difficulty is to decide whether the dilation of ventricles, and subarachnoid spaces together with oedema are the cause or the result of epilepsy. This also applies to the areas of sclerosis so often found especially in Ammon's horn. Many observers point to this part of the brain as the seat of the lesion in epilepsy. Reviewing the literature on the subject Lennox & Cobb (11) remark that "no specific lesion of the nervous system in epilepsy has been demonstrated."

First of all the epileptic is considered to have motor neurones that are unstable and easily irritated, so that comparatively slight stimuli are sufficient to cause widespread muscular action. This is truly an academic theory, and does not attempt to explain this instability, further than to say that patients of the convulsive habit have an epileptic diathesis. Facts are brought forward as substantiation: epilepsy is hereditary in 10% - 16%. Brain (12) found a family history of convulsions in 28% of 200 patients as opposed to 10% of a control series.

Burr (1922) (13) & Myerson (1925) (14) decided that a hereditary factor is not important. During the war 5% of cases having gunshot wounds of the head developed epilepsy. Throughout the combatant countries this percentage remained remarkably constant, which is given as evidence that that number have a predisposition to convulsions.

However there may be conditions in and around the cells that contribute something to the convulsive habit. For instance it is known that a poor oxygen supply to the motor cells may cause fits. If an epileptic is made to over ventilate his lungs by long regular expiratory breathing he is likely to have a fit. If however he is made to breathe oxygen rich air he does not have one. A convulsant drug (strychnine) fails to produce seizures in guinea pigs if the pigs are placed in an oxygen atmosphere. At the present time it is impossible to measure the oxygen consumption of nerve cells so that in the meantime it remains a speculation of great value.

Another factor that influences the activities of living cells is the pH of the fluids in its vicinity; but it is difficult to ascertain the pH of brain tissue. The blood pH is no guide to the concentration in the tissues. Below something will be said of pH in relation to the ketogenic diet.

Another factor that might have an influence on the function of the nerve cells is the degree of permeability of the cell membrane. As has been already stated, in uraemic convulsions the brain substance is moist and oedematous. In general paralysis of the insane oedema and abnormally large amounts of C.S.F. are almost constant features, and more so in those having seizures before death. In fact in mental Hospitals one has learned to diagnose G.P.I. merely by looking at the wasted oedematous brain. Oedema etc. is closely related to blood supply. It has been observed at operation that a widespread constriction of arterioles precedes the onset of a convulsive fit, while in animals it has also been seen when producing artificial fits with strychnine. It must also be noticed that nearly all methods that tend to produce seizures cause constriction of pial vessels e.g. stimulation of cervical sympathetic, injection of adrenalin and pituitrin and use of hyperpnoea. Antagonists to convulsions produce in the main dilatation. Thus vagus stimulation, amyl nitrate inhalation, and CO_2 inhalation, and intravenous injection of acetone have this effect.

Modern work has been directed a great deal along the lines indicated above. It is obvious that the motor cells in epilepsy must play some part whether passive or active but whether they

are activated chemically through the blood stream and by increased permeability of their membranes or by something inherent in themselves, has not yet been decided.

If the view is adopted that the nervous tissue is acted on from without then what evidence is there of abnormality in other systems of the body that might possibly alter nervous stability and action?

It has been already noticed that in convulsions constriction of arterioles occurs. How is this constriction brought about? Until the last few years it was denied that the cerebral vessels were under vasomotor control. However it has been proved beyond question by a large number of investigators, including Forbes and Wolff and Weber, that cerebral vessels do possess a nervous mechanism and that this mechanism is under autonomic control. The vessels are supplied through the cervical sympathetics. The cerebral vessels contract after stimulation of the cervical sympathetics, they dilate after stimulation of the vagus. Histologically nerve fibres have been demonstrated on the cerebral vessels (Stohr) 1922 (15). Moreover as corroborative evidence pial vessels contract on the administration of adrenalin which has a selective action on autonomic nerves. Thus it would seem that the cervical

sympathetics play an important role in causing convulsion. This is one of the most fruitful fields for research in epilepsy. Many investigators notably Bojovitch (1925) (16), Hirsch & others (1927) (17) have removed the cervical sympathetic chains in epileptics with a view to cure. Encouraging results were obtained in a fair number of cases, although it would be too much to hope that removal of one apparent cause should be a complete cure. The autonomic system is greatly complicated and the cervical chains are not the sole activators of these peripheral nerves. For example adrenalin can cause vasoconstriction when applied locally. It may be that endocrine gland substances acting through the autonomic system produce the conditions necessary for convulsions, and that either may still be potent when the other is removed. A point of great significance is that vasodilators are in the main anti convulsants, e.g. amyl nitrite, and belladonna.

There are a great many facts collected in support of the theory that the sympathetic nervous system is abnormal in the epileptic, facts pointing to dysfunction in other parts of the body. For example Tracy (18) describes white spots or areas of cutaneous vasoconstriction. According to him all epileptics possess these white spots. Dermographic reactions of the skin

have also been described, while Bolton (19) believes that the oedema in a variety of conditions resembling epilepsy is due to vasomoter disturbances. Other manifestations such as cyanotic extremities excessive sweating, and excessive lachrymation have been noted by the author.

In the gastro intestinal tract there are no lesions that can be regarded as peculiar to epilepsy. Most patients are constipated but that is the rule more or less in the ordinary population, so that although there may be some truth in the theory of autointoxication no such toxin has ever been isolated.

The glands of internal secretion have long been suspected of playing a major role in the production of convulsions. These glands are closely related to the autonomic nervous system. There is little evidence that the thyroid gland is involved. Fischer (20), Cobb and others have removed the thyroid in rabbits and discovered that convulsions are more easily produced by convulsants. There is not a great deal of corroborative evidence that hypofunction of the thyroid is associated with epilepsy, although a small percentage of patients show a decreased metabolic rate. When however the rate is raised to normal or above there is no decrease in the number of seizures. Hyperfunction as a rule is less associated with epilepsy

than hypofunction, and the incidence of epilepsy in exophthalmic goitre is rare. The parathyroid glands, closely associated anatomically with the thyroid, are of course at fault in tetany, a condition much resembling epilepsy. It has been found by Collip (1926) (21) that the factors influencing the production of tetany are also potent in producing seizures in epileptics. They are (1) tissue anoxaemia, (2) disturbance in ionic equilibrium and (3) pH. These factors increase nerve irritability which is found both in tetany and epilepsy. Certain of the conditions improving tetany such as administration of acid forming salts and breathing of CO_2 may also favourably influence generalised convulsions. Post mortem however little evidence of pathological change has been found in the parathyroid glands.

The adrenal glands owing to their close association with the autonomic nervous mechanism are held to have some influence in producing seizures. Benedek (22) injected adrenalin (1-1.5 cc) in a number of epileptics and found convulsions produced in about 40%. Others have found similar results. However Freedman & Lennox (23) tried this in 70 epileptics and produced a seizure in one only. The author, over a period of some months injected similar amounts of adrenalin (for another purpose altogether)

into over 200 epileptics and found seizures produced in 3 cases only. The Fischers (24) in 1914 removed the adrenals in rabbits and failed to produce seizures by the inhalation of 15 drops of amyl nitrite, although 12 drops had been sufficient before the operation. They also discovered a lack of chromaffin staining material in intact rabbits that had been convulsed by 8-12 drops of amyl nitrite.

These observations induced a number of surgeons to remove one gland in epileptics. Some produced favourable results (Sandersen 4 cases) while a greater number had negative results. The operation is not now recommended. However even if the adrenal glands are at fault in epilepsy it is by no means certain that removal of one will result in cure. The wrong gland for instance may be removed, and the one left may be quite sufficient to maintain the abnormal excitability. These experiments or operations do not negative the opinion that over activity of the adrenal glands is a potent factor in epilepsy.

However there is a sign in disease of the adrenals that the author has found in 80% of epileptics, namely areas of brown pigmentation scattered over the body. This of course is one of the cardinal features of Addison's disease a condition undoubtedly

due to disease of the adrenal glands. According to Halle (26) this bronzing is due to an increase of melanin, the normal pigment. Melanin is formed from tyrosine which is also held to be the precurser of adrenalin. Thus an increase of melanin may be due to at least 2 factors: (1) The adrenal glands may not be able to convert the normal amounts of tyrosine into adrenalin (as in Addison's disease) (2) Tyrosine itself may be greatly increased in the tissues giving an increase not only of melanin but of adrenalin. At any rate this question of bronzing is of very great interest, especially as no more than 25% of the ordinary population exhibit such areas.

On the whole the evidence relating to adrenal gland abnormality is conflicting so that until more is known of their true physiological significance it is difficult to assess the various reports. There can be no doubt however that just before and during convulsions the adrenal glands are very active, but whether this is cause or effect is a moot point.

There is very little in the literature concerning the part played by the pituitary and the thymus in the production of seizures but many authors maintain that in the female the activity of the gonads influence seizures. Many epileptic

women during pregnancy have no fits, while a great many have convulsions coinciding with the menstrual periods. It should be borne in mind here that the adrenal glands and the gonads are closely related embryologically. Unfortunately the evidence in females has not been well collected and systematically tabulated. There is no question that among the lay public menstruation is greatly blamed for the epileptic fit and one must remember that tradition is often fairly accurate.

In epilepsy glandular therapy has not met with success. A few cases here and there are claimed to be cured but when the impartial observer treats a large number of patients he finds no support for an optimistic outlook. Glandular therapy however is in its infancy and not many years ago it was despaired of influencing diabetes by extracts of the pancreas. Addison's disease at present does not respond to adrenal gland treatment but this does not negative the belief that the adrenals are at fault. The glands of internal secretion probably play an important part in the production of seizures.

The blood and cerebro spinal fluid in epileptics have received much attention but no consistent abnormalities are found. Some maintain that 50% of epileptics show abnormality of the cerebro

spinal fluid, but the author has had access to C.S.F. reports at this hospital (Whittingham) extending over eleven years and has found no such evidence. However during severe epileptic fits and nearly always in epileptic furor, greatly increased pressure of fluid is found. Withdrawal of 20 ccs greatly ameliorates the attack in most patients. In status epilepticus the removal of C.S.F. has such beneficial effect that it is now a routine procedure in treatment. There may however be a vicious circle at work here, and the increased pressure may merely be an accompaniment of the seizure.

By examination no abnormal ingredient is consistently present in the urine of epileptics, neither are any of the normal constituents greatly increased or reduced, with the possible exception of ammonia. According to Bisgaard (27) and others the ammonia is increased in the urine in epileptics but bears no direct relation to seizures. They have worked this out on a formula supplied by Hasselbalch (28) who stated that in healthy subjects the ratio of ammonia nitrogen to the total nitrogen of the urine, if plotted against the pH of the urine gives a fairly constant value. This work has focussed attention on acid-base equilibrium. Many workers have given data on pH values in the

blood of epileptics and it is now accepted more or less that although there is no persistent and consistent abnormal equilibrium there is an unusual degree of fluctuation in pH values between normal limits from day to day with a tendency to approach a more alkaline reaction.

The rationale of the Ketogenic diet is based on the foregoing observations. It is an attempt to upset the acid-base relations in the patient by giving a bias towards acidity. Apart from independent observations on the subject conducted in a pure spirit of enquiry there is much empirical evidence in support of the view that acidosis is antagonistic to the convulsive habit. As stated above fasting has a favourable influence on the epileptic and has been practised therapeutically for hundreds of years. Chemically the essential changes produced are in the direction of acidosis. Breathing of CO_2 also inhibits convulsions, a condition again tending to acidosis.

There is as yet no specific treatment for epilepsy. All that can be accomplished is a reduction in the number of seizures. To this end have been used a very large number of drugs mostly of a sedative nature. In conjunction with this medication patients have also been advised as to their mode

of life, the avoidance of exciting occupations and amusements, open air living, restriction in food intake and the eschewing of various articles of diet. There can be no doubt that a quietly requlated life as free from worry as possible is eminently suitable for epileptics, but in modern times when there is great competition in making a living this is very often impossible.

With regard to drugs the most commonly employed is one or other or a combination of the bromide salts. These have been used for a very long time and have certainly proved of great value. When the chloride intake is reduced, bromides have apparently a better effect. This has been well proved by Ulrich (29) in an epileptic colony in Switzerland. He reduced the yearly number of seizures (an average) from 64 (when the patients were having bromide) to 16 when the patients were having bromide and a restricted salt intake. Probably there was also some change in the mode of life of the patients. Bromides are apt to make a patient rather dull mentally, while skin rashes are common. Arsenic often prevents the severer forms of skin rash and should always be combined with bromides.

In recent years another drug has appeared that is

much more potent in preventing seizures than the bromides. This is pheno barbital (luminal). It is a very powerful drug and is usually given in 2 grain doses. Some patients may require three such doses per day until the lowest level of seizures is reached. Gradually the drug is reduced until one dose of 2 grs or 1½ grs is sufficient to maintain the seizure at the low level. Luminal can be given hypodermically (luminal sodium) or intravenously when it is particularly valuable in status epilepticus. The dose necessary in these cases varies from four to ten grains. This, combined with withdrawal of cerebro spinal fluid, nearly always cuts the status short.

One drawback in the use of luminal is that on sudden complete cessation of the drug status is often induced. This has been noticed on a number of occasions in this hospital. Luminal therefore is a drug to be used in general practice with great caution.

Chloral, Borax, opium and many other sedatives have been used but they have no advantages over bromide and luminal and they are not much employed nowadays.

In the treatment of epilepsy much can be done by

studying each patient and giving a great deal of time to him. The epileptic is often rather simple and childish easily pleased and as easily imposed upon. He has great faith in anyone who shows him kindness and consideration and is keen to believe that a new treatment will be his salvation. In other words persuasion and suggestion are of great value and ought always to be used no matter what other form of treatment is being tried.

The Ketogenic Diet.

Dietic treatment of epilepsy is as old as medicine itself. Throughout the ages special articles of diet have been said to be potent in producing seizures. Hippocrates himself gives a list of foods that in his time were supposed to be harmful, e.g., eels, goat flesh. pig flesh, and stag; cock, turtle and bustard; mint, garlic, and onions. At the present time many physicians exclude meat; some exclude oranges, apples, celery and grapefruit. These are excluded purely on empirical grounds and there is no scientific reason why meat should be taboo. The ketogenic diet is based on the theory that acidosis or ketosis is antagonistic to seizures and since experimental work and empirical data support the contention it is worthy of being fully investigated. That is the object of this thesis. Very few observations on this subject of ketosis have been

carried out in this country so that an investigation into the claims made abroad is overdue. It will also be considered how far such a diet is practicable. It must be borne in mind that a treatment depending on self sacrifice and great self control is not easy of accomplishment so that it would appear as if institutional patients who are continually under observation are the best subjects for experiment.

The average number of fits per month of the patients chosen for the diet range from 3.4. to 29.2. All these patients have major epileptic fits. As regards mental condition eight of the patients can give a good account of themselves and are well behaved except before and after fits. Five of these eight employ themselves usefully. Six patients are of the demented class who can give little account of themselves, and who are idle and apathetic except at fitting periods. The remainder (six patients) are in a class between these two extremes, patients who although able to give a fair account of themselves, are idle and apathetic and at times violent and troublesome. The patients were more or less equally distributed between three wards so that the nursing problems could be reduced as far as possible.

Ketosis is the result of deficient metabolism of fat. Fat requires carbohydrate in the diet in sufficient amount before it can be properly combusted. In diabetes where the essential feature is a failure of carbohydrate metabolism ketosis may result if the diet contains too much fat. In diabetes ketosis is the most feared complication as apparently coma is dependent on the degree of ketosis. To produce ketosis in a normal individual the conditions present in diabetes must be produced. This is done by limiting the carbohydrate to a very low point and increasing the fat to a very high point. The diet finally shows that fat is contributing at least four times the calories derived from carbohydrate and protein combined. For an effective ketosis, at least in adults it may be necessary to raise the fat quota so that eight times as many calories are being derived from fat as from carbohydrate and protein. The degree of ketosis can be roughly measured by the intensity of the reaction given by the urine to the nitroprusside test for acetone.

The method of calculating the diet required for each patient was done according to the tables set out by Barborka who worked on the subject in the Mayo Clinic. Data was provided by the researches of Du Bois and Boothby & Sandiford. (30)

The first requirement was a diet so calculated that the patient was receiving sufficient food to provide the calories for his energy requirements and the maintenance of weight. It is not possible in the ordinary way to do this by the respiration chamber so that a rough estimation was used, giving each patient 16 calories per 1 lb of body weight (35 calories per kilogram). Diabetic diets often stop at approximately 14 calories per lb of body weight but the patients here under review were expected to keep up their ordinary activities and there was no point in giving a starvation diet. The following table represents the calory requirements of the patients under observation.

Table II

(see next page)

Table II

Name	wt.	Cs.
M. T.	155	2480
M. G.	107	1712
A. Gr.	101	1616
M. E. C.	122	1952
F. L.	112	1792
A. F.	148	2368
N. K.	90	1440
A. A.	94	1504
H. P.	114	1824
A. C.	118	1888
E. T.	122	1952
E. R.	104	1664
B. C.	112	1792
A. Ga.	132	2112
R. P.	118	1888
M. A. B.	120	1920
A. H.	105	1676
E. W.	104	1664
R. R.	124	1984
M. W.	91	1456

These calories were given to the patient in the form of carbohydrate, protein and fat. At first, however it was necessary to test the diet in order to discover whether or not the calory requirements were correct, so that for ten days a diet not ketogenic was calculated for each patient. According to Woodyatt & Wilder (31) the amount of carbohydrate in grams in the diet necessary gradually to produce ketosis is discovered by multiplying the total calories needed by factors ranging from 0.035 to 0.006. In the first diet therefore the

the carbohydrate ratio was calculated by using the greater factor. The protein requirement in grains is estimated as 1/3 of the body weight in pounds. The fat quota is obtained by multiplying the total calories required by 0.09 or 0.10. The following table shows the values in Carbohydrate Protein and Fat supplied to each patient as calculated on the foregoing plan.

Table III

Name.	C.	P.	F.
M. T.	86.8	51.3	223
M. G.	60	35.6	154
A. Gr.	56.5	33.6	145.4
M. E. C.	68.3	40.6	175.6
F. L.	62.7	37.3	161.2
A. F.	82.8	49.3	213.1
N.K.	50.4	30.0	129.6
A. A.	52.6	31.3	135.3
H. P.	63.8	38.0	164.1
A. C.	66.0	39.3	169.9
E. T.	68.3	40.6	175.6
E. R.	58.2	34.6	149.7
B. C.	62.7	37.3	161.2
A. Ga.	73.9	44	190
R. P.	66	39.3	169.4
M. A. B.	67.2	40	172.8
A. H.	58.6	35	150.8
E. W.	58.2	34.6	149.7
R. R.	69.4	41.3	178.5
M. W.	50.9	30.3	131

Since the amount of carbohydrate in the diet is very small it is considered wise to reach a true ketogenic diet

in easy stages. Therefore at least two diets are interposed between Diet I and the diet necessary to produce ketosis without fail. Thus the carbohydrate is withdrawn gradually and the patient is more willing to cooperate. In the second diet (after any necessary alterations have been made in the total calory requirements as shown by Diet I) the carbohydrate allowed is 4/7 of that in Diet I. In Diet III this amount is reduced to 3/7, and in Diet IV (the ketogenic diet used in the present series of cases) it is reduced to less than 2/7. To allow for the calories lost by the reduction in carbohydrate the fat is increased slightly.

The proportion of Carbohydrate Protein and Fat in Diet IV given to each patient is shown in the table.

Table IV.

(see next page)

Table IV

Name.	C	P.	F.
M. T.	14.8	51.3	248
M. G.	10.2	35.6	171
A. Gr.	9.696	33.6	161
M. E. C.	11.712	40.6	195
F. L.	10.752	37.3	179
A. F.	14.208	49.3	236
N. K.	8.64	30	144
A. A.	9.024	31.3	150
H. P.	10.944	38	182
A. C.	11.328	39.3	188
E. T.	11.712	40.6	195
S. R.	9.984	34.6	166
B. C.	10.752	37.3	179
A. Ga.	12.672	44	211
R. F.	11.328	39.3	188
M. A. B.	11.52	40	192
A. H.	10. 056	35	167
E. W.	9.984	34.6	166
R. B.	11.904	41.3	198
M. W.	8.736	30.3	145

For convenience in working those patients who weighed within a few pounds of each other were treated as if they were the same weight.

In calculating the quantities of the various foods the tables of Harrison & Laurence (32) were used. These tables are compiled from the work of many authors and give a good working standard. There are great difficulties in building these diets. The patients have all been used to high carbohydrate meals so that ketogenic diets are apt to be nauseating. Carbohydrate articles of diet are much more bulky than protein and fat articles

so that a meal looks very small and insufficient. At the same time small concentrated meals rarely relieve the feeling of hunger that the patient brings with her to the table. As far as possible therefore the vegetables containing small amounts of carbohydrate were used instead of the potato. Another and perhaps greater hardship is the cutting down of the bread. Bread is the staple article of diet of all the patients in this hospital, so that at meal times the ketogenic patients cast envious glances at the liberal helpings of their more fortunate friends. It was necessary of course to give all the selected patients their meals at separate tables, specially looked after by a nurse.

It was explained to all the patients capable of appreciating the points just exactly what was intended and what was expected. It has always been our experience that epileptics are easy to handle when they believe that something special is being attempted on their behalf. They will put up with many hardships and at times gladly accept the role of martyr. The other patients in the ward were warned that no food or sweets of any kind were to be given to the special patients. To guard against surreptitious eating was particularly difficult since some of the chosen epileptics had as close friends patients who

were liberally supplied with fruit sweets and extra food. However frequent examination of the urine for the detection of acetone bodies was a good check and timely warnings to suspected patients often had the desired effect. If the urine showed no acetone bodies the patient was immediately taxed with eating extra food, and it was remarkable how often a confession of guilt was received, followed by a resolution to do better in the future. On the whole the regime was well maintained, better than could have been expected. A great deal of the credit is due to the nursing staff who entered into the task with enthusiasm, an enthusiasm quickly communicated to the patients concerned.

A typical day's diet for one of the patients was calculated as follows. The total calory requirements of patient M.G. were 1712. Of this total 10.2 grms of carbohydrate supply 41.8 calories; 35.6 grms of protein supply 140 calories; the remaining calories (roughly 1500) were supplied by 170 grms of fat. It was considered a better idea to assign the protein and fat elements before making up the carbohydrate quota because the type of carbohydrate food required depends to some extent on the fat and protein content of the meal. Protein was

made up mainly from meat, bacon, cheese and egg; fat from butter, cream, bacon, cheese and cod liver oil. Since this patient could only be allowed a little more than 10 grms. of carbohydrate it had to be made up from bread and those vegetables having a poor carbohydrate content. The full diet therefore of this patient was made up as follows. The amounts of carbohydrate, protein and fat in grams is also shown together with the calory value. It will be noticed that a little more than the 1712 calories has been given, but this is made up mainly from fat which merely tends to increase the ketosis.

able V

Food	amt. in ozs.	Carbo-hydrate in grms.	Protein	Fat	Calories
Bread	½	7.5	3		43
Vegetables	3	2.5			10
Meat	2¼		16	16	214
Bacon	2		10	30	311
Butter	2			50	465
Cheese	1		7.5	7.5	100
Cream	2			20	186
Cod liver oil	1½			45	418
				Total Calories	1747

This diet was made up into meals in the following manner. Breakfast consisted of 2 ozs Bacon, Bread ¼ oz., butter 1 oz., cream 1 oz. Tea unsweetened was given ad lib. For dinner the patient had meat 2¼ ozs and vegetables 3 ozs. For tea the menu was bread ¼ oz, butter 1 oz., cream 1 oz., cheese 1 oz. Again unsweetened tea was given ad lib. After each meal ½ oz. of cod liver oil was given. For variety the vegetables could be changed frequently a choice of the following being allowed;- Sprouts, cabbage, tomato, beetroot, cauliflower, swedes and lettuce. Instead of cheese 1 egg was allowed for every ounce. If the diet was calculated to contain 2 ozs of cheese then it was found advisable despite the extra cost to give an egg in lieu of 1 oz. of cheese. Some patients objected to cod liver oil but they were few in number and they were soon advised to look upon it as a medicine for their own good. At times cream or butter was substituted for part of the oil. However if that were done the patient found it difficult to consume so much butter and cream without the help of bread or fruit.

On the whole the diet was well tolerated and the complaints were dealt with easily. The greatest difficulty was the small amount of bread. A diligent search was made for a very

low carbohydrate bread such as is used in severe diabetes but no company could furnish a sample that was satisfactory. The lower the carbohydrate content the dearer was the bread and even the samples containing least carbohydrate would not have been bulky enough for our purpose. Everything considered it was decided to continue with ordinary bread. Various kinds of bran wafers were secured but the patients did not take kindly to them and they were discontinued.

Constipation, generally complained of by epileptics, was treated by weekly doses of magnesium sulphate, but no great difficulties were encountered in this respect as the ketogenic diet is fairly laxative.

The urine of every patient on the diet was collected and examined twice weekly for acetone bodies. If the patients were faulty in habits catheter specimens were obtained. The tests employed were the ordinary nitroprusside test for acetone bodies.

If the urine of any patient was found to be negative by these tests a special watch was kept on that patient and if it still was negative the carbohydrate quota was cut down.

Before treatment commenced a special mental and physical examination was given to each patient so that apart altogether from the number of fits a complete comparison could be effected.

The Individual Cases.

In the following account of the results each patient will be described separately. Those having the greatest number of fits will come first. No attempt has been made to insert opinions on the severity of convulsions. Naturally one has to take all that on trust from the nursing staff and where the memory over nearly a year and a half is exercised it can serve no useful purpose. The weights given below are net weights as 10 lbs is deducted to represent the weight of the clothes. The average number of fits is calculated over the period of eight months immediately preceding the introduction of the diet and the eight months of the diet. The fits are divided into day and night fits.

Case I. Patient A.A.; aged 32 years; weight at commencement of treatment 94 lbs.

Physical Examination. No gross organic abnormalities. Feeble health and undersized.

Mental Examination. She is generally lost & confused, and unable

to give much account of herself. At times violent and noisy. Habits as a rule clean.

Average number of fits per month. 29.2 2.5 by day 26.7.by night

This patient as a rule spends the greater part of her time in bed as the result of great mental confusion and for this reason no great difficulty was encountered in maintaining the diet. The Diet consisted of ~~4.8~~ 9.024 grms carbohydrate;31.3 grms protein; 150 grms fat. At the end of eight months her condition was as follows.

Weight. 95 lb. Increase 1 lb.

Physical Condition. No gross organic abnormalities.

Mental Condition. Still subject to bouts of violent behaviour with great mental confusion.

Average number of fits per month. 33.6 1.1 by day 31.9 by night.

There was no improvement observable.

Case 2. Patient E. R.; aged 28 years; weight on commencement of treatment 104 lb.

Physical Examination. No gross physical abnormalities. Small and undersized.

Mental Examination. She is extremely violent and difficult to

manage. Strikes out without warning and requires frequent Side Room treatment. She cannot engage in conversation or understand much of what is said to her.

Average number of fits per month 26.8; 5.8 by day; 21 by night.

Diet consisted of 9.984 grms carbohydrate; 34.6 grms protein; 166 grms fat.

At the end of eight months

weight 99 lbs. Loss 5 lbs.

Physical Examination as above

Mental Examination. She is less violent and difficult to manage. When very confused can now be nursed in the open dormitory. She is much less noisy. She is more suggestible and in that respect has more appreciation of her surroundings.

Average number of fits 22.6; 7.6 by day; 15 by night.

This patient had an average of 4.2 fits per month less than before treatment. As her mental examination shows she was much more amenable and easily managed and in this respect greatly lightened the task of the nursing staff. She was definitely improved.

Case 3. M.T.; aged 47 years; weight at commencement of treatment 155 lbs.

Physical Examination. She is in fair health. Has had tuberculosis of lungs but that condition is now quiescent. She suffers also from cardiac disease, mitral incompetence.

Mental Examination. She is demented and simple. She takes little interest, never speaks unless asked a question. She is clean but cannot do very much for herself.

Average number of fits per month 20.1; 9.3 by day; 10.8 by night.

Diet consisted of 14.8grms carbohydrate; 51.3grams protein; 248 grams fat.

At the end of seven and a half months

Weight 140 lbs. Loss 15 lbs.

Physical Examination. As above. At times becomes breathless and cyanosed.

Mental Examination. No change.

Average number of fits 11.4; 5.8 by day; 4.3 by night.

This patient averaged 8.7 fits less per month on the diet. Although she lost 15 lbs she was a patient who was stout and in poor condition, and could easily afford to carry less weight. The weights of all the patients were taken weekly and where necessary losses were made good but in this patient a weight of 10 stone was looked upon as satisfactory. The general condition of this patient did not deteriorate. Unfortunately she developed frequent attacks of cardiac incompetence and died quite suddenly.

Case 4. R.P.; aged 37 years. Weight at commencement of treatment 118. lbs.

Physical Examination. She is in fair health without gross organic lesions.

Mental Examination. Very violent patient when fitting striking out at anyone near her. She is lost and confused, cannot render any account of herself and is very bad tempered.

Average number of fits per month 19.9; 12 by day; 8.1 by night.

Diet consisted of 11.328 grms carbohydrate;39.3 grms protein; 188 grms fat

At the end of eight months

Weight 115. Loss 3 lbs.

Physical Examination. As above.

Mental Examination. She has improved considerably, is more easily managed and not nearly so violent. Her general temper is better. From the nursing point of view less troublesome. Still much confused when having fits.

Average number of fits per month. 14.5; 8.8 by day; 5.6 by night.

A decrease here was noted of 5.4 fits per month while the general behaviour and condition were improved.

Case 5. M.W.; aged 31 years. Weight at commencement of treatment 91 lbs.

Physical Examination. Feeble health but no gross organic lesions. Small and undersized.

Mental Examination. Simple and childish, and irresponsible. Very emotional and easily upset. When having many fits appears quite lost and confused but can be thoroughly roused fairly easily. She can give a good account of herself. Is clean in habits.

Average number of fits per month 18.6; 13.9 by day; 4.7 by night.

Diet consisted of 8.736 grms carbohydrate;30.3 grms protein; 145 grms fat

At the end of five months.

Weight 98 lbs. Gain 7 lbs.

Physical Examination. As above but a little more robust.

Mental Examination. There is no change in her mental condition.

Average number of fits per month 13.2; 8.8 by day; 4.2 by night.

This patient is one who occasionally has a great number of fits in a short time, fits that are mild and often with consciousness returning as soon as the clonic stage has passed. At the end of a batch of fits she appears little the worse, so that one is tempted to diagnose these apparent conditions of status as hysterical in origin. It is possible to make her have convulsions by suggestion. However five months after the start of the ketogenic diet she suddenly developed a condition simulating status and it was deemed advisable to discontinue the special diet in favour of a regime more suitable to her condition. The ketogenic diet was started in this patient in order to watch its effect on these pseudo static phases. It failed however to benefit.

Case 6. N.K.; aged 28 years; weight at commencement of treatment 90 lbs

Physical Examination; She is in poor health, undersized. Heart shows mitral systolic murmur, but no evidence of heart symptoms.

Mental Examination. Simple, childish and at times confused. Cannot appreciate her position or give much account of herself. She requires a great deal to be done for her.

Average of fits per month 10.8; 6.9 by day; 3.9 by night.

Diet consisted of 8.64 grms carbohydrate; 30 grms protein; 144 grms fat

At the end of four months.

Weight 87 lbs. Loss 3 lbs.

Physical Examination. No change.

Mental Examination. No change.

Average number of fits per month 15.8;10.5 by day; 5.3 by night.

Report. On December 24th was sent to bed as she was much confused after fits. December 25th went into status. Diet stopped and supporting treatment given. Luminal and morphia hypodermically. Nutrient enemata given. Died on December 26th.

Case 7. M.G.: aged 44; weight at commencement of treatment 107 lbs.

Physical Examination. This patient is tubercular, having suffered from phthisis. At present the condition is quiescent. The heart sounds are not good and she cannot do very much in the way of work.

Mental Examination. She is troublesome, disagreeable and noisy. Throws herself about at times and refuses to answer questions. When not excited is surly and disinclined to say much. She is suspicious.

Average number of fits per month 10; 4.1 by day; 5.9 by night.

History of fits from childhood.

Diet consisted of 10.2 grms carbohydrate;35.6 grms protein; 171 grms fat

At the end of eight months.

Weight 98 lbs. At the end of seven months her weight was 104 lbs, a loss of 3 lbs. She lost 6 lbs in the next month.

Physical Examination. There was no great change. No lighting up of the tubercular mischief. Heart much as it was.

Mental Examination. There is some improvement and she is not so noisy. She is more easily managed and can be left on her own more. She is now doing a little light dusting, and is able to go about the ward like any other patient.

Average number of fits per month 1.6; 0.8 by day; 0.8 by night.

Report. This patient showed a great decrease in the number of fits from 10 to 1.6 per month. In the eight months previous to treatment she had 80 fits. In the eight months of treatment she had only 17. Mentally she was also improved not so irritable or easily upset. She gave less trouble and was able to get about more. She showed definite improvement.

Case 8. H.P. aged 31 years; weight at commencement of treatment 114 lbs.

Physical Examination. She is in fair health but has heart sounds of poor quality. She injures herself frequently by falling in fits.

Mental Examination. She is difficult and troublesome to manage, violent and aggressive at frequent intervals and unable to appreciate her position. Her fits are severe and leave her dazed and confused for a long time afterwards. She appears to have no warning of their approach and in consequence receives many injuries by falling.

Average number of fits per month 8.1; 5.8 by day; 2.2 by night.

Diet consisted of 10.944 grms carbohydrate; 38 grms protein; 182 grms fat

At the end of eight months.

Weight 119 lbs. Gain 5 lbs.

Physical Examination. She is healthier and stronger than she was and looks much better.

Mental Examination. She is more amenable to treatment than she was, although she is not much clearer mentally. She cannot engage in a rational conversation but can answer ordinary questions. She can be more easily managed in bed when having fits.

Average number of fits per month. 6.4; 3.6 by day; 2.8 by night.

This patient showed a decrease of 1.7 fits per month. The greatest improvement noted in this patient was in the severity of the fit. She injured herself much less and was more easily managed in bed. The milder type of fit probably accounts for her better temper. This patient was definitely improved.

Case 9. B.C. Aged 46; weight at commencement of treatment 112 lbs.

Physical Examination. She is in good health and has no gross organic lesions.

Mental Examination. She is troublesome and quarrelsome, makes false accusations and is full of trivial complaints. She is idle and lazy and sits about most of her time. When having fits is lost and confused.

Average number of fits per month. 7.7; 4.6 by day; 3 by night. This average is calculated over four months as she was only admitted that time before treatment began.

The diet consisted of 10.752 grms carbohydrate; 37.3 grms protein; 179 grms fat.

After eight months.

Physical Examination. No change to record.

Mental Examination. No important change. Still idle and full of trivial complaints.

Average number of fits per month 4; 3.2 by day; .8 by night.

This patient had a reduction of 3.7 fits per month. This was the only sign of improvement.

Case 10. F.L. aged 22. Weight at commencement of treatment 112 lbs.

Physical Examination. No gross physical abnormalities.

Mental Examination. She is mentally deficient and has very slow cerebration. Speaks in a hesitating manner. When having fits violent and uncontrollable and requires Side Room treatment. She attacks the staff and other patients.

Average number of fits per month 7.6; 7.3 by day; .3 by night.

The diet consisted of 10.752 grms carbohydrate; 37.3 grms protein; 179 grms fat.

After eight months.

Weight 118 lbs. Gain 6 lbs.

Physical Examination. No change.

Mental Examination. No important change.

Average number of fits per month 7.6; 7.1 by day; .5 by night.

There was no change of any kind to record in this patient.

Case 11. A.F. aged 47; weight at commencement of treatment 148 lbs.

Physical Examination. No gross organic lesions.

Mental Examination. Dull and demented, keeps talking of the one thing all the time. Slow cerebration and unable to appreciate her position. Requires a great deal of prompting to do ordinary things.

Average of fits per month 7.1; 3.7 by day; 3.3 by night.

The diet consisted of 14.208 grms carbohydrate; 49.3 grms protein; 236 grms fat.

At the end of eight months.

Weight 152 lbs. Gain 4 lbs.

Physical Examination. No change.

Mental Examination. No change.

Average number of fits per month. 6.4; 2.5 by day; 3.8 by night.

There was a decrease of 0.7 fits per month which cannot be regarded as satisfactory. This patient had few complaints about the diet.

Case 12. A.H. aged 34; weight at commencement of treatment 105 lbs.

Physical Examination. No gross organic lesions.

Mental Examination. She is an extremely violent and dangerous patient who requires Side Room treatment at frequent intervals. She is destructive, smashes windows and dishes and strikes out at those who are near her. When fitting greatly confused and unable to understand what is said to her.

Average number of fits per month 6.5; 2.7 by day; 3.7 by night.

The diet consisted of 10.056 grms carbohydrate; 35 grms protein; 167 grms fat.

After eight months.

Weight 105 lbs. No change.

Physical Examination. No change. No gross lesions.

Mental Examination. She is not nearly so violent and has now gone nearly four months without requiring Side Room Treatment. She is more amenable, better tempered and rarely strikes anyone. Mentally is not so confused and has more insight into her condition.

Average number of fits per month 3.1; 1.1 by day; 2.0 by night.

This patient showed perhaps the best reaction of all to the diet. From being a very dangerous patient with violent destructive habits she became quiet, able to realize what was being done for her, and willing to help and cooperate. Her fits were reduced by 3.4 per month, a reduction of more than half. Definite improvement.

Case 13. R.R. aged 26; weight at commencement of treatment 124 lbs,

Physical Examination. No gross organic lesions. Suffers from a chronic acne ? rash of face.

Mental Examination. She suffers from recurrent attacks of violent excitement when she is difficult to control. She is simple and childish at ordinary times and will employ herself usefully. She is reduced mentally.

Average number of fits per month 5.8; 2.1 by day; 3.6 by night.

The diet consisted of 11.904 grams carbohydrate; 41.3 grms protein; 198 grms fat.

After eight months.

Weight 116 lbs. Loss 8 lbs.

Physical Examination. There is a decided improvement physically. She has a much clearer skin, the muddy pasty look has gone, and the acne rash has entirely disappeared. She looks much better.

Mental Examination. There is little change except that she is more suggestible than she was and is perhaps more content.

Average number of fits per month. 8.1; 1.3 day; 6.7 night; increase 2.3

There was no great change to record in this patient except the physical improvement which probably reflected the benefits from a restricted diet. The fits were increased (one of the few who showed this change).

Case 14. E.W. aged 28; weight at commencement of treatment 104 lbs.

Physical Examination. She is a strong healthy girl with very good colour. No gross abnormalities.

Mental Examination. She is extremely violent and quarrelsome when having fits and requires careful watching when she becomes irritable. She makes savage attacks on others without provocation. At other times is pleasant and willing to help.

Average number of fits per month 5.5; 1.6 by day; 4 by night.

The diet consisted of 9.984 grms carbohydrate; 34.6 grm protein; 166 grms fat

After eight months.

Weight 107 lbs. Gain 3 lbs.

Physical Examination. No change.

Mental Examination. There is no great change mentally. Still very unreliable and very violent when upset.

Average number of fits per month. 6.9; 1.0 by day; 5.8 by night.

There was no great change to record either mentally or

physically but it has to be noted that the fits increased from 5.5 to 6.9.

Case 15. A.Gr. aged 42; weight at commencement of treatment 101 lbs

Physical Examination. She is in feeble health and has very weak heart sounds. Spends a great deal of her time in bed.

Mental Examination. She is dull & stupid, cannot engage much in conversation or understand what is going on around her. She requires a great deal to be done for her.

Average number of fits per month 5; 3.6 by night; 1.3 by day. History of fits extending over 25 years.

The diet consisted of 9.696 grms carbohydrate; 33.6 grms protein; 161 grms fa

After 4½ months.

Weight 94 lbs. Loss 7 lbs.

Physical Examination. There was rather a rapid decline in health for a week or two before being taken off the diet. She had oedema of feet and legs and difficulty in breathing. She was unable to complain. Sick diet started in place of ketogenic diet.

Mental Examination. There was no change to record in her mental attitude. Still dull and stupid.

Average number of fits per month 0.

From the day this patient was put on the diet until she died nearly five months later she did not have a single fit. Her weight was maintained to within 2 or 3 lbs of her normal weight for nearly 3 months. She didn't begin to fail until her general

health broke up. After she had lost seven pounds it was considered expedient to put her on sick diet. P.M. revealed a great amount of myocarditis with mitral incompetence. There was some fatty degeneration present.

Case 16. M.A.B. aged 23 years; weight at commencement of treatment 120 lbs.

Physical Examination. No gross anatomical lesions.

Mental Examination. She is very sullen and deluded, believes she is being persecuted and attacks other patients and staff as a result. She is dangerous and easily excited and requires frequent Side Room treatment.

Average number of fits per month. 5.4; 1.2 by day; 4.2 by night.

The diet consisted of 11.5% grms carbohydrate; 40 grms protein; 192 grms fat.

After eight months.

Weight 108 lbs. Loss 12 lbs.

Physical Examination. No important change apart from loss of weight which had no apparent effect on her.

Mental Examination. There was no change whatever. Still violent and troublesome and very dangerous.

Average number of fits per month; 3.8; 1.9 by day; 1.9 by night.

She showed a reduction of 1.6 fits per month but otherwise was not improved.

Case 17. A.G. aged 21; weight at commencement of treatment 132 lbs.

Physical Examination. She was in good health.

Mental Examination. When having fits very confused for days, violent and aggressive and quite beyond being influenced. She attacks others and is extremely quarrelsome. At ordinary times is well behaved works well and is appreciative.

Average number of fits per month: 4.5; 3.1 by day; 1.3 by night.

The diet consisted of 12.67% grms carbohydrate; 44 grms protein; 211 grms fat

After eight months.

Weight 132 lbs. No change.

Physical Examination. No change.

Mental Examination. No change.

Average number of fits per month: 7.2; 4.3 by day; 2.8 by night.

There was an increase here of 2.7 fits per month the only change to be recorded.

Case 18. M.E.C. aged 44; weight at commencement of treatment 122 lbs.

Physical Examination. In fair health but shows a mitral systolic Murmur.

Mental Examination. Simple and childish and very much reduced mentally. She cannot give any account of herself or engage in conversation. She is violent and troublesome at times.

Average number of fits per month: 4; 3 by day; 1 by night.

The diet consisted of: 11.71% grms carbohydrate; 40.6 grms protein; 195 grms fat

After eight months.

Weight 114 lbs. Loss eight lbs.

Physical Examination. No change.

Mental Examination. No change.

Average number of fits per month: 2.1; 1.1 by day; 1 by night.

There was a decrease here of 1.9 fits per month, representing nearly half the normal number. Apart from this reduction there was no other observable change.

Case 19. E.T. aged 26 years; weight at commencement of treatment 122 lbs.

Physical Examination. She is in fair health without obvious organic lesions.

Mental Examination. Simple and childish easily upset and just as easily pleased. Keeps herself very clean and tidy and always willing to assist the staff in any work. She gives a good account of herself.

Average number of fits per month: 3.9; 3.1 by day; .8 by night.

The diet consisted of 11.712 grms carbohydrate; 40.6grms protein; 195 grms fat.

After eight months.

Weight 117. Loss 5 lbs.

Physical Examination. No change to record.

Mental Examination. No change.

Average number of fits: 3.9; 2.9 by day; 1.0 by night.

The patient was in much the same condition after eight months as before treatment commenced.

Case 20. A.C. aged 62; weight at commencement of treatment 118 lbs.

Physical Examination. She suffers from arterio sclerosis. Urine shows a few granular casts and slight trace of albumen. Otherwise no abnormalities.

Mental Examination. Very disagreeable, continually making false accusations and causing endless annoyance and trouble to everyone. Is violent and aggressive at times. Quite idle and says she has no intention of doing anything.

Average number of fits per month: 3.4; 1.6 by day; 1.7 by night.

The diet consisted of 11.328 grms carbohydrate, 39.3 grms protein; 188 grms fat.

After eight months.

Physical Examination. No change.

Mental Examination. There is some improvement in her mental attitude, and she is not so troublesome. She has refrained in the last few months from making any false accusations but is continually asking when she is being taken off the diet.

Average number of fits per month: 0.9; .5 by day; .4 by night.

There was a decrease here of 2.5 fits per month. In the first five months she was on the diet she had only 2 fits altogether. Thus there was a decided improvement in this patient both in the number of fits and in the mental condition.

It is now intended to present the salient features of the treatment and its results in a series of tables that will show at a glance the various points brought out. First of all is a re-

cord of the fits each patient had in each month covering the whole period under review, that is 16 months. Here no distinction will be made between day and night fits.

Table VI

(see next page)

Number of fits in each month before treatment

Table VI

	Month 1	mth 2	mth 3	mth 4	mth 5	mth 6	mth 7	mth 8	fits total	aver-age.
A.A.	34	11	32	45	20	21	35	36	234	29.2
E.R.	33	32	28	28	26	27	29	11	214	26.8
M.T.	11	9	24	4	24	40	30	19	161	20.1
R.P.	19	26	13	21	21	20	21	18	159	19.9
M.W.	2	3	4	5	9	10	107	9	149	18.6
N.K.	8	3	11	17	16	11	13	7	86	10.8
M.G.	6	4	12	10	10	22	9	7	80	10
H.P.	17	3	11	5	6	10	7	6	65	8.1
B.C.						6	14	3	23	7.7
F.L.	7	8	8	5	9	10	10	4	61	7.6
A.F.	9	9	3	6	4	14	7	5	57	7.1
A.H.	4	7	7	8	13	6	2	5	52	6.5
R.R.	10	1	8	8	7	7	2	3	46	5.8
E.W.	3	4	8	7	6	7	7	2	44	5.5
A.Gr.	11	4	8	4	4	3	5	1	40	5
M.A.B.	3	3	2	3	7	9	9	8	44	5.4
A.Ga.	4	4	9	2	3	4	7	3	36	4.5
M.E.C.	2	4	7	6	2	4	3	4	32	4.0
E.T.	4	4	3	2	3	6	4	5	31	3.9
A.C.	4	4	3	7	6	2	0	1	27	3.4

Number of fits in each month after treatment
Table VI (Continued)

	Month 1	mth 2	mth 3	mth 4	mth 5	mth 6	mth 7	mth 8	fits total	aver-age
A.A.	24	42	43	14	35	44	34	28	264	33
E.R.	36	28	25	26	35	20	8	13	181	22.6
M.T.	7	3	10	10	12	18	9	died 13	82	10.1
R.P.	19	9	13	21	22	6	8	18	116	14.5
M.W.	9	8	10	9	29	4	15	20	104	13
N.K.	14	11	11	10	33	died			79	15.8
M.G.	2	2	2	2	0	2	1	2	13	1.6
H.P.	14	8	8	4	7	4	1	5	51	6.4
B.C.	1	5	5	7	6	3	4	1	32	4
F.L.	6	7	10	6	8	15	1	8	61	7.6
A.F.	5	9	4	7	5	8	4	9	51	6.4
A.H.	1	3	5	6	3	1	3	3	25	3.1
R.R.	7	9	10	2	7	8	8	14	65	8.1
E.W.	6	7	7	8	9	6	6	6	55	6.9
A.Gr.	0	0	0	0	died 0				0	0
M.A.B.	0	10	1	3	3	7	5	1	30	3.8
A.Ga.	6	6	4	3	22	7	6	4	58	7.2
M.E.C.	3	2	3	1	4	2	2	0	17	2.1
E.T.	5	3	4	6	3	4	5	1	31	3.9
A.C.	0	2	0	0	0	1	2	2	7	0.9

It will be noted that of the twenty patients 13 had a reduction in fits with the ketogenic diet 2 were quite unchanged and 5 had an increase. Thus as regards actual fits 65% were relieved 10% were unchanged and 25% reacted badly. In an institution where large numbers of epileptics are living together any substantial reduction in the number of fits is a boon both to patients and staff so that the above figures are considered satisfactory.

In the individual reports of each patient the fits were divided into day and night fits. Some patients habitually have more day fits than night fits and vice versa. It is interesting to note what effect the ketogenic diet has on the time incidence of fits. Only five patients had an absolute increase in fits, yet nine patients had an increase in night fits, and only four had an increase in day fits. Of those having an increase during the day, two also had an increase during the night. All of the patients having an absolute increase of fits had an increase during the night. Three patients had increased night fits who had over the whole period an absolute decrease in fits. This would seem to show that during the night, the period when the patient is furthest from his meal, the increase in fits generally takes place (during ketosis). This is also the period

when ketosis is at its lowest. It is always better for an epileptic to have his fits at night since he cannot injure himself and since it does not interfere with his daily task. Most epileptics would gladly welcome a regime that changed their time of fits from day to night. Therefore this result of the treatment can be considered very satisfactory.

The next table shows the fluctuations in weight over the same period of time. Not one patient appeared the worse for the restricted diet and some of those who lost weight could well afford to do so: in fact it was thought a desirable result. The weights were taken weekly and tabulated so that a strict watch could be kept. The diet in several patients was frequently adjusted at times to maintain ketosis, at other times to maintain weight. It must be understood that the class of patients treated here is poor, poor mentally and physically. All of them are chronics who have been having fits for many years so that intellectual deficiencies are the rule.

Table VII

(see next page).

Table VII weights.

	July	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.
F.L.	112	112	112	111	114	115	119	116	118
A.F.	148	142	144	145	149	150	148	148	152
A.A.	94	94	89	92	92	91	92	92	95
H.P.	114	112	113	114	116	118	118	118	119
E.W.	104	106	103	103	108	105	108	103	107
M.W.	91	91	90	91	96	98	98	discontinued	
M.T.	155	160	151	148	149	146	145	142	140
M.G.	107	107	107	109	109	108	109	104	98
A.Gr.	101	100	98	99	97	94	deceased		
M.E.C.	122	119	118	118	114	116	114	112	114
A.C.	118	112	115	112	111	111	108	108	110
E.T.	122	116	117	117	114	115	115	115	117
E.R.	104	104	102	102	101	100	98	99	99
B.C.	112	110	119	114	112	112	111	112	108
A.Ga.	132	133	132	131	131	132	131	128	132
R.P.	118	119	118	119	121	121	120	115	115
M.A.B.	120	116	110	108	108	107	107	108	108
A.H.	105	105	108	109	104	103	108	106	105
R.R.	124	124	123	122	120	119	120	118	116
N.K.	90	87	85	86	86	87	deceased		

Comments:-

As was to be expected most of the patients lost weight, but on the whole the losses were within reasonable limits and not one patient appeared the worse for it. It is significant that of the five patients who did not benefit from the treatment three increased in weight and of the other three who gained in weight only one H.P. was really considered to have benefited from the diet. Thus it would seem as if a diet low in calory value is of advantage to epileptics. It decreases the metabolic rate and has much less tendency to create constipation. Indeed apart from epileptics the majority of people could eat less with advantage to their health. Athletes of course look upon superfluous flesh as something to be abhorred; and they are the fittest in the land.

The epileptics treated here are all certified lunatics so that the mental attitude and the behaviour are as important as the number of convulsions. Certification only supervenes on epilepsy when the unfortunate patient is unable to be looked after at home because of violent aggressive behaviour. The epileptic mentality is typical and is based on persecutory ideas. This shows itself in quarrelsomeness, the making of false accu-

sations and the frequent homicidal attacks. Thus epileptics are amongst the most difficult of all mental hospital patients to treat. The following table shows the mental reaction to the ketogenic diet. Any improvement is a distinct gain to an overworked and harrassed staff.

Table VIII

(See next page)

Table VIII. Mental Reaction.

A.A.	Not improved
B.R.	Improved
M.T.	Not improved
R.P.	Improved
M.W.	Not improved
N.K.	Not improved
M.G.	Improved
H.P.	Improved
B.C.	Not improved
F.L.	Not improved
A.F.	Not improved
A.H.	Improved
R.R.	Improved
E.W.	Not improved
A.Gr.	Not improved
M.A.B.	Not improved
A.Ga.	Not improved
M.E.C.	Not improved
E.T.	Not improved
A.C.	Improved

Comments:-

It will be noted that seven of the patients improved mentally. This was reflected in the fewer attacks of excitement and violence, less tendency to quarrel and the making of fewer false accusations. Indeed it was observable on this last head that some patients who habitually complained of ill treatment and lack of consideration began to praise the staff and show appreciation of any little kindnesses. As has been noted before this type of improvement may be due to more time being devoted to the patient and a consequent improvement by suggestion. However that may be the change for the better was there. Only one patient improved mentally who showed an increase in the number of fits (patient R.R. This patient also improved physically), a result only to be expected, especially in epilepsy where the mental attitude is so characteristic that it must be looked upon as the result of the convulsions. All the other patients who improved mentally also had less convulsions. On the other hand 7 patients had less convulsions who did not improve mentally. However, when it is considered that all of the patients are institutional and chronic, improvement can only be expected in the more troublesome andviolent.

When the influence of weight is taken into consideration only one patient improved mentally who gained in weight. This is contrary to what one would expect since most patients who gain weight become less troublesome and more easily managed. A gain in weight is often the first objective of treatment in insanity so that the above result is strange. However when it is also noted that only two patients who gained weight had less fits it suggests that a much lower diet in calory value might be given to all epileptics with advantage. Apparently over feeding does not agree with them. Another explanation is that most of the patients who gained weight might have had access to more food; but with the exception of one patient (E.T.) the ketosis was maintained well throughout the whole period as shown by the acetone content of the urine. The patient mentioned was young was given many privileges and was much above the average in mental acumen. However she lacked a sense of responsibility and she stooped to many dodges to get more food, especially fruit and sweets.

Put shortly then the complete results of the ketogenic diet in the 20 cases under consideration are as follows. Sixty-five per cent had a reduction in seizures (one patient

was completely free of seizures)

Ten per cent were quite unchanged.

25 per cent had an increase in seizures.

Thirty-five per cent improved mentally.

Sixty-five per cent were unchanged mentally.

The results of other investigators shows that the above are a fair average. Most experimental diets have been on children. Peterman (33) treated children with a diet in which the ratio of calories from fat are 2, 3, or 4 times the total calories from protein and carbohydrate. His results were that 57% were free from fits, 25% were improved while the remaining 18% were not improved. He found that the younger the children the better the results and that petit mal attacks were more easily controlled than the major attacks.

Luther& Moriarty (34) had a series of 27 patients: 33% were free of seizures, 41% were improved and 26% were unchanged. All the patients who were freed from seizures were under 13 years of age.

The results of Helmholtz (2) in the Mayo Clinic are as follows: 31% were free of attacks, 23% were improved, 46% were unchanged. These patients were all children and the results

agree fairly well with those of Luther & Moriarty.

Weeks, Allen, Rennen & Wishart (35) fed 6 adult institutional epileptics a very high fat diet (up to 580 grams of fat and only 4 of carbohydrate). They concluded that there was no effect on the number of seizures. Barborka (36) however beginning in 1924 treated 49 epileptic adults by the ketogenic diet. His results were: 14.3% free of seizures; 25% improved; 26.5% were not improved while the remaining 34.2% were only on the diet from 2 - 4 weeks. His results therefore showed that nearly 40% were definitely improved.

C.Bastible (37) reported a series of 29 cases of epilepsy mostly in adult females of the grand mal type, treated by the ketogenic diet. He included biscuits made from bran and "carrigien moss". He found a definite reduction in fits in 20 cases and cessation in two. He combined the treatment later with the exhibition of acid salts and concluded that it had a beneficial effect. He was of the opinion that the ketogenic diet was worth an extended trial.

Conclusions and Comments

The foregoing results show that even in institutional epileptics of the lowest grade ketosis engendered by a high fat diet is antagonistic to seizures in a fair number of patients. The results do not compare very favourably with those gained by Helmholz in children but it has always been recognised that adults are particularly resistive to treatment. Neither are the results good compared with Barborka's (as regards complete cessation of fits). He treated 32 adult patients, but it must be remembered that Barborka's patients were not of the institutional class but selected cases in whom the epileptic attacks were the only evidence of abnormality. At the same time the Mayo Clinic patients were mainly suffering from petit mal, whereas this investigation has been carried out in patients who were having grand mal attacks.

The results show that in adult epileptics of the chronic class much can be done to reduce seizures and limit impulsive behaviour by use of the ketogenic diet. Sixty-five per cent of patients greatly relieved is assuredly a good result especially when dealing with a more than hopeless type of case. There are difficulties in maintaining the diet, but in well regulated hospitals it is by no means above the talents of the staff. Persuasion and suggestion can often avert difficult situations and the patients as a whole are glad

to cooperate. Once the diets are worked out the serving of meals accompanied as it necessarily is with the weighing of all food, becomes a mere routine. Certain members of the staff are detailed to the particular duty of looking after the special diet and theirs is the responsibility of seeing that all the patients get their due allowance.

As has already been said the great complaint against the diet is the small amount of bread allowed. No doubt some form of substitute containing little or no carbohydrate will be found, but at present bran wafers etc are not very palatable. Again the large amounts of fat (especially butter and cream) appear to have a nauseating effect but it is surprising how easily the patients become used to it. As a whole the complaints are more against what is not permitted in the diet than against any particular food allowed.

The results so far are encouraging and I personally am continuing the treatment in the more violent type of case, as they seem to benefit most.

The reason why ketosis should limit the number of convulsions in epilepsy is not easy to discover but the following observations do throw some light on the problem. If the establish-

ment of acidosis in epilepsy is of value in treatment then it would seem logical that the administration of alkali would result in an increase in seizures. In the cases in which this has been done the results are striking. As far back as 1897 Charon & Briche (38) (who believed that acidosis was present in untreated epileptics) gave subcutaneous injections to 8 patients who showed an increased frequency in the fits. Lennox & Cobb gave alkali to a fasting epileptic with a resulting increase in seizures. Another patient of theirs, in whom acidosis had been induced first by fasting and then by administration of $CaCl_2$, was given alkali after each period of acidosis. The result was a great increase in convulsions. In some patients although acidosis is actually present continued administration of alkali results in seizures. This suggests that it is the sudden change from acidosis towards the alkaline side that precipitates the seizures.

It has been already stated that hyperpnoea in epileptics frequently results in the precipitation of a seizure. In rapid deep expiratory breathing the patient gets rid of CO_2 from the blood with the result that the alkalinity increases; seizure is the result. If however the patient is made to rebreathe the air

he has actually expired (air now having increasing amounts of CO_2) the expected seizure does not occur, which apparently must be due to the high content of CO_2 in the inspired air. Again if the patient is made to breathe air that has decreasing amounts of oxygen in it without a corresponding increase in the CO_2, seizures result. This last experiment is carried out by making the patient rebreathe the expired air from which the CO_2 has been absorbed. Relating these experiments and remembering that it is not possible to induce seizures in an epileptic by hyperpnoea if pure oxygen is breathed, it would appear that oxygen lack in the tissues is the fundamental condition. Oxygen is given up to the cells much more readily when the percentage of CO_2 in the blood is relatively high while the converse is equally true. Thus decreasing the CO_2 of the blood has a similar effect to limiting the oxygen supply. A decrease in CO_2 in blood results in a bias towards alkalinity, therefore acidosis is a condition in which the tissues much more readily receive oxygen, and alkalosis a condition in which the tissues find difficulty in consuming oxygen. Apparently it does not matter a great deal how the acidosis or the alkalinity is produced. In epilepsy the cells most affected are the neurones, and of course it is very well

known that in oxygen deficiency the nervous system is the first to suffer. As a rule consciousness is lost in the normal individual without actual tonic or clonic muscular spasms, but in epilepsy it is not to be supposed that the nervous system is ordinarily robust. Probably it reacts to much smaller deficiencies in oxygen supply and reacts in an exaggerated fashion.

It is not being suggested that epilepsy is a syndrome depending on an abnormal alkaline bias in the blood and tissues. This may be the cause but oxygen supply to the tissues can be affected in many ways besides decreasing CO_2 in the blood. For example the blood supply may be at fault as in spasm of arterioles, or stasis of the venous return. The arteriole spasm theory has many upholders at the present time, but it must be remembered that arterial spasm merely leads to the tissues being starved (principally of oxygen since the cells react most quickly to it, probably because no tissue interchange can take place without some oxidation process).

The real cause of epilepsy remains unknown. It is a condition that in its nature is not common in the realm of medicine. It has perhaps some near relations like angina pectoris, migraine, and general muscle cramps. All of these conditions

are alike in that the precipitating factor may be quite different from the real causal factor. The nature of these diseases suggests that there is not one cause but several. The unfortunate thing is that up to a point the seizures may be controlled without the disease being cured. As a rule the discontinuance of a remedy in epilepsy is the signal for a return of the seizures, sometimes increased in force and frequency. A great deal of the confusion in the investigation of this terrible scourge is the result of neglect to differentiate between causal factors and precipitating factors. As has been pointed out the precipitating factor may be an acute oxygen lack in patients having a nervous system not quite physiologically normal. Investigations into oxygen interchange and the conditions modifying it seems to hold out the best hope of ultimate cure in epilepsy.

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