THE TREATMENT OF EPILEPSY

WITH BIOLOGICAL MEDICINES

Harvey M. Good, BA, MD

"It is not in my opinion any more divine
or more sacred than other diseases, but
has a natural cause, and its supposed
divine nature is due to man's inexperience".

Hippocrates

Epilepsy is often diagnosed as a disease, primarily it is a syndrome arising from one of a variety of causes. When a definite cause for seizures is known (as brain injury or tumour) it is termed symptomatic epilepsy; when the cause is unknown, it is called idiopathic epilepsy. Usually in idiopathic epilepsy the first attack occurs before 20 years of age and practically always before 30.

In about half the cases, grand mal seizures are preceded by a warning, or aura, (in adults) consisting of sensations often bizarre and usually localised. In other cases there is no warning. The patient falls suddenly, with complete unconscious ness, in a stage of tonic muscular rigidity followed by a stage of clonic muscular jerking. During the attack the patient often injures himself on falling or bites his tongue. Respiration is very stertorous, and loss of sphincter control is common. There is often complete amnesia for the seizure, which is often followed by deep sleep or sometimes by mental confusion. Status epilepticus consists of a series of rapidly occurring seizures and may end in coma or prolonged deep sleep.

The clinical evaluation of a patient with epilepsy is based on careful analysis of the seizure itself and of the immediate postictal state. Epilepsy may be distinguished from hysteria by the signs of previous injury, complete loss of consciousness and absence of ecstatic attitudes or sounds characterised by the hysterical seizure. Furthermore, the electro-encephalogram usually reveals characteristic changes in epilepsy.

During the seizure the patient should be protected from injury and an object should be placed between the teeth to prevent his biting the tongue. No attempt should be made to arouse the patient should he fall into a deep sleep following the attack.

Table 1

The four major types of epilepsy

Name	Clinical Pattern	Electroencephalogram
1. Grand Mal (Generalised: major motor convulsions)	Generalised convulsion	1. Discharge of rapid spikes
2. Petit mal (Generalised: absence attacks)	Momentary simple unconsciousness with amnesia	2. Slow alternate "spikes and domes"
3. Psychomotor (Complex partial seizure)	Sudden series of automatic co-ordinate activities with amnesia	3. Slow discharge of "flat-topped waves"
4. Jacksonian (Simple partial seizure)	Series of chronic jerks advancing from one point to involve the entire body in regular order.	4. Local point of atypical spike discharges usually found

Since tremors, twitching and massive motor seizures occur quite frequently in infancy and childhood secondary to a rapid rise in temperature the seriousness of this clinical phenomenon is often overlooked by equating a convulsion in a child with a headache in an adult. Any child who has a convulsion should be considered to have an infection or an irritation of the central nervous system either primary or secondary such as might occur during the course of a communicable disease. It should also be noted that in brain-injured children due to the immaturity of the brain convulsive disorders are a common occurrence.

Convulsions are sometimes classified as symptomatic convulsive disorders when studied by electro-encephalography excludes the idiopathic or genetic type. The cause of seizures can be grouped to some degree according to the age of the child.

From birth to six months of age;

1. Brain injuries.

2. Developmental defects of the central nervous system.

3. Bacterial and viral menengitis.

4. Hypoglycemia.

5. Hypocalcemia (rare).

From six to twelve months of age;

1. Febrile convulsions secondary to infections such as roseola infantum, gastro-enteritis or bronchial pneumonia.

2. Bacterial and viral infection of the brain.

3. Secondary to birth injuries or anomalies of the brain.

From two to six years of age;

1. Infections of the central nervous system.

2. Residual of birth injuries and anomalies.

3. Onset of idiopathic or genetic epilepsy.

4. Manifestation of degenerative diseases of the central nervous system.

5. Brain tumours.

From six to fifteen years of age;

1. Genetic idiopathic type of epilepsy.
2. Brain anomalies as at two to six years of age.
3. Brain tumours.
4. Infections of the central nervous system.
5. Degenerative diseases.

The major motor seizures and petit mal seizures in children are not unlike those seen in older individuals. They generally occur most frequently between the ages of four and eight years. A more specific type of seizure for childhood occurs between one and twelve months of age in a brain-damaged child. This type produces a jack-knifing of the body sometimes referred to as a salaam seizure. These brain-injured children usually suffer from some form of mental deficiency.

Another type of seizure that is beginning to be recognised more often is the so called temporal lobe seizure which may manifest itself as a behaviour disorder, in some cases specifically associated with smacking the lips and grasping movements of the hands and a dazed countenance.

Anti-convulsants; anti-epileptics

Drug management of epilepsy began with the observation in 1857 that bromides would reduce the incidents and the severity of seizures. The use of bromides for this purpose became very general and about the year 1900 the annual consumption by one English hospital was estimated at 2 tons. Phenobarbital was introduced for the same purpose in 1912, and these two drugs constitute the sole treatment until the observation in 1938 that diphenylhydantoin (phenytoin) raised the threshold of electrical excitability in animals without producing the same degree of somnolence and ataxia as phenobarbital; clinical trials demonstrated that this chemical was highly effective in grand mal epilepsy. This successful experimental approach to the problem of epilepsy quickly resulted in the introduction of trimethadione (tridione) as the drug of choice in the management of petit mal, and, in turn, has been followed by the development of a considerable number of synthetics with varying patterns of usefulness. Experimental screening procedures include the use of electric shock techniques in animals and the termination of threshold convulsive doses of drugs such as pentylene-tetrazol and strychnine. Low sodium levels, thyroid or cortisone lowers the threshold for convulsions while high sodium levels, thyroidectomy and DOCA raise the threshold; these features may be regulated or varied deliberately in conjunction with the various tests of cortical excitability. EEG patterns are helpful indicators in the experimental procedures.

Bromides

No longer are considered important in the management of epilepsy, and their current interest is related chiefly to frequent instances of bromide intoxication which develops most commonly after self-medication with proprietary sedative mixtures. The cumulative characteristics of bromide are responsible for this type of chronic intoxication their body distribution is largely extra cellular, although the bromide readily enters red blood cells the ratio of bromides to chlorides is relatively uniform in the extra cellular fluids and is about the same in the urine which is the predominant route of excretion. The lack of preferential secretion of bromide over chloride by the kidney is the basis for its relatively slow elimination and its ready cumulation on continued ingestion.

Phenobarbital

More than most barbituates, raises the threshold for electro-shock seizures. This was not recognised until after it had been found imperically to be useful in grand mal epilepsy. Two other barbituates have some similar use with more suita-bility for the petit mal type of epilepsy. These are mephobarbital and metharbital. Primidone is related chemically to phenobarbital the only difference being the presence of two hydrogen atoms in place of oxygen in the urea group.

Diphenylhydantoin (phenytoin)

Probably acts to prevent the spread of excessive discharges in the motor cortex and those originating in the thalamus. In experimental animals, it does not effectively antagonise convulsive drugs such as pentylenetetrazol but modifies greatly the character of the electro-shock convulsions. The inter-seizure EEG in patients with grand mal or with psycho-motor seizures may be improved in terms of diffuse abnormality while an abnormal focus may be defined more sharply. Although widely used there are specific characteristic toxic effects which include hirsutism and gum hyperplasia (resembling a vitamin C deficiency); excessive over-dose produces excitation and psychosis. Mephenytoin is a close chemical variant of phenytoin, bone marrow depression is a serious side-effect in its use.

Trimethadione (tridione) and Oxazolidine derivative

Is conspicuous for the degree to which it raises the threshold dose of drug induced convulsions commonly in petit mal. It abolishes both seizure and characteristic spike-and-wave EEG abnormalities. The oral dose ranges from 1 - 2 grammes daily and the common side-effects include photosensitivity, blood dyscrasias, nephrosis, hepatitis and dermatitis may occur during its administration. Paramethadione (Paradione) is closely related and sometimes may be used as a replacement but may provide other side effects.

Succinimides, Phensuximide (Milontin) and Methsuximide (Celontin)

Have a structural chemical resemblance to Trimethadione, and their spectrum of anti-convulsive action and side-effects are similar. Another member of this group Ethosuximide (Zarontin) has successfully controlled the attacks in patients who have been resistant to Trimethadione and other forms of therapy but continues to exhibit the same side-effects.

Phenacimide (Phenylacetylurea, Phenurone)

Has a relatively broad spectrum of effectiveness both in experimental testing procedures and in the various forms of epilepsy. Toxic side effects are high and include personality changes.

Magnesium

These compounds have the effect of depressing nervous and muscular activity. However, orally administered compounds such as magnesium salts for cartharsis, have no important systemic effects, since they are very poorly absorbed from the gut, and such amounts as are absorbed are excreted readily by the kidney. Traditionally, magnesium sulphate by intravenous and intra-muscular injection have been used to antagonise the convulsions of eclampsia. However, animal experiments indicate a very low margin of safety, with death by respiratory depression, calcium salts (chloride or gluconate) by intravenous injection act as a prompt and spectacular antidote for magnesium depression.

Carbamazepine (Tegretol)

This tricyclic compound related to Imiprimine was originally introduced for the treatment of trigeminal neuralgia. It is recommended for the treatment of grand mal and pshcho-motor epilepsy. It appears to be as effective as Phenytoin and may prove to be better tolerated. Can cause nystagnus and drowsiness. Other adverse side effects include anorexia, ataxia, dizzyness, and diplopia, more serious side effects also include aplastic anaemia, hepatitis, heart block, and lupus erythematosis.

Valproic Acid (Depakene)

Is an anti-epileptic used in the treatment of petit mal seizures. Experiments with this drug indicate that it is also effective for treating generalised tonic-clonic and photo-sensitive seizures, and particularly for myoclonic seizures, which are often refractory to other anti-convulsives. Its mechanism of action has not been well established, although increased brain levels of GABA have been implicated as an

explanation. The drug is rapidly absorbed when orally administrated and has a serum half life of 8 to 12 hours, and is strongly bound (90%) to plasma proteins. Valproic acid can increase Phenobarbital levels when the two drugs are taken concurrently. The most common adverse side effects are, nausea, vomiting, and diarrhoea. Other side effects include hair loss, weight gain, rash, hypersalivation, headache and insomnia have also been reported. Valproic acid can also interfere with platelet function; spontaneous bleeding or bruising are indications for stopping the drug, severe hepatic toxicity has also been reported.

Diazepam (Valium)

This is now the drug of choice in the treatment of status epilepticus. Since it is short acting, dosage can be readily titrated. It is administered by slow intravenous injection or intra-muscularly if necessary. Other drugs which are effective in the treatment of status epilepticus are Phenytoin and Phenobarbital. Any of the drugs used can be lethal if they are given too rapidly or in over-dosage. If these drugs do not suppress continued seizure activity, general anaesthesia may be necessary.

Acetazolamide (Diamox)

This is a carbonic anhydrase exhibitor, and is used occasionally. Its effectiveness is thought to be related to the inhibition of carbonic and hydrase in the central nervous system. Although effective in all types of epilepsy, its usefulness is limited by the rapid development of tolerance. Thus making this drug ineffective in continued use.

Clonazepan (Clonopin)

This is a benzodiazepine and is particularly used for myoclonic and akinetic seizures, which may be resistant to treatment with other anti-convulsives. It is also effective for the treatment of absence attacks, but generally less so than Ethosuximide or Valproic Acid. Like Acetazolamide tolerance may develop to its anti-convulsive effects; frequent adverse effects such as behavioural changes, drowsiness and ataxia may outway the benefits and should never be used in retarded brain-injured or disabled patients.

HOLISTIC CONCEPTS

The biological approach to the patient with epilepsy and/or convulsive disorders is directed towards treating the cause of the disorder not the suppression of symptoms with often life-threatening side effects. The concept proposes that anti-convulsant drugs impair both cortical control of the reflex mechanism for seizures and the maturational and developmental processes by which such cortical control is

ultimately used and established. With this paper it is my intent to issue a cautionary note to the medical world and to the parents of brain-injured children and to individuals suffering from epilepsy regarding the wide spread and sometimes indiscriminate use of anti-convulsive drugs. It has been my experience that the use of anti-convulsant drugs frequently fail to help the individual use his brain effectively and in the case of brain-injured children there is a danger that the drugs themselves further delay the child's neurological growth. It has been noted that brain-injured children who present themselves with convulsions and in taking anti-convulsive drugs show the ineffectiveness of these medicaments. More than half of the children on these medicaments continue to have convulsive disorders.

Serious doubts about the effectiveness of these anti-convulsant agents have also arisen in other medical quarters. This is clearly stated in an editorial in EPILEPSIA (17: XIII-XV, 1976). This editorial discusses a recent view of the previous medical literature on "Prognosis in Epilepsy" which "emphasises the widespread misconception that 70-80% of epileptics are controlled by drugs" does not agree with the published facts. A persistent finding in the studies reviewed is that the longer the duration of follow-up, the worse the prognosis in terms of seizure control. An overall picture that emerges from the literature is that complete seizure control is achieved for two years in 30-37% of patients but this figure falls to approximately 20% at five years and 10% at ten years". The editorial said further the picture revealed by this review "is a consistent one, which surprisingly has not altered throughout this century, despite the introduction of drugs which are so widely used today". This further emphasises the lack of efficacy of the anti-convulsive drugs used today. To this end the objections to the use of anti-convulsant medications include the following:-

1. Ineffectiveness

2. Disfiguring side-effects

3. Insidious and serious alteration of the fundamental processes in the body

4. A capacity for potential fatal reactions

5. Ability to cause inco-ordination and other neurological disorders.

6. Mind-dulling and stupefying actions.

The biological approach to the patient with epilepsy and/or convulsive disorders is directed towards treating the cause of the disorder not the suppression of symptoms with often life-threatening side-effects as demonstrated earlier in this paper. It is especially important with children to withdraw the anti-convulsant medication prior to introducing the biological treatment. It has been my experience that a gradual withdrawal of anti-consulsant medications often causes the frequency of the convulsions to decrease. It has also been my experience that brain-injured children with

convulsions that are not controlled by anti-convulsive medications react favourably to the withdrawal of those medications. It has been noted that upon withdrawal of the anti-convulsive medications the stupor which is asssociated with these drugs is lifted the child is able to respond to the outside world and frequently the process of brain maturation and stimulation is more effective. It is important to note that withdrawal of anti-convulsive medication should be attempted gradually initially beginning with the withdrawal of 10% of the dose each week this would mean that the anti-convulsive medication would be withdrawn completely in a time period of 10-12 weeks. Within this 10-12 weeks the biological treatment can be initiated and favourable results can occur.

Biological Treatment Concepts

The treatment which we offer consists of four parts. We have attempted the treatment of children with convulsive disorders and brain injuries using only one or two or a combination of the four parts and have noted that the results have not been as effective as if all four parts are used. The biological treatment of epilepsy and convulsive disorders consists of:-

1. Nutrition.

The diet we recommend is basically a whole-food diet that means food that is as close to its natural state as possible. It has been noted and documented in the medical literature that certain food colourings affect brain metabolism. It has also been suspected that certain foods can actually trigger convulsions. We therefore recommend the diet of food that is as close to its natural state as possible, not overcooked and free from any additives, preservatives and colourings.

2. Enzyme Substitution.

Enzymes are natural substances which help stimulate the body to function efficiently. The best example we have for enzymes are vitamins. In the case of an individual with convulsive disorders it is important that the patient receives a full complement of B vitamins as they frequently aid in the correct metabolism of the brain. At minimum I recommend B complex. There are other enzymes which affect brain metabolism which can be prescribed depending upon each individual patient. These enzymes fall under the following groups:-

Wobenzyme - digestive enzymes based on a combination of substances, some found in tropical fruit, given at each meal as a source as a source of vegetable and bacterial enzymes.

Piracetam (Nootrop, Nootropil, etc) - this is an entirely new compound of substances which act on the brain. Piracetam seems to act on the cerebral cortex to stimulate the production of ATP within cells, this facilitates the transfer of information between the two cerebral hemispheres. Studies show that Piracetam increases the activity of the enzyme that produces ATP (Nickerson, 1976) and improves learning capacity (Bartus, 1981).

Pyrithioxin, Pyritonol (Encephabol) - is a vitamin B6 derivative without the characteristics of a vitamin which especially influences the development of speech in infancy. This substance increases glucose utilisation and protein synthesis. Previous studies (Hotovy and Enenkel, 1964) showed that Pyriphioxin increased cerebral circulation and psychomotor efficiency.

Centrophenoxin (Helfergin) - this is a synthesised product from amino-alcohol and p-chlorphenoxy-acetic acid. Experiments have established profound influence on cell respiration and glucose metabolism by this substance (k.Nandy). Without changing pulse frequently and blood pressure an increase in spontaneous activity has been achieved in animals. The lipofuscin formation, a morphological expression of the ageing process in the cytoplasm of the neurons, seems to be delayed by Centrophenoxin. The same study demonstrates an increase in the ability to learn and remember. Contingent upon dosage and duration Centrophenoxin activitates the pentosephosphate-cycle (making ribose - 5 - phosphate available for the nucleotide and nucleic acid synthesis) and influences the transport of specific nucleic acids from the cell nucleus into the cytoplasm (K.Kanig, 1977). According to Hoyer a significant increase in circulation is achieved by Centrophenoxin among children suffering from a pathologically reduced brain circulation.

Nicotinic acid compound (Niamid, Nico-Padutin) - lead to a speedy improvement of blood circulation at the periphery. Improvement in circulation in the central nervous system is debatable but distinctive pharmacological effects on the central nervous system have been observed with Nicotinic acid amides.

Membrane activators (Membravit) - these are substances and biocatalytic combinations intended to improve the function of the cytomembranes. The function of the membrane activators is not confined to supplying reduced substances introcellularly; they also facilitate transmembrane movement. Numerous preparations and combinations of vitamins, trace elements and biocatalysts also have this effect. Membravit contains three magnesium compounds, zinc, iodised salt and vitamins B1, B2, B6 and tryptophane.

3. Biological treament

Originally this part of the treatment was known as Cellular Therapy. At one time cells were taken from animals. Foetal animals, primarily sheep, were used to donate cells. These cells were actual tissues from various parts of the animal's body. The cells were freeze-dried, similar to the process used in freeze- drying coffee, and reconstituted at the time of injection.

Therefore, in this part of the treatment, the child is given an injection every five to six months. This injection consists of particles of cells, (brain cells in most cases), that actually stimulate the normal growth and function of the child's brain.

Cellular-Therapy is a therapeutic procedure which delivers biological material from foetal or juvenile donors as "bricks" for revitalisation: the material is injected, implanted or transplanted. The cells (or tissue particles) are used by the receiver-organism in molecular sizes. This method has been used in Europe for more than 50 years in more than five million patients.

Of the innumerable diseases and injuries that are epileptogenic it has not been possible to distinguish the component of the lesion that is responsible for the seizures from one that is not. In other words one cannot say from microscopic examination whether any given lesion was epileptic gliosis, fibrosis, vascularisation, meningocerebral cicatrix have all been incriminated but they occur as well in a patient with non-epileptic phosi. Partial disconnection of groups of cortical neurons from those of the neighbouring cortex, of the other cerebral hemisphere, and of the thalamus seems likely to have occurred or certain systems of inhibiting neurons may have been destroyed. Once gliotic focus of whatever cause, bordered by groups of discharging neurons, becomes epileptogenic, if untreated it may remain so throughout the lifetime of the patient.

It is therefore difficult to recommend specific cell implantations for each specific patient but in general we can divide the treatment of convulsive disorders into specifically two groups. Those patients suffering from petit mal should have the following cellular implantations initially:-

Foetal Mesencephalon
Foetal Medulla Oblongata
Foetal Thalamus
Foetal Cerebellum

Those patients suffering from grand mal, physcho-motor and Jacksonian type seizures would benefit from the implanatation of the following tissues:-

Foetal Cerebral Cortex
Foetal Mesencephalon
Foetal Thalamus
Foetal Cerebellum*

*Note: other cerebral sections may be involved and in following implantations those cerebral sections must be implanted.

It may also be noted that frequently the patient presents himself with other problems note: in children with brain-injuries other areas of the brain must be taken into account and those areas, if deficient, must be implanted. Also in brain-injured children note that the spinal column and lack of peripheral profusion must be treated with spinal column and placenta cells. These may be included in the course of treatment. It is the Author's experience that convulsions improve following the first treatment. It has been noted in certain cases that after three to four weeks the convulsions have stopped altogether and not returned.

4. Peripheral Stimulation

With the above three sections we have taken care that the brain has been:-

i. Fed correctly with proper nutrition

ii. Given the proper enzymes so that brain function has the optimum opportunity at the metabolic level to function properly.

iii. Specifically stimulated at the biochemical level with cellular implants the parts of the brain which have not been functioning properly and have acted as phosi for convulsive activity.

With this last portion of the treatment that we offer individuals with convulsive disorders we are stimulating the brain through the periphery. The traditional approach to convulsive disorders is to suppress the electrical activity of the brain. With the biological approach we stimulate the brain to function properly and efficiently therefore stimulating the electrical activity of the brain to flow efficiently without a build-up to the threshold level so that it is all released at once causing the convulsion. It is important that the brain is stimulated through the periphery so that the electrical activity has somewhere to go. To this end we turn to a system of brain stimulation known as patterning. This system was developed by Doman in Philadelphia. With this system we stimulate the brain through the periphery with an organised patterned method. Therefore we are accomplishing two things. First the electrical activity that is building up in the brain is stimulated to flow to the periphery instead of building up to the threshold level causing a convulsion and two we are retraining the parts of the brain that are injured or deficient. With this treatment we are stimulating from the inside with the cellular therapy and stimulating from the outside with the peripheral stimulation. It would take more space than is available in this article for me to describe the processes of stimulating the brain through the periphery but basically a series of exercise prescriptions are given to each individual patient after evaluation and these exercises stimulate the brain through the periphery. Each patient is re-evaluated after four to six months and the exercise prescription is altered depending upon the progression of each individual patient.

There are many Centres throughout the world which offer varying types of peripheral stimulation. The Author has worked for a number of years with a Centre in Scotland which offers all of the treatments described in this article. This Centre is known as SABIC which is the Society For the Advancement of Brain-Injured Children. At this Centre patients are given counselling in nutrition, they are seen by the Medical Advisor who recommends the enzymes which each child needs and they are also given cellular implantations. They are then evaluated to determine the state of brain maturation. This evaluation takes an entire day and they are given an exercise prescription which they perform for 4-6 months after which they are re-evaluated. and then they are given a re-evaluation. It is noted that the children who receive all

four of the treatment modalities improve dramatically. We have been able to withdraw all anti-convulsive medication from most of the children who we have treated with a marked decrease or total elimination of all convulsive disorders.

CONCLUSION

It is noted that all anti-convulsive medications used in traditional medicine cause profound side-effects and possible brain-damage in and of themselves. With this treatment modality proposed by this article we have shown that individuals with convulsive disorders can be treated using complementary therapies that not only give surprising results in their decrease of the convulsive states but also give good results in the improving of the general health and medical abilities of brain-injured children.