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Convulsive Disorders in Children

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INDEX

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I. UNIVERSITY OF MINNESOTA MEDICAL SCHOOL
CALENDAR OF EVENTS

No. 43

October 23 - 28
Visitors Welcome

Monday, October 23

9:00 - 10:00 Roentgenology Medicine Conference; L. G. Rigler, C. J. Watson and Staff, Todd Amphitheater, U. H.

9:00 - 11:00 Obstetrics and Gynecology Conference; J. L. McKelvey and Staff, Interns Quarters, U. H.

12:30 - 1:30 Pathology Seminar; Parental Influence in Breast Cancer, Report on the Cancer Conference; C. P. Oliver, 104 I.A.

4:00 - School of Public Health; Report of the Meetings of the American Public Health Association; Ruth Grout, Ruth Freeman, Alan Treloar; Womens Lounge; H.S.

Tuesday, October 24

9:00 - 10:00 Roentgenology-Pediatrics Conference; L. G. Rigler, I. McQuarrie and Staff, Eustis Amphitheater, U. H.

11:00 - 12:00 Urology Conference; C. D. Creevy and Staff, Main 515, U. H.

12:30 - 1:30 Pathology Conference; Autopsies; Pathology Staff, 104 I. A.

12:30 - 1:30 Physiology-Pharmacology Seminar; Reciprocal vs. Non-Reciprocal Inervation in the Autonomic Nervous System; E. Gellhorn, 214 M.H. (Series will be re-convened October 31st.)

4:30 - 5:30 Obstetrics and Gynecology Conference; J. L. McKelvey and Staff, Station 54, U. H.

4:00 - 5:00 Pediatrics Grand Rounds; I. McQuarrie and Staff, W-205 U. H.

4:30 - 5:30 Ophthalmology Ward Rounds, Erling Hansen and Staff.

5:00 - 6:00 Roentgen Diagnosis Conference; A. T. Stenstrom, Leslie Anderson, 515-M, U. H.

8:00 - Minnesota Pathological Society; Tumors and Hyperplasia of the Adrenal Glands; T. E. Bratrud; 15 MeS.

Wednesday, October 25

9:00 - 11:00 Neuropsychiatry Seminar; J. C. McKinley and Staff, Station 60, Lounge, U. H.

11:00 - 12:00 Pathology-Medicine-Surgery Conference; Gastric and Duodenal Ulcer, Myocardial Infarct, C. J. Watson, O. H. Wangensteen and Staff, Todd Amphitheater, U. H.

Wednesday, October 25 (Cont.)

12:30 - 1:30 Pediatrics Seminar; Histoplasmosis in Children; Ida Imes; W-205 U.H.

12:30 - 1:30 Physiological Chemistry Literature Review; 116 M. H.

12:30 - 1:30 Pharmacology Seminar;

4:30 - 5:30 Neurophysiology Seminar; Studies on Action Potentials Resulting from Stimulation of Chemo-receptors; Miss E. J. Uehren; 214 M.H.

Thursday, October 26

9:00 - 10:00 Medicine Case Presentation; C. J. Watson and Staff, Todd Amphitheater, U. H.

12:30 - 1:20 Physiological Chemistry Seminar; Use of Spectrographic Methods in the Studies of Hemoglobin; David Molander; 116 M.H.

4:30 - 5:30 Ophthalmology Ward Rounds; Erling Hansen and Staff.

5:00 - 6:00 Roentgenology Seminar; Strangulation Obstruction of Intestine; R. Beiswanger, M-515 U. H.

Friday, October 27

9:00 - 10:00 Medicine Grand Rounds; C. J. Watson and Staff; Todd Amphitheater, U.H.

8:30 - 10:00 Pediatrics Grand Rounds; I. McQuarrie and Staff.

10:00 - 12:00 Medicine Ward Rounds; C. J. Watson and Staff; East 214 U. H.

10:30 - 12:30 Otolaryngology Case Studies; Out-Patient Otolaryngology Dept., L. R. Boies and Staff.

11:45 - 1:15 University of Minnesota Hospitals General Staff Meeting; Diagnosis and Treatment of Patent Ductus Arteriosus, M. J. Shapiro, Powell Hall Recreation Room.

1:30 - 2:30 Medicine Case Presentation; C. J. Watson and Staff, Eustis Amphith.

1:00 - 2:30 Dermatology and Syphilology; Presentation of selected cases of the week; Henry E. Michelson and Staff; W-306 U. H.

1:30 - 3:00 Roentgenology-Neurosurgery Conference; H. O. Peterson, W. T. Peyton and Staff, Todd Amphitheater, U. H.

Saturday, October 28

8:00 - 9:00 Surgery Journal Club; O. H. Wangensteen and Staff, Main 515 U.H.

9:15 - 10:30 Surgery-Roentgenology Conference; O. H. Wangensteen, L. G. Rigler and Staff, Todd Amphitheater, U. H.

9:00 - 10:00 Medicine Case Presentation; C. J. Watson and Staff, Main 515 U. H.

10:00 - 12:00 Medicine Ward Rounds; C. J. Watson and Staff, E-214 U. H.

11:30 - 12:30 Anatomy Seminar; The Gall Bladder in Pernicious Anemia Patients; E. A. Boyden, I.A. 226.

II. CONVULSIVE DISORDERS IN CHILDREN

Irvine McQuarrie

Clinical disorders which are characterized primarily by convulsions, seizures, fits or spells of various types present some of the most challenging problems encountered in the practice of pediatrics. As Hippocrates wisely affirmed more than twenty centuries ago, a generalized convulsion is always to be regarded as a serious omen until thorough examination of the afflicted person and the passage of time have proved it to be but an incidental symptom of some transient or curable disease. A severe seizure of this character in a child is a terrifying experience to witness, particularly for his parents. While certain other types of "spells," such as simple fainting or syncope, or breath holding spells, can be almost as alarming at times, they rarely signify the presence of serious illness in the case of a child, as generalized convulsions so frequently do.

That infants and young children are peculiarly predisposed to convulsive seizures, particularly in relationship to the onset of an acute febrile illness or in response to some profound emotional or metabolic disturbance, has long been recognized. While the cause of this increased convulsive tendency is still enigmatic, it is probably related in some way to such characteristics of the brain tissue in early life as its lack of myelin, its greater water content and its more rapid metabolism. The time-honored assumption that it is due to "greater irritability of the nervous system" at this age loses its validity in light of the fact that the threshold for electrical stimulation is actually higher in infants and young children than it is in more mature individuals. This greater resistance to electrical stimulation in the young applies to the cerebral cortex as well as to the peripheral nerves. A related immaturity in the development of the cerebral inhibitory mechanism may account in part at least for the tendency for convulsions to arise at the lower brain levels more frequently in early life than later.

Perhaps further investigations in the field of electro-encephalography will provide an adequate explanation for the differences in convulsive reactivity observed at different ages. It has already been shown by a number of different investigators that the "brain waves" recorded by the electro-encephalograph are normally slower and less well regulated in infants and young children than they are in older subjects. The Gibbses and Lennox have further demonstrated that the electrical pattern is far more easily "built'up" to higher-than-normal amplitude and slower-than-normal frequency in young children by such changes in physiological state as those induced by hyperventilation of the lungs or by hypoglycemia. Since the rhythm of electrical activity of the cerebral cortex, like most other aspects of physiological homeostasis, is progressively stabilized with increasing maturity of the individual, it is difficult to escape the conclusion that the young child's peculiar liability to convulsions is directly related to the immature development of this function.

Classification of Convulsive Disorders

The convulsive disorders of infancy and childhood may be classified variously according to: 1. etiology or pathogenesis, 2. character of the convulsive attacks (clinical and electro-encephalographic), 3. anatomical location of the seizure's point of origin or 4. age of patient. While all of these criteria must be taken into account in any comprehensive discussion of the subject, the following general etiological classification has proved in our experience to be the most satisfactory for practical purposes:

I. Chronic or Recurrent Convulsive Disorders

- A. Epilepsy
  - 1. Idiopathic (primary, cryptogenic, essential or genuine epilepsy)

a. Hereditary or genetic type.
b. Non-genetic or acquired idiopathic type.

2. Organic (secondary or symptomatic epilepsy--with residual brain damage from previous injuries, either focal or diffuse)

a. Post-traumatic (e.g., from direct laceration of brain tissue)
b. Post-hemorrhagic (e.g., from injury at birth or later, hemorrhagic diseases, pachymeningitis, rupture of miliary aneurysm)
c. Post-anoxic (e.g., from severe asphyxia neonatorum
d. Post-infectious (e.g., following encephalitis, meningitis, sinus thrombophlebitis, or abscess)
e. Post-toxic (e.g., "Kernikterus," encephalopathy following lead, arsenic or other chronic poisoning)
f. Degenerative (e.g., "idiopathic atrophy," cerebromacular degeneration, encephalitis periaxialis diffusa or Schilder's disease)
g. Congenital (e.g., cerebral aplasia, porencephaly, tuberous sclerosis, hydrocephalus, vascular anomalies, such as the Sturge-Weber type)

B. Pyknolepsy

C. Narcolepsy and cataplexy

D. Hysteria ("psychogenic epilepsy")

E. Tetany (hypocalcemia)

1. Hypoparathyroidism

2. Dietary deficiencies (e.g., avitaminosis D and calcium deprivation)

F. Hypoglycemic states

1. Hyperinsulinism (e.g., tumor or hyperplasia of islets of Langerhans)

2. Hypopituitarism (e.g., deficient production of diabetogenic hormone)

3. Hypocorticoadrenalism (Addison's disease)

4. Miscellaneous

G. Uremia

H. "Cerebral" allergy

I. Cardiovascular dysfunction or synocopal attacks (e.g., simple fainting attacks, Stokes-Adams syndrome, hyperactive carotid sinus reflex)

J. Parasitic brain disease (cysticercosis, toxoplasmosis and syphilis)

K. Intracranial neoplastic disease (e.g., chronic, slowly developing brain tumor or cyst)

L. Migraine

II. Acute or Non-Recurrent Forms

A. Intracranial infections (e.g., acute meningitis, encephalitis, sinus thrombophlebitis, cerebral abscess, tetanus, malaria, typhus fever)

B. "Febrile convulsions" (e.g., at onset of extracranial infections such as scarlet fever, pertussis, pneumonia, measles; also high environmental temperature)

C. Intracranial hemorrhage (e.g., from birth or other trauma, hemorrhagic disease of newborn, purpura hemorrhagica, rupture of defective vessels)

D. Toxic

1. Convulsant drugs (e.g., camphor, thujone, metrazol, strychnine)

2. "Kernikterus" in erythroblastosis foetalis foetalis

3. Acute lead encephalopathy

E. Anoxic (e.g., sudden severe asphyxia, inhalation anesthesia)

F. Metabolic or nutritional (e.g., acute hypocalcemic tetany, alkalosis, therapeutic hypoglycemia, malnutrition with dehydration and cerebral sinus thrombosis)

G. Acute cerebral edema (e.g., in acute glomerular nephritis or allergic edema of the brain)

H. Brain tumor (e.g., rapidly growing primary or metastatic neoplasm or rupture of cyst).

In clinical practice consideration of the incidence of different etiological factors at different ages is frequently helpful in arriving at a correct diagnosis and in evaluating prognosis. Convulsions are far more common during the first two years of life than at any other period. The accompanying slide shows that intracranial birth injury (including the effects of anoxia and hemorrhage) and congenital defects of the brain are the most frequent causes of convulsions in very young infants, acute infections (both intra- and extracranial and tetany) occupying places of but secondary importance. In the latter half of infancy and in early childhood, on the other hand, acute infection constitutes the most important single cause. Idiopathic epilepsy, first appearing as an important cause of convulsive seizures at about the third year of life, comes to be the most prominent single factor in later childhood.

Far less important causes of convulsions in infants than those referred to are tetany, true epilepsy, spontaneous hypoglycemia, brain tumor, renal insufficiency, poisoning, asphyxia, spontaneous hemorrhage, postnatal trauma, and others listed in the foregoing classification. In middle and later childhood the chief causes of convulsive seizures other than acute infections and idiopathic epilepsy are congenital defects of the brain, residual cerebral damage from earlier trauma, infection, lead poisoning, brain tumor, acute or chronic glomerular nephritis and certain degenerative diseases of the brain.

Acute or Non-recurrent Convulsive Disorders

As indicated in the foregoing classification the causes of acute convulsive attacks in children are extremely varied. Whereas the seizure itself is the clinical feature of primary concern in genuine epilepsy, it is usually regarded as an incidental symptom of minor importance only in the acute disorders. Any type of seizure may occur as a transient manifestation of acute disease involving the brain, but generalized tonic and clonic convulsives similar to the grand mal attacks of epilepsy are by far the most common. Seizures resulting from extracranial disorders are practically all of this type. A convulsion may merely herald the onset of an acute disease or less frequently it may occur as a terminal or agonal sign in a fatal illness.

If the patient is afebrile and has not shown evidence of infection shortly before the attack, such disorders as tetany, lead encephalopathy, head injury, intracranial hemorrhage, brain tumor, poisoning with a convulsant drug, hypoglycemia, asphyxia, cerebral sinus thrombosis (associated with cachexia), allergy and epilepsy should be considered as possible diagnoses. If the primary disease is of an infectious character, it should be ascertained whether the infection is intracranial or extracranial (prefebrile convulsions). In the case of an intracranial infection, it is necessary to determine whether it is meningitis, encephalitis, abscess, sinus thrombophlebitis or tetanus. Certain other diseases of infectious nature,

such as typhus fever, and malaria may occasionally cause convulsions because they produce local lesions in the brain.

Complete physical and neurological examinations, including inspection of the eye grounds, may give the first clue to the nature of the primary illness. An ophthalmoscopic examination may reveal the existence of choking of the discs, such as occurs in the presence of an expanding intracranial lesion (tumor, cyst, hemorrhage or abscess), acute hydrocephalus or severe encephalitis with swelling of the brain. Or it may show the presence of retinal hemorrhages, suggesting intracranial bleeding from trauma or some blood dyscrasia. Albuminuric retinitis may furnish the first clue to the presence of subacute or chronic nephritis. There may be slight choking of the optic discs in acute nephritis with arterial hypertension (acute uremia). The choreoretinities of toxoplasmosis, the reddish areas of degeneration in the macular region in cerebromacular degenerative disease and the choroidal tubercles of miliary tuberculosis are highly characteristic of these disorders.

The treatment for individual convulsive episodes in the acute disorders is similar to that of grand mal epileptic attacks to be described later. In the case of "febrile" convulsions which occur at the onset of acute extracranial infections, ordinary methods of sedation and reduction of the elevated body temperature usually suffice to prevent their recurrence. On the other hand, seizures due to severe and continuous meningeal irritation, such as occurs in tetanus and the meningitides, heavy sedation or fairly deep anesthesia may be necessary at first for their control. Phenobarbital or chloral hydrate given in medium-size doses may prove to be satisfactory in the milder type of disorder, whereas larger doses of chloral hydrate or avertin by rectum or phenobarbital sodium by vein may be required to control the convulsions caused by direct meningeal irritation. In rare instances it may be necessary to induce general anesthesia for a short period of time by inhalation of ether or chloroform or by the cautious use of such a drug as pentothal sodium intravenously. The latter type of agent should be given by an experienced anesthetist, preferably under hospital conditions, where oxygen therapy and other means of resuscitation are readily available. Whenever anoxia becomes apparent, as in greatly prolonged or frequently repeated convulsions, oxygen should be administered if possible. A quiet and otherwise pleasant atmosphere, reassurance and avoidance of unnecessary annoyance to the patient are important factors in preventing recurrence of convulsions during the period required for diagnosis and active treatment of the primary illness. The introduction of new chemotherapeutic agents, such as the sulfonamide drugs and penicillin, has greatly reduced the period of treatment in many of the acute infections, whether they are generalized or are localized intracranially or extracranially.

For hypoglycemic convulsions glucose or other carbohydrate must be administered at frequent intervals until the underlying cause can be removed. In acute tetany soluble calcium salts (chloride or gluconate) may be administered intravenously or by mouth or parathyroid gland extract may be given subcutaneously or intramuscularly to control the convulsions. If the tetany is of the vitamin D-deficiency type, this vitamin must be administered either parenterally in a single massive dose or at regular intervals by mouth in doses used for the treatment of active rickets. This curative therapy is given only after the convulsions have been brought under control.

Subdural hemorrhage occurring in the newly born infants as a result of bith injury or hypoprothrombinemia is treated by blood transfusion, aspiration of the fresh blood by way of the anterior fontanelle or by removal of a blood clot through a bone flap. It is a sound rule to administer vitamin K parenterally whenever intracranial bleeding is suspected in a young infant. The objective is the same in older children with subdural hemorrhage resulting from head injury, namely early removal of the blood clot and prevention of further bleeding.

Epilepsy

"Epilepsy" is the dreaded, and, therefore, unfortunate term long used to designate a variable symptom complex characterized by recurrent or paroxysmal attacks of unconsciousness or of impaired consciousness with or without a succession of tonic or clonic muscular spasms. Owing to obscurity regarding the underlying pathogenesis and to variability in the character of factors which appear to contribute to the causation of seizures, precise definition and classification of the clinical states coming under this general designation (or the still less desirable one, the "epilepsies"), is unattainable at the present time. Within recent years there has been a growing tendency to reserve the term "epilepsy" for the group of patients showing a chronic convulsive tendency of unknown origin and with no demonstrable evidence of organic brain pathology. Such readily recognizable physiological disturbances as hypoglycemia and hypocalcemia, as well as known convulsogenic febrile and toxic states, are excluded by this more restricted definition. According to the studies of Lennox and his associates, the genetic factor is unusually prominent in the cases falling into this narrower category and there is a higher incidence of abnormal complexes in their electroencephalograms. While disturbances of the electrical rhythms of the brain are admittedly not pathognomonic of cryptogenic epilepsy and while the hereditary factor cannot be demonstrated in an overwhelming majority of such cases, this general viewpoint has given more definite direction to our faltering search for much needed additional information regarding pathogenesis in the chronic convulsive states.

Why some patients included in this more restricted category have one type of seizure predominantly or exclusively and others have other types and why different patients respond differently to a given form of therapy still remains to be determined. So far as is known at the present time, there are no electro-encephalographic peculiarities, no special diagnostic tests and no variations in response to therapy that would in themselves serve to differentiate the genetic from the nongenetic form of idiopathic epilepsy or the "idiopathic" from the "organic" forms. They are all bound inextricably together by one common characteristic, namely, the tendency to recurrent or paroxysmal attacks of disturbed consciousness, which occur spontaneously and without known cause. Such seizures may or may not be preceded by sensory disturbances (auras) and may or may not be accompanied by involuntary tonic or clonic muscular spasms.

Symptomatology of Epilepsy. As implied in the foregoing attempt to define epilepsy, its only characteristic symptoms are those related to seizures, which may be predominantly motor, sensory or psychical, according to the location of the primary focus of abnormal neuronal discharge in the brain.

While all of the seizure types that are ordinarily listed under these headings are known to occur in epileptic children, petit mal (minor fits), grand mal (major fits) and local motor or Jacksonian attacks are far more frequently encountered than are the other forms. Any of these types of seizure may be preceded immediately by a momentary aura in the form of any of a large variety of sensory manifestations, but fewer than a third of epileptic children interrogated on this aspect of their symptomatology can give a definite description of such an experience. Auras precedes grand mal most frequently. In some cases a preliminary, localized spasm or twitching of muscles may precede a generalized seizure. This is often referred to as a "motor aura" or warning. Vague prodromal symptoms or signs, such as irritability, digestive disturbances, myoclonic spasms, headache and mental dullness may forewarn patients or their parents of impending motor seizures or of petit mal attacks. The period intervening may be one of hours or even of a day or two. So-called "secondary symptomatology," which pertains chiefly to personality traits, such as egocentricity, shallowness, religiosity and chronic negativism and which is considered by some author-

ities to be characteristic of epilepsy, is much less prominent in young children than in adult epileptics. When such personality traits are manifested, they usually can be explained most satisfactorily as a result of the patient's response over a long period of time to the strange attitude of other people toward him and his tragic disability and are not to be attributed to the disease per se or confused with the transient behaviour disturbances seen in psychomotor attacks. Similar personality disturbances are frequently seen to develop in victims of Pott's disease of the spine, crippling poliomyelitis, spastic paraplegia or severe, intractable acne vulgaris and on the same general basis.

The petit mal seizure consits of a transient loss of consciousness with no muscular spasms at all or only minor manifestations, such as staring or an upward rolling of the eyes, moving of the lips, drooping or rhythmic nodding of the head or slight quivering of the trunk and limb muscles. Attacks of this type are most frequently described by parents or other associates of the little victim as "staring or dizzy spells," "absences," "lapses" or "fainting turns."

Grand mal seizures are generalized convulsions which usually show two phases so far as the muscular spasms are concerned, the tonic and the clonic. Following a severe generalized convulsion, the patient usually awakens from his post-convulsive sleep with severe generalized headache and feels confused. He may go about in a semi-dazed or stuporous state in which he may perform more or less automatic acts without being able to recollect just what he has gone through after it is all over. These postictal reactions are interpreted as malfunctioning of neurones which have not as yet recovered from the violence of the discharge and the secondary effects of the seizure. These may be so severe at times as to result in prolonged automatism, transient paresis or more rapidly in hemiplegia or other paralytic manifestations of focal injury or hemorrhage. A grand mal seizure may occur at night ("nocturnal epilepsy") without the patient's being aware of having had it until he is informed by some other person who observed him in the attack. A bitten tongue or lip, headache, blood on his pillow or a bed wet with urine may be the only clue to the fit. Generalized motor seizures tend to be predominantly of the tonic character during infancy, although the clonic feature is always present to some degree. In association with this chronic convulsive disorder, infants sometimes exhibit a peculiar "over-response" to ordinary stimuli, instability of their thermoregulating mechanism (indicated by wide diurnal variations in the rectal temperature without fever) and increased refractoriness to anti-epileptic, sedative and anesthetic drugs.

A psychomotor attack ("epileptic equivalent" or "psychic variant") is a vague type of epileptic seizure characterized by variable degress of impairment of consciousness in which a child may become unreasonable, go into tantrums, become destructive, or take on a docile or apathetic attitude without obvious reason. The patient himself does not know why he behaves in this matter and usually has no recollection of his acts when the attack has subsided. Such seizures may be prolonged for many hours or even days, the patient carrying out complicated and purposeful but irrational movements. For instance, he may walk through crowded streets, avoiding traffic as he goes, but is sooner or later taken into custody because of some irrational behaviour.

Focal seizures may be of the sensory or the motor type (Jacksonian epilepsy), depending upon the location of the focal area of abnormal neuronal discharge. A large variety of localized sensory attacks may occur giving rise to symptoms referable to special sensory experiences. While focal seizures, either sensory or motor, may occasionally occur in the absence of organic lesions, they are usually very stereotyped and are indicative of a localized cerebral lesion. Although they are not infrequently preceded by a brief tonic phase, unilateral motor or Jacksonian attacks are typically clonic in character. This indicates their origin in the motor cortex. The

muscles most frequently involved in a Jacksonian seizure are those which are most specialized for voluntary purposes. When such an attack is of brief duration and remains localized to one area, consciousness may not be disturbed. However, when its spread is extensive and rapid, consciousness is lost and generalized convulsion occurs which is indistinguishable from a typical grand mal seizure.

Electro-encephalography and Seizures

The foregoing description of various types of epileptic seizures refers to their clinical or outward manifestations only. What are perhaps more significant are the electrical discharges in the brain. These have been studied extensively during the past decade by means of the electro-encephalograph, an instrument first adapted for this purpose in the human subject by Berger, who found that the essential feature of an epileptic seizure is a profound disturbance in the rhythm of electrical activity in the brain.

In the cerebral cortex there is a summation or synchrony of the action potentials of thousands of individual neurons which normally build up characteristic rhythms. By amplifying these summated brain potentials a million or more times as they are led off from electrodes placed at various points on the skull, it is possible by means of ink-writing oscillographic pens to make a permanent record (electro-encephalogram) on moving paper. Four types of rhythm have been described in the normal human electro-encephalogram. The most common or alfa rhythm consists of a regular series of smooth waves occurring at a frequency of between 8 and 12 per second and having a voltage of 20 to 60 microvolts when led off through the intact skull. It is most prominent in the parieto-occipital cortical areas. The second or beta rhythm most prominent in the frontal cortex is one with lower amplitude but with a frequency of 13 to 32 per second. The least common or gamma rhythm, when recognized at all arises from the frontal lobes and consists of a still more rapid (33 to 55 waves per second) pattern of extremely low voltage. The fourth or delta rhythm consists of waves similar to those of the alfa rhythm but slower, 1 to 8 per second. As a rule the younger the child the higher is his index or percentage of slow rhythm, the normal adult patterns not being fully developed before the eighth or tenth year. Closing of the eyes brings out the slower and more uniform waves. Normal sleep and light anesthesia are accompanied by slower rhythms with waves of higher amplitudes.

Epileptic seizures are always associated with marked disturbances of electrical rhythm, the E.E.G. showing greatly increased voltage and either excessive slowing or speeding up of the wave frequency, depending upon the type of seizure. This fact led Lennox to offer the name, paroxysmal cerebral dysrhythmia as a synonym for "epilepsy." Since a small percentage of supposedly normal people at times show abnormal electro-encephalograms similar to those seen in epilepsy, cerebral dysrhythmia cannot be considered absolutely pathognomonic of the convulsive state. However, even in these cases, it may someday be shown to represent potential epilepsy. Grand mal seizures are characterized by a rhythm showing a great deal of spiking with increased frequency (15 to 50 per second) and high amplitude of the waves in the E.E.G. Petit mal shows a three-per-second complex of alternating spike and sinusoidal wave with very high amplitude. Attracting the patient's attention or getting him to carry out a simple problem in arithmetic will often abolish or modify the dysrhythmia in petit mal. The so-called petit mal variant is characterized by a still slower rhythm, that is, one in which the wave-and-spike pattern occurs at a rate of two or less per second, and in which the spike has a duration greater than one fifteenth of a second. Whereas the faster three-per-second rhythm is very diffuse in its origin and can be partially abolished by CO_2 inhalation or induced almost at will in a victim of petit mal by hypoglycemia or by hyperventilation of the lungs, the slower petit mal variant rhythm tends to

originate in a constant focal area and, according to Gibbs, is practically uninfluenced by the other factors mentioned. Psychomotor attacks show prolonged periods of dysrhythmia with occasional brief periods of normal rhythms intervening. The typical seizure discharge is one consisting of slow flat- topped waves with numerous superimposed small waves (giving them a "saw-tooth" appearance) or slow (4 to 6 per second) sinusoidal waves of high voltage.

While the foregoing rhythm patterns correspond fairly closely to the clinical types as indicated by Lennox and Gibbs, there is considerable overlapping according to the studies of Jasper. The various types of cerebral dysrhythmia may occur for short spaces of time during periods between slinical seizures. They are then referred to as subclinical seizures. The occurrence of discharges of very short duration, such as a single wave-and-spike formation or a short series of grand-mal-like spikes, without clinical manifestations has given rise to the designation larval seizures. These subclinical bursts may foretell the onset of clinical seizures in some cases.

Etiology of Epilepsy--As implied in the above general classification of the chronic convulsive disorders, there are numerous factors which may contribute to the occurrence of epilepsy, but, in addition to these, there is one common underlying etiological factor the exact nature of which remains enigmatic. This may be regarded as an innate functional defect in the brain cells themselves or a chronic change in state which renders them "epileptogenic." This obscure abnormal character may be inherited, as in the genetic type of idiopathic epilepsy and in some cases of organic epilepsy as well, or acquired, as in numerous cases of organic or symptomatic epilepsy and in the presumably non-genetic type of idiopathic epilepsy. The neurones which exhibit this bizarre convulsive reactability show no special morphological alterations which can be detected by present-day histochemical techniques. In cases of so-called pure organic epilepsy, as repeatedly demonstrated by Penfield and his associates, it is not the scar, cyst or tumor tissue itself, but the surrounding altered gray matter, which is endowed with the peculiar convulsogenic reactability.

While the nature of the cellular defect which allows the building up of abnormal electrical potentials in the brain is admittedly quite unknown, some observations hint that the fault lies with the brain cell membrane. For instance, the various physioligical changes which have been observed to favor the occurrence of seizures happen to be those known in general biology to increase cell membrane permeability and those which tend to prevent seizures are those considered to have the effect of decreasing permeability. The more or less specific response of the epileptic patient to forced dilution of the body fluids (pitressin test) to be described later lends additional support to this hypothesis. The inherent abnormality in the mode of functioning of the epileptic's brain cells, no matter what its basic cause, is influenced to a certain degree by many recognizable extraneous factors. In addition to such variations, however, it appears to fluctuate spontaneously from time to time or to manifest itself in peculiar cycles or paroxysms without obvious reasons. The electro-encephalogram shows a greatly increased incidence of larval and subclinical seizures, as well as typical seizure patterns, during such spontaneously occurring periods of increased activity and few or none during periods of remission.

Given this bizarre propensity to seizures, which is the one essential feature of true epilepsy, innumerable accessory or contributing causes can result in one or other of the various types of attack. The pathological lesions that most frequently play a contributing role are listed in the above classification under the heading, "organic epilepsy." At the present time it appears likely that certain injuries to the brain, particularly those involving the structures located supratentorially, may induce more or less permanent alterations in the neurons surrounding the lesion, producing

thereby an epileptogenic focus. Severe birth injury, including the residual effects of anoxia, hemorrhage and direct trauma, deserves special mention as an extremely important cause of organic epilepsy. Ford found that half of the patients surviving such severe injury subsequently had seizures and that 2.5 per cent of all epileptics gave a definite history of birth injury. In our experience this latter percentage is much higher. Convulsions may begin at once or many months after brain injury. Of the many other pathological conditions listed in the foregoing classification under the heading of "organic epilepsy," several deserve special consideration.

Accidental head injuries any time during a child's life may have effects similar to those of birth injury. The importance of the residual damage resulting from lead poisoning has recently been emphasized by Lord and Byers.

Under vascular congenital anomalies of the brain, which may give rise to recurrent seizures, the most important are hemangiomata of the pia and underlying cortex (Sturge-Weber's syndrome) and miliary aneurysm of a small artery. The latter, while congenital, does not manifest itself by rupture and hemorrhage so frequently during childhood as it does in late adult life. However, it should be kept in mind as a possible source of intracranial hemorrhage in older children with coarctation of the aorta or other conditions placing a special strain on the arterial system. Recurrent hemorrhages from this source must be differentiated from those from the much more common condition pachymeningitis hemorrhagica interna.

In the Sturge-Weber syndrome convulsions occur as a result of a hemangiomatous lesion involving the pia and underlying cerebral cortex. This lesion characteristically shows calcification which can usually be demonstrated by x-ray. Associated with the unilateral brain lesion are vascular changes in the eye and a facial nevus vasculosis on the same side as the lesion and hemiplegia, hemiatrophy and Jacksonian seizures on the contralateral side. Surgical treatment is not indicated. However, we obtained most gratifying therapeutic results from deep x-ray therapy over the affected side of the brain in one case. Most cases respond fairly well to ordinary anti-epileptic drugs.

Tuberous sclerosis is another congenital condition of the brain occasionally appearing in several children in the same family. It is characterized by recurrent convulsive seizures, adenoma sebaceum in butterfly distribution over the nose and upper lip, mental retardation and the occurrence of firm nodular masses in the brain and at times in other organs as well. The brain nodules can usually be visualized in a pneumoencephalogram as rounded shadows protruding into the ventricular or subarachnoid spaces. The disorder takes a progressively downward course, few such children surviving beyond the seventh year of life.

Some physicochemical factors which may serve as contributing causes of typical epileptic seizures may be referred to at this point. A disturbance of the acid-base equilibrium of the body fluids toward the alkaline side definitely favors the occurrence of seizures in severe epileptics, whereas acidosis tends to prevent their occurrence. Gibbs and Lennox found consistently low CO_2 values in the blood of patients suffering from frequent petit mal attacks. Voluntary or forced hyperventilation of the lungs (alkalosis) frequently brings on petit mal seizures and occasionally grand mal as well. Breathing an atmosphere with a high partial pressure of CO_2 on the other hand (acidosis) greatly lessens the seizure tendency. The effect of hypoxia on the initiation of seizures is not so important as some reports have indicated. Evidence regarding this relationship is still somewhat equivocal. Excessive water intake under conditions which result in a dilution of the extra-cellular body fluids (e.g., with inadequate salt intake) tends to cause seizures in epileptics but not in non-epileptic subjects, except when this condition is carried to the extreme (so-

called "water intoxication"). Dehydration has the opposite effect, particularly in grand mal epilepsy. Strangely enough epileptic patients show no increase in sensitiveness to convulsive drugs, such as metrazol or strychnine, or to insulin hypoglycemia, when compared with normal or other non-epileptic subjects. In contrast with their convulsogenic effects in tetany, acute infections often tend to reduce the convulsive tendency in epilepsy. These differences in the convulsive mechanisms involved in epilepsy and in other convulsive disorders. This is an additional reason for abandoning the old definition of epilepsy which made it include all convulsive conditions and setting up our present classification. Epileptics are no more sensitive to interference with the blood supply to the brain than are normal persons so far as the induction of seizures is concerned.

Disturbances in mental hygiene, such as enforced idleness, frustration, irregularity of sleep, worry, anxiety, confusion, fright and excessive excitement contribute very prominently to the occurrence of seizures in some cases of epilepsy, particularly those of the petit mal and psychomotor types.

Pathology. Although anatomical lesions of every description and nearly every possible location both within and outside of the brain have at one time or another been described as the cause of epilepsy, it is now recognized by most neuropathologists that there is no constant morphological change which is characteristic of the disorder. Except for cerebral edema, vascular congestion and petechial hemorrhages occurring as a result of violent convulsions in fatal status epilepticus, no gross lesion whatsoever can be demonstrated either during life or postmortem in uncomplicated cases of genuine, cryptogenic epilepsy. Lesions such as scars or hemorrhagic cysts may, of course, develop in these patients as a secondary result of external trauma or of hemorrhage from severe generalized motor seizures. In passing it should be emphasized that any type of chronic lesion may occur in some persons without producing seizures and without developing brain wave rhythms typical of epilepsy. Among 18,000 soldiers with craniocerebral wounds sustained in the First World War, Sargent found epilepsy to develop in but 4.5 per cent subsequently. Similar injuries in infancy and early childhood would probably result in a much higher incidence of post-traumatic epilepsy.

Diagnosis. The clinical diagnosis of epilepsy is highly probable if a long history of recurring petit mal or generalized seizures without obvious cause is obtained. If, in addition, the child complains of a definite preceding aura and gives a family history of a tendency to seizures, this diagnosis is all but certain. Other chronic convulsive states, such as those listed in the above classification of the convulsive disorders (tetany, hypoglycemia, uremia, allergy, hysteria, syncopal attacks, etc.) are eliminated by their peculiar histories and by special tests to be referred to in connection with the brief discussions of these subjects.

The final diagnosis of epilepsy may then be completed or confirmed by special test procedures such as electroencephalography (E.E.G.), pneumo-encephalography (P.E.G.), water and pitressin test, hyperventilation of the lungs (for petit mal) and by the therapeutic test.

The water and pitressin test is carried out as follows: For several preliminary days the patient is maintained on an essentially salt-free, relatively high-carbohydrate diet and any anticonvulsant medication being given is omitted over the same period. Without change in this regime, except for forced water drinking (75 to 100 cc. per Kg. of body weight per 24 hours taken at a fairly uniform rate), the anti-diuretic hormone from the posterior lobe of the pituitary gland, pitressin, is given every 3 hours night and day in doses of 0.3 to 0.6 cc. to prevent water diuresis. The patient is weighed every 6 or 12 hours just after the bladder has been emptied. Before or by the time the net gain due to retained water amounts to 5 per cent of the original body weight (usually between 12 to 36 hours), a typical grand mal seizure is likely to occur if the

test is epileptic. The convulsogenic effect of the procedure is completely nullified if sodium chloride is given. The induction of a clinical seizure might be made unnecessary in the test, if an E.E.G. could be taken periodically to detect early appearance of the typical dysrhythmia ("subclinical seizures").

Prophylaxis. According to our present-day understanding of the problem of epilepsy, prevention has two definite aspects. One is the complete avoidance at all ages of every type of brain injury known (e.g., traumatic, toxic, anoxic, infectious and hemorrhagic), so far as this is possible. The other has to do with the genetic factor. There is no known way of preventing congenital anomalies of the brain and its coverings or the development of tumors which may be responsible for recurrent seizures.

Undoubtedly much more care could be taken, than at present, to avoid brain injuries at the time of birth and thereafter. Improvement is obstetrical management at the time of birth and during the prenatal period should greatly reduce the incidence of severe cerebral anoxia as well as laceration and hemorrhage of the brain. Excessive use of analgesics and anesthetics, unnecessary instrumental delivery and inexpert management of the complications of pregnancy are all too common. The prophylactic use of vitamin K in the mother before and in the infant shortly after delivery is indicated to prevent intracranial hemorrhage which may occur at any time between the second and fifth days of life as a feature of hemorrhagic disease of the newborn now known to be due to hypoprothrombinemia. Prevention of all types of intracranial infections so far as possible is equally desirable. Exposure to lead poisoning in any degree should be scrupulously avoided during infancy and childhood.

The most important prophylactic measure for the individual epileptic patient, aside from that of preventing the seizure itself, which is to be discussed later, is the prevention of accidents to himself and to others during an attack. Infants and young children must be guarded constantly against falling from bed, down stairs, against sharp objects, into a fire, in the street before passing vehicles or into deep water at the time of a seizure. Driving automobiles, climbing to high elevations, swimming or boating alone and working at occupations requiring the use of an open fire, hot or electrified objects or moving machinery should be forbidden epileptics.

Therapeutic management. The complete prevention of seizures and provision, so far as possible, for normal development of his mental and emotional capacities throughout the entire growth period are the prime objectives of antiepileptic therapy in the individual child. The degree of success that one can anticipate depends upon a number of limiting conditions, such as the duration and severity of symptoms, the kind of seizures, the prominence of the genetic factor, the presence or absence of complicating brain lesions, the nature and extent of the latter when present, the number and type of other contributing etiological factors, the special plan of therapy used and, finally, the capacity on the part of the patient and his guardians to cooperate in carrying this out. Where possible, of course, causative factors should be eradicated or at least alleviated. Since the variety of circumstances and agents capable of influencing the occurrence of seizures is practically unlimited, continuous search must be made for such factors and means for their removal. Because of the protean nature of its etiology, this disorder requires the highest possible degree of individualization in treatment.

Surgical treatment of one kind or another is indicated in a small percentage of epileptic children. A survey of the older literature on this phase of the subject reveals the fact that nearly every removable organ in the body has at one time or another been extirpated in the vain hope of curing epilepsy. During recent years, however, surgery has been confined almost entirely to the brain and has given much better results, on the whole, than previously, because of more intelligent selection of cases

and because it has been carried out by well-trained neuro-surgeons. Surgical exploration is indicated whenever the clinical history, results of neurological examination, the pneumoencephalogram or ventriculogram and the electro-encephalogram indicate the presence of a localized lesion which appears to be the site of origin of either Jacksonian or generalized convulsive attacks. Complete extirpation of encapsulated tumors or old traumatic scars has not infrequently resulted in long periods of remission from seizures or complete cure. Drainage of cysts or fresh hematomata and ligation of anomalous vessels may greatly reduce the number or severity of seizures without curing the patient entirely.

The best plan of treatment for all cases of cryptogenic epilepsy and for the great majority of those known to have intracranial organic lesions as well, is that which utilizes at the same time all non-surgical procedures known to favor prevention of seizures. When home conditions make it impossible to carry out all phases of this combined system of therapy, only the simplest procedures can reasonably be advised, but these must be applied consistently if results are to be at all satisfactory. Our important therapeutic resources can be discussed under the following general headings: 1. Hygiene, physical, emotional and mental, 2. Anticonvulsant drugs, and 3. Dietary regimen.

Physical hygiene, while not often a spectacular factor should never be neglected. The first requirement is that all physical abnormalities (such as obstructions of the upper respiratory tract, focal infectious, faulty body posture, adherent clitoris or prepuce, severe constipation, intestinal parasites, eyestrain, anemia and all possible sources of poisoning) be readicated as promptly and as thoroughly as possible. Regular non-fatiguing muscular exercise in the form of organized, constructive and enjoyable work or supervised play should always be provided for the child to keep his body and mind active. Simple outdoor life in the quiet country side is conducive to improvement in most cases. Overeating, a common habit among children, should be prevented.

Of even greater importance in the control of seizures is attention to proper mental hygiene. Parents, teachers, companions, and especially patients themselves are usually only vaguely aware of the close relationship between certain emotional or mental stresses and the occurrence of seizures, until this is brought to their attention by the physician. Even in the case of epileptic infants over-stimulation from sudden loud noises, bright lights or rough handling in connection with bathing, feeding, giving enemas or changing the clothing tends to cause recurrence of seizures. In older children a careful survey of the social relationships and a search for contributory emotional factors should be made from time to time with the hope of eliminating or avoiding mental conflicts, unnecessary anxiety and undue excitement of all kinds. An intelligent and tactful social service worker can often render valuable assistance in ferreting out the significant social factors. Where the personality, mental and emotional factors are complex and are obviously involved, the cooperation of an experienced child psychiatrist is frequently invaluable.

Drug Therapy. Since the introduction of bromides in the treatment of epilepsy by Leacock in 1858, drug therapy has been the choice and usually the only form of treatment used by physicians. Even today, as already implied, other therapeutic resources are utilized but rarely. This tendency to rely upon medication alone was encouraged by the more or less accidental discovery by Hauptman (1919) that phenobarbital (luminal) is from most viewpoints an even better therapeutic agent than bromides. Subsequently specific dietotherapy came into limited use for a time as a result of the discovery that fasting, the ketogenic diet and restriction of the water intake all tend to prevent epileptic seizures. Following the discovery by Putnam and Merritt (1937) of a new anticonvulsant chemical agent, phenytoin sodium or dilantin (sodium diphenylhydantoinate), which is effective in many cases of epilepsy not controlled successfully by phenobar-

bital, the tendency to depend entirely upon drug therapy has again increased. A number of forms of medication other than these three have also been found to be of value in some cases.

Phenobarbital remains the drug of first choice for use over a long period of time in the average case of juvenile epilepsy, where non-soporific doses are effective. The dosages range between 1/8 grain (8 mg.) one to three times daily in an infant and 1-1/2 grains (0.09 gm.) one to four times daily in an older child or adult with a severe form of the disease. It should be given regularly. Mebarol or prominal (methyl-ethylphenylmalonylurea) is another barbiturate which has been found of value in some cases of epilepsy. The dose is approximately double that recommended for phenobarbital. The most valuable antiepileptic drug available today, next to phenobarbital, is phenytoin sodium (dilantin or epanutin). It is administered regularly in dosages ranging between 1/4 grain (15 mg.) one to three times daily in infants and 1-1/2 grains (0.09 Gm.) one to three or four times daily in older children and adults. The dosage, as in the case of phenobarbital, is adjusted by the method of trial to meet the patient's individual requirements. The chief advantage of dilantin over phenobarbital is that it acts as an efficient anticonvulsant without producing excessive sedation or drowsiness. It should be given a trial as a substitute, therefore, in all cases requiring phenobarbital in such large doses that they suffer from mental depression or intolerable skin eruptions. Replacements should be made gradually, however, when such a substitution is to be carried out, because the modes of action of these two drugs appear to differ somewhat. The chief disadvantage of phenytoin, when compared with phenobarbital, is its greater tendency to produce toxic reactions. Fortunately, the majority of patients can take effective doses of this drug, as they can of phenobarbital, with impunity. It has recently been found advantageous for the average patient to use these two therapeutic agents simultaneously, administering them alternately in proportions of one part of phenobarbital to two parts of sodium phenytoin. In this way sufficiently small doses of each drug can be given to prevent toxic reactions, while insuring an effective antiepileptic response.

The bromide salts, while definitely relegated to a third place among antiepileptic agents still have a place in cases which do not respond satisfactorily to the other drugs. At times they may be used with advantage also in conjunction with one or other or both of these agents. Bridges has recently found definite improvement to follow use of benzedrine in cases of petit mal. Price, Wallsch and Putnam have reported benefit in cases of petit mal epilepsy from feeding deglutamic acid hydrochloride in amounts (4 to 6 Gm. three times daily) sufficiently great to increase the acidity of the urine (pH around 5.0). This adjunct had little effect on grand mal and Jacksonian attacks. On the basis of its specific effects on the water and electrolyte exchanges of the body, which are in some essential respects antagonistic to those of pitressin, Anderson and Ziegler and the author in a preliminary study found the synthetic corticoadrenal substance, desoxycorticosterone acetate, to interfere with the induction of grand mal attacks by the pitressin test. Given sublingually in propylene glycol at 8 hour intervals, it has prevented grand mal seizures almost entirely over a period of three years in one extremely severe case of genuine epilepsy. It did not appear to prevent petit mal seizures in the one case of this type which was treated. However, until further clinical studies have been carried out to determine its special indications and limitations, this comparatively expensive form of therapy cannot be advised as a substitute for the better understood and far cheaper drugs.

Special Diet Therapy. The idea which prevailed among physicians of a previous generation, that epileptic children are gluttonous by nature and bring on their convulsions by eating to excess, is no longer considered to be correct. However, it remains true

that under special conditions the dietary factor may play a significant role in relationship to the occurrence of seizures or to their prevention.

It has been demonstrated beyond question that fasting causes cessation of grand mal seizures in a majority of epileptic children, the effect usually manifesting itself shortly after ketosis appears on the third day and lasting thereafter for the duration of the fast. A strongly ketogenic diet, furnishing the body tissues with a metabolic mixture very similar to that of prolonged fasting, has a comparable anti-convulsive effect after ketosis has developed. Stringent restriction of the water intake along, even when the diet is non-ketogenic, results in cessation of grand mal seizures in a large majority of those patients who are known to respond favorably to fasting or the ketogenic diet. Establishment of a negative water balance, either by restricting the intake or by increasing the output, intensifies the anticonvulsive effects of the ketogenic regimen. Administration of alkaline salts in sufficient amounts to neutralize the acidogenic effect of fasting or of the ketogenic diet abolishes anticonvulsive action of the latter, whereas administration of inorganic acids or acid-forming salts fortifies or intensifies such action.

The modus operandi of the ketogenic regimen, which not only reduces the seizure tendency but at the same time affects the patient's mental clarity most favorably, is not fully known. Logan and Baldes found that the electroencephalographic records of those patients who responded favorably were improved. The chief physiological effects of fasting and of the ketogenic diet are: 1. the accumulation of mildly anaesthetic or sedative acetone bodies in the tissues, 2. the production of a mild degree of compensated acidosis with loss of fixed base, and 3. a small net loss of water from the body. These changes and possibly others induced by the regimen appear to counteract the abnormalities in function of the central nervous system which are responsible for the occurrence of seizures. It is highly probable that the beneficial results are due to a combination of all three of the primary physiological effects.

It has long been recognized that exclusive drug therapy may not only fail to prevent but may increase the tendency to mental deterioration in the epileptic patient. It should be noted in contrast that the dietary regimen does not have this deleterious effect. In fact, what little evidence is available on this aspect of the subject suggests that prolonged, consistent and exclusive use of the dietary regimen in suitable cases may actually help to correct the underlying cellular defect to a variable degree. The possibility of such a response may be regarded as a special indication for this form of therapy in young patients with cryptogenic epilepsy.

Dietary treatment is usually more successful if it is carried out in a well regulated hospital during the first week or two. Intelligent older children or the parents of younger patients can be taught the details of the dietary management and the technic of determining the presence of acetoacetic acid in the urine and the urinary specific gravity, if water restriction is to constitute one phase of the therapeutic program, as it may well do in the more resistant cases during the first few weeks or months. Dietotherapy is most likely to succeed when the specific gravity of the urine is made to range above 1020 and the urine turns a dark brown to deep burgundy red on addition of an excess of 10 per cent ferric chloride solution. It is essential that the various constituents of the diet be weighed carefully at first, if success is to be expected. The diet should be made palatable and varied so far as possible, and must contain adequate amounts of proteins, minerals and vitamins. Failure in this form of therapy is usually attributable to dissatisfaction and uncooperativeness on the part of the patient. Much ingenuity on the part of the dietitian or mother in the selection and preparation of natural food stuffs and to a certain extent of some special food substitutes will insure success in some difficult cases which would otherwise be doomed

to failure.

Calculation of trial diets for epileptic children of different ages is facilitated by use of the following formulae:

1. For Children of Preschool Age (or body weight up to 19 Kg.)

Total water	30 to 50 cc. per Kg. of body wgt.
Protein	2 grams " " "
Carbohydrate	0.7 grams " " "

$$\text{Fat (Gm.)} = \frac{60 \times \text{Kg. of body wgt.}}{9}$$

2. For Children between the Ages of 5 and 10 years (or 20 to 32 Kg. body weight)

Total water	25 to 40 cc. per Kg. of body wgt.
Protein	1.5 Gm. " " "
Carbohydrate	0.5 Gm. " " "

$$\text{Fat (Gm.)} = \frac{50 \times \text{Kg. of body wgt.}}{9}$$

3. For Children above the age of 10 Years (or above 33 Kg. of body wgt.)

Total water	20 to 30 cc. per Kg. of body wgt.
Protein	1.5 Gm. " " "
Carbohydrate	0.4 Gm. " " "

$$\text{Fat (Gm.)} = \frac{40 \times \text{Kg. of body wgt.}}{9}$$

The basic physiological water requirement which must always be provided varies so greatly with muscular activity and changes in clothing and environmental temparature that only an approximate estimate can be made at first, final adjustments being made empirically by trial. Existence of impairment of renal function, acute infection, vomiting or diarrhea contraindicates restriction of the water intake. If the patient's caloric needs are too greatly exceeded by the contents of the diet offered, loss of appetite or nausea will intervene to interfere with the success of this form of treatment. When the diet is adequate and is properly used, experience has shown that it is compatable with normal health over a long period of time, if, after the first few months, it is gradually made less strongly ketogenic.

For the majority of patients who show a favorable response to the combined ketogenic, water-restriction regimen, it is found advantageous to insist on maintenance of a mild or moderate degree of ketosis but to add to this the use of a medium to small dose of phenobarbital or phenytoin sodium (or both) daily to insure freedom from seizures without the inconvenience and unpleasantness incident to the use of an extremely rigid and monotonous regimen. Administration of 10 to 20 grams of dl-glutamic acid hydrochloride daily as an adjunct to this regimen may prove to be helpful in refractory cases of petit mal and psychomotor epilepsy. Careful attention to the mental hygiene is an additional essential in this combined form of preventive therapy.

Chronic Paroxysmal Disorders Simulating Epilepsy

Pyknolepsy ("myriad spells") is the designation used by Adie to describe a clinical state in which minor fits of unconsciousness practically indistinguishable from mild petit mal seizures suddenly appear in great numbers in otherwise normal children between the ages of two and a half and ten years. Characteristically the condition lasts for a period of a few months or several years and then disappears suddenly and permanently without having caused any mental deterioration or other sequelae. The occurrence of grand mal attacks precludes the diagnosis of phynolepsy. There are no muscular spasms or falling to the ground during spells and no mental confusion or drowsiness afterwards. Ordinary anti-epileptic drugs (at least in therapeutic doses), the ketogenic diet and fluid restriction are ineffectual in controlling

the spells. The etiology is a complete mystery. A genetic factor has not been established for this condition, as it has for petit mal epilepsy. Whether or not it is a rare manifestation of the latter disorder or a disease sui generis is not definitely known at the present time, but the former is likely. The one possible psychological advantage of making this special diagnosis in a given case is that it appears to offer a much more favorable prognosis than petit mal epilepsy. Electroencephalography shows the spike and wave pattern characteristic of minor epilepsy during the active phase and normal rhythms after seizures have stopped. Ephedrine sulfate and benzedrine sulfate in fairly large doses have both been hailed as beneficial drugs in its treatment.

Narcolepsy is a more or less specific symptom complex characterized by recurrent, diurnal attacks of irrepressible sleep, usually precipitated by a sudden emotional change. It occurs but rarely in children. It is said to be more frequent in boys than in girls.

The spells resemble those of epilepsy in their brevity, in the abruptness of their onset and in their paroxysmal and involuntary nature. The overpowering sleep of narcolepsy may come on suddenly while the patient is engaged in some form of activity such as talking, walking or driving. Although the mechanism of narcolepsy differs from that of the natural sleep in most respects, the electroencephalogram during an attack resembles that of deep sleep very closely, showing a marked tendency to slow or delta rhythm formation. Benzedrine sulfate has proved to be very much more effective than ephedrine or other drugs. The dosage varies between 1/12 and 1/6 grain (5 to 10 mg.) every four to six hours.

Breath holding spells which are comparatively common in early childhood are sometimes complicated by convulsions. Bridge found this to happen in more than half of 90 children brought to a children's hospital specifically for such spells. A follow-up study of these cases showed a small percentage to be epileptics. Such spells usually have their origin in disturbances of behavior which may require the services of a child psychiatrist for their satisfactory control. Rarely they are due to hypoparathyroid tetany.

Hysterical fits can resemble true epileptic seizures in a superficial way. Although they appear to occur far less frequently in children today than formerly, they are still observed from time to time. Since neurotic children presenting behavior problems not infrequently show some abnormalities in the electro-encephalogram, hysterical patients may do so likewise. However, the types of dysrhythmia characterizing the different manifestations of epilepsy are not found in hysteria. The treatment of hysterical seizures is that for the underlying psychogenic disorder, namely, psychotherapy.

Chronic hypocalcemic tetany due to hypoparathyroidism, dietary deficiency or excessive loss of calcium by way of the intestinal tract is not infrequently misdiagnosed at first as idiopathic epilepsy. The history relating to the onset of seizures, however, reveals the fact that in tetany they are frequently ushered in by an acute febrile illness, whereas in genuine epilepsy such a febrile episode tends to give relief from seizures. In active hypocalcemic tetany the serum calcium is reduced to 5 or 6 mg. per cent or less. The inorganic phosphorus is usually elevated above normal. In latent tetany the serum calcium values are intermediate between these and the normal level of 10 to 12 mg. per cent, e.g., 7 or 8 mg. per cent. The Salkowitch qualitative test for calcium in the urine shows a reduction of this element when the serum calcium is low.

The mechanism of convulsions in active hypocalcemic tetany involves a disturbance in water, as well as in calcium metabolism. The brain tissue has been shown to contain an excess of water during the active phase of tetany and the water and pitressin test is positive at that time also. The latter test is consistently negative when the serum calcium has been restored to

normal by parathyroid or dihydrotachysterol (AT-10) medication or by calcium administration.

Recurrent attacks of spontaneous hypoglycemia manifest themselves at times in the form of severe generalized convulsions, resembling grand mal epileptic attacks fairly closely. Petit mal-like spells, temporary amnesia and queer behavior resembling that seen in psuchomotor attacks may also result from prolonged hypoglycemia. These symtoms are usually preceded by feelings of hunger or gauntness, weakness, tremulousness and "cold sweats." Hypoglycemic reactions almost always occur at times most remote from meals. The lowering of the blood sugar may be caused by adenoma, hyperplasia, or carcinoma of the islets of Langerhans, by hypopituitarism or by hypocorticoadrenalism.

The physiological mechanism of the hypoglycemic convulsinn is not known. The former assumption that it is due to anoxia was disproved by the author and his associates, who found that insulin convulsions could actually be prevented from occurring in the presence of extreme degrees of hypoglycemia by having dogs used in the test breathe an atmosphere containing but 5 per cent of oxygen. Marked hypoglycemia causes a disappearance of alfa waves and the occurrence of slow waves of high amplitude in the electro-encephalogram. Curative treatment consists of surgical removal of an islet adenoma, if this is found to be present on exploration of the pancreas or extirpation of a substantial portion of the tail and body of this organ in case hyperplasia is found. It has been demonstrated that alloxan (the ureide of mesoxalic acid) exhibits a semi-specific poisoning or inhibiting action on the insulin-producing islet cells of the pancreas. When given in properly regulated doses, it was found by Brunschwig and associates to be beneficial in a case of intractable hyperinsulinism due to inoperable metastasizing carcinoma of the islet tissue. If the hypoglycemia is caused by hypocorticoadrenalism or hypopituitarism, endocrine replacement therapy is indicated.

Syncopal attacks of various types due chiefly to transient cerebral anemia are frequently complicated by slight tonic and clonic convulsive reactions of short duration confined mostly to the face and upper extremities. The most common form seen in early life is the simple fainting spell, which is brought on reflexly in certain children when a simple procedure such as removal of a sliver or insertion of a needle into the skin is carried out or the patient sustains a sudden fright or painful stimulus while in a standing or sitting posture. The susceptibility to fainting in such children appears to be related to defective reflex regulation of the vascular system, which manifests itself as a sudden relaxation of the visceral capillary bed with bradycardia and a fall in blood pressure. A slight convulsive attack may occur near the end of such a simple fainting spell. Holding the patient in a horizontal position or with the head tilted downward at a 45 degree angle for a minute will tend to shorten the period of unconsciousness. When it is necessary to subject a child known to faint easily to some painful test or treatment, it is advisable to have him lie on a table with his head lowered slightly below the horizontal position. Vigorous crying before and during a procedure, such as taking a blood sample, tends to prevent fainting. In an older child active gripping of some object in the hand and voluntary contraction of the abdominal muscles has the same effect.

In the Stokes-Adams syndrome, which occurs in heart block, a short convulsive reaction often accompanies the syncopal attack. The latter appears within 10 to 20 seconds after the onset of asystole. The diagnosis is made by examination of the heart or pulse at the time of onset and during a typical attack. Treatment consists of measures directed toward the solution of the underlying problem of heart block. Syncopal attacks of similar character have been reported in patients as a result of paroxysmal tachycardia and they occur fairly frequently following excessive muscular effort in young children with

certain congenital anomalies of the heart, such as the tetralogy of Fallot.

A hyperactive carotid sinus reflex manifests itself by episodes of unconsciousness with or without brief tonic and clonic convulsive attacks. Pressure over the carotid sinuses in the anterior neck region causes a marked slowing or temporary arrest of the pulse in individuals subject to such attacks. Associated with the asystole are symptoms of faintness, weakness, loss of consciousness and finally the convulsive reaction.

Cysticercosis of the brain should be suspected and examined for whenever recurring convulsive attacks are met with in a child showing eosinophilia, particularly if the circumstances indicate the possibility of invasion by cysticercosus cellulosae, the larvae of taemia soleum, the pork tape worm. This infestation is comparatively rare in the United States, but is not extremely uncommon in parts of China, India, Egypt, and other countries where sanitary conditions are poor. The diagnosis is often confirmed by finding the larvae in subcutaneous nodules which can easily be subjected to biopsy. Fairly typical triangular calcified areas (dunce-caps) may be seen in the x-ray of the brain or muscles. Medical treatment is ineffectual, but, if the lesions in the brain are single or few in number and are accessible, surgical removal is indicated.

Encephalomyelitis caused by the protozoan, Toxoplasma hominis, was first described as a clinical entity in man by Wolf and his associates in 1937. Since that time increasing importance has been attached to the disease as more cases have been discovered in different parts of the country. While other organs are also frequently involved, the brain is a common site of invasion. Here the somewhat crescent shaped, nucleated parasites cause necrotizing lesions which become calcified. Another common result of the invasion is an extensive chorioretinitis. Impairment of vision, retardation of mental development and recurrent generalized convulsions are the most common clinical manifestations.

The disease is seen in its most severe form in early infancy when the mortality is extremely high. In such cases it appears to be congenital in origin. Sabin has shown that the blood of infected young infants and their mothers contain complement fixing and neutralizing antibodies for the Toxoplasma. Test for these antibodies have considerable diagnostic value. When it occurs in newborn infants it is frequently referred to as fetal encephalitis. Acquired forms occur in older children and in adults, who may show extensive ophthalmoscopic evidence of the disease without other manifestations. If acquired prenatally or in early infancy, it is likely to cause either microcephalus or hydrocephalus. Apparently many cases of the acquired type in older individuals to unrecognized as such at the present time. No satisfactory form of therapy has as yet been discovered.

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III. GOSSIP

After a long summer absence it is good to be back on the job trying to collect items which will be of interest to our readers. Most staff members were able to get away at intervals this summer and found that the work went on in their absence. Mayo Clinic staff members were recently told that the largest registration in the history of the clinic was anticipated in the months to come. The importance of taking time off was stressed as nothing makes the job go better and easier than a change from the routine. "Medical vacations" are the best of all for physicians who tell us that the opportunity to get away and see what the other fellow is doing, is both restful and stimulating at the same time. A group of 43 physicians from all sections of the U.S. took a "medical vacation" at the Center for Continuation Study last week and attended a course in Internal Medicine sponsored by the American College of Physicians. Cecil J. Watson and associates assisted by representatives from the Mayo Foundation put on an interesting program which covered certain aspects of diseases of the blood, liver, lung, endocrine organs, virus diseases, infectious diseases, and gastroenterology problems of medical and surgical interest. Staff members on the program included George N. Aagaard, John M. Adams, Wallace D. Armstrong, Clarence Dennis, Charles A. Evans, Gerald T. Evans, Frederic W. Hoffbauer, Bernard G. Lannin, Thomas Lowry, Irvine McQuarrie, J. A. Myers, E. R. Rickard, Leo G. Rigler, M. J. Shapiro, W. W. Spink, and R. L. Varco. Mayo Foundation representatives were Malcolm M. Hargraves, Wallace E. Herrell, Horton C. Hinshaw, F. Raymond Keating, Jr., Edwin J. Kepler, Edward H. Rynearson, and Thomas H. Seldon. Registrants numbered physicians from Kansas, Texas, Alberta, Ohio, Utah, Illinois, North Dakota, New York, District of Columbia, Michigan, Wisconsin, West Virginia, Nebraska, Virginia, Oklahoma, Pennsylvania, Iowa, South Dakota, Virginia, and Minnesota. Noble P. Sherwood, Professor of Bacteriology and Head of the Department at the University of Kansas was registered. He graduated from our medical school and has many friends on the faculty and in the profession. The group was outstanding in every respect as it contained a higher number of well trained men than usual. There were many keen fellows in the class and they provided plenty of stimulation for those who met with them.... ..For the next three weeks, a special course for "nurse trainers" will be the offering. Nurses who have a bachelor or master degree in nursing education are in attendance. A group of twenty women from this area are taking this course which is sponsored by the University in cooperation with the United States Public Health Service. Every member of the class is living in the building during the period of instruction, including nurses from the Twin Cities. There are many advantages to be gained by staying at the Center during a course of instruction. The current course for nurse trainers is one of several that will be sponsored during the coming year. All students are given scholarships by the Federal Agency for the purpose of improving the quality of nurse education and service in this area. Similar programs are conducted elsewhere.....A large delegation of physicians from Minneapolis attended a special showing of Sister Kenny's moving picture at the Nile Theater, Thursday, October 12, at 10:30 P.M. The picture has teaching value in that it demonstrates to physicians the concept of Infantile Paralysis upon which the Kenny method is based. It also answers the question of how much functional recovery must be present before considering that the patient has reached maximum improvement. The picture is long (1-1/2 hours) and is badly in need of editing as all physicians will object to certain features in the presentation.....Minnesota is enjoying unusual weather. Fall colors are at their best, and the countryside is beautiful. We have had our early frosts and the gardens are largely a thing of the past. The University Grove gardens again had a flourishing year. I had reserved a certain amount of space in this column to describe my large blue-Hubbard squash which weighed over 30 pounds. I was sorry I hadn't taken it to the State Fair, until one of the janitors in the Zoology Building brought his 47 pound squash to school, which silenced the opposition.....