ment of the extradural hematoma be invoked. The diagnosis and emergency treatment have been outlined.

Summary

The fulminating extradural hemorrhage classically has three stages—concussion, recovery, and then relapse of unconsciousness with ipsilateral dilated fixed pupil, contralateral hemiplegia, and terminally decerebrate rigidity. The fulminating extradural hematoma is often rapidly fatal. The patient should not be transported long distances prior to intracranial decompression. The responsibility for early treatment lies with the general surgeon who first attends the patient.

Treatment by intracranial decompression through an enlarged bur hole should be carried out with haste, since irreversible changes occur rapidly in the midbrain. After intracranial decompression, the patient should be placed in the care of a neurosurgeon and accompanied by the physician en route.

References

1. Schneider, R. C., and Tytus, J. S.: Extradural Hemorrhage: Factors Responsible for High Mortality Rate, Ann. Surg. **142**:938-948 (Dec.) 1955.

2. Odom, G. L.: Neurosurgical Care of Severely Injured Patient, J. A. M. A. **168**:2087-2090 (Dec. 20) 1958.

3. Lazorthes, G.: La paralysie totale du III; la mydriase unilatérale dans les traumatismes craniens et dans l'engagement temporal: étude anatomique: Conclusions pathogéniques et pratiques, Neuro-chir. **1**:52-69, 1955.

4. Robinson, R. G.: Control of Bleeding in Extradural Hemorrhage, Australian & New Zealand J. Surg. **27**:303-306 (May) 1958.

5. Mullan, S.: Essential Don'ts in Treatment of Craniocerebral Injuries, S. Clin. North America, pp. 115-122, Feb., 1958.

TREATMENT OF HYPSARHYTHMIA WITH ACTH

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Hypsarhythmia is a type of epilepsy which has, in the past, had an extremely poor prognosis. Eleven per cent of the patients died before the third year of life, and 87% of those who lived were feeble-minded. The present series of 60 children were treated with corticotropin for one year, with marked improvement in 36 and almost complete relief in 5 as judged by electroencephalographic criteria and subjective symptoms. The mode of action of the drug was not explained, and its effectiveness in the individual case could not be predicted from a knowledge of the etiology. By contrast with the poor results obtained in the past, these recent results with corticotropin are encouraging.

In 1957 at the International Congress of Neurological Sciences in Brussels, Sorel and Dusaucy-Bauloye [1] presented an exhibit showing that ACTH is highly effective for the treatment of hypsarhythmia and infantile spasms. In March, 1958, Sorel came to Chicago to attend a conference organized by the Brain Research Foundation to discuss this treatment and its implications.[2] A full-length report by Sorel and Dusaucy-Bauloye has been published recently.[3]

After seeing Sorel's exhibit in Brussels, we began, in October, 1957, to treat patients with hypsarhythmia with ACTH. The present article is a report on the first 60 consecutive cases of hypsarhythmia in which this treatment was used. Low [4] has reported a similar study with comparable results. Infantile spasms with hypsarhythmia is a distinct entity.[5] The characteristic electroencephalographic findings are random slow waves and spike discharges of very high voltage [5b]; these are present in both waking and sleeping states (fig. 1, 2, and 3). The spike discharges vary from moment to moment in both duration and location. At times they appear to come from a single focus, and a few seconds later they seem to originate from multiple foci. Occasionally the spike activity becomes generalized, but a highly organized pattern like that of either petit mal variant or true petit mal does not occur.

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The pattern of hypsarhythmia usually develops between the 3rd and the 12th month of life. However, some of our patients were 1 day old, and one child developed spasms with hypsarhythmia at the age of 3 years. When the illness starts in the first few months of life severe mental and physical retardation usually results. Many of these children were unable to hold up their heads at 6 months of age, and many were unable to stand at the age

of 2 years. Several of the 6-year-old children could speak only indistinct single words. When hypsarhythmia develops after 12 months of age there may be a very rapid deterioration of the child's intellectual and motor status.

The spasms, which are the most usual clinical manifestations, are characterized by sudden jerking or flexion of the body; often the eyes roll up, and there is an outward flinging of the arms and quivering of the entire body. The attacks are short, but not so short as myoclonic seizures. Some of the infants have tonic-clonic convulsions that are classifiable as grand mal. The spasms are most likely to occur as the child awakens, and they tend to repeat, forming an interrupted series. Sometimes they are so numerous that several thousand spasms occur in a day.

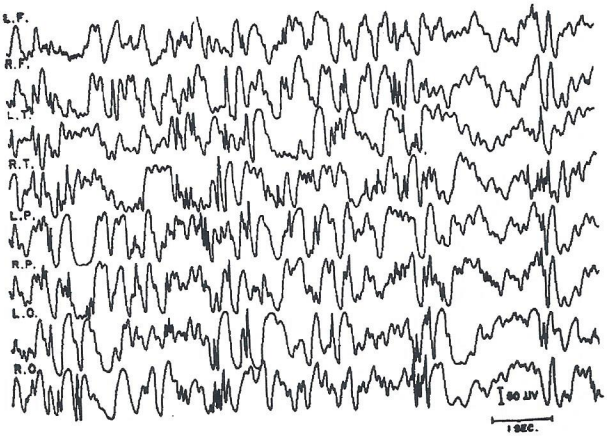

Fig. 1.—Electroencephalogram showing severe hypsarhythmia (waking and sleeping states indistinguishable), recorded on 7½-month-old infant with frequent brief spasms of turning the head, upward rolling of the eyes, and twitching of the arms, lasting for a few seconds. Onset at age of 3 months; retarded motor development; child does not sit up and is unresponsive; etiology unknown. Time calibration shows one second. Voltage calibration indicates the deflection for 50 μv.

The prognosis for a child with infantile spasms was extremely poor before the introduction of treatment with ACTH.[6] Eleven per cent of the patients died before the third year of life, and 87% of those that lived were feeble-minded. Although the seizures tend to subside by the fourth year of life even without treatment, retardation is permanent.

Materials and Method

An electroencephalogram was obtained on each child suspected of having hypsarhythmia, and the diagnosis was established before treatment with ACTH was begun. All recordings were made with the patient in both waking and sleeping states. The recordings were monopolar; interconnected ear lobes were used as a common reference, but this is unimportant because hypsarhythmia is a disorder that can be seen as easily in bipolar as in monopolar recordings.

As soon as the electroencephalographic diagnosis was established treatment with ACTH was begun. Infants were given (intramuscularly) 5 units of corticotropin gel (Purified Corticotropin-Gel Wilson) daily for five days. This was increased to 10

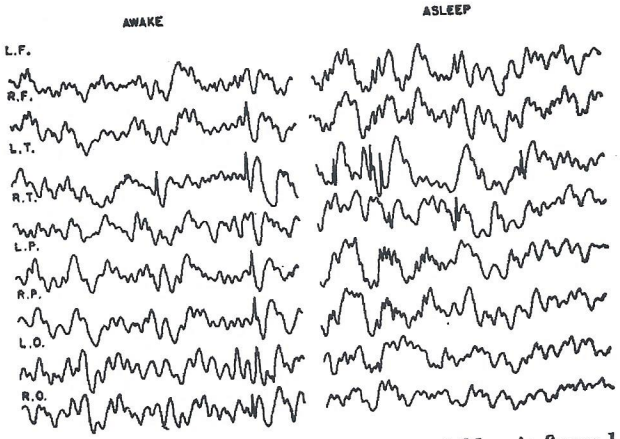

Fig. 2.—Electroencephalogram of same child as in figure 1 after 18 daily injections of 16 units of ACTH gel. Brief seizures are reduced in number and electroencephalogram is improved.

units after 5 days and 15 units after 10 days. On the 15th day the electroencephalogram was repeated. If there was clinical or electroencephalographic evidence of improvement the dosage of 15 units per day was maintained. If not, the dosage was increased gradually up to a maximum of 50 units per day. In one case the electroencephalo-

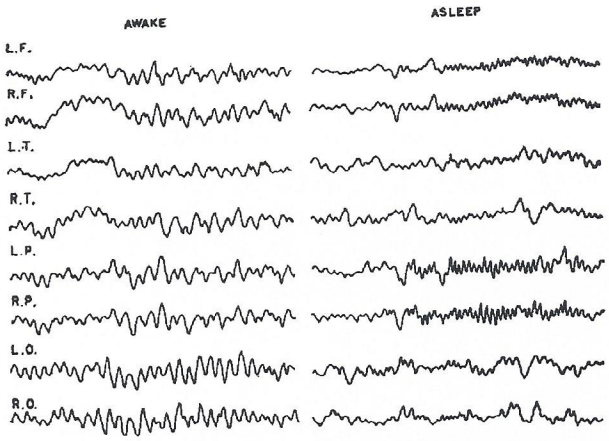

Fig. 3.—Electroencephalogram of same patient 30 days later after total of 54 daily injections of 16 units of ACTH gel. Normal electroencephalogram; no seizures have occurred for 20 days; child is able to sit up by himself and get up on his knees; he is responsive, alert, and apparently of normal intelligence.

gram normalized with the patient in both waking and sleeping states after 20 injections; the infantile spasms stopped completely and there was marked mental and physical improvement during the ensuing month. In a few cases, in order to obtain maximum benefit it was necessary to give as many as 120 daily injections.

Results

The table shows the number of patients whose electroencephalograms normalized and who became seizure-free. The number whose general clinical condition improved and the number unimproved are also shown. From these figures it will be seen that when the spike discharges disappear from the electroencephalogram the prognosis is good. In the five patients with complete normalization in both waking and sleeping states, all became seizure-free; three became completely normal clinically, two improved, none remained unimproved, and none showed relapse.

Among the 31 patients with marked electroencephalographic improvement, 42% were seizure-free, 40% were greatly improved, and only 18% were unimproved as far as seizures were concerned. The general improvement in motor performance and intellectual activity was similar to the improvement in the seizures; 10% became clinically normal and 50% were greatly improved. However, 30% showed relapse.

Further confirmation of the prognostic value of the electroencephalogram appears when one considers the 24 patients who were unimproved electroencephalographically; none were seizure-free and 96% were unimproved as far as seizures were concerned. None became clinically normal, and 96% were clinically unimproved.

Relationship Between Electroencephalographic and Clinical Response to ACTH Treatment

No. of Cases	EEG After Treatment	Seizures						Motor Performance and Alertness							
		Eliminated		Decreased		Unchanged		Normal		Improved		Unimproved		Relapsed	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
5	Normal	5	100	0	0	0	0	3	60	2	40	0	0	0	0
31	Improved	13	42	12	40	6	18	3	10	15	50	13	40	9	30
24	Unimproved	0	0	1	4	23	96	0	0	1	4	23	96	1	4
Total 60		18	30	13	22	29	48	6	10	18	30	36	60	10	17

We have tried to analyze the etiology to determine the most usual cause of hypsarhythmia and to see if we could establish any relationship between etiology and response to ACTH. Each of the common infectious diseases of childhood was implicated in a few cases, but none seemed to be particularly likely to produce hypsarhythmia. In 28 of our 60 cases there was no history of illness just before the onset of spasms and the symptoms appeared suddenly without apparent cause. In 10 cases hypsarhythmia developed after encephalitis. Various diseases were involved: chickenpox, measles, virus pneumonia, and German measles. In one case triple vaccine injections were held responsible, but the association may have been coincidental. There were single cases in which the disorder was secondary to meningitis, otitis, and Mongolism respectively. Among the five cases in which ACTH normalized the electroencephalogram, made the patient seizure-free, and produced a general clinical improvement, no relationship could be found between the etiology and the therapeutic response. In this maximally responsive group each of the following etiologies was responsible for one case: German measles, roseola, upper respiratory infection, and cerebral palsy; in one case there was no assignable cause. When hypsarhythmia occurs in a patient with cerebral palsy it is usually difficult to decide whether the hypsarhythmia is the result of a developmental defect, anoxia at birth, or trauma. The situation is further complicated by the fact that babies with hypsarhythmia often become spastic after a number of years. The conclusion is not justified that spasticity indicates that the cerebral palsy is the cause of the hypsarhythmia.

In the conference organized by the Brain Research Foundation,[2] the question arose as to whether chlorpromazine might increase the effectiveness of ACTH therapy. Sorel had used chlorpromazine in the patients he treated with ACTH, and the incidence of great clinical improvement and normalization of the electroencephalogram in his series of cases was somewhat higher than in ours in which no chlorpromazine was used. We placed seven patients who did not respond to ACTH alone on therapy with chlorpromazine and ACTH. One patient became completely normal, three improved, and three patients remained unimproved. The question arose as to whether anticonvulsants might increase the therapeutic effect of ACTH. One patient who returned to normal was not receiving anticonvulsants. All others were on therapy with various combinations of diphenylhydantoin (Dilantin) sodium, phenobarbital, trimethadione (Tridione), primidone (Mysoline), and methsuximide (Celontin). A relationship between tranquilizers and anticonvulsants and the therapeutic effect of ACTH has not been established. The mode of action of ACTH in causing improvement in some cases of hypsarhythmia is not understood. It is also not clear why some patients fail to respond to this form of therapy. At the present time one cannot predict in which case of hypsarhythmia the patient will respond to ACTH.

About 15 of the total series of 60 patients were hospitalized, and their electrolyte balance and steroid levels were studied. These investigations will be reported in a subsequent paper.

Summary and Conclusions

Before the introduction by Sorel of ACTH for the treatment of hypsarhythmia, the prognosis for patients with this condition was extremely poor; 85% became mentally retarded and 10% died. Elec-

troencephalographic and clinical studies on 60 consecutive patients with infantile spasms with hypsarhythmia, some of whom have been followed up for over a year, indicate that ACTH therapy results in a dramatic improvement in at least 30% of such cases. When a good response to ACTH is obtained, the electroencephalogram normalizes, a great clinical improvement occurs, the spasms cease, and further retardation is prevented.

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The corticotropin gel used for this investigation was supplied as Purified Corticotropin-Gel Wilson by Wilson Laboratories, Chicago.

References

1. Sorel, L., and Dusaucy-Bauloye, A.: A propos de 21 cas d'hypsarhythmia de Gibbs: Son traitement spectaculaire par l'ACTH, exhibit at the International Congress of Neurological Sciences, Brussels, 1957.

2. Molecules and Mental Health, ACTH Treatment of Hypsarhythmia—Third Scientific Conference, Brain Research Foundation, Chicago, March 31, 1958, Philadelphia, J. B. Lippincott Company, to be published.

3. Sorel, L., and Dusaucy-Bauloye, A.: A propos de 21 cas d'hypsarhythmia de Gibbs: Son traitement spectaculaire par l'ACTH, Acta neurol. et psychiat. belg. **58:**130-141 (Feb.) 1958.

4. Low, N. L.: Infantile Spasms with Mental Retardation: II. Treatment with Cortisone and Adrenocorticotropin, Pediatrics **22:**1165-1169 (Dec.) 1958.

5. (*a*) Vazquez, H. J., and Turner, M.: Epilepsia en flexión generalizada, Arch. argent. pediat. **35:**111-141 (March) 1951. (*b*) Gibbs, F. A., and Gibbs, E. L.: Atlas of Electroencephalography, vol. 2, Epilepsy, Cambridge, Mass., Addison-Wesley Press, 1952. (*c*) Gibbs, E. L.; Fleming, M. M.; and Gibbs, F. A.: Diagnosis and Prognosis of Hypsarhythmia and Infantile Spasms, Pediatrics **13:**66-72 (Jan.) 1954. (*d*) Gastaut, H., and Roger, A.: Symposium sur les convulsions de l'enfance: Etude électroencéphalographique des convulsions infantiles, Pédiatrie **42 (n.s.8):**603-614, 1953. (*e*) Hess, R., and Neuhaus, T.: Das Elektroencephalogramm bei Blitz-, Nick-, und Salaamkrämpfen und bei andern Anfallsformen des Kindesalters, Arch. Psychiat. **189:**37-58, 1952. (*f*) Kellaway, P.: Myoclonic Phenomena in Infants, Electroencephalog. & Clin. Neurophysiol. **4:**243 (May) 1952. (*g*) Thiebaut, F.; Sacrez, R.; Rohmer, F.; and Isch-Treussard, C.: Corrélations électrocliniques dans 25 cas d'hypsarhythmia de Gibbs, Rev. neurol. **93:**455-460, 1955. (*h*) Druckman, R., and Chao, D.: Massive Spasms in Infancy and Childhood, Epilepsia **4:**61-71 (Nov.) 1955. (*i*) Livingston, S.: Diagnosis and Treatment of Convulsive Disorders in Children, Springfield, Ill., Charles C Thomas, Publisher, 1954, p. 110. (*j*) Illingworth, R. S.: Sudden Mental Deterioration with Convulsions in Infancy, Arch. Dis. Childhood **30:**529-537 (Dec.) 1955. (*k*) Baird, H. W., III, and Borofsky, L. G.: Infantile Myoclonic Seizures, J. Pediat. **50:**332-339 (March) 1957.

6. Reference 5*a*, *b*, and *c*.

GASTRIC PERFORATION IN THE NEWBORN INFANT

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Perforation of the stomach wall in the newborn infant was first described by Siebold in 1825, and 81 cases have since been reported. Mortality is 81%. Peptic ulceration was initially considered the cause of perforation, but congenital defects of the stomach wall and other etiological factors have now been defined. The first attempt to close such a perforation was in 1929, but survival after operation was not recorded until 1950. There should be little difficulty in making an early diagnosis and instituting proper treatment, if the possibility is kept in mind. Prompt identification and adequate supportive management during the preoperative and postoperative periods should decrease mortality.

Until recent years little had been written about perforation of the stomach in the newborn infant. This is not surprising, in view of the paucity of known cases. Vargas and others [1] have credited Siebold with publishing the first report of this entity in 1825. During the next century fewer than 10 cases were reported. However, within the past two decades more cases have been recognized and reported, bringing the total to 81. The over-all mortality in the cases reported is 81.5%.

Etiology

The cause of perforation in the initial cases was ascribed to peptic ulceration. In 1943 Herbut [2] shed new light on the subject when he found the perforation in a newborn infant to have resulted from a localized congenital defect in the musculature of the stomach. This finding has been confirmed by other observers.[3] Overwhelming septicemia with ulceration and necrosis of the stomach,[1] gastric ulceration resulting from intracranial hemorrhage sustained at birth,[4] stress and anoxia with resultant gastromalacia,[5] ruptured diverticulum,[6] distal obstruction,[7] intubation from tracheal suction or gavage feeding,[1] and abdominal trauma during delivery [8] have been cited as etiological factors. Cases have been reported in which no cause for the perforation could be found.[9]

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