observations of the effective dosage of the optically active isomers and of the racemic compound were completed. Two cases of post-encephalitic Parkinson's disease have also been under observation for several months, and while it is more difficult to quantitatively evaluate therapy in this disease than in narcolepsy, the relative effectiveness of the isomers is clearly apparent. One case of postural hypotension has also been studied with the isomeric compounds. In all cases studied the method was to determine a minimal effective dosage of each compound that produced comparable degrees of effect.

Dextro-amphetamine was found to be much more active than the levo isomer in all the cases studied. The ratio of their relative activities varied from 2 to 4. It was likewise found that the dextro isomer was more active than the racemic compound, which in turn was more active than the levo isomer. Theoretically, if the levo : dextro ratio is as 1 : 4 for their activities, the corresponding racemic : dextro ratio should be as 5 : 8. Our observations indicated that the activity of the dextro isomer was indeed from about 1.5 to 2 times that of the racemic compound.

Some supplementary observations† have been carried out on 10 normal individuals with regard to the comparative effects of the dextro and the racemic compounds on alertness and mood. These observations naturally have a low degree of precision and depend upon subjective impressions, but the dextro isomer was very clearly the more active.

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Electroencephalographic Studies in Relatives of Epileptics.*

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(Introduced by R. J. Block.)

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In studying heredity in nervous and mental diseases it has proved useful to study not only the incidence of identical clinical entities in other members of the family but also to observe the occurrence of other personality or physical trends, which appear to be related in some way to the disease under study. Such characteristics may be

† These observations by Dr. Harvey Lewis.

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found in many members of the family who may, nevertheless, not manifest clinical evidence of the disease itself. In studies of heredity it is obviously important not only to study the direct line of descent with regard to the factors under analysis but also the total family including siblings where the latent element may possibly occur.

The development of electroencephalography has revealed that abnormal electroencephalograms can be found in epileptics not only during seizures but also in many cases between seizures.[1, 2, 3] Considering the findings in the electroencephalogram as possible evidence of either the manifest or latent existence of an epileptic tendency it seemed important to study to what extent electroencephalographic abnormalities are present in the relatives of known epileptics.

Methods. Electroencephalographic studies were performed on all the relatives possible to contact, of epileptics committed to one of the large state hospitals of New York and diagnosed as "idiopathic epilepsy." The relatives included the parents, when possible, and all the siblings possible. A short history was taken on every relative with special reference to the incidence of nervous and mental disease and particularly of convulsive and epileptoid trends. Whenever some organic disease involving the nervous system seemed probable in a relative a complete neurological examination was performed. To date, 93 relatives of 31 epileptics have been examined.

A 2-channel electroencephalograph with ink writing recorders, constructed by one of us (W.E.R., Jr.), was used. Standard records were taken with 2 pairs of electrodes placed symmetrically in both frontal and occipital regions so that we obtained trans-frontal, trans-occipital and right and left fronto-occipital records. Patients were lying down at rest, in a darkened room, with the eyes closed.

Observations. Three types of electroencephalograms (EEG) were differentiated. These were called normal, abnormal and suspicious records. Under the classification of abnormal were included those which showed serial activity of 3 or 6 or between 3 and 6 cycles per second of an amplitude of at least 50 microvolts. In the classification of suspicious records were included those showing either similar series of lower amplitude or similar slow frequencies in relatively large numbers but without forming series. Normal records were considered as those showing none of these findings. The appearance of series of slow potentials exclusively after hyperventilation was considered as abnormal only when it occurred in adults.

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As stated above, our preliminary study to date includes 93 relatives of 31 epileptics. The number of relatives studied varied from 1-9 in the various families. Table I summarizes these results. Twenty-five members constituting 26.9% of the examined relatives gave definitely abnormal records. Of the 93 relatives examined 30 were parents of the epileptic patients. Seven of these or 23.3% of such parents showed abnormal records. Of the 63 siblings of the epileptic patients 18, constituting 28.6% gave abnormal records. Of the 31 epileptics whose families were examined at least one person with an abnormal record in the family was found in 14 cases or 45%. Definite abnormality of at least one parent was present in 8 cases or 34.8% of the 23 cases in which one or both parents were examined. Abnormal records in at least one sibling were found in 11 or 46% of the 23 cases in which the siblings were examined.

TABLE I.
Incidence of Abnormal Potentials in the Relatives Studied.

Group	Case No.	Parents Found			Siblings Found		
		Normal	Suspicious	Abnormal	Normal	Suspicious	Abnormal
Normal Records	1	1			2		
	2	1					
	3	1					
	4				2		
	5	1					
	6	2			4		
	7	1			2		
	8	1					
	9	1			4		
	10	2			4		
	11	2					
	12				1		
Suspicious Records	13					1	
	14					1	
	15		1				
	16	2				1	
	17				1	1	
Abnormal Records	18			1	6	2	
	19					1	2
	20	1	1		2	1	1
	21	1				1	2
	22		1			1	2
	23	1		1	1		
	24			1			
	25	1		1		1	1
	26			1	2		1
	27						2
	28			1	1		2
	29	1		1			2
	30	1					1
	31				1		2

The records in general revealed 2 family groupings. One family group consisted of those cases in which several persons with abnormal records were found. The other group consisted of those in which the relatives did not show any evidence of electroencephalographic abnormalities. Thus it is clear that the abnormal records were not equally distributed throughout the various families.

In the first group mentioned above, namely, that in which abnormal records were found in one or several relatives of the patients, there were 14 cases or 45% of 31 families examined. Fifty-three relatives of these 14 patients were examined and abnormal records were found in 25 cases or 47.2%. Normal records were found in 19 cases or 35.8% and suspicious records were found in 9 cases or 17%. In 3 cases overt familial epilepsy was present. In a total of 10 cases or 71.5%, some other clinical symptom related to epilepsy, such as epileptoid personality, migraine, etc., was present. A possible symptomatic cause for the convulsive disorder was found in only 2 cases. In the remaining 12 cases or 85.7%, a history indicating only "idiopathic epilepsy" was obtained. It is clear from the above that one group of these patients showed a high incidence of abnormal or suspicious electroencephalographic findings in the relatives examined, associated with a high incidence of clinical "epileptoid" features in the relatives and a history suggesting idiopathic epilepsy in the patients.

The second group included those cases in the relatives of which no abnormal electroencephalographic patterns were found. All that can be said at present is that such abnormal potentials were not found even with hyperventilation. Since abnormal potentials are not always present and cannot always be produced by hyperventilation, even in overt epileptics, it is possible that abnormal records in some of the examined subjects were missed. In some cases, in addition, it was not possible to obtain records on all relatives of the patient. Thus, it is again possible that some of those relatives were missed who might have shown abnormal records if recorded. Preliminary observations, however, to date indicate the probability of the existence of these 2 groups of relatives and final answer can be obtained only as the study is continued in a large number of cases. It is of interest that this group of 12 patients in which 32 relatives were examined with no abnormal electroencephalographic findings, showed clinical epileptoid characteristics in only 4 cases or 33⅓% of the relatives and a history very probable of symptomatic epilepsy in 6 cases or 50%.

Although, as mentioned above, the relatives examined tended to

separate themselves out on the basis of their electroencephalographic records into a group with a high incidence of abnormal records and a group with no abnormal records, there was a small third group of 5 epileptics with 8 relatives in which no definitely abnormal but some suspicious records were found. Of the 8 examined relatives in this small group normal records were found in 3 cases or 37.6% and the suspicious records in 5 cases or 62.5%. Clinically epileptoid trends in the family were found in 3 cases or 60% of these 5 families and a history of "idiopathic epilepsy" in all of the cases. Although we feel that ultimately the suspicious records will have to be included in the group of pathological or abnormal records these records are being kept for the present in a separate group until the problem is more definitely controlled on a largr series of cases.

Discussion. As a result of the preliminary studies made so far it is evident that many subjects with abnormalities of the electroencephalogram can be found in the families of some epileptics and also that similar abnormalities are not found in the families of other epileptics. On the basis of these 2 groups of electroencephalographic findings it seems possible that in time, on the basis of the electroencephalogram, at least 2 forms of epilepsy may be established; one with abnormal brain potentials in the family and one without abnormal brain potentials in the family. It is highly probable that many cases now diagnosed as "idiopathic epilepsy" in our hospitals are not definite idiopathic epileptics but are related to some more specific, as yet undetermined causes, which would place them in the group of symptomatic convulsive disorders. Further studies are being made to determine whether these 2 groups of patients, as determined by the incidence of abnormal electroencephalographic findings in their families, correspond to the 2 groups which on careful clinical examination might be separated out into the idiopathic and the symptomatic convulsive disorders.

A still more important question arising from these findings, certainly from the practical genetic or therapeutic angles, is the question as to whether relatives, clinically non-epileptic, showing abnormal electrical patterns may develop overt seizures at some time or other. This would seem to be especially important in those young siblings of epileptics, in which the abnormal electroencephalographic findings are present even though overt seizures have not occurred. It seems highly probable that only a small percentage of relatives with abnormal electroencephalographic findings ever develop overt clinical seizures. A long study and follow-up will have to determine whether those cases which will, at some time or other, develop overt seizures

can be separated out from the other relatives who, although they manifest abnormal electroencephalographic findings, fail to develop overt seizures. In addition, another important question is whether such cases can be detected in early childhood and preventive measures of some sort taken to eliminate the probability of the onset of overt seizures. Finally, the problem as to the "carrier" nature of such relatives with regard to the heredity of convulsive disorders is a highly important one on which it is hoped the long controlled series of observations now under way at the New York State Psychiatric Institute may shed future light.

Summary. Upon examination of parents and siblings of patients diagnosed as idiopathic epileptics it was shown that 23% of the parents and 28% of the siblings showed definitely abnormal EEG findings. The material fell roughly into 2 groups, that is, those families showing a high incidence of abnormal EEG findings and those families showing no such evidence. The diagnostic, therapeutic and genetic problems are briefly reviewed in relation to these observations.

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Fluorescence and Absorption Spectra of Flavin Isolated from a Toxic Culture Filtrate of *C. diphtheriae.*

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This note* reports the isolation of flavin elaborated by *C. diphtheriae,* strain No. 3203, grown in synthetic medium. Flavin was separated by ultrafiltration from the toxin and extracted by chloroform from the filtrate after it had been treated with ether to remove the porphyrins soluble in ether and any other ether-soluble substances. The chloroform extract was subjected to chromatographic

* This study is a continuation of previous studies[1,2,3] of toxigenic growth of the diphtheria bacillus in synthetic medium. I wish to thank Miss Amy Walker for her collaboration in the technical work.

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