of the significance of minor abnormalities in the E.C.G.s of apparently healthy people makes it hazardous for us to acquaint the patient with their presence or to advise alterations in job or way of life. In this way much unwarranted cardiac invalidism might be engendered. Certainly none of our "high-risk" subjects were acquainted at any time with the nature of their E.C.G.s. Indeed, even in retrospect it is difficult to know what advice could usefully have been given them. Our present limitations in individual prognosis are underlined by the fact that of the 20 men re-examined in group B2 (who had the grossest changes in 1954-7), 13 are still absolutely free of cardiac symptoms (Table VI) and four of these now have no abnormality in the post-exercise E.C.G. Thus, although the risk of the subsequent development of clinical coronary heart disease is clearly high in persons with such changes, we must agree with Weitzman and Smith (1959) that in a patient with chest pain the presence of RS-T depression of even 1 mm. after exercise does not necessarily mean that the particular pain complained of is due to coronary heart disease, nor, we can add, does it mean that he will certainly develop symptoms over the next five years.

Our results raise some interesting theoretical points. The re-examination of a sample uncovered a surprisingly large proportion of persons suffering from undoubted but undiagnosed coronary heart disease. This emphasizes the deficiencies of the indirect postal follow-up technique. The results also suggest that a high proportion of cases of coronary heart disease can be found months or years before the clinical onset of the disease. A further study limited to men over 40 and including persons with asymptomatic hypertension could be expected to yield a large group with RS-T depression after exercise who would be suitable both for analysis of aetiological factors and for therapeutic trial.

Oliver (1962) has drawn attention to the fact that reduction of plasma cholesterol either by modification of diet or by drugs does not appear to alter the prognosis in persons who have suffered myocardial infarction. He favours the trial of such procedures in young men without symptoms, in the hope that irreversible changes will not already have been produced in their coronary arteries. It is unknown to what extent RS-T depression after exercise in symptomless men is a manifestation of an irreversible change. However, such men would seem to be a group in whom the trial of measures designed to increase collateral circulation or to reduce circulating cholesterol would be worth while.

Summary

Six hundred and sixty men in whom there was no clinical evidence of heart disease were examined by means of an electrocardiogram before and after exercise in 1954-7. The E.C.G.s were classified as "normal" or "anomalous." The subsequent fate of the men has been followed to the end of 1961 and news was obtained of all but six of them. In the interval a significantly higher proportion of the anomalous group than of the "normal" group had suffered a definite episode of clinical heart disease for which medical care had been required.

With precautions to avoid bias, 73 of the remaining men in the anomalous group and 104 controls from the normal group were re-examined in 1961. Fourteen additional cases of coronary heart disease were uncovered in this way—11 in the anomalous group and 3 in the

normal group. All 11 of the men whose E.C.G.s had been judged anomalous in the 1954-7 survey and had subsequently developed coronary heart disease had shown flat or sagging depression of the whole RS-T segment of 0.5 mm. or more after exercise.

The results show that it is possible, by means of an E.C.G. before and after exercise carried out in symptomless men, to identify a population with a higher-than-average risk of developing coronary heart disease in the next five years. The limitations of the method in individual prognosis are pointed out, and its theoretical and practical implications are discussed.

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A FOLLOW-UP STUDY OF LATE-ONSET EPILEPSY

I. NEUROLOGICAL FINDINGS

BY

E. A. SERAFETINIDES, M.D., D.P.M.

Research Assistant, Guy's-Maudsley Neurosurgical Unit,
Maudsley Hospital

AND

J. DOMINIAN, M.A., M.B., M.R.C.P.Ed., D.P.M.

Senior Registrar, the Bethlem Royal and Maudsley Hospitals

An examination of the relevant literature on epilepsy of late onset reveals two important findings. The first is that the condition is not rare. Thus in a study of 245 patients investigated for seizures after the age of 12 years Martin and McDowell (1954) found an incidence of 43% starting after the age of 35; and Alajouanine *et al.* (1959), analysing 7,745 cases from the literature between 1901 and 1955, gives a figure of 32.7% in which epilepsy started after the age of 20. The second relates to the incidence of tumours. The incidence found may well reflect the source of reference, and it is not surprising to note that neoplasms and trauma are given as the commonest causes by Penfield and Jasper (1954). If unselected material is considered it has been shown repeatedly that tumours account for only a small proportion. Walker (1936), in a study of 100 cases with an age of onset after 20, found only 16 tumours and 4 head injuries. Sheehan (1958), in a study of 1,000 cases after the age of 20, could find a causal factor in 552 cases only, and 139 of these were tumours, giving an overall incidence of nearly 14%. A study reported by Du Saucy-Bayloye and Sorel (1959) of 265 patients over the age of 40 shows 20% of tumours. Raynor *et al.* (1959), reporting on 141 patients with a follow-up of 3 to 15 years, found only 16 certain tumours.

So far as we know, no detailed examination has been made of late-onset epilepsy accompanied by psychiatric illness. This study presents the results of a review of 51 patients seen at the Maudsley Hospital, and is concerned primarily with the aetiological and seizure data. Detailed psychiatric and social studies are reported in Part II.

Method

All patients who developed epilepsy after the age of 25 and who were seen consecutively between 1952 and 1956 were studied. A total of 51 patients (29 males, 22 females) were found to fulfil these criteria. Our dividing age is later than most recent studies but is in agreement with the view of Alajouanine *et al.* (1959). Clinical details were abstracted from their notes and the patients were seen personally by one or other of us and independently by the psychiatric social worker. All except one were traced, and sufficient details are available to assess their current epileptic and psychiatric state. Five had died, and a history regarding the mode of death was obtained from either the nearest relative or the hospital concerned. The majority of these patients were under the care of Dr. Denis Hill, the remainder being under the care of various physicians of the hospital. All had E.E.G.s, which were carried out and reported upon in the department of clinical neurophysiology of the Institute of Psychiatry. All but five of the patients were investigated as in-patients.

Findings

Age of Onset and Duration.—In nearly 70% of the patients the seizures started under the age of 40. The remainder were spread over a wide range as shown in Table I. Patients were referred after having been under the care of their general practitioners or investigated at other hospitals and when first seen had already a long history of epilepsy, the minimum average duration for any age group being 5.5 years and the maximum 18.8

TABLE I.—*Findings on Admission*

	Age-group								Total
	25–	30–	35–	40–	45–	50–	55–	60+	
No. of patients ..	11	13	11	4	3	3	2	4	51
Infrequent ..	8	5	3	1	2	3	1	3	26
Frequent ..	0	2	3	1	0	0	0	1	7
Very frequent ..	3	6	5	2	1	0	1	0	18
Major ..	3	5	2	1	1	2	0	2	17
Psychomotor ..	2	6	5	2	2	0	0	0	17
Mixed ..	6	2	4	1	0	1	1	2	17
Average years of duration when first seen ..	18.8	13.8	15.3	8.75	12	5.7	5.5	7	

years. If to this is added an average follow-up of 5.4 years it will be seen that no patient in this study suffered epilepsy for less than 10 years at the time of the follow-up, and nearly 70% had had the condition for 15 years or longer.

Previous History.—The previous history was examined with regard to details of birth, milestones, childhood illnesses, ear disease, head injuries, and positive family history of epilepsy. Of 45 cases with recorded details of birth, 42 were listed as normal; abnormal milestones were recorded in one patient; childhood severe exanthemata were recorded in six cases and ear disease in one case. Infantile convulsions were not present in any case. Nine patients had a positive family history of epilepsy—six on the paternal side and three in their sibs.

Head Injuries.—A total of 17 patients gave a history of head injury ranging from the trivial to the most severe. They were assessed in their severity by the period of unconsciousness and amnesia, both retrograde and post-traumatic (Ritchie Russell, 1934), and the interval between the injury and the onset of epilepsy was carefully examined. By means of these criteria seven cases were selected in which the head injury was considered to have been severe.

Neurological Examination.—This was carried out in all cases. Seven patients were found to have abnormalities: the signs in three were incidental and included two cases of strabismus and one of facial weakness from an old Bell's palsy; two had continuing signs from head injuries, including a partial third-nerve paresis and a complete upper quadrantic hemianopia; one man had slurred speech, nystagmus, intention tremor, and ataxia as part of cerebellar degeneration accompanied by epilepsy; and one patient had a facial paralysis of the central type as a sequel of a hypertensive incident.

Special Investigations

These are summarized in Table II and include 49 routine skull x-ray examinations, 31 air encephalograms (A.E.G.), 50 blood W.R., 40 C.S.F./W.R., and 11 angiograms. Eleven routine skull x-ray films were found to

TABLE II.—*Summary of Special Investigations*

	Normal	Abnormal	Not Done
C.N.S. examination ..	44	7	0
Skull x-ray examination ..	38	11	2
W.R. (blood) ..	50	0	1
W.R. (C.S.F.) ..	38	2	11
Air encephalogram ..	8	23	20
Angiogram ..	9	2	40

be abnormal—three showed intracranial calcification, three cranial defects, two elevation of the petrous bone, one hemiatrophy of the right side, one a smaller middle fossa on the left, and one osteoma of the left frontal sinus. Marshall and Whitty (1952) found that in those patients who had their first fit between the ages of 20 and 40 the A.E.G. was of no further help if routine neurological examination was normal, and Martin (1954) expressed a similar view, although he qualified this by indicating that cortical atrophy may be shown by the A.E.G. These views do not coincide with our experience, since out of 31 A.E.G.s 23 were assessed as abnormal. In 21 cases the disturbance, usually minor, was associated with the ventricular system—dilatation of the lateral and third ventricle in five cases, dilatation confined to one of the lateral ventricles alone in six, and the other 10 showed a distortion in the temporal horn outline. This finding is not surprising in view of the preponderance of temporal-lobe epilepsy in our material. Widening of the sulci was present in eight cases, in six associated with ventricular abnormalities. Careful assessment of such small abnormalities is of great help when considered in conjunction with the other routine investigations and in particular the E.E.G. This finding may be related to the high incidence of temporal-lobe cases under investigation.

Epilepsy

The patients were divided into three groups according to the type of seizure: those showing either major or psychomotor seizures alone and those showing both, designated as mixed. Their distribution by age is shown in Table I. Each type contributed 17 patients.

The frequency of attacks was divided into three categories: infrequent refers to an upper limit of six attacks in a year, frequent to more than one attack a month, and very frequent to more than one attack a week. Frequency on admission (Table I) was not significantly related to age of onset under the age of 45; over this age 9 of the 12 patients had an infrequent incidence. This finding does not reach statistical significance, but the trend is in keeping with other studies (Smith and Wilson, 1958). Frequency and type of seizure were clearly and significantly related (Table III). Clinical impressions are thus confirmed: the difference between the frequency of occurrence of major and psychomotor attacks is significant ($\chi^2=7.6$ for 2 d.f., $P<0.05$). The mixed group lies somewhere midway

TABLE III.—Frequency and Type of Epilepsy

Type	Infrequent	Frequent	Very Frequent
Major	13	1	3
Psychomotor	3	4	10
Mixed	10	2	5

but nearer to the distribution for the major type. Frequency and duration of epilepsy were not found to relate with any statistical significance.

Electroencephalograms

All 51 patients have been studied electroencephalographically. Most of them have had their records taken by an eight-channel Ediswan apparatus, but some have had further studies with a 16-channel apparatus of a similar type. After the routine recording from the scalp, all but a few had sphenoidal electrodes inserted and an intravenous injection of thiopentone, so that a sleep-recording could be obtained. Reports on this technique have been published elsewhere (Pampiglione and Kerridge, 1956). Eleven patients had normal E.E.G.s, 40 abnormal.

A further subdivision of these 40 E.E.G.s shows that 28 of them had specific abnormalities, whereas seven had non-specific abnormalities, and five had both types. By specific abnormalities we mean the existence of spikes or sharp waves suggestive of epileptic discharges, and by non-specific abnormalities the presence of slow or irregular slow waves, as well as asymmetries of the background activity.

Table IV shows the E.E.G. abnormalities and their relation to the type of seizure and outcome. The total number of 47 cases shows an excess of seven which belong to more than one abnormal category. It will be seen that 31 of these patients had a temporal location—26 of these were associated with a specific E.E.G. abnormality (10 right, 10 left, and 6 bilateral). This high

TABLE IV.—E.E.G.

	Specific						Non-specific						Normal
	Temporal			Non-temp.		Bil.	Temp.		Non-temp.		Bil.		
	R	L	Bil.	R	L		R	L	R	L			
Major ..	2	3	1	2	—	1	—	1	1	1	2	5	
Psychomotor ..	7	5	4	1	1		1	1	—	—	2	—	
Mixed ..	1	2	1	1		3	1	2	—	—	1	6	
On follow-up:													
Improved	6	4	4	3	1		1	3	1	1	1	8	
Unchanged	4	6	2	1		3	1	1	—	—	3	3	
Deteriorated						1							
Follow-up not known ..											1		
Total ..	10	10	6	4	1	4	1	4	1	1	5	11	

Bil. = Bilateral.

incidence of temporal-lobe involvement reflects the particular interest in this type of epilepsy in the department during the years under consideration. No statistically significant clinical correlations were found, but it is noteworthy that 7 of the 10 patients with a right temporal focus had "pure" psychomotor epilepsy. The follow-up showed that with regard to epilepsy the group with the best prognosis was the one with normal E.E.G.s.

Deaths

Five patients had died by the time of the follow-up: two had suffered from cerebral arteriosclerosis, one succumbed to peritonitis, the fourth to carcinoma of the oesophagus (he was an alcoholic), and the fifth committed suicide.

Treatment

Seven patients were treated surgically by Mr. Murray A. Falconer at the Guy's-Maudsley Neurosurgical Unit, the rest received anticonvulsants. The pathology found in the operated cases consisted of scars (2), meningioma (1), capillary angioma (1), tuberous sclerosis (1), hamartoma with oligodendrogliomatous changes (1), glial infarct (1).

Outcome

The follow-up since first seen at hospital consisted of a minimum period of four years and a maximum of eight, with an average of 5.4 years. All but one of 51 patients were followed up, including two of the deaths, for which cases we had a follow-up of two years and one year respectively. In fact, the total duration of the epilepsy, including the follow-up period, was very much longer (Table I). Follow-up studies covering this duration of epilepsy are remarkably few in the literature, and our study is comparable only to that of Raynor *et al.* (1959), covering a period of up to 3–15 years, and of Livingston (1956), who studied 689 patients of this age-group and followed up 490 for 10 years and 152 for five years.

The criterion for the outcome of the epilepsy was frequency of seizure, and this was assessed as unchanged, improved, or deteriorated. The patient's account was supplemented by the independent report of the psychiatric social worker, who visited the home and contacted relatives, usually the spouse, and in a few cases by hospitals and G.P. reports.

So far as epilepsy is concerned, 28 (56%) patients had improved, 19 having no fits (this period of freedom was in all cases at least one year and frequently much more); 21 (42%) remained unchanged; and only one had deteriorated. These results have been statistically analysed with respect to age of onset, type of seizure, initial frequency, and psychiatric state before and after onset, and no significant relationships have been found. These results are in marked contrast to the psychiatric outcome.

Discussion

As has already been suggested, the findings and therefore the conclusions of any paper dealing with late-onset epilepsy will depend a great deal on the sample of population selected for study. It is only natural to expect and to find the greatest incidence of tumours from studies carried out with neurosurgical material. From this point of view our patients represent an opposite extreme, having been referred to a psychiatric hospital for psychological reasons. It is thus not surprising to find only three tumours in our series. Miscellaneous conditions found in the other four cases operated upon

consisted of two scars, one case of tuberous sclerosis, and one of a glial infarct. The incidence of trauma in seven cases is probably the major aetiological factor, and cerebrovascular syphilis accounts for two cases. The two scars belong to the traumatic category, leaving 37 cases (74%) with unknown aetiology.

These 37 cases were further examined in relation to significant organic and psychological factors. Indirect evidence of probable brain damage, as assessed by E.E.G., A.E.G., skull x-ray film, previous head injury, and positive neurological findings, was found in 30 cases. In 20 of the 37 we found in addition evidence of clear, severe, and unequivocal emotional strain. The only paper that refers to emotional disturbance in late-onset epilepsy is Livingston's (1956), which singles out 6 out of 689 patients as having psychogenic precipitation. In Part II we describe the life situation confronting the 20 cases at the time of the initial precipitation of seizures, and consider the significance of brain damage. Among previous studies, Livingston, using 689 patients over the age of 20 who were initially referred to him after the exclusion of tumours, and metabolic and acute cerebral disease at the Johns Hopkins Hospital, found 78% with unknown aetiology. Berlin (1953), studying 125 men over the age of 34, found an incidence of 50% of unknown aetiology. Du Saucy-Bayloye and Sorel (1959), who examined 265 patients over the age of 40, found 57% with unknown aetiology. It is possible, however, that these cases of unknown aetiology could, in the light of similar investigations to our own, show indirect evidence of brain damage.

The high incidence of temporal-lobe epilepsy is in part related to the special interest devoted to this subject both in investigating and in treating such cases at this hospital (Falconer *et al.*, 1955). At the time of the follow-up all but 5 of the 50 patients traced were still on their anticonvulsants (in this context the five deceased are included—all of whom were taking their tablets up to the time of their death). Improvement was shown by 56%, indicating the benign prognosis of this condition when the full therapeutic measures including surgical intervention are employed (Hill, 1958). This finding and the absence of any evidence of a shorter life expectation in these patients is in agreement with the findings of Berlin (1953), White *et al.* (1953), and Livingston (1956).

Summary

Fifty-one cases of late-onset epilepsy accompanied by psychiatric illness were studied.

Frequency of attacks was not related significantly to the duration of epilepsy nor to age of onset in those under 45 years, but it was related to the type, being greater in the psychomotor ones.

A low incidence of tumours and a benign outcome of the epilepsy found in other studies is confirmed.

Of 40 patients with abnormal E.E.G.s, 26 had a temporal focus.

Patients with normal E.E.G.s had a better prognosis for epilepsy. Small abnormalities in the air encephalogram were frequent and were of particular value when taken in conjunction with other routine tests, especially in the temporal-lobe cases.

There was direct evidence for brain damage in 14 cases and indirect evidence for probable damage in another 30. It is considered that these brain lesions alone or in conjunction with other factors such as emotional strain play a major part in the aetiology.

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A FOLLOW-UP STUDY OF LATE-ONSET EPILEPSY

II. PSYCHIATRIC AND SOCIAL FINDINGS

BY

J. DOMINIAN, M.A., M.B., M.R.C.P.Ed., D.P.M.
Senior Registrar, the Bethlem Royal and Maudsley Hospitals

E. A. SERAFETINIDES, M.D., D.P.M.
Research Assistant, Guy's-Maudsley Neurosurgical Unit, Maudsley Hospital

AND

M. DEWHURST, B.Com.
Psychiatric Social Worker

Since the time of Hughlings Jackson (1931) and Gowers, attention has been paid to the role of the emotions in the precipitation of epileptic seizures. Gowers (1901) suggested that fright, excitement, and anxiety are the potent factors. Fremont-Smith (1933) studied 36 unselected private patients between the ages of 10 and 53 and found in 24 of them a close relationship between their seizures and emotional disturbance such as fear, guilt, or frustration. The period of follow-up in this study was three years. Hendrick (1940), studying two patients, Bartemeier (1943) and Greenson (1944), studying one patient each, suggest that aggression which reaches a high peak prior to the attack is responsible for it. Aring *et al.* (1947) accept emotional conflict as the precipitating factor in subsequent attacks after the onset of epilepsy. Barker (1948), describing a typical petit mal patient, concludes that the attack "abolishes consciousness when unconscious emotional demands endanger consciously acceptable patterns of behaviour." All these authors are primarily concerned with the emotional state prior to the occasion of a seizure in established epilepsy. The findings are based on a small series of