onset over the age of 40, a history of under 5 years' duration, focal attacks (though in long-standing temporal lobe epilepsy the findings are more likely to be negative), abnormal physical signs, and a bruit.

Electroencephalography is of positive value, particularly if localizing delta activity is present.

Pneumoencephalography is the most useful initial neuro-radiological investigation for the detection of early cases of tumour, and cerebral atrophy is also revealed by its use.

Angiography is the best method of visualizing the angiomas, but these malformations are an uncommon cause of epilepsy of late onset and can usually be diagnosed on clinical grounds; it is, however, of no special value in atrophy and may be misleading. In arteriopathy, although no disaster occurred in this series, angiography carries a risk of hemiplegia if angiospasm occurs.

The results suggest that electroencephalography, combined with pneumoencephalography by the lumbar route, is the most suitable combination of investigations in epilepsy of late onset unless prominent lateralizing signs or bruit are present, when angiography is preferable. Repetition may be necessary in two to three months or at a longer interval. The patient's co-operation is more likely to be obtained if he has not been subjected to angiography in addition to pneumoencephalography on the first occasion.

Summary

A series of 200 cases of epilepsy starting over the age of 20, excluding traumatic cases and those with papilloedema, have been surveyed in an attempt to assess which investigations are indicated to detect the causal lesion.

The C.S.F. findings have not been considered.

A group of 100 cases, after clinical evaluation and straight x-ray examination, were investigated by pneumoencephalography.

The investigations employed in the second group of 100 cases were E.E.G. (100%), pneumography (88%), and angiography (68%).

The diagnoses showed a close similarity in the two groups.

Contrast radiography might be negative in the presence of a tumour which produced a focal abnormality in the E.E.G.

Pneumoencephalography was slightly more reliable than angiography in detecting tumours at an early stage, and demonstrated cerebral atrophy. Angiomatous malformations were an uncommon cause of epilepsy, and the presence of their characteristic clinical features indicated the need for angiography.

It is concluded that after clinical and straight x-ray examinations electroencephalography with pneumoencephalography is a suitable combination of techniques for the investigation of epilepsy of late onset, unless frank lateralizing signs or a bruit are present, when angiography is preferable.

I wish to express my thanks to Sir Russell Brain and Mr. D. W. C. Northfield for permission to use their clinical records at Chase Farm Hospital E.M.S. Neurological Unit, and to Dr. M. H. Jupe, for his reports on the radiographs. I am indebted to my colleagues at Maida Vale Hospital for allowing me access to their case records and investigations.

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VASCULAR DISEASES OF THE NERVOUS SYSTEM

A SERIES OF 315 CASES

BY

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Vascular diseases of the nervous system are the fourth most common cause of death in this country. While intracranial aneurysms and cerebral angiomas have received much attention lately because of new methods of diagnosis and treatment, the majority of deaths from cerebral vascular disease are due to cerebral thrombosis and haemorrhage. Wright and McDevitt (1954) estimated that in the United States there were 10 cases living in any one year for each death due to a cerebral vascular accident. The application of this factor here gives a figure of nearly 700,000 people suffering from some sort of stroke or its after-effects. As Wright and McDevitt point out, many of these people are still in the productive period of life and may be the main support of their family. Their frequent need for prolonged attention cannot always be met by a suitable relative, and the care of the paralysed is nowadays falling increasingly on hospitals and other institutions.

Between 1943 and 1953 the number of deaths a year due to vascular diseases of the nervous system rose from 49,000 to 68,000—that is, from 10% to 13% of the total annual deaths for England and Wales (Registrar-General, 1954). The rise in deaths from this cause, both absolutely and in relation to other causes of death, is largely due to the increasing age of the population and to the decreasing numbers of deaths from pneumonia and other infections since the advent of the sulphonamides and antibiotics. However, it is not clear why, even after allowing for the different numbers and ages of each, the rise is slightly greater in women than in men.

In view of the size and increasing importance of the problem, and of present developments in treatment, as by cervical sympathetic injection (Leriche, 1952) or by operation, it was felt that a study of the recent natural history of this group of diseases would be of value. All cases of vascular disease of the central nervous system admitted to St. Mary Abbots Hospital in the years 1951–4 inclusive have been reviewed. Selection on the basis of admission to hospital has been inevitable and is discussed below. It was thought that the cases excluded would be mainly the very mild and the immediately fatal, so that those admitted would be the ones most likely to benefit from recent therapeutic advances. Although there are limitations to the method of retrospective analysis, information has been obtained on age and sex incidence, mortality, degree and duration of recovery, and certain clinical features. In addition, a brief description is given of some special aspects of the population and districts from which most of the cases came.

Material, and Diagnostic Criteria

In the four years covered, 315 cases fell into the group of vascular diseases of the nervous system. This is 6% of all in-patients in that period, but since these cases stay longer than the average they take up more than 6% of hospital beds and time, particularly nursing-time.

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The cases were split up as shown in Table I.

The initial clinical diagnosis of cerebral haemorrhage was not always correct, but in all 73 cases included here the diagnosis was confirmed at necropsy (62 cases), by lumbar puncture (43 cases), or both.

TABLE I.—*Vascular Disease of C.N.S., St. Mary Abbots, 1951-4*

Diagnosis	Total	Male	Female	Total Deaths	Mortality %
Thrombosis	164	69	95	60	36.6
Haemorrhage	73	32	41	71	97.5
Embolism	6	1	5	4	66.6
Arteriosclerosis ..	7	5	2	0	—
Subarachnoid haemorrhage	31	11	20	7	22.6
? Thrombosis or haemorrhage	16	7	9	16	100
Transient group ..	16	5	11	1	6.3
Others	2	2	0	0	—
Total	315	132	183	159	50

Cerebral thrombosis was differentiated from haemorrhage by recovery (104 cases), absence of blood in the cerebrospinal fluid (69 cases), or necropsy (41 cases). If it is postulated that some mild cases of cerebral haemorrhage can recover, then some may be included under thrombosis. If such cases show little or no blood in the cerebrospinal fluid, differentiation from thrombosis is difficult or impossible.

In 16 cases no definite distinction between thrombosis and haemorrhage could be made. In none was lumbar puncture or necropsy performed. However, in view of their severity (eight started with unconsciousness) and their rapid course (all were dead within six days) it is thought that most of the 16 were cases of haemorrhage.

The cases of subarachnoid haemorrhage all had a typical picture of sudden onset of headache and signs of meningeal irritation with blood in the cerebrospinal fluid.

All seven cases of arteriosclerosis showed sudden changes, such as confusion or minor disturbances of consciousness with no focal signs. Although insignificant in this series, many such cases occur, but they are more likely to reach mental hospitals.

The diagnosis of embolism is difficult to prove, and some cases may have been included under cerebral thrombosis. Of the six cases listed, one, with mitral stenosis, had had repeated embolic episodes, one had subacute bacterial endocarditis, two occurred during attacks of coronary thrombosis, and two had peripheral emboli as well.

The transient group of 16 cases is of great theoretical interest, and is discussed more fully below.

The two other cases in the table were included, as both presented with hemiplegia. One had general paralysis of the insane; the other may have had a stroke or a cerebral abscess or a secondary deposit following lobectomy for carcinoma of the lung three months before.

Age and Sex Incidence

The slight preponderance (57%) of women in the cerebral haemorrhage and thrombosis groups may be due to the higher proportion of women in the population at risk (see below). It is also seen in the annual death rate for these groups given by the Registrar-General. The greater excess of women in the subarachnoid haemorrhage group has been noted previously by Falconer (1954), but has not been explained.

While the bulk of cases of vascular diseases of the nervous system occurred in the older age groups (Table II), 30% were under 60. This is a little lower than the 33% under 60 found by Brain (1954) in a series of 100 private patients,

TABLE II.—*Age Incidence*

Diagnosis	Mean Age in Years	Range
Cerebral thrombosis ..	70.8	35-90
" haemorrhage ..	65.6	46-86
Subarachnoid ..	53.7	16-74

and much less than the 63% under 60 in his hospital series. The latter was weighted by a higher proportion of cases of subarachnoid haemorrhage and cerebral angiomas, which occur in younger people. On the other hand, in the present series, while cases of subarachnoid haemorrhage occurred at earlier ages than the cerebral haemorrhages and thromboses their mean age was still quite high, and in fact 42% of the cases of subarachnoid haemorrhage were over 60 and 64% over 50. These figures should be compared with those of Falconer (1954), who found that of 100 cases with demonstrable aneurysms 35 were over 50. Of 250 cases of sudden death from intracranial aneurysm collected by Simpson (quoted by Falconer, 1954) 73% were over 50. All the figures suggest that degenerative changes may play a more important part in producing subarachnoid haemorrhage than has often been assumed hitherto.

Clinical Features

Speed of Onset.—This is shown in Table III. By sudden is meant a more or less dramatic attack reaching a climax in a minute or two. Gradual cases may not develop maximum impairment until a few hours or days. Where paralysis

TABLE III.—*Speed of Onset*

	Sudden	Gradual	Overnight	Unknown
Cerebral thrombosis ..	58%	20%	13%	9%
" haemorrhage ..	62%	18%	8%	12%
Subarachnoid ..	80%	—	—	—

is first found on waking in the morning the rate of onset during sleep cannot be given. The unknown groups should probably go in the "sudden" or "night" groups. They consist mainly of patients living alone who were found paralysed and speechless or too confused to say what had happened. There is no relation between speed of onset and prognosis within the cerebral thrombosis group. When cases of thrombosis are compared with those of cerebral haemorrhage it is seen that the latter are altogether more rapid and more often fatal. There was initial loss of consciousness in 22% of the thrombosis cases, 62% of those with cerebral haemorrhage, and 33% of those with subarachnoid haemorrhage. Although initial unconsciousness is much more common in cases of cerebral haemorrhage as a whole, it is of no diagnostic value in the individual case. However, cases of cerebral haemorrhage develop rapidly. Practically all these patients died—just over one-third on the first day and two-thirds in the first week (median = four days). By contrast, one-third of the fatal cases of thrombosis were in hospital over four weeks (median = 14 days). One-third of the surviving cases of thrombosis were in hospital over eight weeks (median = 36 days). The mortality in cases of thrombosis with initial unconsciousness was higher than in those without—18 out of 36 (50%) compared with 42/128 (33%), but the difference is not quite significant.

Blood Pressure.—The range of blood pressures was very wide, but hypertension was common in all groups, although the known lability of blood pressure makes detailed comparison suspect. If the somewhat less variable diastolic pressure only is taken the frequency distributions in the cerebral thrombosis and haemorrhage groups overlap considerably, but hypertension is slightly more common in the latter. In 69% of the cases of thrombosis and in 83% of the cases of haemorrhage the diastolic pressure was 100 mm. or over ($P < 0.05$). The diastolic pressures in the cases of subarachnoid haemorrhage did not differ significantly from those in cerebral thrombosis, 62% having a diastolic pressure of 100 mm. or more. This, like the moderately high age of the cases of subarachnoid haemorrhage, suggests that congenital aneurysms are not the sole factor.

Cerebrospinal Fluid.—Lumbar puncture was performed in 69 of the 164 (42%) cases of thrombosis, in 43 of the

73 (59%) cases of cerebral haemorrhage, and in all cases of subarachnoid haemorrhage. In cases of thrombosis the cerebrospinal fluid protein varied widely, from 20–130 mg. per 100 ml. No close relation between protein level and prognosis (measured in arbitrary grades, see below) could be discovered, though the scatter suggested that very high protein values were associated with a worse prognosis. Interpretation is made more difficult by the fact that lumbar puncture tended to be done less often in the elderly but more often in the more severe cases.

Prognosis

Surviving cases of cerebral thrombosis were divided into three arbitrary grades of recovery, defined as follows: (1) poor—little or no recovery of function, little or no limb movement; (2) fair—moderate movement of arm, walking only with help or a stick; and (3) good—no or minimal disability.

TABLE IV.—Cerebral Thrombosis. Change in Death Rate and Degree of Recovery with Age

	Numbers in Each Age Group			
	Under 60 Years	60–69 Years	Over 70 Years	Total
Died ..	9 (28.2)	13 (27.1)	38 (45.7)	60 (36.8)
Recovery grade {	12 (37.5)	9 (18.7)	6 (7.2)	27 (16.6)
	9 (28.2)	21 (43.8)	34 (41.0)	64 (39.4)
	2 (6.2)	5 (10.4)	5 (6.0)	12 (7.3)
Total ..	32 (100.1)	48 (100.0)	83 (99.9)	163* (100.1)

Figures in parentheses = No. in grades at each age as % of total at that age.
* No information on fate of 1 patient.

Deaths and degrees of recovery are shown in relation to age in Table IV. The Chart shows the relation more clearly, expressing the number of cases in each grade at a given age as a percentage of the total at that age. Most cases fall into grade 2. It should be noted that the grading is based mainly on the final state and takes less account of the severity of the initial attack.

Change in death rate and degree of recovery with age in 163 cases of cerebral thrombosis. X—X=Deaths, $P<0.05$. ○—○=Grade 1, $P<0.01$. ●—●=Grade 2, $P>0.05$. ●—●=Grade 3, $P>0.05$.

the more severe cases are nearly all fatal; the rest do fairly well. It is only at the younger ages that patients survive a thrombosis big enough to cause severe disability.

At first sight the data suggest that complete lack of recovery was more often found in the arm than in the leg, but the figures are not significant.

It is interesting to note that even in these days most patients with thrombosis who recover go home or to a relative, as in the following 104 cases: home (including relatives), 83; institution, 15; transfer (in acute stage), 5; still in, 1.

Transient Group

The 16 cases in the transient group were all diagnosed originally as hypertensive encephalopathy. The characteristic features were the sudden onset, in all cases, of focal signs such as hemiplegia, monoplegia, visual or speech disturbances, and, in many, of initial loss of consciousness. These signs were transient and, except in the one patient who died, had completely disappeared within 24 hours. The average stay in hospital was only 13 days (range 2 to 28, except one patient who stayed 117 days and had several attacks, including a definite thrombosis). The fatal case was a hypertensive woman of 72 who developed a left hemiplegia and unconsciousness. She had had several previous attacks lasting half an hour. At necropsy there was no evidence of thrombosis or cerebral infarction.

Pickering (1948) has argued that these cases are not essentially different from those of cerebral thrombosis, but are simply due to the production, by minor thrombi, of mild lesions which rapidly recover. In support he points to the often brief nature of the symptoms known to be due to organic obstruction in cases of cerebral emboli. The concept of vascular spasm, however, is very widely accepted and has been strengthened by the experimental work of Byrom (1954) in rats.

The present series of cases was examined to see if they lent support to either theory. The three features considered were duration of illness, blood pressure, and initial unconsciousness.

If the transient and thrombotic groups are one and the same, the duration of cases in the two groups should give a smooth frequency distribution curve. If the transient group is a separate entity characterized by a rapid course, an irregular curve with a second peak in the lower range might be seen. However, the transient group formed such a small percentage of the whole that no significant effect could be found.

Hypertension was common among the transient group, the mean diastolic pressure being 115 mm. (range 70–140), and 82% having a diastolic pressure of 100 mm. or more. This is greater than the incidence of hypertension in the cases of cerebral thrombosis, which is not what one would expect if the transient cases were really the mildest of the thromboses. Again, however, the figures are too small to be significant.

Initial unconsciousness was much more common in the transient group, occurring in 10 out of 16 cases (62%), compared with the thromboses, in which 36 out of 164 (22%) lost consciousness initially. This difference is highly significant ($P<0.01$). On general grounds one would not expect to find a higher incidence of unconsciousness in milder cases, and, indeed, as stated above, unconsciousness is related to a poorer prognosis. The finding of unconsciousness in so high a proportion of the transient group suggests, therefore, that this group differs fundamentally from the cerebral thromboses and is not just the mildest section of them.

Source of Patients

In a survey of this kind it is important to know how the patients were selected and from what sort of population. So far as the availability of beds allowed, all patients from the hospital area for whom admission was requested either by a doctor or by the Emergency Bed Service were accepted, and, while no exact figure can be given, certainly the majority of cases of strokes were admitted.

A sample of all in-patients over three months in 1954 showed that 47% were from Kensington, 21% from Westminster, 18% from Fulham, and 5% from Hammersmith. Fulham and Hammersmith are largely residential boroughs in which the age and sex structure, marital state of the population, and the size of households is almost the same as for London as a whole. Kensington and to a less extent Westminster, however, have an unduly large proportion of women, of single people, of small households, and of people

living in hotels or institutions. The incidence of vascular diseases of the nervous system in these boroughs, corrected for age and sex, is much the same as in the rest of London, but the factors mentioned in Kensington and Westminster would increase the pressure on beds, since many patients have no one at home to look after them.

Summary

A series of 315 cases of vascular diseases of the nervous system admitted to a general hospital over a four-year period are reviewed.

The diagnosis, age and sex incidence, and certain clinical features are discussed.

Evidence is presented in support of the separation of some cases with transient cerebral attacks from the cerebral thrombosis group.

The population from which cases were received is briefly described.

I am indebted to Dr. B. Gottlieb for much encouragement and advice. I thank both him and Dr. H. Gainsborough for permission to use records of their cases, and the records staff of St. Mary Abbots Hospital for much help.

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Medical Memorandum

Effect of a Barbiturate Antagonist in Chronic Barbiturate Intoxication

Chronic barbiturate intoxication may be associated with spectacular neurological manifestations which may mimic organic disease of the central nervous system. The signs observed include ataxia, dysarthria, dysdiadokokinesis, hypotonia, tremor, decrease in the abdominal reflexes, and extensor plantar reflexes. There are no sensory changes, and the deep tendon and corneal reflexes are usually unchanged unless an acute intoxication is superimposed on the chronic state (Isbell, 1950). The electroencephalogram is of great value in establishing the diagnosis, as in chronic barbiturate intoxication there is an increased number of beta waves (fast waves with frequencies of 15-30 a second), whereas in acute barbiturate intoxication large slow waves resembling normal sleep waves are seen (Isbell, 1950).

A new barbiturate antagonist, bemegride (β -ethyl, β -methylglutarimide; "megimide") has been shown to be of value in the treatment of acute barbiturate intoxication (Shulman *et al.*, 1955). The effect of this substance in a patient suffering from chronic barbiturate intoxication is shown in the following case.

CASE REPORT

A housewife aged 50 was admitted to hospital on November 28, 1955, because of a small haematemesis from a chronic duodenal ulcer.

On examination she was nervous and agitated and there was some intellectual impairment. A pronounced coarse tremor of the right hand at rest was present. The pupils reacted briskly to light and constricted on convergence; the fundi were normal; and no abnormality was found in the cranial nerves. She had nystagmus to the right, a coarse tremor of the extended arms which was more evident on

the right, a marked intention tremor of the right arm, and dysdiadokokinesis which affected both arms, the right more than the left. There was no sensory ataxia. The power and tone of the upper limbs were normal, there was no muscle wasting, but the tendon reflexes were slightly exaggerated on the right side. Sensation, superficial and deep, in the upper limbs was normal. The abdominal reflexes were present. In the lower limbs power and tone were normal. The "knee-heel" test showed slight unsteadiness in the right leg. The knee-jerks were present and equal, but both ankle-jerks were absent. The plantar reflex was flexor on both sides. Sensation, superficial and deep, was normal. No abnormality was detected in the cardiovascular, respiratory, or abdominal systems.

On close questioning it was revealed that five years previously she had been treated in a mental hospital for "nerves," and that since then she had been taking from 6 to 9 gr. (0.4 to 0.58 g.) of amylobarbitone sodium and 2 gr. (0.13 g.) of phenobarbitone daily.

Investigations.—The urine was normal. The Wassermann reaction was negative. X-ray films of the skull and chest and the E.C.G. were normal. Lumbar puncture: pressure normal; free rise and fall on jugular compression; protein, 40 mg. per 100 ml.; cells, 0 per c.mm.; Wassermann reaction, negative; colloidal gold test, 0000000000. An electroencephalogram taken in May, 1953, was normal, but the record now showed a generalized excess of high-voltage fast activity (beta waves) mixed with fairly regular alpha waves. There was also patchy slow activity over the right temporal area.

The patient was treated on a gastric regimen, phenobarbitone, 1 gr. (65 mg.) twice daily, and amylobarbitone sodium, 3 gr. (0.2 g.) at night. This large dose of barbiturate was given to prevent the delirium and epileptiform confusions which may follow abrupt withdrawal of barbiturates from chronically intoxicated persons. A fortnight after admission 10 ml. of a 0.5% solution of bemegride was given intravenously; this resulted in an immediate and dramatic improvement in the neurological signs. The intention tremor of the right arm became less marked, the nystagmus and dysdiadokokinesis disappeared. This improvement persisted for two hours, but although there was slight regression the signs were not as marked as they had been before the injection of bemegride. The next day a further intravenous injection of 10 ml. of a 0.5% solution of bemegride was given while the patient was under electroencephalographic examination. Before the injection a generalized excess of high-voltage fast activity mixed with fairly regular alpha waves was seen. After the injection, in a matter of minutes, there was a complete disappearance of the beta waves, and the record continued during the period of observation with no further abnormalities. It was noted that after the second injection of bemegride there was no reappearance of the neurological signs. The patient was discharged and her doctor was requested to supervise a gradual withdrawal of barbiturates over a period of six weeks.

My thanks are due to Dr. Max Valentine for his reports on the electroencephalograms.

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The Medical Superintendents' Association of New Zealand, at a recent conference in Wellington, endorsed a change in hospital policy for child patients. By a unanimous vote the conference approved the principle of the closest possible association between mother and child while the child is a hospital patient.