

SOME ASPECTS OF  
CAROTID ARTERY OCCLUSION

Thesis

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## INTRODUCTION

Carotid artery occlusion has long been recognised as a sequel to penetrating wounds of the neck, and is known to accompany local infections and tumour formation in the vicinity of the carotid sheath.

During the eighteenth and nineteenth centuries it was recognised that carotid occlusion could occur from the extension of a thrombus from aortic aneurysms. Von Haller in 1749 described a case where blood clot had spread into the left common and internal carotid arteries from an aneurysm of the thoracic aorta, and Petit (1765) also recorded a similar finding, where the right common carotid artery was occluded. In this country Davy (1845) referred to a patient under his care who presented with a sudden hemiplegia, and in whom the left carotid artery was almost entirely occluded.

However, general recognition that spontaneous occlusion of the carotid vessels could occur as a result of local arterial disease was long delayed. This is indeed surprising for Thomas Willis probably recorded the first case of this type in 1684. It is interesting to recall his actual words, for not only did he record his findings but he also speculated on the alterations in cerebral blood flow which had occurred with the occlusion of the artery.

"It is not long since we dissected the dead body of a certain man, whom a great Scirrhus or hard Swelling within the Mesentery, growing at last ulcerous, had killed. When his Skull was opened, we beheld those things belonging to the Head, and found the right Carotid, arising within the Skull plainly bony or rather stony, its cavity being almost wholly shut up; so that the influx of the blood being denied by this passage, it seemed wonderful, wherefore this sick person had not dyed before of an Apoplexy; which indeed he was so far from, that he enjoyed to the last moment of his life, the free exercise of his mind and animal function . . . . This Gentleman, about the beginning of his sickness, was tormented by a cruel pain of the Head towards the left side. The cause whereof I know not how better to explain, than that the blood excluded from the right Carotid Artery, when at first it rushed more impetuously in the left, had distended the membrane."

Like so many observations in medicine his writings were either unknown or disregarded by others. It was not until 1872 that Kussmaul described two patients with carotid artery occlusion, in one of whom there was a local "endarteritis". Chiari (1905) observed that atherosclerotic plaques were often found in the carotid sinus, and if thrombus were deposited on them might cause obliteration of the vessel. Gowers (1893) was also well aware that carotid occlusion occurred secondary to atheroma lying in the sinus, and it was he who pointed out that the clinical picture arising from the occlusion was a variable one, and was comparable with that occurring after ligation of the artery.

This variation in symptomatology in spontaneous carotid artery occlusion was well known to the German workers in this field. In Kussmaul's two patients the symptoms were slight; one complained of headache and transient visual disturbances before death, and the other of left-sided headache with vertigo and epileptic attacks without showing any paralysis. On the other hand, Penzoldt (1881) described a patient who had developed sudden unilateral blindness with a contralateral hemiplegia, and at post-mortem examination thrombus was found in the left common, internal carotid and left middle cerebral arteries. Oppenheim (1908) also appreciated the variability of symptoms and signs following carotid artery occlusion. He drew attention to the progressive hemiplegia which sometimes followed "obliterative arteritis" of the vessel, and quoted the paper of Brissaud and de Massary (1898) who had described a similar mode of presentation.

Hunt (1914) from America, emphasised the importance of carotid artery occlusion in patients presenting with a hemiplegia of vascular origin. On examining the carotid pulsation in twenty such patients, he found it absent on the appropriate side in four instances. He suggested a more thorough study of the cervical portion of the carotid artery at autopsy. In his paper he wrote:- "In the realm of pathology such condition as chronic oedema, indurative and

softening processes of the brain in which the main vessels of the circle of Willis are free from obstruction should always give rise to the suspicion of impaired circulation in the carotid artery". His good advice was ignored by clinicians and pathologists alike, presumably because the cervical carotid artery lies in a "no man's land" between general pathology and neuropathology, and at post-mortem examination it tends to be neglected.

With the introduction of arteriography by Moniz in 1927 a tremendous impetus was given to the study of vascular syndromes of all types. Following his paper (Moniz et alia 1937) in which he described four cases of carotid artery occlusion demonstrated by this new technique, there was a spate of literature on the subject, mainly from continental and American sources.

Shimidzu (1937) reported one case with a three-year history of insomnia, loss of memory, depression and dysphasia, the diagnosis before arteriography being that of Pick's disease. In the following year Chao et alia (1938) described two cases, one of which presented with a hemiplegia without loss of consciousness. Reichert (1938) reported three cases, and Sorgo (1939) eight cases in which he called attention to the migrainous headaches, mental deterioration, fleeting attacks of paraesthesiae, and weakness of the extremities which many of his patients experienced. From America Galdston et alia (1941) described two cases of thrombosis

of the carotid arteries demonstrated by arteriography, whilst King and Langworthy (1941) reported three cases in which the diagnosis was made on purely clinical grounds by reason of a unilateral optic atrophy and a contralateral hemiplegia.

Andrell (1942) reviewed the then known literature on the subject, collected twenty-three cases confirmed by arteriography, and added nine cases of his own. He, in particular, was well aware that many of these cases did not suffer from hypertension and emphasised that the headache which often preceded other symptoms by months or years, was frequently situated on the same side as the obstructed carotid artery. Like Sörgo, he drew attention to the prodromal attacks of numbness, paralysis and speechlessness, and recognised that once the hemiplegia appeared its distribution was characteristic of an occlusion of the middle cerebral artery.

Krayenbühl and Weber (1944) and Krayenbühl (1945) also described headache and brief paralytic attacks in their patients, and added that some of them had experienced transient blurring of vision and Jacksonian epilepsy before the onset of a hemiplegia.

Ameli and Ashby (1949) from this country, presented six cases in their paper on "Non-Traumatic Thrombosis of the Carotid Artery". They emphasised that in them the first symptom was commonly a transient



weakness of one of the extremities, which was often succeeded by recurrent exacerbations of their weakness over several weeks or months before a permanent hemiplegia developed. Headache was uncommon in their experience.

Johnston and Walker (1951) collected 101 cases from the literature and added six of their own. They came to the conclusion that patients suffering from carotid artery disease presented three distinct clinical pictures. The largest group had transient attacks of hemiparesis, paraesthesiae and dysphasia which not infrequently terminated in a hemiplegia, whilst the others presented either a sudden hemiplegia without previous warning, or, less frequently, developed a slowly progressive hemiparesis which took several months to become stabilised.

Although most of the recorded cases have been examples of internal carotid artery occlusion, Galdston et alia (1941) described two cases with common carotid artery occlusion, and Webster et alia (1950) recorded three cases in which the internal, external and common carotid arteries were occluded on the same side. Incomplete occlusion of the artery is also well recognised for Andrell, Krayenbühl and Weber, Ameli and Ashby and Taptas and Pecker (1948) all mention such cases. However, whether the occlusion is complete or incomplete, there appears to be no significant difference in the resulting syndrome.

But not all patients showing carotid artery occlusion develop dramatic symptoms. Symonds (1955) mentioned headache as the sole manifestation, and Darling and Clark (1915) have described asymptomatic total occlusion of the carotid artery which was discovered accidentally at post-mortem examination.

Now it is this variation in symptomatology which has intrigued observers over the past century and many theories have been advanced in an attempt to explain the underlying mechanism in carotid artery occlusion. Chiari, from the study of his pathological material, favoured cerebral embolism, whereas Hunt related the cerebral damage in his cases to failure of the collateral blood supply through the circle of Willis. More recently Hultquist (1942) published his extensive monograph dealing with the pathological findings in the entire carotid system in 1400 post-mortems, and studied the site, aetiology, histology and propagation of the thrombus within the artery, and gave a detailed account of the resultant changes in the brain. He came to the conclusion that embolism of the cerebral vessels from detachment of thrombus with the carotid artery was the principal cause of the cerebral damage.

Yet Fisher (1951) in his excellent paper, made a clinico-pathological study of four of his eight cases, and ascribed the clinical picture and resulting cerebral damage to defects in the circle of Willis causing a failure of the collateral blood flow.

Denny-Brown (1951), from study of his cases, has agreed with Hunt's theory that the syndrome can be ascribed to a reduced blood flow through an apparently normal circle of Willis. More recently Symonds in his Harveian oration has speculated on the functions of this circle, and has related the clinical findings following carotid artery occlusion to a similar mechanism.

No work has yet been published in which the clinical picture shown by patients after carotid occlusion has been related to the arteriographic findings and the underlying pathological changes.

In this thesis it is proposed to analyse the clinical syndrome of thirty patients presenting with carotid artery occlusion, to describe the arteriographic findings, and to relate the clinical picture with the pathological findings in seven of them. This study throws further light on the alterations in cerebral blood flow which may occur after carotid occlusion.

CLINICAL ANALYSIS

Of the thirty patients studied, twenty-five of them were suffering from spontaneous carotid artery occlusion. They are considered in Section A.

The remaining five patients are considered separately in Section B. In three of them the occlusion was associated with aneurysmal formation in the cavernous sinus (Cases 5, 23 and 27); in another with embolism from rheumatic heart disease (Case 14); and in the last patient the occlusion occurred immediately after a major operation to the spine, (Case 28).

SECTION A

Spontaneous Occlusion of the Carotid Artery

Age and Sex

In this group of twenty-five patients, twenty-one were male and four were female. In the males the age at which the carotid artery occlusion was discovered ranged from twenty-four to seventy years, and in the females between forty-eight and seventy-three years. The maximum incidence for both males and females lay in the fifth decade and, as the following table shows, was only slightly less common in the fourth and sixth decades:-

<u>Age</u>	<u>Number of Patients</u>
20-30	1
30-40	1
40-50	7
50-60	9
60-70	5
70-80	2

Side

Partial or complete occlusion of the internal carotid artery was found in fourteen patients on the left side and in ten patients on the right; in one other patient the left common carotid artery was occluded, the sole example in this group.

Family History

In almost half of these patients there was a significant family history of degenerative cardiovascular disease in either their parents or siblings. Five patients claimed relatives who had had "heart attacks" in late middle life (probably coronary thrombosis), and the relatives of another six died following cerebrovascular accidents. In this connection the family history of Case 30 is of more than passing interest. Her father and one brother both died following acute cerebrovascular episodes in middle life, and her mother died of an illness characterised by an alternating hemiplegia with aphasia.

One can only speculate on the underlying pathology in these cases but it is possible that some of them did suffer from carotid artery occlusion. In particular the history of an alternating hemiplegia was highly suggestive of a bilateral occlusion of this vessel.

Antecedent Disease

Six patients in this group had suffered from disease or injury which may have influenced or predisposed to the carotid artery occlusion which was discovered subsequently. Two patients (Cases 4 and 17) had had moderately severe concussional head injuries two and ten years before symptoms of carotid occlusion appeared; they had apparently made a complete recovery in the interval.

In Case 2 four years elapsed between a crush injury of the neck and the subsequent development of the syndrome.

In another two patients unilateral carotid occlusion followed some time after local irradiation to the neck. Case 1 developed symptoms four years after successful x-ray treatment of a carcinoma of the alveolus with associated glandular involvement, and Case 16 had had local radium treatment for a carcinoma of the tonsil six years before the development of the syndrome. In this latter case treatment had also been successful, for at post mortem examination there was no sign of local recurrence or of secondary glandular involvement.

One patient in this group (Case 25) was found to have diabetes mellitus, which had been discovered three years before the onset of his symptoms of carotid occlusion.

### Symptomatology

The basic feature in the majority of these cases was an hemiplegia of variable severity which was commonly preceded by transient symptoms including weakness and paraesthesiae of the extremities, dysphasia and vertigo. Headache was experienced by well over half of them some time during the development of the syndrome. The mode of presentation in these patients has been variable, as was the subsequent course, but broadly speaking they can be conveniently divided into the following groups:-

1. Those with a sudden onset of hemiplegia with few or no prodromal symptoms.
2. Those developing a variable degree of hemiparesis after several premonitory symptoms.
3. Those with a superficially progressive syndrome.

#### 1. Sudden onset with few or no prodromal symptoms

Nine patients presented in this fashion (Cases 4, 12, 13, 15, 16, 17, 18, 19, 21). Two patients (Cases 12 and 16) suddenly lost consciousness without warning and on recovery showed a total hemiplegia. In another two patients (Cases 18 and 21) the hemiplegia was less abrupt in onset and in them consciousness was retained.

Case 18 awoke one morning with a left facial paralysis and by the evening his left hand had become clumsy. A few hours later he awoke with a severe left hemiplegia.

In case 21 the onset of the hemiplegia was even more delayed. His symptoms commenced with severe headache which was succeeded after several hours by a mild dysphasia. Next day the dysphasia was most marked but a further twenty-four hours elapsed before he suddenly became aphasic and hemiplegic.

Three other patients (Cases 4, 15 and 17) also developed a relatively sudden hemiplegia but all had had premonitory symptoms or signs. Case 4 presented with a right main en griffe and sensory impairment along the ulnar border of the hand and forearm. He was thought to be suffering from a compressive lesion of the lower cervical cord and exploration was advised. However, he refused further investigation and subsequently recovered sufficiently to join the Malaya Police Force. Eighteen months elapsed before he developed a total right hemiplegia associated with loss of consciousness. The other two patients had less spectacular premonitory symptoms. Case 15 had transient numbness of the right hand one month before the appearance of his hemiplegia, and Case 17 had had transient weakness of the right side of the face with dysphasia one week before the sudden onset of a moderately severe hemiparesis.

Two other patients (Cases 13 and 19) in this group presented with transient weakness of the extremities which was succeeded by recurrent attacks of hemiparesis.



Case 13 noticed a transient diplopia two days before he lost his senses. On recovering consciousness he had weakness of the right arm and leg which disappeared within an hour. Over the next ten days he experienced recurrent attacks of hemiparesis and dysphasia which finally culminated in a severe right hemiplegia with total aphasia.

The other patient (Case 19) presented in an unusual fashion. He suddenly became speechless and paralysed in all four extremities but recovered completely within a few hours. However, over the next six weeks he had several short-lived attacks of dysphasia together with weakness and numbness of the right arm and leg. When the attacks ceased he showed slight weakness of the right face and hand and a nominal dysphasia.

With the exception of Case 19 all patients in this group had a severe degree of hemiplegia which showed little sign of recovery even after several months had elapsed.

## 2. Cases with several prodromal symptoms

Twelve patients presented with prodromal symptoms spread over a variable period of time before persistent or permanent neurological deficit appeared (Cases 1, 3, 6, 8, 10, 11, 20, 22, 24, 25, 26, 29). These commonly included transient paraesthesiae, numbness and weakness of the face or the extremities,

often accompanied by dysphasia if the dominant hemisphere were involved.

The presenting symptom in this group of patients was variable, but over half of them (Cases 3, 6, 8, 11, 20, 22, 29) had an initial weakness or numbness of one side of the face or one hand which usually disappeared within a few minutes, hours or days, and was followed some time later by similar symptoms in the ipsilateral arm, face or leg.

Occasionally, when patients experienced unilateral facial weakness, they complained of twitching of the affected muscles (Cases 8 and 20) but on the whole local irritative motor phenomena were uncommon.

When the dominant hemisphere was involved in this process some degree of expressive dysphasia was frequently present but dysphasia as the sole presenting symptom was only encountered once (Case 25).

As a rule these patients experienced three or more episodes of this kind separated by weeks or months of comparative freedom from symptoms before a variable degree of hemiparesis with or without speech deficit developed.

Case 10 is illustrative of this group. She was a woman of forty-nine years, who two years before admission to hospital experienced short-lived pins and needles and clumsiness of her right hand. She remained well for a further seventeen months, when a slight

dysphasia developed. This disappeared within a few days but was followed two months later by difficulty in reading. After a further interval of two months the right side of her face became weak and this was soon followed by a second attack of dysphasia and weakness of her right arm. When admitted to hospital several days later she showed a moderately severe hemiplegia with a severe degree of global dysphasia.

Although in the majority of these patients the time interval between such episodes has been measured in weeks or months, this is not always the case. One patient (Case 6) had an interval of over one year between the initial attack of pins and needles in the right hand and the subsequent development of a severe right hemiplegia with aphasia. It must be admitted, however, that in this interval he had had two brief attacks of stiffening of the right extremities on awakening in the morning.

In another (Case 29) the time interval appeared to be much longer. Seven years before her admission to hospital she had several transient attacks of weakness of one hand which ceased after six months. Four years later she had another isolated attack, and after a further year had an episode of transient weakness of both legs with loss of consciousness. This was followed after several months by two attacks of weakness of her left arm accompanied by some clouding

of her conscious state. Eventually, after a bout of severe right-sided headaches, she developed a mild left hemiparesis with blindness of the right eye.

In contradistinction to those patients presenting with few isolated episodes spread over several months, five patients in this group complained of frequent attacks of numbness, weakness or stiffness of the extremities (Cases 1, 11, 20, 22, 25). These lasted anything from several minutes to half-an-hour and might occur several times daily.

At first such attacks were followed by complete recovery but eventually in three patients (Cases 1, 11, 20) some degree of permanent weakness and sensory impairment remained when the attacks had ceased. Two others (Cases 22 and 25) showed slight dysphasia only when their condition became stabilised.

Case 1 was illustrative of this highly important group. He presented with a sudden left hemiparesis which rapidly recovered. Over the next four weeks he had literally more than 100 attacks of stiffening of the left arm and leg lasting twenty minutes at a time with complete recovery between each attack. They ceased after he had developed a permanent left hemiplegia. Case 22 presented a similar picture which was ushered in by sudden clumsiness of the right hand and an expressive dysphasia. Over the course of the next few days these symptoms

improved but were followed by transient attacks of numbness of his right hand occurring twice each day. After six weeks similar attacks of numbness affected his right leg but ceased spontaneously after three months. When seen three months later he showed a mild nominal dysphasia with weakness of the right side of his face but no motor or sensory deficit in the extremities.

Although in the majority of these patients the clinical course suggested an episodic and progressive affection of the cerebral cortex in the region of the pre- and post-central gyri, two patients have shown evidence of more widely disseminated lesions of the cerebrum. Case 3 had a transient clumsiness of the left hand followed after three months by a left facial weakness. Two months after this he developed signs of parietal lobe disorder including constructional apraxia, topographical and spatial disorientation and agnosia of the left half of visual space. Case 26 had attacks of visual blurring with headache which was followed by signs of parietal lobe dysfunction. Later clumsiness of the left hand appeared and finally dysphasia and giddiness complicated by a severe left hemiplegia.

In these twelve patients two developed a total hemiplegia (Cases 1, 13), one had a moderately severe hemiparesis (Case 8), four a mild hemiparesis (Cases 6, 20, 24, 29), and five mild degrees of

weakness of the face and/or arm with or without dysphasia (Cases 3, 11, 22, 25, 26).

### 3. Cases with a superficially progressive syndrome

In this series four patients presented with an apparently progressive syndrome (Cases 2, 7, 9, 30). However, on closer questioning all admitted to some episodic deterioration in their condition, although for the most part the picture was one of a progressive weakness and numbness of the affected extremities terminating in variable degree of hemiplegia.

The clinical course pursued by these patients usually extended over several months, but in one of them (Case 9) a transient clumsiness of the left hand was quickly followed by a progressive weakness of the left arm and leg terminating in a moderate degree of hemiparesis several weeks later.

At the other end of the scale is Case 2, whose syndrome took two years to develop. His first symptom was progressive numbness and weakness of the right arm which at that time was thought to be due to a local cervical cord lesion. Exploratory laminectomy showed no abnormality. Gradually the right arm became weaker and numbness spread over the right side of his head and neck. Sixteen months later the right leg also became weak and numb and shortly afterwards he had mild left frontal headache accompanied by deterioration

of vision in the left eye. When examined two years after the onset of his illness, he showed a mild right hemiparesis with sensory impairment and a left optic atrophy.

The initial symptoms in patients with carotid artery occlusion is usually referred to the hand or face but in this group two of the four patients presented with initial involvement of the leg. For instance, Case 7 developed a gradual weakness of the right leg which remained static over several weeks. Then he awoke one morning with a sudden increase in weakness of the leg complicated by weakness of the right hand together with dysphasia. Case 30 showed a progressive weakness of the left leg over seven months before it was accompanied by recurrent attacks of weakness of the left arm. Eventually, after several months she developed a severe hemiplegia which, however, was maximal in the affected arm.

This primary leg affection has not been a prominent feature in cases reported in the literature, and has not been seen in other patients in this series.

When the condition of the four patients in this group became finally stabilised one had a total hemiplegia (Case 30), two had moderate degrees of hemiparesis (Cases 7 and 9), and the last (Case 3) had a mild degree of hemiparesis with a contralateral optic atrophy.

Headache

Fourteen patients with carotid occlusion complained of headache some time during the development of their syndrome (Cases 1, 2, 3, 7, 9, 10, 18, 19, 20, 21, 24, 26, 29, 30). In more than half of them, it was either localised or more severe on the side of the obstructed artery, was commonly situated in the frontal or temporal regions, and was more often aching than throbbing in character. Its presence and severity did not appear to be related to the extent of the final neurological deficit, and indeed in most cases headache ceased once the syndrome had become stabilised. It was often complained of by patients presenting an episodic picture but was less frequent in those with a sudden explosive onset or a slowly progressive course.

In two patients throbbing headache was present for many years before symptoms of carotid occlusion developed (Cases 1 and 15). Both were hypertensive and arteriosclerotic and for this reason it seemed unlikely that their headaches bore any relationship to their subsequent carotid artery occlusion.

However, in seven patients (Cases 1, 2, 7, 18, 19, 21, 26) headache was clearly related to the occlusion and heralded or accompanied the appearance of other symptoms.



In two of them (Cases 7 and 19) intermittent gnawing temporal headache was present on the same side as the occluded carotid artery for several weeks before the onset of their strokes, and in another (Case 21) severe continuous left-sided headache preceded the development of a right hemiplegia by four days.

In another five patients headache accompanied the appearance of other symptoms. In cases 1 and 18 severe unilateral throbbing headache persisted for several hours during the onset of a contralateral hemiplegia, and gradually ceased once it had become established, and in Case 2 nagging left temporal pains appeared intermittently during the development of a slowly progressive weakness of the right arm.

On the whole headache accompanying transient neurological disturbances was uncommon and only two patients showed this association. Case 19 complained of nagging temporal pain with each hemiplegic episode and in Case 26 aching frontal headaches ushered in the syndrome, were occasionally accompanied by attacks of transient blindness, and ceased as symptoms of permanent neurological dysfunction appeared.

In another five patients (Cases 3, 9, 10, 20, 24) headache developed late in the syndrome and did not appear to have any close connection with the

episodic deterioration in their condition. In three of them (Cases 3, 9, 10) it was situated in the forehead above both eyes and was described as a "mild aching" (Cases 9 and 10) but in Case 3 it was throbbing in character and was more severe on the side of the obstructed artery.

In two other patients (Cases 20 and 24) headache was confined to the occipital region. In Case 20 it was described as an "occasional dull ache". In Case 24 it was obviously much more severe and gradually subsided over several months without any obvious deterioration in the patient's clinical state.

It is worth noting that patients who have experienced prominent visual symptoms have all complained of headache. Case 2 had mild frontal aching when vision in his left eye was failing, and Case 29 had severe throbbing headache in the right temple for several hours before she became blind in this eye. Both patients showed a primary optic atrophy presumably the result of a vascular occlusion of the central retinal artery.

None of these patients had noticed any dilatation of the scalp vessels or excessive redness or watering of the eyes during their attacks of headache.

### Vertigo

Four patients showing carotid artery occlusion complained of giddiness (Cases 6, 8, 20, 26).

In two of them the sensation was one of general unsteadiness rather than a true vertigo (Cases 6 and 26), but in the other two patients (Cases 8 and 20) attacks of true vertigo ushered in the syndrome.

In Case 8 a brief vertiginous attack caused the patient to fall to the ground and was accompanied by twitching of the right facial muscles. Later in the development of his syndrome a similar episode of vertigo accompanied weakness of his right hand. Case 20 also experienced short-lived attacks of vertigo at the onset of his illness. They occurred at intervals of a fortnight and soon after their onset were accompanied by transient numbness of his right index finger and twitching of the right facial muscles. They ceased after three months when transient attacks of weakness of his right leg appeared.

None of these patients admitted to any defect of hearing, and clinically none has shown any deafness or suggestion of labyrinthine involvement. It must be admitted, however, that no detailed otological examination was made in any of them.

#### Visual Symptoms

Visual symptoms were uncommon in these patients. Contrary to the older concept that carotid artery occlusion was characterised by unilateral blindness and contralateral hemiplegia, only two patients (Cases 2 and 29) in this series have shown this

combination of signs. Both had an established hemiplegia of many months' duration before they became blind in the contralateral eye.

Transient diplopia was experienced by two patients (Cases 13 and 26). In the former a horizontal diplopia lasting for ten minutes heralded the onset of a mild hemiplegia which appeared two days later, and in the latter vertical diplopia sometimes accompanied the fleeting attacks of blindness from which he suffered.

Transient blindness has not been a prominent feature in these patients with carotid occlusion. Two of them (Cases 6 and 17) complained of "slight blurring of vision" late in the development of their syndrome, and in Case 6 it was present during an attack of speechlessness and weakness of the right arm. Unfortunately, by the time they were interviewed one could not gain an accurate impression of what they had experienced because of the severe degree of dysphasia and intellectual deterioration which was present.

Case 26, however, was first seen shortly after his symptoms commenced. Then his chief complaint was of transient blindness, each attack lasting a quarter of an hour (patient's own estimate of time), during which vision faded until there were several negative scotomata in the visual field. After five minutes these would slowly disappear and vision return to normal. They recurred over several months but ceased as symptoms of parietal lobe dysfunction appeared.

In one other patient (Case 24) excessive brightness of vision lasting five days was the presenting symptom of his carotid artery occlusion.

In these patients with transient disturbances of vision none has shown any permanent impairment once the attacks had ceased.

Although eight cases in this series have shown a complete hemianopia, few of them complained of this disability, and indeed patients were often unaware of its presence until it was demonstrated to them.

#### Other Symptoms

Mental or emotional changes preceded the onset of the syndrome in one patient (Case 15) and in three others (Cases 2, 13 and 26) were amongst the presenting symptoms of the disease.

Case 15 complained of impaired memory for several months before the carotid occlusion declared itself, but as she had suffered from the effects of cerebral atherosclerotic disease for some years, it would be bold to ascribe this change solely to the effects of carotid occlusion.

In Cases 13 and 26 mild irritability accompanied symptoms of parietal lobe dysfunction early in the development of the syndrome, and were no doubt attributable to the effects of the carotid artery disease.

The relationship between the development of neurological signs and the appearance of mental symptoms was less clearcut in Case 2. Shortly after his right arm became weak he became depressed and was unable to concentrate or recall day-to-day events. As there was an adequate exogenous cause for his depression it seemed unlikely that these symptoms were the result of the carotid occlusion subsequently discovered.

Of course, as the disease progressed, nearly all patients showed organic intellectual impairment which varied in severity, but was more marked in those showing a severe degree of hemiplegia.

The onset of epilepsy after the development of the syndrome was not unexpected and was encountered in three patients in which it appeared three to eighteen months after the onset of their illness (Cases 12, 18, 19). The follow-up period in the other patients varied considerably and it may well be that more of them will develop epilepsy in the future.

### Signs

In these patients with carotid occlusion the basic feature shown by them was a weakness of the affected extremities. Although the basic pattern was a fairly constant one, the actual clinical picture ranged from a complete hemiplegia with marked sensory impairment to slight unilateral facial weakness. Dysphasia of some degree was always present when the dominant hemisphere was involved.

A severe degree of hemiplegia was encountered in five of the six patients presenting with a sudden onset (Cases 4, 12, 15, 16, 17), in only two of the four patients with a progressive story (Cases 1 and 30), but was rarely seen in patients presenting an episodic course (two of the twelve patients).

Three patients developing a sudden severe hemiplegia were seen within a few days of the onset of their symptoms, and all showed a total flaccid weakness of the affected face, arm and leg.

As recovery took place the distribution of the weakness was characteristic of other patients in this group in that the maximal weakness was present in the arm and tended to spare the facial muscles.

In those patients with a severe hemiplegia sensory impairment was invariably present. In half of them all forms of sensation appeared to be equally affected, but in the other half the impairment was chiefly cortical in type, represented by absent or impaired joint position sense and two-point discrimination in the fingers and toes.

A complete hemianopia was found in the majority of these patients. When the dominant hemisphere was involved all showed a severe degree of dysphasia in which the expressive aspect of speech was outstandingly affected.

Five patients presented with a moderate degree of hemiparesis, with the characteristic distribution of maximal weakness in the affected arm (Cases 7, 8, 9, 10, 13). All showed some degree of cortical sensory impairment in the affected hand, but in two of them (Cases 8 and 9) other forms of sensation were also to some extent impaired. In Case 8 there was slight tactile impairment over the hand and arm, and in Case 10 painful stimuli were less well appreciated over the affected face and arm. In three of them the dominant hemisphere was affected; one patient (Case 7) had a mild degree



of expressive dysphasia, whilst the other two (Cases 10 and 13) had a severe dysphasia both expressive and receptive in type which was unexpected in view of the degree of hemiplegia present. A complete hemianopia was not encountered in any of them but two patients showed a slight inattention defect to simultaneous stimuli presented in both visual fields.

Eleven patients showed lesser degrees of motor deficit varying from a mild hemiparesis, maximal in the arm, to a slight weakness of the affected face or hand (Cases 2, 3, 6, 11, 19, 20, 22, 24, 25, 26, 29). In the majority of these patients sensory impairment was less marked than in the other groups and was chiefly confined to defective joint position sense and two-point discrimination in the hand. However, in three patients with minimal weakness of the face and/or the arm no sensory impairment was demonstrated, and in one other (Case 20), showing a mild hemiparesis, the only sensory abnormality was slightly impaired joint position sense in the foot.

In those with a dominant hemisphere lesion some degree of dysphasia was present, usually restricted to a slight nominal defect of speech or a mild expressive dysphasia, but in one of them (Case 6), with a minimal degree of hemiparesis and cortical sensory impairment, there was both an expressive and receptive dysphasia accompanied by alexia and agraphia which suggested that

there were at least two distinct lesions present - one causing the hemiparesis and the other the speech deficit.

In these eleven patients three showed a complete hemianopia (Cases 3, 6, 26) and one other a right upper quadrantic field defect (Case 24). All had minor degrees of motor and sensory deficit yet had well-marked signs of parietal lobe dysfunction including dyscalculia, alexia, agraphia, constructional and dressing apraxias and visual agnosia in varying combinations.

These findings suggested that the lesion or lesions of the cerebral hemisphere producing these signs were more posteriorly situated than is usually encountered in these patients.

#### Optic Atrophy

In this series only two patients presented with a unilateral optic atrophy (Cases 2 and 29), which in both instances was preceded by pain confined to the temple on the same side. In the former the visual acuity was gradually reduced over some weeks to finger counting, was associated with marked constriction of the visual field and fundal appearances consistent with a primary optic atrophy. In the latter the affected eye was quite blind and the optic disc, when seen several days after the event, showed slight swelling and grey pallor suggesting that there had been a vascular occlusion of the ophthalmic artery.

### Papilloedema

Only one patient (Case 30) presented very early swelling of both optic discs which appeared soon after the development of a severe hemiplegia and was presumably due to swelling of the infarcted hemisphere. Two other patients (Cases 10 and 13) showed a questionable "blurring" of the nasal side of both optic discs, but subsequent observation over some weeks showed little change and the appearances were probably within the limits of normality.

### Ptosis

Ptosis was encountered once (Case 18). This patient was admitted to hospital shortly after the acute onset of an hemiplegia, was drowsy and apathetic, and had a moderately severe bilateral ptosis without any other signs of internal or external ophthalmoplegia. This finding was probably related to his mental state and otherwise had no neurological significance.

### Pupillary Changes

In one patient (Case 29) with unilateral optic atrophy the pupil of the affected eye was slightly dilated and reacted sluggishly to direct light. In two others (Cases 13 and 26) the pupil on the side opposite the cerebral lesion was dilated yet reacted adequately to light stimuli and on convergence. Both these patients had some degree of hemianopia and it is possible that this pupillary inequality was due to a tract lesion

as suggested by Walsh and Smith (1952). In the remaining patient the pupil on the side of the cerebral lesion was dilated (Case 16) and it is possible that this was a residuum of a partial III nerve palsy caused by temporal herniation of the infarcted hemisphere when he developed his hemiplegia two years before.

#### Mental and Emotional Signs

Although few of these patients were subjected to prolonged psychological testing, the majority of them have shown some degree of organic intellectual impairment which tended to be more pronounced in those with the severer neurological deficit. There was often a failure of recent memory and of concentration which in many of them was complicated by an aphasia.

Sometimes this involvement of higher cerebral functions declared itself in an excessive lability of mood (Cases 4 and 30), and very occasionally patients were noted to be demanding and critical (Case 16).

Even in those patients where brief clinical testing did not show any obvious deterioration (Cases 12 and 20), their relatives had observed subtle changes which were not remarked on by the casual observer. With the onset of the disease they had become rather irritable, were less interested in their surroundings and unable to perform tasks requiring continued concentration.

#### Carotid Pulsation

In sixteen patients alteration in the carotid pulse was looked for but this was only found in two

of them (Cases 10 and 19). The occluded internal carotid artery did not pulsate under the examining finger. In one other patient in whom a right carotid occlusion was suspected there was no difference in the pulsations felt on either side of the neck, but a low-pitched systolic bruit was heard over the artery on the side opposite the cerebral lesion, suggesting an increased blood flow through this vessel. Subsequent arteriography demonstrated a block in the right carotid syphon; the left carotid artery was hypertrophied and supplied blood to both cerebral hemispheres.

It may seem surprising that differences in the carotid pulse has not been encountered more frequently in these patients when the artery is occluded in the neck. Indeed, I think the figure given here is erroneous, as it has only been recently appreciated that one should palpate the arteries high in the neck and thus avoid confusing the pulsations in the external carotid with those in the internal carotid artery. It may well be that with this new technique differences will be noted in a higher proportion of cases.

#### Signs of Arterial Disease Elsewhere

In five patients of this series the peripheral arteries and retinal vessels showed atherosclerotic changes (Cases 1, 3, 6, 11, 15). All had some degree of hypertension which in three of them was systolic in type with blood pressure readings in the neighbourhood

of 160/90, whilst in the other two there was a sustained hypertension with readings fluctuating around 210/130.

In Case 3, with a history of intermittent claudication, no pulsation was felt in either dorsalis pedis or posterior tibial arteries. At post-mortem examination both femoral arteries were found to be obstructed by old thrombus laid down upon atherosclerotic plaques which had narrowed the lumen and reduced the blood flow.

Case 15 suffered from a mild hemiballismus which presumably had an arteriopathic basis, although at post-mortem examination no significant abnormality was seen in the basal ganglia, thalami or corpus luyisii.

Five other patients also had a mild degree of hypertension but none of them showed gross evidence of atherosclerosis.

## INVESTIGATIONS

### 1. Cerebrospinal fluid.

The cerebrospinal fluid was examined in eleven patients (Cases 2, 3, 4, 7, 8, 11, 18, 22, 24, 29, 30) and in all but four of them was normal. The fluid obtained from one of these four was ventricular in origin and had been contaminated with blood. In another two (Cases 7 and 11) the lumbar cerebrospinal fluid examined two to four weeks after an hemiplegic episode contained a protein of 70 and 75 mgms.% respectively. The fluid from one other patient (Case 24), examined nine days after the onset of a profound hemiplegia, contained 1800 red blood cells, 10 white cells (90% lymphocytes), a protein of 120 mgms.% with a Lenge curve reading 5555431000.

The raised protein in Cases 7 and 11, and the grossly abnormal fluid findings in Case 24, do no more than reflect the size, type and position of the infarct which in these cases was probably in close proximity to the subarachnoid space or ventricular system.

### 2. X-rays of skull

Straight x-rays of the skull were never helpful but films were taken in every case. Only three patients showed any abnormality (Cases 6, 11, 15). In them small flecks of calcification were seen overlying the pituitary fossa in the region of the

carotid syphon, but as this is a not uncommon finding in any patient with atherosclerosis, this appearance had no diagnostic value.

### 3. Blood Wassermann

No patient in this series has had a positive blood Wassermann reaction.

### 4. Air studies

In this series four patients had air studies (Cases 1, 17, 24, 30). All had severe degrees of hemiplegia yet the radiological changes varied considerably from patient to patient. Cases 1 and 24 showed mild dilatation of the lateral ventricle on the affected side, but in Case 17 there was a mild degree of generalised cortical atrophy. Case 30, with a recent aggravation of her hemiplegia, showed slight flattening of the temporal horn of the affected hemisphere. At post-mortem examination some days later the whole hemisphere was seen to be swollen and oedematous, and presumably this radiological finding showed where the oedema first appeared.

### 5. Arteriograms

Twenty-one of the twenty-four patients suffering from spontaneous carotid artery occlusion were subjected to arteriography. Partial or complete occlusion of the internal carotid artery was found on the right side in seven patients and on the left side in thirteen patients; in one other patient (Case 10) the left common carotid artery was blocked.



The commonest site of obstruction lay in the region of the carotid sinus in the neck. The following table details the site of obstruction in these twenty cases:-

SITE	RIGHT	LEFT
At the origin	3 complete occlusions 1 partial occlusion	1 complete occlusion 2 irregular filling defects in lumen
½ cm. above origin	2 complete occlusions	---
1 cm. above origin	---	6 complete, 1 incomplete occlusions
2 cm. above origin	---	1 complete occlusion
3½ cm. above origin	---	1 complete occlusion
In the carotid syphon	1 complete occlusion	1 complete occlusion
In common carotid	---	1 complete occlusion

N.B. In one patient (Case 30) the right internal carotid, anterior and middle cerebral arteries hardly filled with the dye and no satisfactory conclusion could be drawn from this finding. A few days later post-mortem study showed the internal carotid artery to be incompletely blocked by a large atherosclerotic plaque upon which a recent thrombus had been deposited.

Arteriography was also carried out in four of the five patients suffering from non-spontaneous carotid occlusion.

The following table details the site of obstruction:-

	RIGHT	LEFT
Aneurysms in region of carotid sinus		
Occlusion at origin		1
$\frac{1}{2}$ cm. above the origin		1
$1\frac{1}{2}$ cms. above the origin	1	
Embolism of internal carotid artery		
At carotid T		1

In this section the arteriographic findings of both spontaneous and non-spontaneous occlusion will be considered together as they show some of the alterations in cerebral haemodynamics which may occur after obstruction of the carotid artery.

The radiographic appearance at the site of the occlusion has varied, but most commonly a blind rounded stump was seen just proximal to the origin of the internal carotid artery in the neck (eight cases) (Fig. 1). The next most common finding was a conical or rat-tailed narrowing over a distance of 1-2 cms. before complete blockage occurred (Fig. 2). Case 21 presented a similar appearance but the narrowing occurred over a distance of 3-4 cms. before the block became complete; in this case the occlusion was due to a dissecting aneurysm of the carotid artery (Fig. 3).



Fig. 1.



Fig. 2.



Fig. 3.

In a further two patients the internal carotid artery was blocked in the syphon just proximal to the origin of the ophthalmic artery; one of these patients (Case 24) showed the interesting congenital anomaly of a carotid-basilar anastomosis so that the contrast flowed freely into the posterior cerebral circulation (Fig. 4). In one patient (Case 14) with embolic occlusion of the artery in its distal part the anterior and middle cerebral arteries were faintly outlined (Fig. 5).

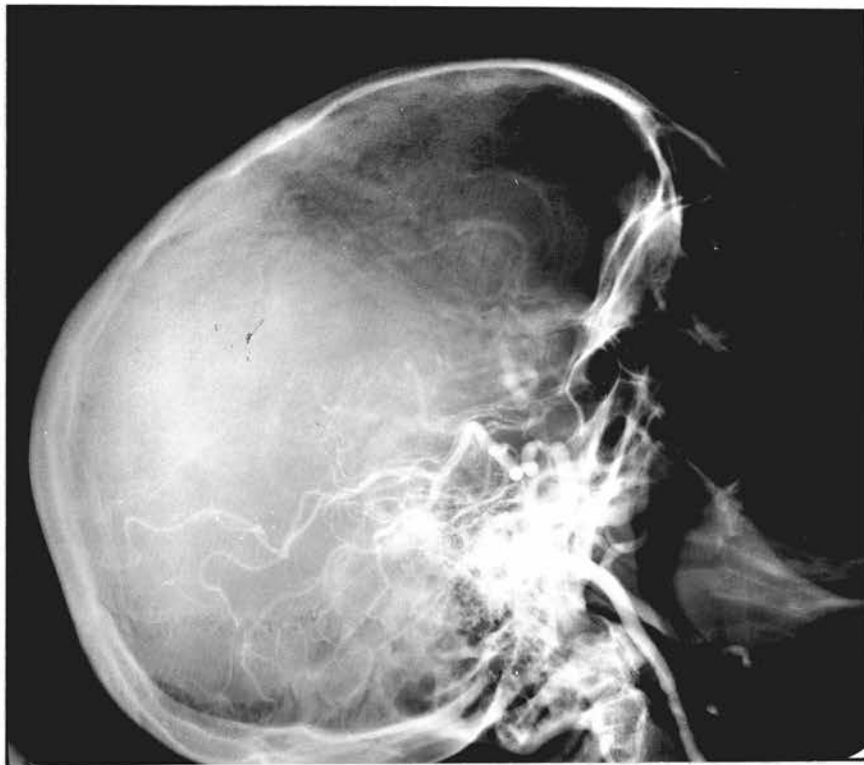


Fig. 4.



Fig. 5.



Fig. 6.

In three patients the internal carotid artery did not fill with the contrast medium. After careful inspection of the films one was always able to see a slight irregularity in the column of dye where the origin of the internal carotid should be and it was presumed that thrombus had spread from the sinus to the very mouth of the artery. (Fig. 6).

In four patients the lumen did not appear to be entirely occluded for dye flowed sluggishly up the carotid artery into the cerebral vessels.



In three of them a constant filling defect narrowed the lumen in the region of the carotid sinus (Fig. 7). In the other (Case 26) an irregular filling defect was present in the horizontal loop of the carotid syphon (Fig. 8). When the arteriogram was repeated one year later the vessel was found to be occluded just distal to its origin in the neck. This finding suggested that



Fig. 7.

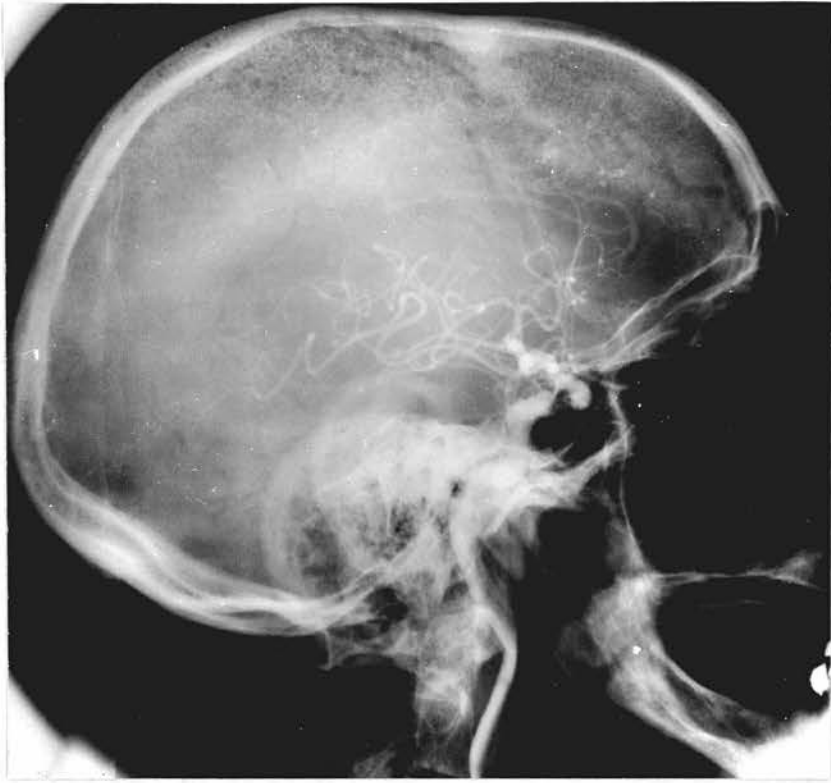


Fig. 8.

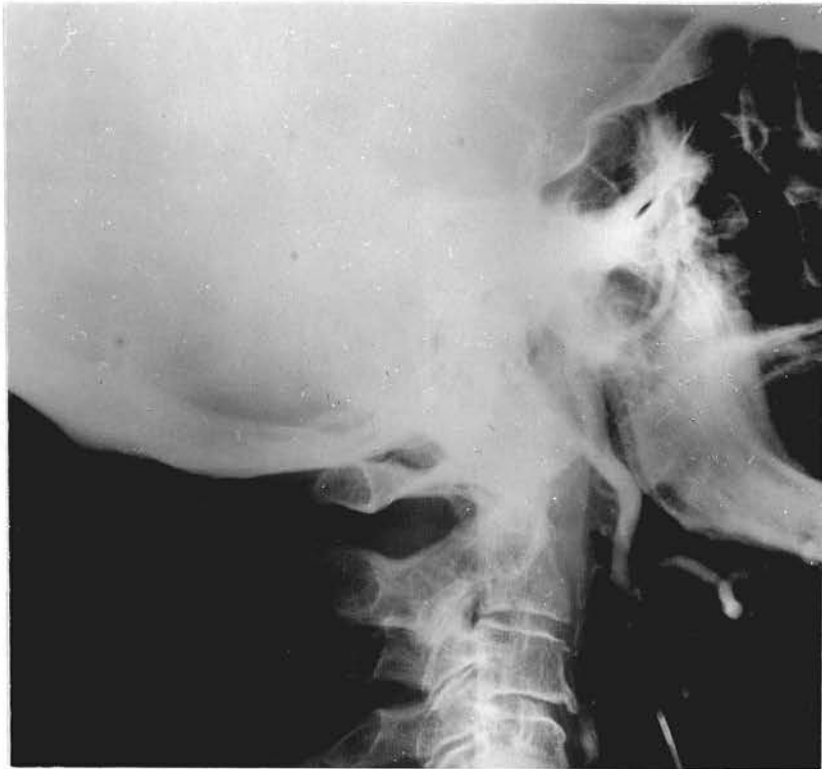


Fig. 9.

with the slowing of the blood stream secondary to partial occlusion of the vessel, retrograde thrombosis had taken place (cf. aneurysms) (Fig. 9).

In this series there was no significant difference in the clinical syndrome presented by patients showing complete or incomplete occlusion of the carotid artery.

#### Collateral supply.

In this series the internal carotid artery appeared to be totally occluded in five patients (Cases 5, 7, 8, 24, 25), yet in later films (taken a few seconds after the injection and normally showing venous filling) contrast medium was seen within the intracranial vessels on the same side.

In two cases (Cases 5 and 7) the dye flowed upwards through an apparently hypertrophied external carotid artery, and through its maxillary branch to numerous large arteries around the orbit. From there it could be seen passing backwards along the ophthalmic artery to fill the intracranial portion of the internal carotid artery and the middle cerebral group of vessels (Fig. 10). In another patient (Case 25) the contrast medium followed the same pathway via the external carotid anastomotic channels and filled both the anterior and middle cerebral arteries on the same side.



Fig. 10.

In Case 24, where the internal carotid artery was occluded in the syphon, dye flowed backwards through an anomalous carotid-basilar anastomosis and filled the ipsilateral anterior and middle cerebral vessels through the posterior communicating artery. This to my knowledge is the sole example where the posterior communicating has functioned as a collateral channel in carotid artery occlusion. As a congenital anomaly was present it may be that the circle of Willis was also abnormal, and the anterior communicating artery absent, so that this unusual collateral channel opened up to compensate for the reduced blood supply occasioned by the carotid artery occlusion.

In another patient (Case 8) the right carotid artery was also blocked at the syphon and dye filled the superior cerebellar arteries through anastomoses between enlarged musculo-cutaneous branches of the occipital artery and the basilar and vertebral arteries. The significance of this finding was far from clear, as when contrast medium was injected into the left carotid the anterior and middle cerebral arteries filled on both sides indicating that the circle of Willis was functioning as an anastomotic channel. Perhaps the posterior cerebral artery originated from the internal carotid and the occipital vessels had become hypertrophied in an effort to compensate for the reduction in blood supply consequent upon the carotid occlusion.

From these observations it would appear that in twenty-five per cent of these cases with carotid artery occlusion nature provided an alternative blood supply through the external carotid artery and its branches. But this is not the only collateral channel through which blood may be supplied to the intracranial vessels on the same side as the occluded artery.

In four patients contrast medium injected into the non-occluded carotid artery has filled the cerebral vessels of both hemispheres (Cases 8, 13, 23, 27).

In two of them (Cases 8 and 23) both anterior and middle cerebral arteries were filled (Fig. 11) and in another (Case 27) both anterior cerebrals were outlined. In Case 13 contrast medium injected into the unobstructed right carotid artery filled both anterior cerebrals but only the right middle cerebral artery. In the light of pathological findings in other cases one may presume that the left middle cerebral artery in this patient was occluded by thrombus.

In these eight patients in whom a collateral supply was demonstrated, three had no symptoms referable to the occlusion (all were associated with aneurysms in the cavernous sinus region), three had relatively mild degrees of weakness of the affected extremities and two had a severe hemiplegia. It is worthy of note that Case 8, in whom collateral channels were available through the external carotid and the opposite internal carotid artery via the circle of Willis, had a





Fig. 11.

severe hemiplegia.

Unfortunately, many of these patients did not have cross-circulation studies and there is no means of knowing the availability of the collateral blood supply via the circle of Willis. The number in this series in which a collateral supply was demonstrated is too small to allow for a statistical analysis, but the findings suggest that in patients with an alternative route through which blood may reach the affected

hemisphere, the symptoms of carotid artery occlusion are usually less pronounced.

#### Dangers of arteriography

That arteriography is not without its dangers in carotid occlusion is well illustrated by four cases in this series.

Case 11 presented with a mild hemiparesis. Arteriography demonstrated an irregular filling defect in the lumen of the internal carotid artery at its origin. The circulation in the carotid tree was obviously sluggish but the anterior and middle cerebral arteries were filled. Unfortunately blood clotted within the needle and repuncture of the artery was necessary to secure further pictures. On this occasion the appearances were similar except that the anterior cerebral artery did not fill. Within an hour of the second injection he developed a profound hemiplegia, lapsed into coma and died within a few days.

At post-mortem examination the filling defect in the lumen of the internal carotid artery was accounted for by a large atheromatous plaque lying in the wall, upon which recent blood clot had been deposited. The territory of the middle cerebral artery showed recent massive haemorrhagic infarction and some of the smaller branches of the middle cerebral artery contained coiled-up blood clot which appeared to be embolic in origin.



Before arteriography Case 30 presented a severe left hemiplegia but was reasonably alert and co-operative. After puncture of the right common carotid artery the arteriographic pictures were unsatisfactory and showed only slight filling of the internal carotid and cerebral arteries on the same side. After this procedure she became progressively more drowsy and died within eight hours. At post-mortem examination the right internal carotid artery at its commencement was almost completely occluded by old organised fibrous tissue attached to which was recent thrombus. In the right cerebral hemisphere there was recent extensive infarction of the middle cerebral artery territory without evidence of any organic occlusion of the larger cerebral vessels.

Two other patients have also shown deterioration in their clinical state following arteriography, but in them pathological examination was not possible as both survived. Case 24 became totally hemiplegic after the injection of the contrast medium, which outlined a complete block in the carotid syphon. The cerebrospinal fluid examined nine days after this event showed changes which were compatible with a large infarction of brain in close proximity to the subarachnoid space.

The arteriogram in Case 22 revealed an irregular filling defect at the origin of the internal carotid artery in the neck, and after the injection was

completed he complained of partial blindness in the ipsilateral eye. Examination then showed an altitudinal field defect resulting from occlusion of the superior temporal artery.

It is perhaps important to note that three of these four cases did not have a complete occlusion of the vessel. However, the mechanism underlying the sudden deterioration in these cases following arteriography is far from clear. Admittedly, in Case 11 a few emboli were found in the cerebral vessels, but were not of sufficient size or number to account for the massive infarction of the brain, and in the other (Case 30) no organic occlusion of the larger cerebral vessels was demonstrated. Although embolism may occur, presumably from the thrombus lying in the carotid sinus, some other factor must play a part. The possible nature of this factor is discussed in considering the mechanism of the symptoms and signs underlying carotid occlusion (*vide infra*).

SECTION B

In this group of five patients the carotid artery occlusion was associated with aneurysmal formation in the cavernous sinus in three of them (Cases 5, 23, 27), in another the occlusion was due to an embolus (Case 14), and in the last patient the occlusion followed soon after the successful removal of a spinal meningioma (Case 28).

In two of the three patients (Cases 23 and 27) suspected of harbouring aneurysms, there was radiological evidence of a partly calcified ring shadow of considerable size lying behind the orbit in the region of the cavernous sinus, which had partly eroded the floor of the middle fossa. This finding when taken in conjunction with the clinical history confirmed that a large aneurysm was present, although of course it did not fill at subsequent arteriography as the internal carotid artery was blocked at its origin in the neck.

However, in Case 5 the presence of an aneurysm could only be presumed. She was a hypertensive woman of sixty-seven years, who two years before her admission to hospital had experienced mild giddiness with an unsteady gait due to a sudden diplopia. These symptoms

disappeared within two months, although her relatives noted that her left eye did not move out properly. Four months later she awoke with severe headache and photophobia and later vomited. The headache persisted for several weeks, then gradually diminished and disappeared completely some months later. At the time of her admission to hospital she showed a partial third and complete sixth nerve palsy, and with the exception of a mild bilateral ptosis there were no other abnormal neurological signs. It was thought that she had an intracranial aneurysm, which was not demonstrated by arteriography when the left internal carotid artery was found to be occluded at its origin in the neck. Although no aneurysm was demonstrated, there was strong presumptive evidence that such an anomaly was present, and had given rise to the symptoms of which she complained.

None of these three cases had any symptoms or signs referable to their carotid artery occlusion.

Another patient (Case 14), who was known to have had at least three previous embolic accidents from rheumatic heart disease, developed a sudden hemiplegia, the onset and course of which was exactly similar to those cases of spontaneous carotid artery occlusion presenting in a sudden manner. An arteriogram showed an obstruction in the region of the intracranial carotid bifurcation, presumably indicating where the embolus had lodged.

The last patient in this group was most interesting (Case 28). She was a woman of sixty-one years who developed a hemiplegia after the removal of a spinal meningioma under general anaesthesia. She died within a few hours of this happening, and at post-mortem examination recent blood clot was found in the intracranial portion of one internal carotid, together with extensive infarction of most of the middle cerebral artery territory on the same side. Unfortunately, the state of the carotid artery in the neck was not investigated, and unfortunately the histological preparations of the brain had been lost and could not be replaced.

PATHOLOGICAL FINDINGS IN CAROTID ARTERY OCCLUSION

Post-mortem studies were made on six of the patients who had suffered from spontaneous carotid artery occlusion. Serial sections of the cerebral hemispheres were not made but approximately eight representative sections of the brain in each case were studied in detail (Cases 3, 11, 15, 16, 21, 30).

A further patient (Case 28) in whom thrombosis of the carotid artery had occurred post-operatively was also studied but unfortunately the examination was confined to the naked eye changes as the sections of the brain and obstructed artery were lost and could not be replaced.

SPONTANEOUS CASES1. The occluded carotid artery.

In every patient the carotid arteries were examined throughout their length in the neck and intracranial cavity.

In four of them (Cases 3, 11, 16, 30) the occluded artery was marked by tough yellowish craggy tissue laid down in the vessel wall in the region of the sinus. This had caused considerable eccentric narrowing of the lumen which in two cases was reduced to  $\frac{1}{2}$  to 1 mm. in diameter. This narrowing steadily diminished above this level so that the lumen assumed a roughly inverted conical shape with its apex downwards. Recent ante-mortem thrombus was adherent to these masses, which in two of them

(Cases 11 and 30) was continued upwards for a short distance as a loosely adherent tongue of tissue.

In the other two cases recent ante-mortem thrombus had completely occluded the lumen of the artery, and in Case 16 extended upwards for one inch above the sinus, where it was limited by a large yellow atheromatous plaque, whilst in the other (Case 3) it had extended into the middle cerebral artery.

In Case 15 the maximal site of atherosclerotic narrowing lay in the carotid syphon just proximal to the origin of the ophthalmic artery. Recent thrombus filled the internal carotid artery to its origin in the neck. Here another large plaque of atheroma was present.

In Case 21 the internal carotid artery had been occluded by a dissecting aneurysm, probably on an atherosclerotic basis, and recent ante-mortem clot extended upwards into the anterior and middle cerebral arteries of the same side.

The opposite internal carotid artery appeared to be healthy in three of these six cases, but in the other three atherosclerotic changes were present to a varying degree. In Case 15 small plaques lay in the sinus but in Case 16 the change was much more extensive and had resulted in ring calcification which had considerably reduced the available lumen. In Case 11 the carotid sinus was free from atheroma but the intradural portions of both carotid arteries were

narrowed by yellowish plaques. Thrombosis had not occurred at any of these sites.

Histologically the appearances at the site of maximal narrowing of the obstructed artery have been strikingly similar in five of these six cases. The lumen was eccentrically narrowed by a mass of subintimal fibrous tissue and progressively organised thrombus upon which had been deposited recent blood clot (Fig. 1).

1. Recent blood clot
2. Organised blood clot
3. Fibrous tissue
4. Internal elastic lamina



Scattered throughout the more superficial layers (i.e. near the media) were many clusters of cholesterol crystals and calcium deposits, around which lay foreign body giant cells, together with small round cells which were more diffusely distributed throughout this tissue (Fig. 2).



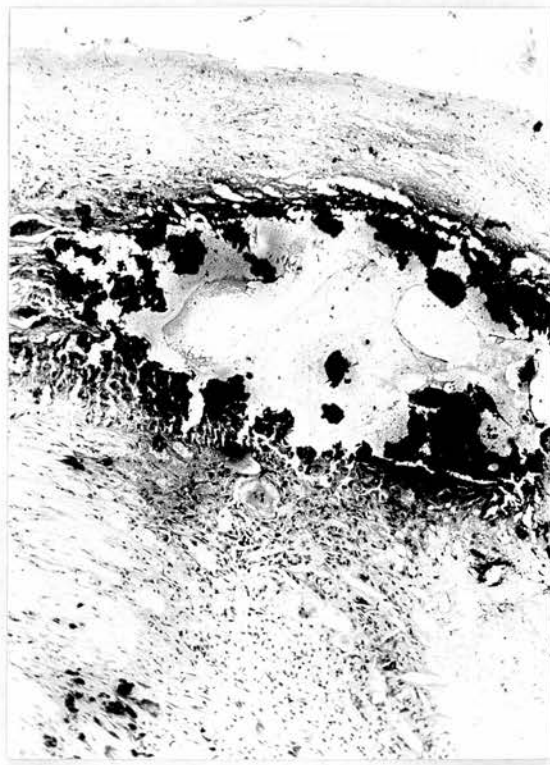


Fig. 2.

In three cases (Cases 3, 15, 16) there were small endothelial lined channels scattered throughout the organising thrombus. Some of these channels contained red blood cells (Fig. 3) and it was thought that they represented attempts at recanalisation.

The internal elastic lamina of the artery was often crenated and sometimes reduplicated and thinned but the media, adventitia and neighbouring veins were always healthy in appearance.

In Case 21 the histological appearances were naturally different. The intima had been separated from the underlying media and thrombus of recent origin occluded the carotid artery; the media and adventitia were healthy.

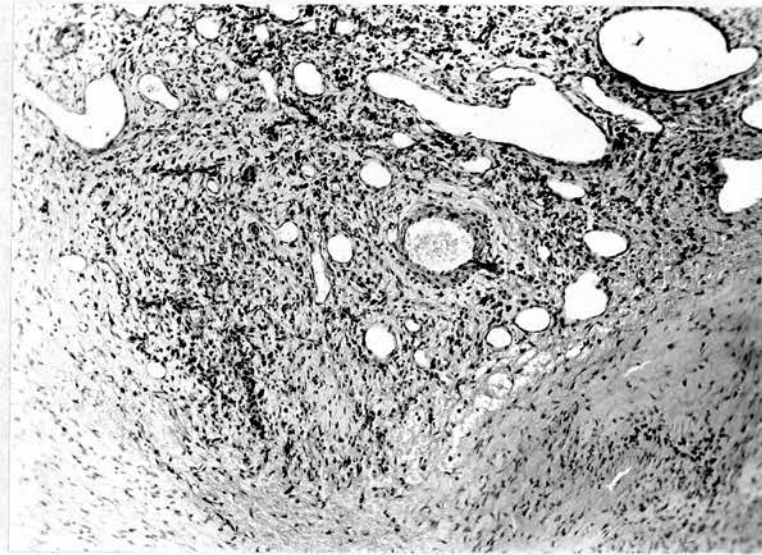


Fig. 3.

## 2. Macroscopic changes in the cerebral blood vessels.

In every case the larger cerebral vessels at the base of the brain have shown atheromatous changes, which were pronounced in Cases 15 and 16.

The circle of Willis was symmetrical in each one, with the exception of Case 30, where the left posterior communicating artery was small. However, the corresponding artery on the right side was larger than normal as if nature had attempted to compensate for the underdevelopment of its fellow.

To the naked eye occlusion of the larger cerebral vessels was noted in two cases only (Cases 3 and 16). In Case 3 the middle cerebral artery at the

Sylvian point was free from recent blood clot but was thinned and greyish-white over a distance of  $\frac{1}{2}$  cm. This appearance was consistent with an old-standing thrombosis at this point. A small cortical artery over the convexity of the occipital lobe presented a similar appearance and was clearly related to an old scarred infarct in the underlying cortex. In Case 16 recent thrombus was present in the anterior cerebral artery in the region of the splenium of the corpus callosum, but whether this was thrombotic or embolic in nature was not determined.

### 3. Macroscopic changes in the brain.

The hemisphere on the same side as the occluded carotid artery has always shown macroscopic change which was most evident in the territory of the middle cerebral artery. The area of infarction, whether old or recent, was fairly constant in distribution and was most severe at cortical and subcortical levels. As a rule it involved the mid-part of the convexity of the frontal lobe including the inferior and mid-frontal convolutions, the pre- and post-central gyri in almost their full extent, the inferior parietal convolutions and the outer surface of the occipital lobe. It also frequently extended into the superior and middle temporal gyri except in one of them (Case 16), where the cortical infarction was less extensive (Fig. 4). Medially the infarct often involved the supero-lateral part of the corpus callosum, putamen and globus pallidus, especially

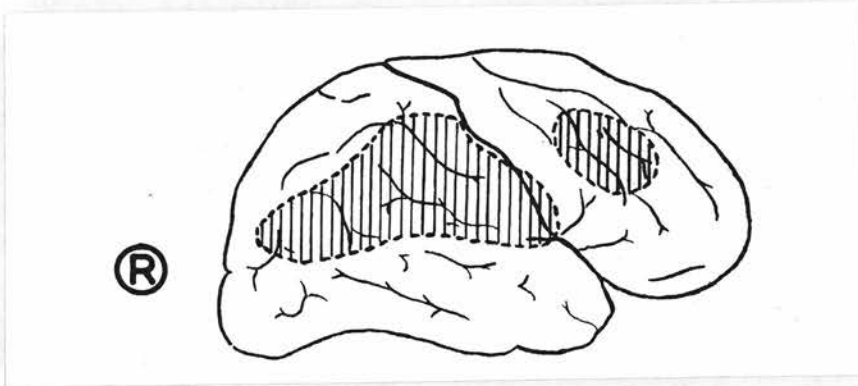


Fig. 4.

in Cases 3, 11 and 16, but always spared those parts of the brain supplied by the anterior cerebral and Heubner's artery.

In those patients who died following aggravation of their cerebral symptoms (Cases 3, 11, 15, 30) parts of this infarct were stippled with minute haemorrhages and in Case 30 the leptomeninges overlying the convexity were oedematous and blood-stained.

#### 4. Histological changes in the brain and cerebral blood vessels.

The histological changes in the affected hemisphere have always been more widespread than was suggested by the naked eye appearances. Throughout the distribution of the middle cerebral artery in both grey and white matter there were scattered areas of

focal brain damage surrounded by regions of more diffuse but less severe ischaemic change. Except for Case 21, where these lesions were all of recent origin and of the same age, all the other cases (Cases 3, 11, 15, 16, 30) have shown areas of focal damage of differing ages as shown by the cellular reaction and degree of gliosis present. These lesions varied in severity from complete dissolution of the cerebral tissues to slight ischaemic cell change. In general the older areas of infarction lay mainly in the more peripheral parts of the middle cerebral artery territory. In the anterior and middle parts of this territory the infarction was haemorrhagic in type, and the extravasated blood was mainly periarteriolar in distribution (Fig. 5). However, this ischaemic

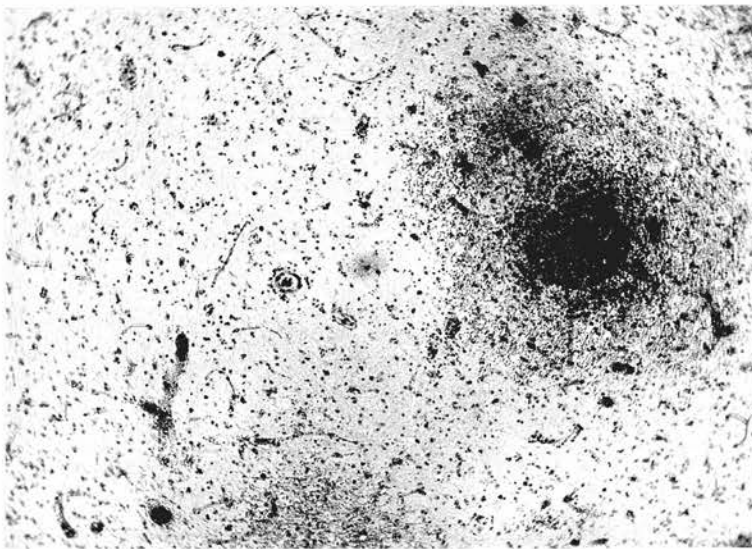


Fig. 5.

damage was not solely confined to the middle cerebral artery territory. In three cases (Cases 15, 16, 30) there were regions of focal ischaemic change within the anterior cerebral artery distribution, which in two of them (Cases 15 and 16) was frankly haemorrhagic in type. In one further case (Case 3) the damage was less severe but more diffuse and was restricted to the cortex in the anterior and posterior cerebral territories, where the nerve cells were shrunken and distorted (Fig. 6 ).

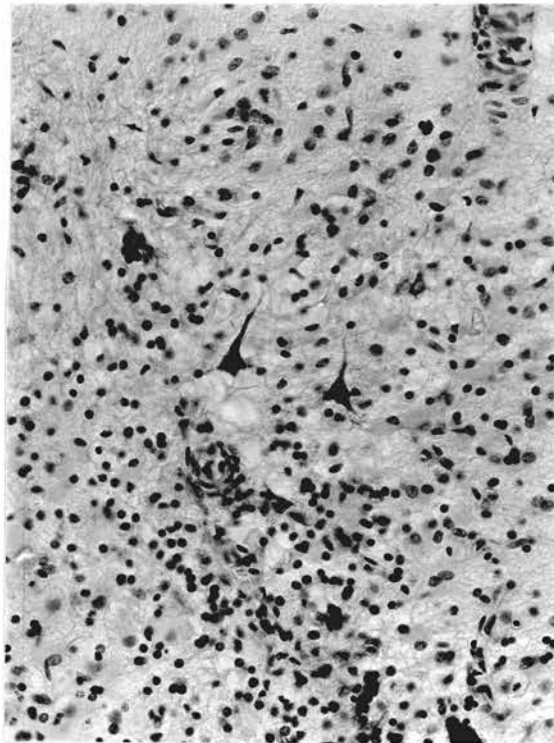


Fig. 6.

In the infarcted regions in three of these six cases blood clot was seen in some of the smaller cerebral arterioles (Cases 3, 11, 30). The occluded vessels lay chiefly in the more peripheral branches of the middle cerebral artery and in some of them thrombus

infiltrated by small round cells blocked the lumen. In others it was eccentrically placed and had been partly reabsorbed (Fig. 7) or had been recanalised (Fig. 8).

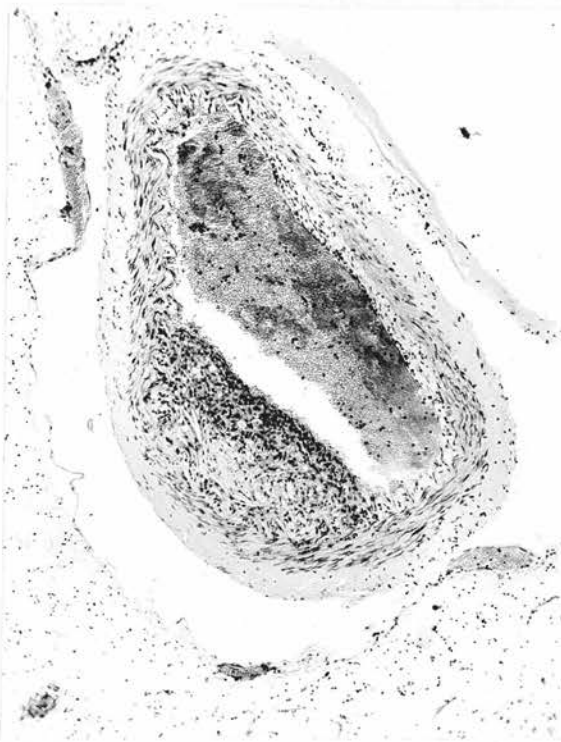


Fig. 7.

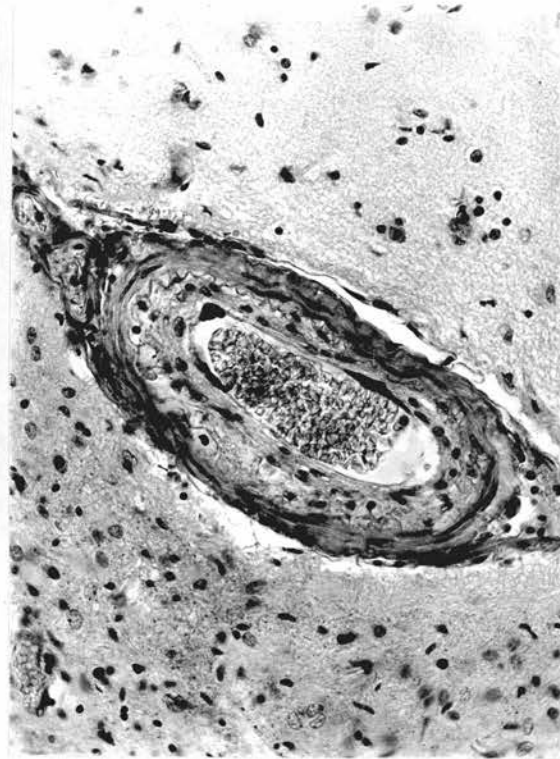


Fig. 8.

Occasionally small arterioles were seen to be occluded by cholesterol crystals, and sometimes fibrous tissue which was infiltrated by small round cells; it was thought that these appearances were consistent with the end result of a long-standing thrombotic occlusion, as the type of vessels affected were not those usually involved in an atherosclerotic process. It was usually possible to relate these small vascular occlusions with ischaemic infarcts in the neighbouring brain substance (Fig. 9).

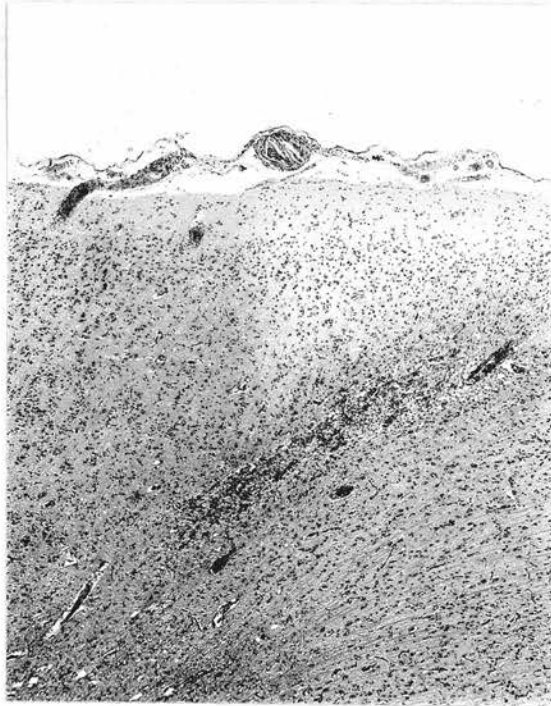


Fig. 9.

Histologically it was often impossible to be sure whether these changes represented embolic

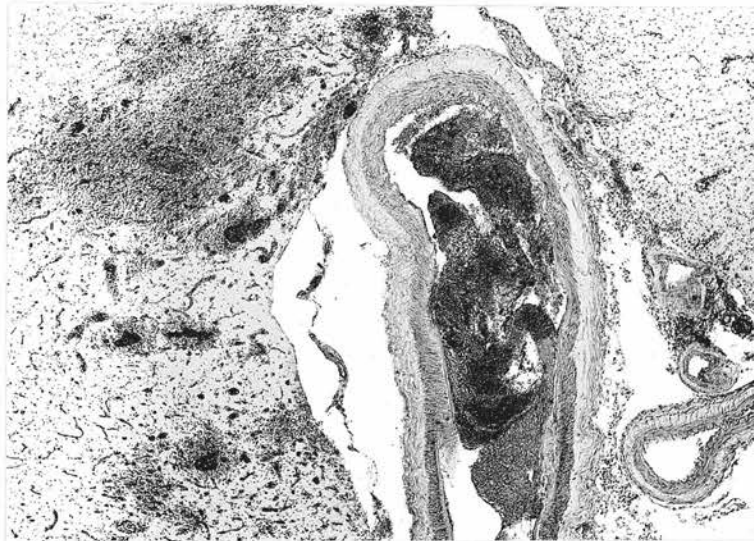


Fig. 10.





Fig. 11.

or thrombotic occlusion, but in one of them (Case 11) coiled-up blood clot was seen in a few of the larger branches of the middle cerebral artery, and it seemed reasonably certain that these were embolic in nature (Fig. 10).

In these three cases arterioles of a similar calibre appeared to be normal, and one frequently saw healthy vessels lying in the neighbourhood of those occluded by thrombus.

In the other three cases thrombus was not found in the smaller cerebral blood vessels. In two of them (Cases 15 and 16) several of the larger branches of the middle cerebral artery were narrowed by subintimal connective tissue infiltrated by a few small round cells,

and it was uncertain whether this change represented the edge of an atherosclerotic mass or an old organised thrombus lying within the lumen. In the other case (Case 21), where the infarction was of recent origin, all the smaller vessels were dilated and packed with red cells.

In those cases where the infarction was of recent origin the vessels in the neighbouring sulci were often surrounded by small round cells, polymorphs and compound granular corpuscles, but these cells never infiltrated the vessel walls (Fig. 11).

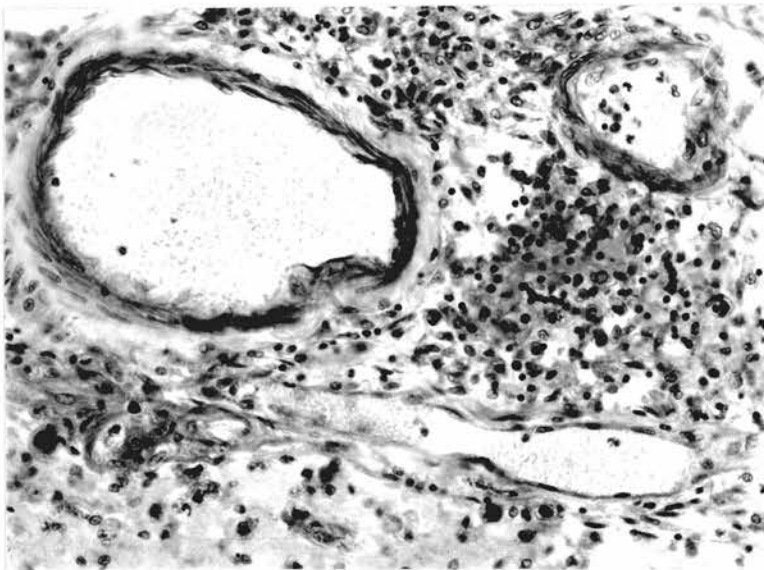


Fig. 11.  
H.P. view

This was well illustrated by Case 30 where in addition to these changes the leptomeninges overlying the infarcted areas were swollen and infiltrated by these cells.

Apart from subpial gliosis the cerebral hemisphere on the side of the unobstructed carotid artery appeared to be healthy and no significant changes were seen in the smaller cerebral vessels.

### 5. Changes elsewhere in the body.

Atherosclerotic changes were not entirely confined to the cerebrovascular tree, and both the coronary arteries and abdominal aorta have been affected in these cases. In one of them (Case 16) the coronary artery was so narrowed that myocardial infarction had resulted. In another (Case 3), where the atherosclerosis was more widespread, both femoral arteries were almost totally occluded over a distance of 1 to 2 cms. in their course; the histological picture presented by these vessels was similar to that seen in the obstructed carotid artery. In addition to these changes recent ante-mortem thrombus had been deposited on a patch of atheroma on the wall of the aorta midway between the superior and inferior mesenteric arteries. The mouth of the former vessel was blocked by recent thrombus with resultant infarction of most of the small intestine. The left ventricle in this case also contained a ball thrombus consisting of laminated blood clot. It seemed unlikely that this thrombus had caused the pathological changes in the right cerebral hemisphere for several reasons. Firstly the left cerebral hemisphere appeared to be healthy, and surely if emboli had entered the systemic circulation they would have been commoner on this side, and secondly the lumen of the right internal carotid artery was reduced to  $\frac{1}{2}$  mm. which would make the passage of emboli difficult. Thirdly, with the exception of

the occlusion of the superior mesenteric artery, which may have been embolic in nature, the results of emboli were not observed in the rest of the systemic circulation.

#### NON-SPONTANEOUS CASES

In Case 28 the intracranial portion of the right internal carotid artery was filled with recent blood clot which extended into the right middle cerebral artery. The right cerebral hemisphere was swollen and congested and almost the entire distribution of the middle cerebral artery infarcted.

Unfortunately the cervical portion of the carotid artery was not investigated and the histological sections of this case were lost and could not be replaced.

## DISCUSSION

### The aetiology of the carotid artery occlusion

There has been much discussion in the past on the underlying mechanism of spontaneous carotid occlusion but there is now fairly general agreement that atherosclerosis is the basic factor in the majority of these patients. Much of the evidence for this rests on histological examination of resected portions of the occluded vessel during life (Sorgo, Reichert, Andrell, Webster et alia) but both Fisher and Hultquist have confirmed its presence in their patients coming to post-mortem. In particular Hultquist's figures are most impressive for in the ninety-one cases of carotid occlusion which he studied all were secondary to an underlying atherosclerosis of the vessel.

This may seem surprising for cases of spontaneous carotid artery occlusion have been described from the age of seven years (King and Langworthy), and are by no means uncommon in the second and third decades when one would not usually expect to find atherosclerotic changes of such a nature as to predispose to thrombosis. However Chiari, who examined the carotid vessels in 400 routine post-mortems, found atherosclerotic changes in the carotid sinus in two boys aged twelve and eighteen years and in two women aged twenty-three and twenty-five years in whom there was little evidence of atherosclerosis elsewhere in the body. Keele (1933)

in fifty-five consecutive post-mortem examinations discovered atherosclerosis of the carotid sinus in fifty of them. It was present in a patient of sixteen years but tended to be more severe in the older age groups and paralleled atherosclerotic changes in the iliac arteries. Therefore the pathological evidence that atherosclerosis is the fundamental change in most cases is a strong one.

However, not all authors subscribe to this view for Sargo, Antoni, Andrell, Sunder-Plassman (1941), Krayenbühl and Weber thought that thromboangiitis obliterans was the basis of the carotid artery occlusion in some of their cases.

The evidence for this was based upon histological examination of resected portions of the occluded artery during life. The diagnosis was made on the presence of mural inflammatory cells and delicate fibrillar connective tissue lying within the lumen of the vessel, although Andrell reported slight small-celled infiltration of the media and adventitia in one of his cases. With this one exception these changes were confined to the intima. Five of the cases in this series presented similar appearances, and it must be admitted that in the advanced stages of thromboangiitis obliterans there may be a close resemblance to extensive atherosclerosis. However, focal collections of chronic inflammatory cells and even giant cells are seen in undoubted cases of atherosclerosis, and the delicate

fibrillary connective tissue is probably the late result of organisation of a thrombus. Another pointer in favour of atherosclerosis is the normal appearance of the media and adventitia and the fact that the neighbouring veins are never involved in this process. Therefore before thromboangiitis obliterans is accepted as a cause for carotid occlusion more convincing evidence must be brought forward.

Although atherosclerosis appears to be the commonest cause of spontaneous carotid artery occlusion, there are rarer causes which should not be overlooked. Gilmour (1941) reported two cases of giant-cell arteritis which had caused stenosis and occlusion of the carotid vessels, and Darling and Clark described local syphilitic arteritis leading to occlusion of the carotid artery in the neck. Moniz (1937) too thought that syphilis was the factor underlying the occlusion in one of his cases. His evidence for this assumption rested solely on a past history of syphilis in the presence of negative serological reactions, and it is doubtful if in fact this was the underlying cause of the occlusion.

Budinova-Smela et alia (1949) found a positive blood Wassermann reaction in one of their cases but they did not have the opportunity for pathological study of the occluded internal carotid artery. One cannot therefore confidently attribute the occlusion to a syphilitic arteritis, as atherosclerosis is commonly

met with in the presence of positive serological reactions. With the exception of this one example the serological reactions have all been negative in other cases reported in the literature. Syphilis therefore is probably a very rare cause of carotid artery occlusion.

Trauma has often been invoked as the underlying factor in the spontaneous vascular occlusion suffered by these patients but there is little direct evidence that it plays any great part.

Wolfe (1948) advanced the theory that thrombotic occlusion of the carotid artery might result from small intimal tears, akin to those which have been found in the femoral and popliteal arteries in young adults indulging in unaccustomed exercise. <sup>There</sup> ~~This~~ is no strong evidence that this does in fact happen except when the artery receives a direct or indirect concussion injury. In any case the carotid artery is much less liable to major stresses and strains than the major limb vessels and this supposition does not explain why carotid occlusion is much commoner in later life. There is, however, no doubt that occlusion can occur after blunt injuries to the neck, for Verneuil (1872) reported a case where the intima of the artery had been torn following the injury and had provided a suitable nidus for subsequent thrombus formation which blocked the vessel. Greco (1935) had a similar case and Northfield and Morgan (1944) found recent occlusion of the carotid



artery in a young soldier who died shortly after a rope had been wound round his neck.

But intimal tears of the carotid artery leading to thrombotic occlusion of the vessel can also follow trauma to the head. Moniz (1941) has described a patient who died soon after a head injury, and at post-mortem examination one carotid artery was found to be distended by recent blood clot which had been laid down on an intimal tear. He suggested that the head injury had resulted in excessive stretching of the artery with rupture of the intima. Elkington (1954) also had a similar case under his care.

In all these cases the carotid artery occlusion followed closely on the injury and was directly attributable to it. The literature on spontaneous occlusion contains several instances of head injury preceding the discovery of the occlusion, and it will be recalled that two patients in this series had had concussionial head injuries several years before their symptoms developed (Cases 4 and 17).

In another one (Case 2) a severe crush injury of the neck antedated the onset of his symptoms by four years. In these cases the long time interval between the injury and the subsequent development of symptoms argues against the injury being the direct cause of the occlusion. However, it could be that a small contusional injury or actual tear of the intima of the carotid artery could result in local thrombus formation, which became

organised and eventually incorporated into the vessel wall and thus resembled a primary atherosclerotic change. On this intimal thickening thrombus might be again deposited, and after this cycle had been repeated several times it could lead to narrowing of the lumen and changes which would be indistinguishable from atherosclerosis (Duguid 1946, 1948). Eventually occlusion of the artery might result.

That such a chain of events might occur is borne out by this histological study of the material in this series. With the exception of Case 21, where a dissecting aneurysm had resulted in relatively sudden occlusion of the carotid artery, in the others the occlusion has been more gradual. In these cases it was impossible to say whether the initial change in the vessel wall followed on primary atherosclerosis (Rokitansky, 1852) or an organised thrombus. But there is no doubt that whatever the primary change may have been, at some future date fresh thrombus was deposited upon this roughened area and again became organised, and this process was probably repeated several times until extensive narrowing of the lumen occurred. At this stage the blood flow through the artery is slowed, as has been demonstrated by arteriography (cf. Case 11), and eventually the narrowed portion of the vessel is occluded by thrombus which may remain localised, or extend upwards into the intracranial part

of the internal carotid artery, and even into one or more of the major cerebral vessels. When the clot remains localised recanalisation may take place. By far the commonest site for this narrowing lay in the region of the carotid sinus (four cases) but in one other (Case 15) the maximum site of narrowing lay in the carotid syphon and thrombus filled the lumen of the artery downwards to its point of origin in the neck. That this was a retrograde extension of the clot is suggested by Case 26, who on his first arteriography showed a constant filling defect in the carotid syphon, presumably due to a large atherosclerotic plaque, with considerable slowing of the blood stream in the whole carotid tree. Subsequent arteriography one year later showed the carotid artery to be occluded just distal to its origin in the neck.

Hultquist in his series also found that occlusion of the carotid artery was commoner in the region of the sinus and much rarer in the syphon. He emphasized that fresh thrombus was often deposited on these sites in the carotid artery shortly before death but in several of his cases the thrombus had spread so far that he could not be sure of its point of origin.

Although in the six cases in this series which came to post-mortem the underlying cause of the occlusion was undoubtedly atherosclerosis whatever its primary basis, there were nineteen others demonstrated

by arteriography where it was presumed to be present. There are strong grounds for this assumption. The majority of these cases were in the age group when atherosclerosis is common, and the strong family history of degenerative cardiovascular disease and the predominance of males are all significant pointers in this direction.

In three other patients in this series the carotid artery occlusion was associated with aneurysmal formation in the region of the cavernous sinus. In two of them large partly calcified ring shadows lay in the region of the sinus and were of sufficient size to have caused compression of the carotid artery with consequent slowing of the blood stream and retrograde thrombosis of the vessel to its point of origin in the neck. In the third patient the presence of an aneurysm in the same situation could only be presumed. The finding of isolated unilateral III and VI nerve palsies and a history compatible with a previous subarachnoid haemorrhage pointed to aneurysmal formation, and moreover these isolated signs have rarely been reported in uncomplicated carotid artery occlusion. Le Beau et alia (1949) called attention to a similar patient with carotid occlusion who complained only of headache but had unilateral third and fourth nerve palsies. Under these conditions one can only guess at the size of the aneurysm but it is probable that the mechanism of the associated carotid occlusion was the same as in the

other two patients described above.

In one other patient (Case 28) the carotid artery occlusion occurred immediately after a major operation to the spine. At post-mortem examination recent ante-mortem clot distended the intracranial part of one internal carotid artery with infarction of most of the brain supplied by the middle cerebral artery.

Fisher in particular has met with this condition in several patients following operation or vascular collapse from other causes and has always found the occluded artery to be narrowed at its origin in the neck by atherosclerosis. He postulates that a sudden fall in blood pressure, in the presence of an impeded circulation in the vessel, results in a massive thrombosis throughout its entire length. Although the origin of the internal carotid artery was not inspected in Case 28 it seems reasonable to assume that the mechanism was similar to that postulated by Fisher in his cases.

The aetiology of the pathological changes found in the brain and cerebral vessels with carotid artery occlusion

Although the pathological changes in the carotid artery have been described by a number of authors, cases in which the brain and cervical portions of the carotid artery have been investigated are relatively uncommon, and it is rare to find cases where the histological changes in the brain and cerebral vessels have been studied.

The early German writers including Penzoldt and Oppenheim (1898) merely described softening of the brain with occlusion of the carotid artery, but Chiari in 1905 recorded five cases of cerebral embolism following detachment of a thrombus from the carotid sinus in the neck; in one of these the carotid artery was entirely occluded. Hunt in his paper on the clinical effects of occlusion was well aware of the resulting changes in the brain including "chronic oedema, atrophic and softening processes" but gave few details of his own observations.

Saphir (1935) as well as Hunt called attention to the importance of examining the carotid arteries carefully throughout their entire length in cases of "unexplained" cerebral infarction. He illustrated this point when he described three patients with "serpentine aneurysms" of the intracranial carotid artery in whom occlusion of the vessel had occurred in the syphon. In two of them there was extensive haemorrhagic infarction of the capsular region and in the other the temporal, parietal and occipital lobes were damaged. Although he briefly alluded to the histological changes in the brain he made no reference to the state of the smaller cerebral arteries. Fisher in his excellent paper on the clinical and pathological results of carotid artery occlusion described his findings in two of his cases with unilateral occlusion. In both there was extensive infarction of the territory supplied by the

anterior and middle cerebral arteries, and in them he found the anterior communicating artery was functionally deficient. However, none of these observers examined the histological changes in the brain and cerebral vessels in any detail.

Sorgo (1939), however, made a detailed study of two of his cases with unilateral occlusion and reported in one of them destruction of the cerebral tissues at the base of the second and third frontal convolutions within the boundary zone between the anterior and middle cerebral arteries, whilst in the other there was an extensive area of infarction of the hemisphere on the same side as the occluded artery and in addition small foci of cortical and subcortical damage in the opposite hemisphere.

In one of these cases he saw changes in the smaller cerebral vessels which he attributed to thromboangiitis obliterans. Antoni (1941) found softening of the parietal lobe in one of Andrell's cases, and observed similar changes in the cerebral vessels which he too thought were typical of thromboangiitis obliterans. Judging from the descriptions given by Sorgo and Antoni, and from the latter's illustrations, the vascular changes which they observed were similar to those seen in this present series of cases, and it is doubtful if they can be ascribed to thromboangiitis obliterans (*vide infra*).

It is obvious from these reports that the extent of the brain infarction resulting from carotid artery occlusion may vary widely from case to case. Hultquist in his painstaking and extensive monograph has confirmed this impression. His observations were based on ninety-one post-mortem examinations in carotid artery occlusion, in thirty-one of which he made a detailed histological study of the brain and cerebral blood vessels. In a few of these cases no evidence of any cerebral change was found but in the majority there was macroscopic damage visible in the territory of the middle cerebral artery on the same side as the carotid artery occlusion. This damage tended to be more severe in the anterior half of the middle cerebral territory, and was most marked in the region of the insula and operculum. The histological appearances of the parenchyma were similar to those seen in any other occlusive cerebrovascular disease, consisting of degeneration of the ganglion cells and nerve fibres together with reactive changes in the glia with scar tissue formation. These changes were not uniform throughout the affected area and tended to be patchy in distribution. In many of his cases areas of severe focal necrosis of all the cerebral tissues were surrounded by regions of more diffuse ischaemic cell damage, which were more pronounced in the cortex of the inferior frontal and central gyri. However,



this damage was not entirely localised to the territory supplied by the middle cerebral artery. In about a quarter of his cases similar but less severe ischaemic damage was present in the adjacent anterior and posterior cerebral artery territories, and very occasionally both focal and diffuse changes were seen in the cortex of the opposite cerebral hemisphere. In this present series of six cases the extent of the cerebral infarction tended to be more widespread than in Hultquist's material. In general it involved the mid-part of the convexity of the frontal lobe, the pre- and post-central gyri, the inferior parietal lobule and the outer surface of the occipital lobe, and often spread medially to involve the corpus callosum, putamen, globus pallidus and internal capsule. In two of these six cases the anterior cerebral artery territory showed haemorrhagic infarction, and in one other case (Case 3) the cortex within the anterior and posterior cerebral artery distribution showed ischaemic cell damage similar to that described by Hultquist.

The greater extent of this cerebral infarction in these cases, which approximates to that described by Fisher in two of his cases, is probably related to the source of the material. Hultquist obtained many of his cases from the Department of Medicine of his University, and although clinical details were often lacking, it would appear that some of them died from incidental causes and not from the effects of the carotid

occlusion, and this fact may well explain the greater extent of cerebral infarction which was observed.

The histological appearances of the brain in this series did not differ from those described by Hultquist. The regions of more severe damage were predominantly cortical and subcortical in distribution and were often haemorrhagic in type. Within these regions were focal areas of damage varying from complete necrosis of all the tissues to lesser degrees of ischaemic change of the nerve cells. Around the foci of severe damage more diffuse areas of ischaemic change were found, suggesting that the blood supply to these areas had been reduced but not completely cut off. These areas of focal damage were not all of the same size or age and lay scattered throughout the grey and white matter, although the older areas were more commonly found in the peripheral parts of the territory of the middle cerebral artery.

The underlying mechanism of these cerebral changes intrigued Hultquist and he naturally turned his attention to the carotid cerebro-vascular tree, searching for a possible explanation. He found that thrombosis in the internal carotid artery anywhere in its cervical portion resulted in cerebral changes in one in three to one in four of his cases, yet when the thrombus extended upwards to the origin of the ophthalmic, anterior communicating or posterior communicating arteries, fifty per cent showed cerebral changes. If, as in Cases 3

and 21 of this series, the thrombus extended beyond the termination of the internal carotid artery into the anterior and middle cerebral arteries all cases showed extensive changes in the affected hemisphere.

In Case 21 the thrombus in the carotid artery and the anterior and middle cerebral vessels was of recent origin, and although the resulting changes in the affected hemisphere were patchy in distribution, they were of the same age. In Case 3, however, there were regions of older ischaemic damage which could not possibly be related to the recent occlusion of the middle cerebral artery, and in the other cases in this series similar changes have been observed when there was no demonstrable occlusion of the major cerebral vessels. Hultquist also observed this phenomenon in many of his cases, as did Turner (1954) in his material, and on looking at the smaller cerebral arterioles they found blood clot in varying stages of organisation lying within many of their lumina.

Similar appearances were seen in smaller cerebral vessels in three cases in this series (Cases 3, 11, 30). The affected arterioles lay in the more peripheral parts of the middle cerebral arterial tree in the region where the older areas of brain infarction tended to be present, and one was often able to correlate these vascular changes with the underlying areas of infarction.

Both Hultquist and Turner thought these changes in the vessels represented cerebral emboli, and therefore suggested that many of the focal changes in the brain substance could be explained on this basis. However, Hultquist admitted that the number and size of the visibly occluded vessels could not possibly account for the extensive areas of brain infarction which were present in his cases and so he suggested that either the emboli had become absorbed, or that the particular section of the vessel which was blocked was not seen in the section, and that serial sections of the brain would be necessary to demonstrate it. Yet he agreed that in some of his cases with focal areas of damage no obstruction of the smaller cerebral arteries was discovered, although in a few of them the veins draining these areas were occluded by recent thrombus. To explain this phenomenon he suggested that these areas of focal damage could be the result of reflex dilatation or spasm of the arterioles secondary to the action of breakdown products of the infarcted cerebral tissues.

At this juncture it is pertinent to enquire whether these changes in the cerebral vessels represent embolic occlusion. From their histological appearance all one could say was that ante-mortem thrombus lay within the lumen but because of its age one could not distinguish whether it was embolic or thrombotic in nature. Some vessels were partially or completely occluded by

thrombus which was infiltrated by small round cells, and therefore of fairly recent origin, whilst in other areas the thrombus had become recanalised by small endothelial-lined channels, or, when lying eccentrically, had become incorporated into the vessel wall. That these appearances represented embolic occlusion was suggested by the following points. Firstly the affected vessels lay almost entirely in the territory of the middle cerebral artery and thus accord with the known distribution of emboli entering the carotid circulation. Secondly there was an ample source for such emboli in the internal carotid artery itself. Thirdly no primary change was ever observed in these vessel walls, and lastly, one so frequently saw healthy vessels of a comparable size lying in their immediate neighbourhood.

However, undoubted recent embolic occlusion of one or two of the larger branches of the middle cerebral artery was seen in one case (Case 11). In all probability these emboli were detached from the carotid artery in the neck by the needle puncture during arteriography, or the manipulation had predisposed to clot formation with subsequent detachment. As the cerebral embolism occurred in the presence of special conditions, i.e., arteriography, it does not necessarily mean that it frequently happens in all cases of carotid occlusion. But the findings of Fisher and Adams (1951) support the view that cerebral embolism may occur

frequently in them. They examined sixty-six cases with haemorrhagic arterial infarcts of the brain and in all but three there was evidence of embolism. They did not state what their evidence was, but in common with cases in this series the infarcted brain tissue was partly haemorrhagic and the rest pale. They suggested that the underlying mechanism of the haemorrhagic arterial infarction was one of embolic occlusion. They postulated that a vessel became blocked proximally by blood clot which rendered its territory anaemic, then the blood clot fragmented and passed distally. With the restoration of the blood supply the more proximal parts of the infarct became haemorrhagic. This is an attractive theory and is supported by the work of Harvey and Rassmussen (1951) who were able to produce haemorrhagic infarcts in the monkey's brain by clipping a main vessel for fifty minutes then relieving the obstruction.

However, one cannot accept Fisher and Adams' theory unreservedly, for in one case in this series (Case 15), with massive haemorrhagic infarction of the anterior and middle cerebral arterial territories, clot was not found in any of the blood vessels.

Again, the focal and diffuse changes in the brain are not solely confined to the middle cerebral artery territory, and are sometimes met with in both the anterior and posterior cerebral territories of the same

hemisphere, and occasionally also to a lesser degree in the opposite hemisphere. While embolic occlusion from blood clot in the internal carotid artery can presumably occur in the anterior cerebral arterial tree it is unlikely to occur in the posterior cerebral arterial territory, and is most unlikely in cases where opposite cerebral hemisphere is affected. Hultquist suggested that the more diffuse changes which occurred in the territories of all three cerebral arteries were related to a reduction in blood flow following incomplete obstruction of the blood vessels from oedema of the brain, or vasospasm associated with damage to cerebral tissues, or to the passage of an embolus, or alternatively to failure of the collateral blood supply. There is no doubt that vasospasm can occur with direct mechanical and chemical injury of the blood vessels (Penfield 1938), and there is much suggestive evidence that it does occur with cerebral embolism. Villaret and Cachera (1939) observed widespread spasm of the dog's cerebrovascular tree following the introduction of glass emboli into the intracranial circulation. The resulting spasm lasted for hours to weeks and led to haemorrhagic infarction of the hemisphere.

However, cerebral embolism apparently does not occur in every case of carotid artery occlusion (cf. Case 15), and surely with such severe degrees of infarction seen in these cases one would be justified in expecting to find more evidence of recent embolic occlusion of the cerebral vessels. Therefore some other

mechanism must be responsible, and I hope to prove that most of these changes in the cerebral parenchyma are due to failure of the collateral blood supply.



The question of cerebral thromboangiitis obliterans

In discussing the pathology of cases showing occlusion of the carotid artery several authors observed changes in the cerebral blood vessels which they ascribed to thromboangiitis obliterans (Sorgo, Antoni, Andrell, Krayenbühl (1945)).

In three of Antoni's cases with unilateral carotid artery occlusion several of the smaller cortical arteries on the same side as the occlusion were blocked by thrombus, whilst in other areas vessels of a similar size had become recanalised. There were few if any reactive changes in and around the vessel walls, and the internal elastic lamina was always intact. These vascular changes were most apparent in the more peripheral branches of the middle cerebral artery and were prominent in those vessels lying in the frontal lobe. He likened their appearance to the "Fullgewebe" of Jager, and pointed out that Spatz (1935) in his cases of cerebral thromboangiitis obliterans found the diseased cerebral vessels in much the same situation as in his cases. In Antoni's experience the cerebral veins were mostly unaffected, except in his Case 1, when some of them were seen to contain recent blood clot.

In one of his three cases the clinical picture of carotid artery occlusion was complicated by intermittent claudication of the legs, and this he took to support the

pathological diagnosis he had made, although he did not investigate the condition of the peripheral vessels in the legs. This therefore cannot be accepted as confirmatory evidence in favour of thromboangiitis obliterans, as about fifteen per cent of patients with carotid artery occlusion have peripheral vascular disease on a purely atherosclerotic basis (Denny Brown).

It is also of interest that the internal carotid artery in two of his three cases presented "sclerotic changes", which he did not think were typical of thromboangiitis obliterans. Krayenbühl and Sorgo also found similar changes in the cerebral blood vessels in some of their cases, which they ascribed to thromboangiitis obliterans .

In the literature on cerebral thromboangiitis obliterans it is surprising that such a large proportion of the reported cases had a thrombosis of the internal carotid artery as the principal or sole lesion, but in many of them the histological changes were not observed or were assumed, chiefly because of the absence of other known causes of carotid artery occlusion. Evidence of involvement of the peripheral limb vessels was seldom an outstanding feature.

Davis and Perrett (1947) explored eleven of their patients whom they thought were suffering from cerebral thromboangiitis obliterans, as they gave a history of transient cerebral attacks similar to those given by some patients in this present series. In nine

of them the smaller cortical arteries in the frontal, parietal and temporal lobes were thickened and blocked over short distances in their course. In the cerebral substance underlying these occluded arteries lay scattered infarcts of varying ages. Histological examination of portions of the vessels removed at operation showed changes identical with those described by Antoni, Krayenbühl and Sörgo. There were never any frank inflammatory changes in the vessel walls, and although the process mainly affected the cortical arteries, some of the smaller veins were blocked by thrombus. Davis and Perrett observed that in many of their patients there was a unilateral carotid artery occlusion, and the cerebral changes were always confined to the hemisphere on the same side as the occluded vessel in the neck.

Scheinker (1945) in describing one case, which he thought was an example of cerebral thromboangiitis obliterans, found similar changes in the cortical arteries of one hemisphere. These vessels often showed subendothelial thickening of the intima with secondary thrombus formation, and sometimes recanalisation of occluded vessels had taken place. Apart from round celled infiltration of the thrombus material within the lumen of these vessels, reactive changes were absent and the vessel walls appeared to be otherwise healthy. On the same side as these cerebrovascular changes the internal

carotid artery was occluded in the neck, a finding which he held to be incidental.

In their pathological study of twenty cases of cerebral thromboangiitis obliterans Lindenberg and Spatz (1939) observed comparable histological changes mainly in the cortical arterioles. But in addition some of the vessels lying in the sulci in the neighbourhood of recent areas of cerebral infarction were surrounded by small round cells, some of which had infiltrated the adventitia, although the media always appeared to be healthy.

The localisation of the resulting cerebral infarction in these cases fell into two groups. In one there was an extensive malacia in the region of one of the larger cortical arteries and in the other similar but smaller lesions were found in the border zone between the three main cerebral arteries, i.e., in the distal parts of the middle cerebral artery territory. Stender (1936) also noted that the cerebral damage in his cases of cerebral thromboangiitis obliterans was chiefly found in the anterior and middle cerebral artery territories, was more pronounced in the latter, and more often than not situated on the left side of the brain. He did not specifically state whether there was an associated carotid artery occlusion but in many of Lindenberg and Spatz's cases it was present.

Surely it is significant that so many cases described as cerebral thromboangiitis obliterans show unilateral carotid artery occlusion, that the changes in

the cerebral arterioles are frequently confined to one hemisphere, that reactive or inflammatory changes are rarely if ever seen in the vessel walls, and that the site of the cerebral infarction is similar in distribution to that seen in atherosclerotic occlusion of the carotid artery. Again, in many of these cases there has been little or no evidence of involvement of the peripheral limb vessels, and so frequently the clinical syndrome presented by them was identical with that seen in spontaneous occlusion of the carotid artery following atherosclerosis.

In some of the cases in this present series the vascular changes in the cortical arteries were similar to those described by Antoni, Sorgo, Krayenbühl and Davis and Perrett, except that thrombus was never seen in the cerebral veins. This however was not an outstanding feature in the reported cases of thromboangiitis obliterans, and Hultquist has seen small venous thromboses in some of his cases with undoubted atherosclerotic carotid occlusion.

The sub-endothelial thickening described by Scheinker is, I believe, comparable to that found by Duguid in atherosclerotic coronary arteries, and should therefore be interpreted as the late result of organisation of a thrombus lying within the lumen of the vessel which has become covered by a layer of endothelial cells, and thus resembled a primary change in the vessel wall.

The description of these vascular changes are very different from those given by Buerger (1924) in his classic book on thromboangiitis obliterans. He described an acute inflammatory process involving all coats of the vessel, which was infiltrated by polymorph leucocytes, and the lumen of which was filled with recent blood clot. In the peripheral portion of this clot foci of leucocytes formed small miliary abscesses which rapidly organised into foci containing endothelioid and giant cells, and the clot then became recanalised and organised. Although all the vessel wall was infiltrated by white cells the media showed the most intense change. Later the cellular elements disappeared and fibrous tissue bound the arteries and veins together. These appearances, as described by Buerger, are so different from those observed in the cases of Antoni and others that doubt must be cast on the validity of their diagnosis. Frank inflammatory changes in the vessel walls were never seen, and leucocytic infiltration of the thrombus within the lumen of the occluded vessel was surely a reaction to the blood clot and should not be accepted as evidence of "inflammation".

Although in some of Lindenberg and Spatz's cases the adventitia of freshly occluded arteries in the sulci lying near areas of recent infarction were infiltrated by small round cells, the media was never affected and these changes were therefore not typical of classical Buerger's disease. Similar changes were

present in Case 30 of this series, where the subarachnoid space was literally packed with leucocytes, small round cells and scavenger cells, which in some regions appeared to lie in the adventitia of the occluded vessels. This I think was a result of the cerebral infarction when products of the damaged tissue were drained along these spaces to the surface, and should not be accepted as evidence of primary disease in the vessel wall.

The papers of Foerster and Guttmann (1933) and Hausner and Allen (1938) only add to the confusion surrounding the subject of cerebral thromboangiitis obliterans. Their observations were based on clinical grounds and lacked pathological confirmation. They assumed that the association of peripheral vascular disease, repeated attacks of transient hemianopia, hemiplegia, confusion and aphasia and perhaps coronary artery disease, indicated vascular involvement secondary to thromboangiitis obliterans. This assumption is now known to be incorrect, for a similar clinical picture can arise from atherosclerotic disease of the carotid and peripheral limb vessels, a fact which is well illustrated by Case 3 of this present series. He suffered from intermittent claudication and repeated cerebral attacks due to atherosclerotic occlusion of one carotid and both femoral arteries.

Cerebral thromboangiitis obliterans probably does occur, but I would suggest that many of the cases recorded under this title were examples of unrecognised

atherosclerotic carotid artery occlusion with or without peripheral vascular disease on a similar basis.



### Clinico-pathological Correlation

In this series of thirty patients it was possible to relate the clinical picture with the pathological findings in six of them. Two of these patients had several prodromal symptoms before the onset of a hemiplegia (Cases 3 and 11), three developed their hemiplegia with little or no warning (Cases 15, 16, 21), and one other presented an essentially progressive syndrome (Case 30).

In these six patients their hemiplegia was due to infarction of the brain tissue in the territory of the middle cerebral artery, which also explained the dysphasia, hemianopia, cortical sensory impairment and mental changes from which they suffered. In four patients who died soon after the onset of their hemiplegia (Cases 11, 15, 21, 30) the affected hemisphere was grossly swollen and death had resulted from tentorial herniation. In the other two patients the cause of death was different; one died from exhaustion following a combination of cerebral damage and infarction of the small intestine, and the other from myocardial infarction in combination with bronchopneumonia.

This much is clear but when one attempts to explain the mechanism of their cerebral symptoms and signs considerably difficulties arise.

In the two patients (Cases 3 and 11) with several prodromal symptoms there was much that could not be satisfactorily explained on a morbid anatomical and histological basis.

It will be recalled that Case 3, six months before his death, had experienced slight weakness and numbness of the left hand which disappeared after one week. Three months later he developed a transient left-sided facial weakness, which was eventually succeeded by symptoms of parietal lobe disturbance and finally by a left hemiplegia. At post-mortem old areas of infarction were seen in the right inferior and mid-frontal regions, the cingulate gyrus and lateral convexity of the occipital lobe. In the lower part of the precentral gyrus within the region of the cortical representation of the hand, the brain tissue showed recent infarction but no evidence of any long-standing change.

It is possible that the symptoms referred to the hand were due to oedema surrounding the initial infarction of the mid-frontal region, and extending backwards gave rise to mild but reversible changes in the pre- and post-central gyri. However, the facial weakness could not be explained on this basis.

On histological examination of this hemisphere one was struck by the numerous small infarcts of varying ages which lay mainly in the peripheral parts of the middle cerebral artery territory. Here some of the smaller arterioles were occluded by blood clot in varying

stages of organisation, and one was therefore tempted to ascribe the clinical picture to embolic infarction of the brain. The finding of an old-standing partial occlusion of the middle cerebral artery on the convexity of the occipital lobe, seemed to strengthen this concept but one could not be certain that these appearances were embolic and not thrombotic in nature. There was a source for emboli in the occluded internal carotid artery. It is possible that this was the underlying mechanism of some of the earlier symptoms, but no fresh emboli were found in the cerebral blood vessels to account for the recent extensive infarction of the brain.

In Case 11 recurrent short-lived attacks of clumsiness and paraesthesiae of the right hand and face accompanied by mild dysphasia were present during the four weeks prior to the onset of profound right hemiplegia with motor fits affecting the left leg following arteriography.

In the affected cerebral hemisphere one was again struck by the fact that old areas of infarction lay in the more peripheral parts of the middle cerebral territory in the regions where the smaller cerebral arterioles were partly or completely occluded by blood clot of differing age. The rest of the middle cerebral territory showed recent infarction. The picture was similar to that described in Case 3. In a few of the larger branches of the middle cerebral artery near the Sylvian point lay coiled-up blood clot which had

presumably become detached from the thrombus lying within the internal carotid artery. The evidence for embolism here seems strong but if one accepts it as the sole factor responsible for this patient's symptoms, one is immediately confronted with difficulties. It is virtually impossible to incriminate embolism as a cause for the recurrent daily episodes of clumsiness and paraesthesiae of the hand and face, and moreover most of the older infarcts lay in the distal parts of the middle cerebral territory, whereas his symptoms indicated transient vascular disturbance in the lower part of the pre- and post-central gyri. Again, one cannot explain the contralateral motor fits affecting the left leg on this basis, as careful examination of the right hemisphere failed to reveal any pathological change in the cerebral parenchyma or blood vessels. It seems reasonable to assume that there was a functional disturbance of this hemisphere causing these fits which left no visible change.

Obviously embolism does not account for the whole picture.

In two of the three patients with the sudden onset of a hemiplegia the mechanism underlying their symptoms and signs was relatively clear (Cases 16 and 21) but in the third it was obscure (Case 15).

Case 21 suddenly developed severe frontal headache which was followed by slight expressive dysphasia and right-sided facial weakness, progressing over twenty-four hours to a complete right hemiplegia with

aphasia. He died in coma five days after the onset of his symptoms. Post-mortem examination showed that the occlusion of the left internal carotid artery was due to a dissecting aneurysm. Recent blood clot filled the lumen of the artery throughout its course and extended into the anterior and middle cerebral arteries with consequent infarction of most of the left hemisphere.

Case 16 presented with a sudden left hemiplegia two years before death. Over several months this disability improved but he still retained a spastic weakness of the affected extremities which was maximal in the arm. Three weeks before death from myocardial infarction and bronchopneumonia, there was a sudden increase in weakness in his left leg. In this patient the right internal carotid artery was almost completely occluded by fibrous tissue and organised thrombus above which recent blood clot closed the lumen. The long-standing hemiplegia was the result of old infarction of most of the middle cerebral territory but the mechanism of this infarction was obscure. The middle cerebral vessels were healthy with the exception of small areas of subintimal fibrous tissue in some of the larger branches near its origin. These appearances may have represented the end result of organisation of blood clot lying within the lumen of the vessels, but if that were so one could not be sure whether the clot was embolic or thrombotic in origin. The recent exacerbation of

weakness in the left leg was related to infarction of the anterior cerebral territory, probably caused by blood clot occluding the anterior cerebral artery at the splenium of the corpus callosum; whether this was due to embolism or thrombosis within the vessel could not be determined.

In Case 15 the mechanism of the pathological findings was most obscure. She had experienced slight numbness of her right hand with a mild expressive dysphasia five weeks before the fatal onset of a right hemiplegia with aphasia. At post-mortem the left internal carotid artery was almost totally occluded in the siphon by atherosclerosis and organised blood clot, below which recent thrombus filled the lumen of the vessel to its origin in the neck. In the left cerebral hemisphere most of the middle cerebral artery territory showed recent massive infarction but a few regions of older infarction lay more peripherally in its distribution; in addition, most of the anterior cerebral territory also showed recent infarction. The cerebral damage in the region of the lower pre- and post-central gyri was severe but of only a few days' duration, and one could not relate the disturbance of speech and sensation in the hand, which appeared five weeks before death, to this area of infarction. The cerebral vessels did not contain blood clot and the smaller cortical arteries were dilated and packed with red cells, but were otherwise healthy. Here indeed one is forced to the conclusion that these

areas of recent infarction in the distribution of the middle cerebral artery were not the result of organic occlusion of the cerebral vessels. One would have expected to find thrombus in some of them if this had been the underlying mechanism of the brain damage.

In the one patient presenting an essential progressive syndrome (Case 30) the picture was even more complex. Her symptoms commenced with a progressive stiffness and weakness of the left leg which was followed after eighteen months by recurrent attacks of transient weakness of the left arm occurring several times a day. These ceased after two months but were succeeded by a severe left hemiplegia one month before death. Arteriography showed poor filling of the right internal carotid and cerebral vessels; she died within a few hours of this procedure. At post-mortem examination the left internal carotid artery at its origin was found to be almost entirely occluded by atherosclerosis and organising blood clot, to the surface of which recent thrombus adhered.

In the right hemisphere older areas of infarction lay in the upper part of the central sulcus in the distribution of the anterior cerebral artery, and this accounted for the weakness of the left leg, but did not explain the progressive nature of this complaint. In the peripheral parts of the middle cerebral artery territory there were numerous infarcts of differing ages and in these regions some of the smaller arteries were occluded by thrombus. Throughout the rest of the middle

cerebral territory the infarction was mainly of recent origin (several days) but lying here and there were smaller regions of infarction of several weeks' duration, and some of these lay in the lower parts of the pre- and post-central gyri. Occluded vessels in relation to these latter infarcts were rarely seen. One may therefore be justified to some extent in accepting the weakness of the left hand as being embolic or thrombotic in nature, but as in Case 11 one cannot possibly explain their recurrent nature on this basis.

Thus in many of these patients one is left with the unsatisfactory conclusion that whilst cerebral embolism can and probably does occur, presumably from thrombus within the internal carotid artery, there are many features which cannot be explained in this way. Why are the infarcts and changes in the cerebral blood vessels situated in the more peripheral parts of the middle cerebral territory, whilst the symptoms in most of these patients indicate a vascular disturbance in the more proximal parts of its territory? Again, why does one so rarely find evidence of recent occlusion of the cerebral vessels in those patients with large regions of recent infarction, especially when there is an adequate source for emboli in the internal carotid artery? And why does arteriography in those patients with an incomplete carotid artery occlusion so often have a fatal outcome? What is the basis of these recurrent



attacks of transient cerebral disturbance and how can one explain the progressive nature of some of their symptoms?

These intriguing questions invite an answer which is not to be found in a purely morbid anatomical and histological study.

Mechanism of Syndrome

Clinically patients suffering from carotid artery occlusion may present in one of four ways:-

- (i) with the sudden onset of a hemiplegia;
- (ii) those with several prodromal symptoms before signs become established;
- (iii) those with a superficially progressive syndrome;
- (iv) those where the arterial occlusion remains symptomless.

About one-third of the reported cases in the literature presented with a sudden hemiplegia with or without loss of consciousness. However, loss of consciousness occurring without immediate neurological sequelae is less well recognised (cf. Case 29). Krayenbuhl and Weber however reported such a case with two attacks of unconsciousness preceeding the onset of a hemiplegia by one or two months, and one of Andrell's patients suddenly fell down unconscious but quickly recovered without sequelae.

Over one-half of the patients with carotid occlusion had several prodromal symptoms before the syndrome finally became established. These commonly included short-lived attacks of paralysis, numbness and tingling of the extremities, speechlessness and giddiness (Fisher, Andrell, Sorigo, Krayenbuhl and Weber), and Moniz regarded them as characteristic of carotid occlusion. In this series there were several patients

who had repeated attacks of numbness and paralysis, often occurring several times daily, which were at first unaccompanied by any permanent neurological deficit. Both Andrell and Fisher had patients with similar symptoms under their care. The former described a patient who had transient attacks of paresis in the arm occurring over four months, and Fisher's case 1 had more than one hundred episodes of dizziness and speechlessness with numbness and paralysis of the right arm during the eight months before a hemiplegia developed (cf. Case 1).

Those patients presenting a progressive syndrome are well recognised in the literature, and according to Johnston and Walker some 25% follow this course, which usually develops over several months. However, their clinical course may be longer (cf. Case 2 where a right hemiparesis slowly developed over two years), and Krayenbühl and Weber have a well documented case in which hemiplegia gradually developed over thirteen years. An important feature, which has rarely been commented upon is the tendency for some of these patients to present with an initial weakness or numbness of the lower extremity, which is quite contrary to the usually accepted course in which the hand or face is first affected. Ameli and Ashby recognised this feature, and in this series no less than two of the four patients with a progressive syndrome presented in this manner.

Many theories have been advanced in an attempt to explain the mechanism underlying the varied clinical picture shown by these patients.

Theory of Vasospasm

Moniz, Reichert, Sorgo and Andrell believed that the thrombosed carotid artery might result in reflex spasm of the smaller cerebral vessels, and thus cause the transient attacks of numbness and paralysis which were described by some of their patients. They partly based this theory on the fact that on arteriography incomplete occlusion of the carotid artery could be met with in the presence of a fully developed clinical syndrome. Sunder-Plassmann also believed that vasospasm was largely responsible for the transient symptoms in his cases, but thought that it was mediated through the superior cervical ganglion, causing slowing of the blood-flow in the cerebral arteries, with the production of cerebral ischaemia. Krayenbuhl (1944) at first subscribed to this theory and divided the sympathetic chain in the neck with a view to dilating the cerebral blood vessels. According to Denny-Brown he has now abandoned this procedure and presumably no longer believes that cerebral vasospasm plays a major part in the syndrome.

Now it would be important to establish whether vasoconstriction does occur in carotid artery occlusion but there is no direct evidence that it does. The work of Byrom (1954) in rats confirms that vasoconstriction of the cerebral arteries can occur in experimentally produced hypertension, and may be severe enough to cause

focal oedema and local necrosis of the arterial wall. But in patients with carotid occlusion transient recurrent attacks of cerebral dysfunction are met with whether they are hypertensive or not, suggesting that some other mechanism may well be responsible for these attacks.

It is most unlikely that the diseased carotid artery in the neck could stimulate the cervical sympathetic pathway sufficiently to cause the cerebral vessels to go into spasm, for according to Dumpke and Schmidt (1944) the response of these vessels to sympathetic stimulation is insignificant. However, the papers of Risteen and Volpitto (1946) and Gilbert and de Takats (1948) would suggest that cerebral vasospasm may be a significant factor in cerebro-vascular accidents. They have both reported alterations in the course of cerebro-vascular disturbances following cervical sympathetic block, and Russek and Zohman (1948) noted remarkable changes in brief cerebral paralytic disorders with large doses of papaverine. Since the course of cerebro-vascular accident is a highly variable one owing to the size of vessels involved and the availability of the collateral circulation, the significance of these results becomes a statistical problem for which there is at present no conclusive answer. There is strong presumptive evidence that vasodilatation and not vasoconstriction follows occlusion of a carotid artery (Brackett 1953). The lowered oxygen and increased carbon dioxide tension and the

accumulation of metabolites which follow occlusion of the artery are all powerful vasodilators.

Fisher, recognising this argument, suggested that the transient cerebral attacks might be due to intermittent spasm of the internal carotid artery which was not totally occluded. Judging from the degree of atherosclerotic change present in the artery in many of these cases, it is doubtful whether the lumen of the vessel could alter in calibre as Fisher suggested.

In the patients in this series it was striking that so many of them suggested by their recurrent symptoms that one small region of the same hemisphere was affected in the same way several times daily, and it was not unusual to hear of these recurrent attacks spreading to adjacent parts of the cerebral cortex. For instance, Case 22 after an initial clumsiness of the right hand developed transient attacks of weakness of the right arm which were accompanied after several weeks by similar attacks in the right leg. Surely it is unusual for cerebral vasospasm to affect one part of the carotid tree repeatedly in this manner.

### Theory of Cerebral Embolism

Chiari, Hultquist, Herfarth (1926) and Turner all suggested on pathological grounds that cerebral embolism might be the underlying factor in carotid artery occlusion. It must be admitted that in those patients developing a sudden hemiplegia the clinical picture is identical with embolic occlusion of the middle cerebral artery (cf. Case 14), and it may therefore seem reasonable to assume that their prodromal attacks could also be explained by embolic occlusion of the smaller cerebral blood vessels. That these episodes were frequently short-lived, lasting for several hours to several days before disappearing, is not unknown in cerebro-vascular occlusion (Pickering, 1948), but it is unusual for symptoms to progress over several days before disappearing, unless one were to postulate a spreading thrombosis within the occluded cerebral vessel.

Again, in the majority of patients presenting with several prodromata the initial episode indicated an involvement of the cortex in the centre of the middle cerebral artery territory, i.e., weakness of the hand or face, which was often followed at a later date by similar symptoms again referred to the face, arm or occasionally the leg on the same side, and finally after several attacks by an established hemiparesis (cf. Case 10). Surely it must be unusual for cerebral embolism to recur in the same part of the carotid tree with such



unfailing regularity? Moreover, several of these patients complained of transient attacks of numbness or weakness of the arm and leg recurring several times daily in the midst of their syndrome, which one cannot possibly attribute to cerebral embolism or to spreading thrombus, as they occurred in the same region of the brain, were so short-lived and were followed by complete recovery between each attack. Surely these transient episodes must follow intermittent ischaemia without organic occlusion of the cerebral blood vessels, and it is tempting to attribute their more permanent signs to more severe degrees of ischaemia.

In the clinico-pathological study of the one patient in this series who had several prodromal symptoms (Case 3), cerebral embolism could not be entirely ruled out, but in three other patients showing a recent hemiplegia with widespread cerebral infarction (Cases 11, 15, 30) no significant organic obstruction of the major cerebral arteries was seen. If one accepts the theory of Adams and Fisher that the infarcted area was due to an embolus which had been arrested proximally, fragmented, then passed distally into the smaller peripheral vessels, it is difficult to explain the fact that the thrombi in the peripheral vessels were of differing ages in two of them (Cases 11 and 30), whereas in the third no organic obstruction of the cerebral arteries was found (Case 15). Surely there is no other explanation

than that the brain infarction was due to simple cerebral ischaemia.

Theory of alterations in the cerebral blood-flow.

Although Sörgo believed that vasospasm was the basis of the transient cerebral attacks, he related the permanent neurological deficit to cerebral infarction following a failure of the collateral blood supply from the opposite carotid artery through the circle of Willis.

Wilson (1940) postulated that with unilateral carotid occlusion the blood-flow in the peripheral branches of the carotid artery became markedly slowed with resultant ischaemia of the cerebral tissues. But Chao et alia thought that the atherosclerotic degeneration in the carotid artery resulted in a sensitive carotid sinus reflex, which in turn caused alterations in the cerebral blood-flow. Galdston et alia agreed with this theory and observed that pressure over the unobstructed carotid artery in the neck caused an aggravation of the cerebral symptoms. They therefore suggested that carotid occlusion was due to a hypersensitive carotid sinus reflex on the non-obliterated side which caused a fall in the systemic blood pressure with subsequent thrombosis in the atherosclerotic artery; they further suggested that denervation of this sensitive carotid sinus might protect the brain from further damage. It is possible that stimulation of the carotid sinus may produce symptoms (Forster et alia, 1942) but this overactivity is usually a functional one and no pathological changes are seen. Moreover, in the electro-encephalogram one does not see any gross

disorder of the cerebral rhythms such as has been demonstrated in cerebral ischaemia (Marsh and Rancy, 1942). Therefore it is unlikely that this mechanism plays more than a minor role in these cases.

Fisher has recently expressed similar views to Sörgo, and thought that it was usually possible to relate the extent of the cerebral damage to anatomical defects in the circle of Willis.

For a clearer understanding of the mechanism underlying the clinical picture and pathological findings seen after occlusion of one carotid artery it is necessary to know of the alterations which may occur in the cerebral blood-flow.

Alterations in cerebral blood-flow following unilateral carotid artery occlusion.

Fortunately in recent years we have gained some knowledge of what may happen to the cerebral blood-flow after carotid artery occlusion from both animal and human experiment. The results have substantiated Thomas Willis' concept that the circle which bears his name functions as an anastomotic channel.

Cerebral angiography in man has enabled us to follow the course of radio-opaque substances injected into the major vessels feeding the brain. In 1937 Moniz described bilateral filling of the anterior and middle cerebral arteries in one of his cases with unilateral carotid occlusion when contrast medium was injected into the non-occluded carotid artery, and Sörgo demonstrated that with compression of one carotid artery in the neck contrast medium injected into the other normally filled the anterior and middle cerebral arteries on both sides of the brain. This has now become an established procedure in assessing the available collateral circulation when ligation of one carotid artery is contemplated, e.g. for intracranial aneurysms. This contralateral filling was demonstrated in patients in this present series and will presumably only occur if the anterior communicating artery is of sufficient size to conduct blood to the opposite side of the brain.

It has also been shown (Takahasi 1940, Frøvig 1946) that in the presence of bilateral carotid artery occlusion contrast medium injected into the vertebral arteries may fill all the intracranial vessels via the posterior communicating arteries.

However, in arteriography the contrast medium is injected under pressure, and therefore may not give an accurate picture of the alteration in cerebral haemodynamics which may follow occlusion of one or more of the major vessels.

But the recent experimental work of McDonald and Potter (1951) tends to confirm these arteriographic findings. They introduced methylene blue dye indirectly into the carotid and vertebral arteries of the living rabbit without disturbing the existing pressure relationships in these vessels, and studied its distribution in the circle of Willis and cerebral arteries, the brain being exposed by operation. They showed that dye entering one carotid artery flowed into the anterior and middle cerebral arteries and to a point halfway along the posterior communicating artery. Dye injected into one vertebral artery passed upwards in the basilar trunk unmixed with blood issuing from the opposite vertebral, and flowed into the ipsilateral posterior cerebral artery and to a point halfway along the posterior communicating artery. They postulated that under normal conditions a "dead point" existed halfway

along the posterior communicating artery where the pressures from the carotid and vertebral arterial trees were equalised and therefore no flow occurred through this vessel.

If however these pressure relationships were upset by occluding one carotid artery blood from the vertebral artery flowed along the posterior communicating artery and supplied blood to the whole hemisphere.

Unfortunately in the rabbit there is but a single anterior cerebral artery and therefore no anterior communicating vessel. However, if one applies these principles to the results of arteriography in man it will be recalled that radio-opaque substances injected into one carotid artery normally fills the anterior cerebral artery on the same side only, and it therefore seems likely that there is another "dead point" halfway along the anterior communicating vessel.

Therefore under normal conditions the human brain is fed by three separate streams of blood - one from each carotid and another from the basilar balanced against each other at the "dead points" in the anterior and both posterior communicating arteries. When one carotid artery is occluded the pressure within this system presumably falls and blood from the opposite carotid flows across the "dead point" in the anterior communicating vessel.

In spontaneous carotid occlusion the reduction in blood flow is a gradual process, and as we have seen

from arteriographic studies allows for dilatation of the potential collateral channels between the external carotid and the ophthalmic artery so that the direction of the normal flow in this latter vessel is reversed, and blood reaches the internal carotid artery above the site of the obstruction and fills the cerebral arteries. No doubt the external carotid artery contributes to the blood-flow of the hemisphere on the side of the carotid occlusion but the main source of supply must come across the anterior communicating artery, so that the non-obstructed carotid artery contributes blood to both hemispheres.

McDonald and Potter also demonstrated "dead points" in the superficial cortical arteries between the posterior and middle cerebral territories, and we know that with the gradual reduction in blood-flow these potential anastomotic channels dilate and blood flows over these "dead points" into the middle cerebral artery. But from the post-mortem studies in man we also know that the middle cerebral territory is predominantly or solely affected suggesting that the blood-flow through the anterior cerebral artery is reduced to a lesser extent than in the middle cerebral artery. It is possible that similar "dead points" exist in the junctional zone between these two arteries in man, and that some flow may take place from the anterior towards the middle cerebral territory.



Now it would be interesting to know the extent to which the pressure falls after occlusion of one carotid artery, and recently there have been several pertinent observations made in man. Bakay and Sweet (1952) measured the intra-arterial pressures in the cervical carotid and in the anterior and middle cerebral arteries and their branches down to a diameter of 0.4 mm. Under normal conditions the pressures even in the smaller cerebral vessels ranged from 65% to 92% of the pressure within the cervical carotid artery. Woodhall et alia (1952) also made similar measurements, and found that after occlusion of the carotid artery in the neck the pressure fell distal to the site of the occlusion by 35% of the original value in the intracranial internal carotid artery, and by 44% in the main branches of the middle cerebral artery, these observations being made for periods up to half-an-hour following ligation.

Bakay and Sweet (1953), using an improved technique, found the percentage fall in pressure to be about 50% of the original value in nine patients following carotid ligation in the neck. In seven of them the original fall had been maintained up to twenty-four weeks following their ligation.

Now these observations are interesting but cannot be directly applied to spontaneous carotid artery occlusion. In the first place Bakay and Sweet assumed that the pressures within the circle of Willis and cerebral vessels on the ligated side some time after

the event were comparable to those in the cervical carotid above the site of ligation, and although this may be so there is no direct evidence for this assumption.

Secondly, the reduction in blood supply in the majority of patients with spontaneous occlusion is a slow event and allows for a more gradual development of the collateral circulation with the result that the pressures may be maintained at their original level. However, there is indirect evidence that some fall in pressure does occur in the internal carotid artery and cerebral vessels above the site of the occlusion in spontaneous cases.

Milietti (1950), recognising that the retinal arteries are mere prolongations of the intracranial blood vessels, has measured the pressures within them using Baillart's technique. He found that in unilateral carotid occlusion the systolic retinal pressures were reduced on the same side as the occluded vessel, although the diastolic pressure remained unchanged. If the non-occluded carotid artery were then obstructed there was a decrease in the arterial pressures in both eyes which, however, was more marked on the side of the occluded carotid artery. Denny-Brown has also observed blanching of the retinal vessels on the same side as the occluded artery when the non-obstructed carotid artery was compressed in the neck. In this same case who had peripheral vascular disease of the legs in addition to symptoms arising from the carotid occlusion, vasodilators caused an aggravation of his cerebral symptoms, which

improved once the drug was discontinued. Surely these observations mean that with spontaneous carotid artery occlusion the blood-flow to the intracranial carotid artery and its branches are often delicately balanced, and any mechanism which will lower the general systemic blood pressure will result in a failure of the collateral blood supply, with the production of cerebral ischaemia.

It has already been pointed out that for the equitable distribution of blood to both hemispheres an anterior communicating artery of sufficient size is the first requisite, but it is probable that the cerebral vessels of both hemispheres must also play a part. Corday et alia (1953) in their experiments on the monkey found that by occluding one carotid artery with a clamp and reducing the systemic blood pressure to low levels, bilateral changes appeared in the electro-encephalographic recordings from both hemispheres which were consistent with ischaemic changes in the brain. If the blood pressure were then raised the abnormal record disappeared from the hemisphere on the side opposite the occluded artery.

Now Symonds, aware that Schurr had seen bilateral electro-encephalographic changes over the cerebral hemispheres after unilateral common carotid ligation in man, suggested that with the reduction in total cerebral blood-flow the hemisphere on the obstructed side might claim more than its fair share of blood by reason of the vascular dilatation accompanying ischaemia,

with a corresponding vasoconstriction in the vessels of the hemisphere on the non-obstructed side. This concept finds support in Doring's (1936) observation that bilateral ischaemic lesions of the hemispheres sometimes accompanies carotid artery ligation.

Now after spontaneous carotid artery occlusion when the cerebral blood-flow is at times less than normal, the cerebral hemisphere on the obstructed side may claim more than its fair share of blood with corresponding ischaemia in the opposite hemisphere. This supposition is supported by the presence of bilateral ischaemic lesions of both hemispheres in some of Hultquist's material and from the evidence presented by several cases in this series. It will be recalled that Case 19 suddenly became speechless and paralysed in all his limbs but recovered completely within several hours. Then followed transient attacks of weakness and numbness of the right arm and leg with dysphasia which ceased after six weeks. Surely these sudden, but relatively short-lived, attacks of cerebral dysfunction could only be due to transient ischaemia. This mechanism must also explain the attacks of loss of consciousness without neurological sequelae suffered by Case 29, when the degree of bilateral cerebral ischaemia produced was insufficiently severe or prolonged to cause signs of permanent cerebral damage. That this was so is suggested by the findings in Case 11 who, after

developing a severe right hemiplegia, had focal motor fits affecting the left leg, yet showed no visible change in the right cerebral hemisphere at post-mortem examination several days later.

Mechanism underlying the clinical syndrome and pathological changes seen in carotid artery occlusion

When carotid artery occlusion remains symptomless one may assume that the various compensatory mechanisms have come into play and have proved adequate for the supply of blood to both hemispheres.

However, if the anterior communicating artery is deficient, as in two of Fisher's cases, widespread infarction of the cerebral hemisphere will result since an adequate collateral circulation cannot develop under these circumstances. But the anterior portion of the circle of Willis is within normal limits in 90% of patients (Dandy, 1947), and in the post-mortem studies of six patients in this series, the anterior communicating artery appeared to be adequate yet all of them showed severe degrees of brain infarction. In two other patients (Cases 8 and 13) an apparently adequate blood flow was demonstrated through the anterior communicating artery at arteriography but both had severe hemiplegias. Therefore this mechanism must be uncommon in most patients with carotid artery occlusion.

After unilateral carotid artery occlusion the blood flow to the hemisphere on the same side is reduced, and despite the functioning of the compensatory mechanisms, it must often be in a precarious state. Any fall in the systemic blood pressure or a temporary disturbance in the balance between vasoconstriction and vasodilatation will cause local cerebral ischaemia, often in the centre of the middle cerebral artery territory,

which if at all prolonged, will lead to infarction with reversible or irreversible loss of function.

It is suggested that the recurrent brief attacks of cerebral dysfunction result from a transient failure of these compensatory mechanisms, whereas the permanent degrees of neurological deficit can be related to a more prolonged and severe breakdown. Surely this explains the difficulty Hultquist and Turner experienced in finding emboli in the cerebral vessels in some of their cases with widespread brain infarction, and incidentally also explains the complete absence of organic obstruction in the cerebral blood vessels in Case 15. This view is further supported by the finding of ischaemic changes in the anterior and posterior cerebral artery territories in some of these cases with carotid occlusion.

These changes, which were usually less severe than those in the middle cerebral territory, are surely not due to vasospasm from the passage of emboli but are the result of the attempts of the ischaemic middle cerebral artery territory to claim more than its equal share of blood. In this way the flow to the anterior and posterior cerebral arteries is diverted into the middle cerebral trunk with resulting ischaemia of their territories.

Although simple cerebral ischaemia without organic occlusion of the cerebral vessels appears to be the principal mechanism of the brain damage in these cases, one cannot overlook the older peripheral infarcts with associated changes in the smaller cortical vessels.

Their appearance was compatible with their being embolic in origin, yet there is a more feasible explanation for their presence.

Normally the pressures within the smaller cerebral arterioles must fall towards the capillary end of the vessel. In carotid occlusion this fall in pressure will be more pronounced but is to some extent lessened by the dilatation and increased blood flow through the collateral channels between the three main cortical arteries. If however some of these channels in this junctional zone were narrowed by atherosclerosis, the blood flow to these regions would be correspondingly reduced, and the integrity of the tissues might be held in a precarious balance. Should the compensatory mechanisms governing the redistribution of the blood flow be further upset, these regions would be rendered ischaemic, with resulting local cerebral infarction and damage to the delicate endothelium of the smaller blood vessels with subsequent local thrombosis. As these infarcts lie in relatively "silent" areas of the brain no symptoms would necessarily arise from their presence.

In those patients where the evolution of the clinical picture is essentially a progressive one, it is difficult to visualise any mechanism other than a gradual reduction of the blood flow to the affected hemisphere. In this present series two patients showed the characteristic sequence of symptoms and signs, commencing



with weakness in one hand or one side of the face, and terminating after some time in a hemiplegia. But in the other two patients symptoms first appeared in one leg, progressively worsened, and were succeeded after several weeks or months by similar symptoms in the arm on the same side. One was able to relate the clinical picture with the pathological findings in one of them (Case 30). It will be recalled that there was an old infarct in the upper part of the central sulcus within the anterior cerebral artery territory, which no doubt accounted for the weakness of the contralateral leg but did not explain its progressive nature.

All the major cerebral vessels showed atherosclerotic degeneration, and although the anterior cerebral artery was not carefully examined throughout its length, it is possible that there was local narrowing of some of its branches. With the gradual reduction in blood flow caused by the carotid artery disease, local ischaemia would inevitably result.

The significance of thrombus within the major cerebral vessels.

Löhr (1936), Hyland (1933) and King and Langworthy all found thrombus in the internal carotid artery which extended upwards into the major cerebral vessels, and they therefore attributed the cerebral infarction in their cases to this mechanism.

In two patients in this present series (Cases 3 and 21) with recent hemiplegias, thrombus in the internal carotid artery extended upwards in continuity into the cerebral vessels. In Case 21, where the carotid occlusion was of relatively sudden onset, the ischaemic changes in the brain were of a similar age, and one was inclined to attribute the cerebral damage to thrombotic occlusion of the major cerebral vessels. However, in Case 3 where recent thrombus extended into the middle cerebral artery, there were older infarcts in the more peripheral parts of its territory which could not be related to the recent organic occlusion of its trunk. If one is correct in believing that the cerebral damage in most cases is due to failure of the collateral blood supply, could not this thrombus within the cerebral vessels be a secondary result of slowing of the blood stream and therefore not the primary cause of the cerebral damage? That recent thrombus is often found at post-mortem in the internal carotid artery in the presence of widespread areas of brain infarction, without organic occlusion of the major cerebral vessels, tends to support this view.

### Dangers of Arteriography

In the light of the foregoing discussion on the mechanism underlying the recent brain infarction shown by these patients, it is interesting to enquire why arteriography with solutions of diodone is sometimes accompanied by a deterioration of their condition, which may be followed by a fatal outcome (Cases 11 and 30).

This deterioration can occur whether the carotid occlusion is radiographically complete or incomplete. The results of the post-mortem examinations in Cases 11 and 30 left no doubt that arteriography had precipitated a profound disturbance of the existing blood flow through the middle cerebral artery with consequent infarction of most of its territory. That a few emboli were found in Case 11 was largely incidental, and although they may have contributed to the extent of the brain damage they were not its sole cause.

Broman and Olsson (1949) have drawn attention to the irritating effect of the diodrast group of contrast media on the vascular wall resulting in vasoconstriction and pain. They also conducted experiments in rabbits using a 35% solution of diodone which was injected into the carotid artery in combination with trypan blue. Normally there was little or no permeability of the vessel walls as judged by the staining of the cerebral tissues, but when the same solution was allowed to come into contact with the cerebral vessels for

20 seconds or more severe oedema of the brain with venous congestion and punctate haemorrhages occurred on the side of the injection.

In all cases where arteriography was harmful (Cases 11, 24, 30), the cerebral circulation was slowed. It is suggested that in them the blood flow through the diseased carotid tree was just sufficient to prevent serious cerebral ischaemia but that with the diodone injection, vasoconstriction occurred and the blood brain barrier was also deranged, causing widespread infarction and oedema of the hemisphere.

### Mechanism of Headache

In the literature on carotid artery occlusion there are many references to headache. In almost half of the reported cases it was a prominent symptom, was often generalised, and frequently preceded the appearance of other symptoms by some time. Less commonly it accompanied the development of a hemiplegia, and was then more often localised to the frontal and temporal regions on the side of the occluded carotid artery. Moniz and Andrell both described headache occurring either several years before, or in the later stages of the manifestation of the disease. Five of Andrell's nine patients complained of periodic headache which was situated on the same side as the occluded artery in the neck, and Symonds has recently described headache as the only symptoms of carotid artery occlusion.

Unfortunately many observers did not state its type, duration and precise relationship to the syndrome. However, Fisher who carefully observed these factors in four of his patients who complained of headache called attention to its migrainous-like characteristics, its situation above the eye on the side of the diseased carotid artery, and its presence for several months before other symptoms appeared. In one of his patients the headache was unique and accompanied each transient attack of hemiparesis, during which he observed the temporal vessels on the same side to pulsate vigorously.

He suggested that the headache was due either to referred pain from the carotid sinus or to local vascular dilatation.

In the patients of this present series headache was usually confined to the same side of the head as the occluded carotid artery, was frequently in the frontal or temporal regions and usually ceased once the syndrome had become established. It was commonly aching in character and in over half the patients preceded or accompanied the development of other neurological signs. In particular in Case 19 the association of headache with deterioration in his neurological status was striking, for as in Fisher's case, unilateral temporal pain accompanied each hemiplegic episode. When visual symptoms were prominent headache was always present. In one patient with transient attacks of blindness, frontal headaches accompanied each episode, and in two others aching or throbbing temporal pain was present before the onset of unilateral blindness. In some patients however, headache appeared late in the development of their syndrome and did not seem to have any close connection with the episodic deterioration in their condition.

Believing that the mechanism underlying the clinical picture of carotid occlusion is due to ischaemia, and that nature attempts to overcome the reduction in blood flow by providing blood through other channels,

it was tempting to ascribe these headaches to dilatation of these collateral channels as Willis had done over 300 years ago. Now Wolff (1948a) has shown that when the walls of an artery in the head are dilated beyond physiological limits headache results, and Fisher's observation that headache was accompanied by dilatation of the scalp vessels surely indicate that Willis' explanation was the correct one.

In nearly all the patients in this present series the external carotid artery was dilated on the same side as the diseased internal carotid artery, and in some of them was seen to conduct blood to the intracranial vessels on the same side. In those patients who experienced headache it was frequently situated in the anterior part of the head but in one patient where the occipital vessels were dilated and supplied blood to the intracranial vessels, headache was referred to the occiput. That their headaches frequently preceded or accompanied deterioration in their neurological condition is surely of significance. It is suggested that with the variations in blood flow through the diseased carotid artery the various compensatory mechanisms come into play, and the blood flow through the collateral channels is increased with consequent dilatation of these vessels and the production of headache. Should this increased flow prove adequate no other symptoms will develop but if it should prove inadequate for the demands of the hemisphere, a hemiplegia will result.

Mechanism of Vertigo

Dizziness has often been reported in the literature but the authors frequently alluded to this symptom so briefly that no definite conclusion could be drawn from their descriptions. Reichert, Seigert (1938) and Krayenbühl and Weber all mentioned dizziness, and in one of Moniz's cases dizziness accompanied headache and weakness of the right arm. Andrell was more specific in his description for one of his patients had several attacks of vertigo which caused her to fall down. Fisher also described rotatory vertigo but was uncertain of the underlying cause in his case as there was an associated thrombosis of the basilar artery in addition to the carotid artery occlusion.

In the two patients in this series who complained of true vertigo such attacks occurred early in the syndrome, and were accompanied by transient weakness or numbness of the contralateral hand or by twitching of the facial muscles. There is little doubt that the underlying cause of these attacks was ischaemia of the temporal lobe.



## Mechanism of Visual Symptoms

### 1. Optic Atrophy

Optic atrophy was encountered in only two patients of this present series, and Johnston and Walker in their review of 101 cases of carotid occlusion reported in the literature found that only 10% of them had an associated optic atrophy. This is not surprising, for Elschnig (1893) demonstrated by injection experiments in the cadaver that there was a free anastomosis between the branches of the external carotid and the ophthalmic artery. More recently Walsh and King (1942) have confirmed the observations of Elschnig, and in addition found that with both internal carotid arteries occluded in the neck contrast media could pass via one external carotid artery into both ophthalmic arteries. That these collateral channels are usually adequate to prevent blindness developing with unilateral carotid occlusion is well illustrated by the observations of Dandy (1938). He was able to ligate the internal carotid in the neck, and again distal to the origin of the ophthalmic artery without producing blindness.

In this present series of patients the arteriographic studies have shown that blood can flow in the reverse direction along the ophthalmic artery from the external carotid on the same side, and also from the opposite internal carotid artery through the

anterior communicating artery. No doubt the flow through these collateral channels was sufficient to prevent the development of optic atrophy in the majority of these patients.

In the two patients where unilateral optic atrophy was found on the same side as the occluded carotid artery the fundal appearances differed. In one (Case 2) the optic disc was white in colour and the retinal arteries narrowed, suggesting there had been a vascular occlusion of the central retinal artery, whereas in the other (Case 29) the disc was grey and slightly swollen but the retinal arteries appeared to be of normal calibre, suggesting that any considerable involvement of the central retinal artery was unlikely and that the lesion lay in the small nutrient vessels to the optic nerve arising from the ophthalmic, internal carotid and anterior cerebral arteries. In them the visual defect appeared late in the development of the syndrome, after other neurological signs had become established, yet neither had had any previous symptoms referable to the eyes. In both, the external carotid artery on the same side was dilated and presumably the blood flow through the ophthalmic artery was augmented thereby, and had been sufficient to prevent any severe degree of ischaemia in the retinae or optic nerves. Yet both patients experienced unilateral headache when their optic atrophy developed, suggesting that there was a local vascular insufficiency which had promoted

dilatation of the collateral channels in the neighbourhood, but that the increased blood flow had been insufficient to overcome the local vascular defect. Whether this atrophy followed simple local ischaemia or actual thrombosis within the vessels concerned could not be ascertained. Confirmation of the underlying mechanism must await good clinico-pathological studies.

## 2. Mechanism of the transient attacks of blindness.

In this present series transient attacks of blindness were complained of by one patient only (Case 29) early in the development of the syndrome, were associated with frontal headache, and ceased when symptoms of parietal lobe dysfunction appeared.

With the exception of Moniz and Andrell, who briefly alluded to attacks of blindness in some of their cases, they have been rarely commented upon by other authors. However, no less than four of Fisher's eight cases complained of such attacks, and it was he who recognised their diagnostic importance. He pointed out that this symptom is probably commoner than is generally believed, for unless patients are questioned closely about their vision they tend to refer to these attacks as "blurring of the eyes" or "trouble with the eyes" and the true nature of the symptom is thereby overlooked. Again, unless these patients are seen before the onset of considerable intellectual impairment and aphasia, the relevant history may be impossible

to obtain. In Fisher's cases the transient blindness occurred on the same side as the occluded carotid artery, appeared at irregular intervals and lasted from half to five minutes at a time, were more frequent before the onset of their hemiplegia, but ceased once it had become established. Yet in Andrell's case the attacks commenced after the stroke and gradually diminished over several months. In Fisher's Case 2 unilateral blindness was sometimes accompanied by numbness in the contralateral hand, which disappeared when vision became normal again.

Fisher, who was unaware that a satisfactory ophthalmoscopic examination had been made during an attack of blindness, was unable to account for this symptom on any satisfactory basis, and suggested that the attacks might be the result of vasospasm of the retinal arteries.

But Walsh and Smith (1952) saw the retinal arteries become narrowed during an attack of blindness, and Denny-Brown has seen blanching of the retinal vessels on the same side as the diseased artery when the non-occluded artery was obliterated by digital compression. Surely this must mean that these attacks are due to retinal ischaemia following a reduction in the collateral blood supply.

Now we know that under normal circumstances the blood flow in the occluded internal carotid artery and its branches is reduced and that the external carotid artery on the same side hypertrophies and supplies blood

to the internal carotid artery above the site of obstruction via the ophthalmic artery. If the blood flow through the anterior communicating artery is decreased this fall will be automatically reflected in the ophthalmic artery on the same side. Should the blood flow through the external carotid artery be insufficient to prevent ischaemia blindness will result with the possible increase or appearance of neurological signs referable to ischaemia of the hemisphere (cf. Fisher's case 2).

But it is rather uncommon for transient blindness to occur with signs of neurological disturbance elsewhere. It is suggested that under these circumstances the reduction in blood flow in the obstructed carotid tree is insufficient to give rise to serious ischaemia of the hemisphere but this alteration in cerebral haemodynamics calls forth a generalised vasoconstriction throughout the body, which includes the territory of the external carotid arteries. If the local conditions of vascular supply to the eye are precarious, i.e., insufficient blood flow through the ophthalmic artery, then blindness will result. When the blood flow through the anterior communicating artery is increased by the rise in systemic blood pressure occasioned by this vasoconstriction, vision is then restored to normal. That these attacks usually cease once permanent neurological signs appear probably

indicates that the external carotid artery has dilated sufficiently to prevent further ischaemia developing.

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A P P E N D I X

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CASE 1 A.R. aged 70 years

OCCUPATION Retired jockey

FAMILY HISTORY

No relevant history.

PAST HISTORY

Thirty years ago he was kicked on the head by a horse with resulting laceration of the scalp; the wound healed well.

Eight years ago his appendix was successfully removed.

Four years ago he developed a carcinoma of the alveolus which was treated by local excision, glandular clearance of the neck and deep X-ray therapy; there had been no recurrence.

For many years he had suffered from intermittent throbbing bitemporal headaches which had become more severe in recent months.

PRESENT ILLNESS

One month before admission to hospital he suddenly found his left arm stiff and useless and the left side of his face "drawn". This was accompanied by severe right-sided throbbing temporal headache and inability to speak, which lasted twenty minutes. Over the next twenty-four hours the left arm and face gradually returned to normal, although during the next three weeks he had intermittent attacks of numbness and stiffness of the left arm and occasionally

also of the left face and leg. Such attacks lasted about twenty minutes and recurred up to four times daily. They were occasionally associated with incontinence of urine, but never by loss of his senses.

One week before admission he fell down on account of a sudden severe weakness and numbness of the left arm and leg. Since then there had been a slow improvement of power in the arm and leg, although he had had throbbing temporal headaches on most days.

For the past month his memory had been poor.

#### EXAMINATION

He was drowsy and complained of right temporal headache.

There was no evidence of organic intellectual impairment in excess of his age.

#### Cranial nerves

Visual acuity was 6/9 in each eye and although the optic discs were normal, the retinal vessels were slightly thickened.

There was a left homonymous congruous hemianopia sparing the macula.

Both pupils were equal, moderately dilated, and reacted sluggishly to light and on convergence.

A marked left central facial weakness was present, otherwise no abnormality was found in the cranial nerves.

Motor

There was an almost complete left hemiplegia with only slight flexion movements possible at the hip.

Tone was slightly increased.

The tendon reflexes in the left extremities were increased, the left abdominal reflexes absent, and the left plantar response extensor.

Sensation

All forms of cutaneous sensibility were impaired over the left side including the face. Sense of passive movement was absent in the left extremities with the exception of the hip where gross movements were correctly appreciated.

General examination

No abnormality was discovered apart from slight thickening of the peripheral arteries: the blood pressure was 160/100.

Both carotid arteries were pulsating equally in the neck.

INVESTIGATIONS

X-ray skull and chest

No abnormality was seen.

Electro-encephalogram

The alpha rhythm was slowed to 8 c/sec., a finding which was probably related to his drowsy state. No difference was noted between the two hemispheres and there was no evidence of any cortical damage.



Right carotid arteriogram.

The internal carotid artery was occluded at its origin: the external carotid artery and its branches were well filled.

The appearances were similar to those seen in Case 6.

CASE 2 S.F. aged 50 years

OCCUPATION Tobacco blender

FAMILY HISTORY

No relevant history.

PAST HISTORY

Six years ago he was crushed between two motor vehicles and received a blow on the back of his neck. He was not rendered unconscious and made a good recovery from this injury within a few weeks.

Fourteen months ago he was swindled by his partner and lost all his money; since then he had been depressed and complained of failing concentration and memory.

PRESENT ILLNESS

Two years before admission to hospital he had noted a progressive stiffness and weakness of the right hand together with pins and needles and numbness in the tips of all his fingers. Over the next three months this hand became weaker and numbness spread up the arm to the shoulder. From time to time he had nagging pains in the left temple. At this juncture he was admitted to the National Hospital for Nervous Diseases, Queen Square.

Examination revealed no abnormality in the cranial nerves, but he had a marked weakness of all the small muscles of the right hand and of the wrist extensors

and flexors; the reflexes were increased in this extremity. Cutaneous sensibility was impaired over the hand and forearm, together with gross impairment of the sense of passive movement at the fingers and wrist. The whole hand was swollen. X-rays of the cervical spine showed a crush fracture of the body of C5. The cerebrospinal fluid was found to be under a normal pressure and showed a free rise and fall on jugular compression: cells 2 per c.mm.; protein 35 mgms.%. The Wassermann reaction was negative in both blood and fluid.

He was considered to be suffering from a compressive lesion at C3 and an exploratory laminectomy was carried out. This showed no significant abnormality and he was eventually discharged home.

Thereafter his condition slowly deteriorated and over the next year his right arm became weaker and numbness gradually spread from the arm over the right cheek, head and neck.

Six months ago, the right leg had suddenly become numbed and weak, and within recent months this weakness had progressed further and he was inclined to stammer and hesitate in speech. Recently he had experienced mild left frontal headache and had been aware of some deterioration of vision in his left eye.

EXAMINATION

Cranial nerves

Visual acuity was 6/36 (uncorrected) in the right eye:

hand movements only were appreciated in the left eye.

The right optic disc was normal, the left being pale.

The right visual field was full but the left showed marked concentric constriction.

The left pupil responded less briskly to light than the right, but both responded briskly on convergence.

Apart from a mild right central facial weakness, no other abnormality was discovered in the cranial nerves.

Motor

There was a moderate degree of weakness with a severe spasticity in both right arm and leg.

The tendon reflexes were markedly exaggerated in the right extremities, the abdominals were present and equal and the right plantar response was extensor in type.

Sensation

Cutaneous sensibility was impaired over the right half of the body and face.

The sense of passive movement was diminished in the right fingers and toes and vibration sense was diminished at the ankle and wrist.

General examination

No abnormality was discovered except for a blood pressure of 170/100.

INVESTIGATIONSX-ray of skull

No abnormality was seen.

Electro-encephalogram

There was a normal 8-9 c/sec. alpha rhythm with a constant voltage asymmetry, the left side being quieter. There were also low voltage 1-2 c/sec. slow waves with a vague localisation to the left parietal region. The record was consistent with a slowly progressive organic lesion in this area, or could be the residuum of a cerebro-vascular accident.

Left carotid arteriogram.

The external carotid artery was well filled but the internal carotid was occluded  $1\frac{1}{2}$  cms. from its bifurcation in the neck. The appearances were similar to those seen in Case 6.

Air encephalogram

The left lateral ventricle was dilated throughout and the septum pellucidum was displaced 1 cm. to the left of the midline. The right lateral ventricle was also dilated. The cortical air channels over the left hemisphere were enlarged. The appearances were those of a gross left-sided cerebral atrophy.

CASE 3 F.S. aged 49 years

OCCUPATION Fitter

FAMILY HISTORY

No relevant history.

PAST HISTORY

This man had enjoyed excellent health until the age of 42 years when he developed intermittent upper abdominal discomfort and pain which were attributed to duodenal ulceration. After treatment with diet and alkalies his symptoms rapidly subsided and had not recurred. Eleven months prior to his admission to hospital in May 1947 he had experienced intermittent aching, cramping pain in the left foot when the weather was cold. The skin overlying the foot was often blue in colour and occasionally became dead white. After two months the pain and colour changes disappeared.

PRESENT ILLNESS

Six months before admission to hospital his left hand became mildly clumsy and he had difficulty in manipulating small objects between the thumb and index finger. This disability increased during the course of the next few days and was accompanied by slight tingling in the index finger. Within one week the whole hand was clumsy and he had experienced tingling in all the left fingers in turn.

Three months later he was unable to keep an eyeglass in his left eye, and about one month later he complained to his relatives of "mental confusion", i.e., he was unable to find his way home easily, was unable to see out of the corner of his eyes, and became confused when reading blueprints and in dressing. His relatives also found that he had become irritable, bad-tempered and generally forgetful.

Two weeks before admission he had complained of almost constant throbbing frontal headaches, more pronounced over the left side of his head. They were aggravated by exertion and occasionally radiated towards the left temple. He was right handed.

#### EXAMINATION

On admission he was rather distressed. There was no dysphasia, but he showed a well-marked apraxia of the left hand with an apraxia for dressing. He also showed a constructional apraxia and gross topographical disorientation, together with a disturbance of spatial orientation and visual synthesis: he had a marked agnosia for the left half of visual space.

#### Cranial nerves

Visual acuity was 6/9 in each eye.

There was a left homonymous hemianopia sparing the macula. A moderate degree of left central facial weakness was present.

No other abnormality was discovered in the cranial nerves.

Motor

Apart from slight weakness of the left hand together with an increase in tone, in the more distal parts of the left upper extremity, there was no other abnormality discovered.

Sensation

Changes were confined to the left upper extremity.

Appreciation of light touch was diminished over the left hand and sense of passive movement was lost in the left fingers and about 50% correct at the wrist and elbow.

Two-point discrimination was recognised at 6 cms.

over the left fingers, whereas it was correctly appreciated at  $\frac{1}{2}$  cm. separation on the right finger pads.

General examination

There was no significant abnormality in the general examination, with the exception that the peripheral vessels were slightly thickened and no pulsation felt in either dorsal pedis or posterior tibial arteries.

Blood pressure was 160/90.

INVESTIGATIONS

X-ray of skull. No abnormality seen.

Electro-encephalogram.

There were low voltage 4-5 c/sec. waves recorded from the right parietal and both frontal areas. There



were also runs of pathological activity in the anterior parts of both hemispheres. These changes represented a disorder of long standing.

Cerebrospinal fluid

Pressure 140 mm. with a free rise and fall on jugular compression.

Cells: 5 lymphocytes per ml.

Protein: 40 mgms. per 100 ml.

Lange curve: 0000000000

Wassermann reaction was negative.

Blood count

Red blood cells 6.04 million per c.mm.

Haemoglobin 110%

White blood cells 7,600 per c.mm.

Polymorphs 61%

Lymphocytes 35%

Monocytes 1%

Eosinophils 2%

Basophils 1%

PROGRESS

One month after admission the left face, arm and leg became markedly weak. A few days later he suddenly complained of upper abdominal pain and frequently vomited a copious, slightly blood-stained fluid. He died two days later from exhaustion.

POST MORTEM EXAMINATION

The heart showed slight left ventricular hypertrophy, with extensive fibrous replacement of the myocardium at the left ventricular apex.

The right coronary artery was narrowed by pale firm thickening over a distance of 1 cm. about 10 mms. from its point of origin. The left coronary artery was healthy. A laminated ball thrombus of partly pale and partly red clot measuring 2 cms. in diameter was adherent to the posterior wall of the left ventricle.

The aorta was atheromatous in the thoracic and abdominal parts and a recent small thrombus was adherent to its anterior wall midway between the origins of the coeliac axis and the inferior mesenteric artery. The superior mesenteric artery was blocked near its origin by recent thrombus extending over a distance of 2 cms.

There was recent early infarction of the small intestine from the duodenal-jejunal flexure to about two feet above the caecum. The involved intestine was dilated, covered with fibrin and contained fluid blood.

The right femoral artery showed a luminal narrowing over a length of 1.5 cms. at its origin and the left was completely occluded over a distance of 1 cm. in Hunter's canal. The veins appeared to be healthy.

The left carotid artery was healthy.

The right internal carotid was markedly stenosed at its origin and the available lumen reduced to  $\frac{1}{2}$  mm. For 1.5 cms. above this level the lumen was still reduced by pale, firm eccentric narrowing which progressively decreased so that the lumen resembled an inverted cone with its apex downwards. Above this the lumen was subtotally blocked by brownish-red jelly-like clot which extended upwards into the middle cerebral artery but stopped short of the posterior communication artery.

Histologically the right internal carotid artery at its origin was occluded by fibrous tissue and old organised thrombus (Fig. 1).



Fig. 1. LP view of occluded partially recanalised internal carotid artery.

Near the centre the cellular and organised thrombus lay eccentrically and appeared to be partially recanalised. Lying outside this there was a layer of organised fibrous thrombus in which lay calcium and cholesterol deposits, with related foreign body giant cells (Figs. 2 and 3). The internal elastic lamina was crenated, sometimes reduplicated and thinned. The media and adventitia and the veins were healthy. The occluded portions of the femoral arteries presented similar changes.

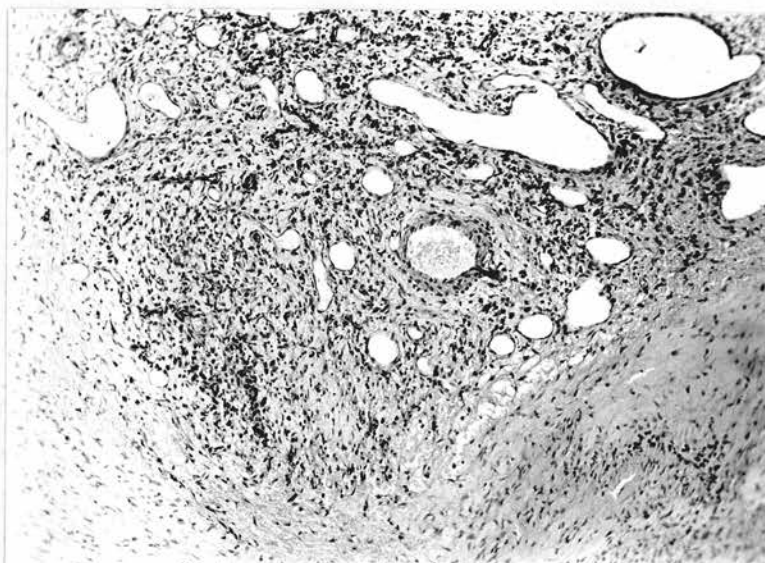


Fig. 2. Medium power view of part of occluded carotid artery.

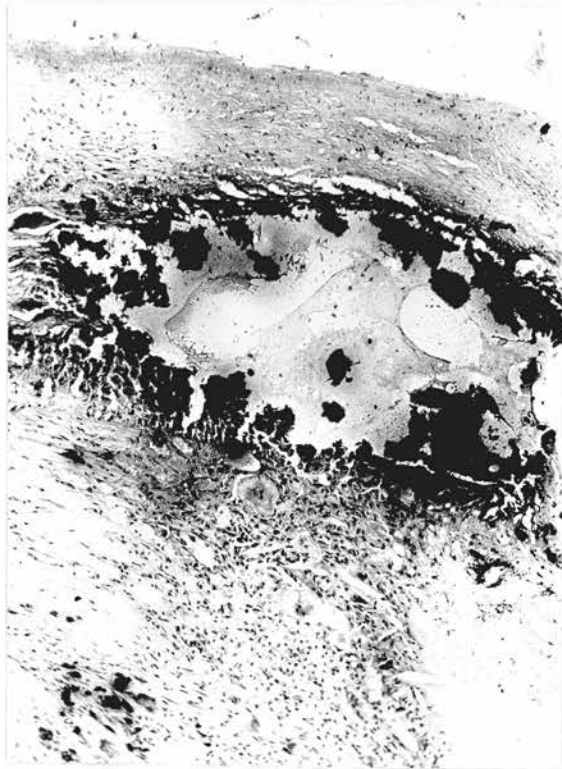


Fig. 3. HP view of Fig. 2. Note atheroma with related foreign body giant cells.

The right hemisphere showed old orange coloured infarction of the grey matter and old cystic infarction of the white matter affecting the inferior frontal gyrus and both superficial and deep parts of the underlying white matter. Further back the middle frontal gyrus and supero-lateral quarter of the corpus callosum were involved. More posteriorly the lentiform and caudate nuclei were infarcted. The gyrus cinguli was also involved, the infarct

commencing where it lay above the genu of the corpus callosum and increasing until the level of the infundibulum was reached. At this level the first and second temporal convolutions were involved together with much of the white matter. Further back both pre- and post-central and both inferior and superior parietal lobules were affected. The cortical infarction extended backwards into the occipital lobe involving the central three-fifths of the convexity. (Fig. 4).

The middle cerebral artery at the Sylvian point was pale and thickened over a distance of 1 cm. presumably due to an old-standing thrombotic occlusion. On the convexity of the occipital lobe there was a small scarred surface depression associated with an old thrombotic occlusion of a small cortical vessel.

Histologically the cerebrum presented infarcts of varying sizes and ages. Older lesions with scarring and glial fibre formation were scattered indiscriminately throughout the cortex but especially in the region of the superior frontal gyrus, the cingulate gyrus and the outer surface of part of the occipital lobe.

Elsewhere in the distribution of the middle cerebral artery many of the lesions appeared to be of more recent origin. In the region of the pre- and post-central gyri there was an area of massive necrosis

of very recent origin with destruction of all elements and infiltration with fat filled phagocytic cells (Fig. 5).

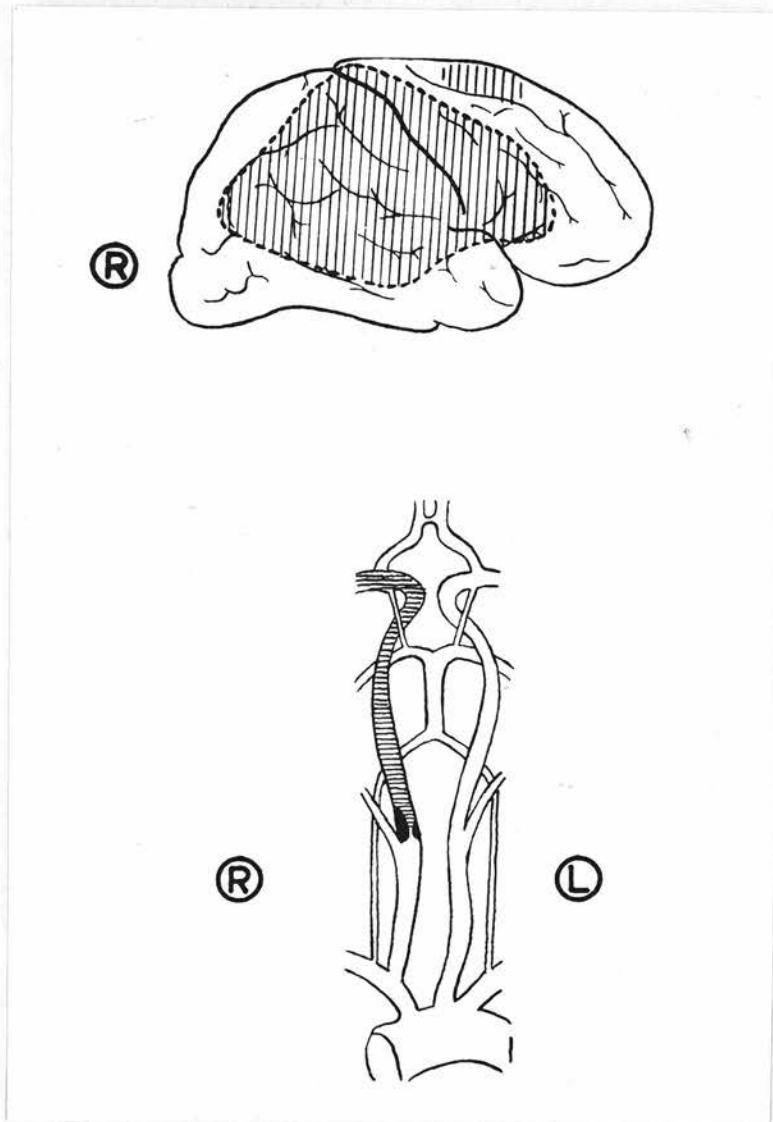


Fig. 4. Diagram of carotid artery obstruction and the area of cerebral infarction.

■ Atheroma

▨ Thrombus

It was limited by severely damaged, but surviving cortex. In the underlying white matter were areas of glial fibre formation. The thalamus showed some nerve cell degeneration and scarring.

The rest of the cortex in the anterior and posterior cerebral arterial distribution showed ischaemic nerve damage with shrunken and distorted cells (Fig. 6).

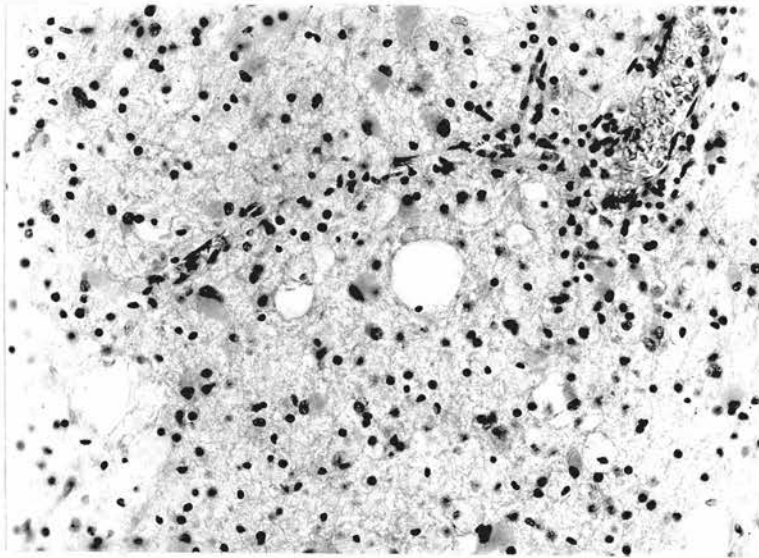


Fig. 5. Border of recent area of infarction with vacuolation of cerebral tissue.

Some of the branches of the middle cerebral artery contained organising blood clot of differing ages, some showing early signs of organisation whilst



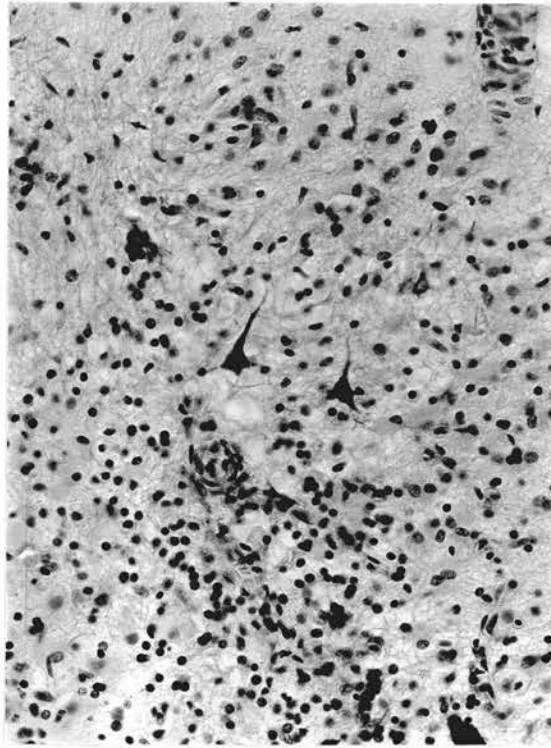


Fig. 6.

others, especially in the smaller cortical branches, had become recanalised. Frequently one saw vessels containing organising clot lying in close proximity to others which appeared to be perfectly healthy.

The opposite cerebral hemisphere showed slight subpial gliosis, but no other gross changes.

With the exception of occasional capillary endothelial hyperplasia the vessels appeared healthy.

CASE 4 R.L. aged 24 years

OCCUPATION Sergeant Malaya Police

FAMILY HISTORY

No relevant history.

PAST HISTORY

At the age of ten years he suffered from "rheumatism" characterised by aching pain in his joints which subsided in a few months.

Four years before admission he fell from a horse, was concussed and remained unconscious for two hours: there were no sequelae.

The following year he had septicaemia from which he made an excellent recovery.

PRESENT ILLNESS

Seventeen months before his admission to the National Hospital for Nervous Diseases, Queen Square, he began to drop things out of his right hand and was unable to hold his pen properly. On this account he was admitted to hospital elsewhere and found to have marked wasting and weakness of the muscles of the forearm and right hand, resulting in a main en griffe. Cutaneous sensibility and vibration was diminished over C8 and T1 dermatomes. Within three months his condition improved and apparently completely disappeared, for he was accepted for service in the Malay Police some ten months later.

In Malayahe remained very well for four months. Then after a game of rugby he felt suddenly tottery and generally unwell. He thought he had an attack of malaria and retired to bed early. Next morning he was found with a right hemiplegia and was unable to speak more than the word "Smithy", the name of his friend. Thereafter he had only a hazy recollection of events until the tenth day, when he was aware that his right arm and leg were useless and that he was still unable to speak. At first he was inclined to weep, especially as he was unable to read or calculate, although he could understand everything that was said to him. Gradually his condition improved and four months later he was able to walk and to make his wants known, but had little use in the right hand.

#### EXAMINATION

He was pleasant and co-operative. The Bellevue Scale placed him in the high normal range. His understanding of spoken speech was normal, although he showed a mild expressive dysphasia.

Reading was grossly impaired from an inability to recognise visual letters and to form visual images of letters.

Writing was grossly disorganised.

Reading and writing of numbers was correct and slow, but calculation was grossly impaired.

Right-left identification was also slow, but otherwise correct.

#### Cranial nerves

Visual acuity was 6/18 uncorrected in both eyes with normal fundal appearances.

There was a right congruous hemianopia splitting the macula.

Apart from a slight right facial weakness on emotional movement only, no other abnormality was seen in the cranial nerves.

#### Motor

There was a severe right hemiparesis more marked in the arm than the leg.

Only slight movement was possible at the right shoulder and in the leg he could barely flex the hip and knee, but could dorsiflex the foot against moderate resistance.

The tendon reflexes in the right extremities were markedly exaggerated, with diminished right abdominal reflexes, and a right-sided extensor plantar response.

#### Sensation

There was a hypalgesia over the whole right side of the trunk and extremities, including the face: touch was normal.

Sense of passive movement was grossly impaired in the right fingers, wrist and elbow, and to a lesser extent in the right toes.

Appreciation of two-point discrimination was absent over the right fingers, with marked astereognosis in this hand.

#### General examination

No abnormality was discovered, in particular the peripheral vessels appeared healthy and the blood pressure was 130/90.

There was no difference in the pulsation of either carotid artery in the neck.

#### INVESTIGATIONS

##### Blood count

Red blood cells	6.02 million per c.mm.
Haemoglobin	102%
White blood cells	5,200 per c.mm.
Polymorphs	50%
Lymphocytes	47%
Monocytes	1%
Eosinophils	2%
Clotting time	5 minutes (Lee and White)

##### Cerebrospinal fluid

Pressure 150 mm. with a free rise and fall on jugular compression.

Cells: 0 per c.mm.

Protein: 35 mgms. %

Lange curve: No change.

Wassermann reaction: negative.

##### X-ray of skull

No abnormality seen.

Electro-encephalogram

The alpha rhythm was normal and regular over the right side, but was almost entirely absent from the left. Generalised slow activity of low voltage at about 6 c/sec. was more prominent over the left side, mixed with slower, irregular low voltage waves.

The evidence for destruction of cerebral tissue was minimal.

Left carotid arteriogram

The external carotid artery was well filled. The internal carotid was occluded 1 cm. from its origin. The obstruction was of conical shape, with its base downwards, similar to that seen in Case 20.

CASE 5 J.B. aged 67 years

FAMILY HISTORY

Her mother suffered from migraine.

PAST HISTORY

From her early teens she had suffered from bifrontal migrainous headaches, which ceased at the menopause.

PRESENT ILLNESS

Two years before admission to hospital she experienced giddiness with unsteadiness of gait due to the sudden onset of double vision. The diplopia only occurred when she looked to the left side and the images produced lay vertically parallel to each other: it persisted for two months then disappeared and was unaccompanied by any headache or facial pain.

About this time it was noted that her left eye was not moving out properly, and at the same time hearing was less acute in the right ear and was accompanied by occasional ringing tinnitus.

Six months after the onset of her illness she awoke one morning with severe left frontal headache, experienced photophobia and later vomited. The headache continued unchanged for several weeks, thereafter gradually decreasing until it disappeared completely five months later.

EXAMINATION

She was an anxious woman, who did not appear to have any intellectual deficit.

Cranial nerves

Visual acuity was 6/18 uncorrected in both eyes, and the fundi were normal in appearance.

External ocular movements of the right eye were full and free. The left eye was strongly adducted and showed evidence of a partial III and a complete VI nerve palsy.

The right pupil reacted briskly to light and on convergence; the left did not react at all to light and only slightly on convergence.

There was a moderate bilateral ptosis.

Motor

The upper and lower extremities were entirely normal. The tendon reflexes in the arms were brisk, those in the legs natural and equal with bilateral flexor plantar responses.

Sensation

Sensation was normal throughout.

General examination

No abnormality was discovered with the exception of the cardiovascular system. The blood pressure was 214/128 with mild peripheral arteriosclerosis.

INVESTIGATIONS

X-ray of skull and chest

No abnormality seen.



Cerebrospinal fluid

Pressure 95 mm. with free rise and fall on jugular compression.

Cells: 1 per c.mm.

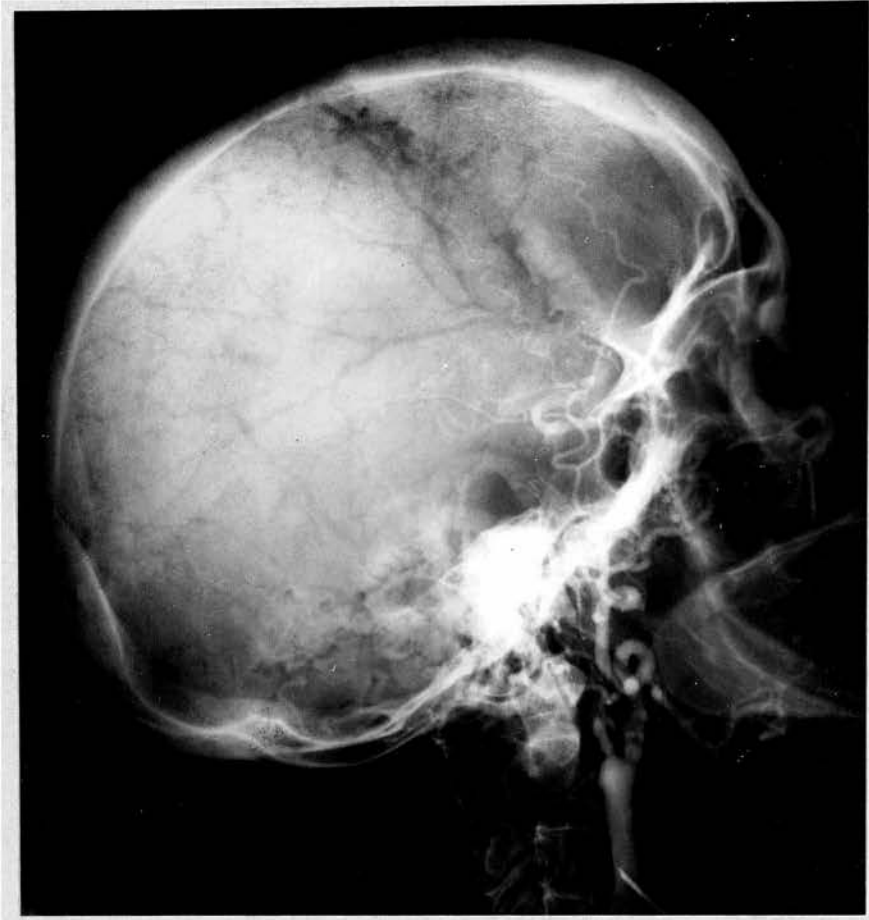
Protein: 35 mgms.%

Lange curve: no change

Wassermann reaction: negative

Left carotid arteriogram

The left internal carotid was occluded at its origin from the common carotid artery. Only a small column of contrast was visualised in the proximal centimetre of the artery. In later films, however, the middle cerebral artery was seen to be filled. No actual communication between the carotid syphon and the point of thrombosis was seen. The contrast may have percolated through a small channel in the occluded internal carotid artery, or alternatively have passed through the collateral circulation in the external carotid system, thus reaching the ipsilateral middle cerebral artery.



CASE 6 F.T. aged 63 years

OCCUPATION Retired traveller

FAMILY HISTORY

No relevant history.

PAST HISTORY

When aged 60 years he developed peritonitis following a ruptured duodenal ulcer. This was repaired and he made an excellent recovery.

Eighteen months ago he developed "asthma" without any associated cough or haemoptysis. This "asthma" consisted of awaking breathless during the night, and was relieved by sitting upright.

During the past two years he had lost three to four stones in weight.

PRESENT ILLNESS

Fifteen months ago his right hand became clumsy and he was unable to hold a pen correctly or to feel coins in his trouser pocket. These disabilities persisted throughout his illness.

Twice in the past year he had awakened with stiffness and numbness of the right arm and leg which passed off after an hour or two.

Six weeks before admission, when reading a book, he suddenly experienced a "dumb feeling" at the back of his neck passing down over the right side of his chest. The right arm was useless and he was unable to speak, although he could understand what others said to him.

He was generally dizzy and his eyesight slightly blurred. There was no true vertigo or loss of consciousness.

After seven days his speech improved, but he still could not read or write or see out of the right side of his eyes.

Since this stroke his memory had been impaired.

#### EXAMINATION

He was feeble and tremulous, although alert and correctly orientated.

There was evidence of mild organic intellectual deterioration.

He showed a marked expressive and nominal dysphasia with a slight comprehensional speech defect, complete alexia and agraphia with considerable dyscalculia, right-left disorientation and finger agnosia.

#### Cranial nerves

Visual acuity was 6/9 in both eyes with normal fundal appearances.

There was a complete right congruous hemianopia sparing the macula.

Otherwise there was no abnormality in the cranial nerves.

#### Motor

A generalised slight to moderate loss of power was present in the right arm and leg, although there was no alteration of tone.

The tendon reflexes were increased in the right arm and to a lesser extent in the right leg. The abdominal reflexes were present and equal with bilateral flexor plantar responses.

#### Sensation

There was a right side hemihyphaesthesia and hypalgesia sparing the face.

Sense of passive movement was grossly impaired at the right finger and wrist, with profound astereognosis in the right hand.

#### General examination

No abnormality discovered with the exception of the cardiovascular system.

All the peripheral vessels were sclerotic, although the heart was normal. Blood pressure was 160/90.

Both carotid arteries were pulsating equally in the neck.

#### INVESTIGATIONS

##### X-ray of skull

A small linear calcification lay in the region of the sella in the region of the carotid syphon.

##### X-ray of chest

No abnormality seen.

##### Erythrocyte sedimentation rate

7 mm. in 1 hour.

##### Electro-encephalogram

The right side was normal. Over the left side the abnormality was limited to the anterior temporal region

where there was a clear focus of 3-4 c/sec waves of moderate voltage. This was compatible with a destructive lesion at this site.

Left carotid arteriogram.

Only the proximal 1 cm. of the left internal carotid artery was filled. The external carotid artery and its branches were well filled.



CASE 7 W.E. aged 50 years

OCCUPATION Miller and borer

FAMILY HISTORY

A brother aged fifty-four years died of an heart attack.

PAST HISTORY

Pleurisy one year ago from which he made an excellent recovery.

PRESENT ILLNESS

Five months before admission to hospital he developed aching pain in his lower back radiating into the right anterior thigh. He had retention of urine for five days. His doctor thought he was suffering from sciatica and confined him to bed for three weeks. Gradually the pain subsided, but some nine weeks after the onset of his sciatica he began to drag the right leg.

Four weeks ago he began to have intermittent left-sided headaches, appearing at any time of the day and lasting several hours at a stretch.

Two weeks ago he awoke to find his right leg much weaker than heretofore and in addition the right arm was also weak and clumsy and he kept losing it under the bedclothes. He also had difficulty in finding and pronouncing words.

Since then these headaches have continued unchanged, and although power in the right arm improved,

the right leg remained weak. For the past month his memory had been impaired.

#### EXAMINATION

Co-operation was limited owing to a moderate degree of intellectual impairment. He showed a mild expressive dysphasia without any nominal defect.

#### Cranial nerves

Visual acuity J 1 on the right, J 2 on the left.

Both fundi were normal and both visual fields full.

A slight right central facial weakness was present,

otherwise there was no abnormality in the cranial nerves.

#### Motor

There was a moderate weakness of the right extremities, more marked in the leg than the arm. Tone was slightly increased in the right arm, and appeared to be extrapyramidal in type.

The tendon reflexes in the right arm and leg were increased, with absent abdominals and a right-sided extensor plantar response.

#### Sensation

A vague hypaesthesia was present over the right trunk and extremities with slight impairment of the sense of passive movement in the right fingers and toes.

#### General examination

This revealed no abnormality with the exception of blood pressure 220/150.

Both carotid arteries were pulsating equally in the neck.



INVESTIGATIONS

Blood count

Red blood cells	5.28 million per c.mm.
Haemoglobin	106%
White blood cells	6,800 per c.mm., with normal differential count

X-ray of skull and chest

No abnormality seen.

Cerebrospinal fluid

Pressure: 140 mm.

Cells: 1 per c.mm.

Protein: 70 mgms.%

Lange curve: No precipitation

Wassermann reaction: negative

Electro-encephalogram

A flat record in which the only activity was slight regular alpha rhythm.

Left carotid arteriogram

Complete occlusion of the left internal carotid artery 2 cms. from its origin. The external carotid artery was well filled. With a solution of 50% diodone the external carotid and intracranial portion of the internal carotid and the middle cerebral arteries were seen: the anterior cerebral artery was not filled.

It was postulated that there was an anastomosis between the external and internal carotid systems through the ophthalmic artery filling the intracranial vessels.



CASE 8 F.E. aged 61 years

OCCUPATION Lorry driver

FAMILY HISTORY

His mother died at the age of thirty-four years from a stroke.

PAST HISTORY

Thirty-eight years ago he injured the left eye, and although vision was unimpaired, the pupil had always remained small.

He had suffered from intermittent attacks of lumbago and sciatica over the past twenty-five years.

PRESENT ILLNESS

When out walking nine weeks before admission he suddenly became dizzy, lost his balance and rolled over into a ditch. He picked himself up and was none the worse for his experience, although his wife noticed that his face twitched most of the night.

A few days later he had two attacks of tingling and numbness of the left hand lasting five minutes at a time, during which the hand felt dead and useless.

Three days ago, when driving a lorry, his left hand became suddenly clumsy and he persisted in steering into the oncoming traffic. Within ten minutes he felt dizzy, and his hand had become weak. This weakness progressed and within two hours the hand and arm were virtually useless.

At no time had he experienced headache.

EXAMINATION

He was apathetic, although correctly orientated in time and space.

There was a mild degree of organic intellectual impairment in excess of his age.

Cranial nerves

Visual acuity was 6/6 in each eye.

The right optic disc was pink, the nasal margin blurred, and the vessels atherosclerotic; the left was not seen due to the small aperture of the pupil caused by his old eye injury.

Both visual fields were full.

The right pupil was slightly irregular in outline, but reacted normally to light and convergence; the left pupil was small and eccentric, reacting minimally to light and on convergence.

The external ocular movements were full.

There was a mild left central facial weakness.

The remaining cranial nerves showed no abnormality.

Motor

There was a left hemiplegia with the maximal incidence in the arm. Both left limbs were hypotonic, with commencing spasticity in the elbow flexors.

In the arm weakness was profound for all movements, whereas in the leg there was only moderate weakness for all movements, more marked peripherally.

All tendon reflexes were brisker in the left arm and leg, with absent abdominal reflexes and a left extensor plantar response.

Sensation

Light touch was not perceived over the left hand and forearm.

Sensation was otherwise normal with the exception of two-point discrimination which was impaired over the fingers of the left hand at  $\frac{1}{2}$  cm. separation, but was normally appreciated at 1 cm. separation.

General examination

General examination was normal except for thickened and slightly tortuous peripheral arteries.

Blood pressure was 140/80.

Both carotid arteries were pulsating equally in the neck; there was a loud systolic bruit heard over the left carotid vessel.

INVESTIGATIONS

X-rays of skull and chest

No abnormality seen.

Cerebrospinal fluid

Pressure not recorded

Cells: 1 per c.mm.

Protein: 15 mgms.%

Lange curve: No precipitation

Wassermann reaction: Negative.

Electro-encephalogram

An alpha rhythm at 7-8 c/sec. was present and symmetrical after overbreathing. Low voltage slow waves occurred transiently over the right hemisphere. The changes recorded were slight.

Right carotid arteriogram

The right internal carotid artery was occluded at a point in the carotid syphon just proximal to the ophthalmic artery. The vessel was also narrowed at its origin in the neck. The superficial temporal artery was unduly large and the occipital arteries were tortuous and dilated and the musculo-cutaneous branches well seen. The superior cerebellar arteries were filled possibly through anastomoses with the cutaneous branches through the basilar and vertebral arteries.

Left carotid arteriogram

There was good filling of the internal carotid artery and its branches. The contrast medium filled both anterior and middle cerebral vessels. The appearances were similar to those seen in Case 23.

CASE 9 R.R. aged 56 years

OCCUPATION Civil Servant

FAMILY HISTORY

No relevant facts.

PAST HISTORY

When fourteen years old he had an attack of rheumatic fever from which he made a good recovery. One year ago he had a carbuncle on the back of his neck which disappeared under conservative treatment.

PRESENT ILLNESS

Three months prior to admission he suddenly developed difficulty in moving the fingers of his left hand; this disappeared within half-an-hour. One week later the left hand and arm became gradually useless over a period of some hours. Five weeks later the left leg became similarly weak and he had difficulty in placing it correctly on the ground. When taking his bath hot water felt lukewarm on this leg. At the same time the left arm became stiff and he had difficulty in appreciating its position in space, and the left side of his face became insensitive. He had occasional mild aching frontal headaches.

EXAMINATION

He was anxious and showed a mild degree of organic intellectual impairment.

Cranial nerves

Visual acuity was 6/12 in both eyes.

Both fundi were normal in appearance and both visual fields were full except to the extreme left periphery where there appeared to be a slight inattention when simultaneous stimuli were presented in both visual fields.

Except for a slight left central facial weakness, no other abnormality was discovered in the cranial nerves.

#### Motor

There was a left spastic hemiplegia, more marked in the arm.

He was barely able to abduct the arm at the shoulder, but was unable to extend the wrist or fingers.

In the leg all movements were moderately weak.

All the tendon reflexes in the left arm and leg were brisk with diminished left abdominal reflexes and bilateral flexor plantar responses.

#### Sensation

All forms of sensation were impaired over the left half of the body, except for vibration sense which appeared to be normally appreciated.

#### General examination

No abnormality was discovered.

The peripheral vessels were healthy and both carotid arteries pulsated equally in the neck.

Blood pressure was 150/90.

#### INVESTIGATIONS

##### X-ray of skull

No abnormality was seen.



X-ray of chest

A shadow was present in the right lower lobe which was suggestive of a neoplasm.

Electro-encephalogram

In the anterior temporal region on the right side there was a low voltage continuous 5-6 c/sec. activity. In transfrontal records it was also possible to distinguish low voltage slower waves.

The record was consistent with a local destructive lesion in the right fronto-temporal region.

Right carotid arteriogram

The external carotid artery and its branches were well filled. The internal carotid artery was blocked  $\frac{1}{2}$  cm. from its origin in the neck. The common carotid artery was then compressed above the site of the needle and the circulation of the arm occluded. Further injections of contrast medium showed retrograde filling of the common carotid and innominate arteries and both vertebrals, the basilar and both posterior cerebral arteries were well filled.

The appearances were similar to those seen in Case 6.

CASE 10 J.C. aged 49 years

OCCUPATION Housewife

FAMILY HISTORY

No relevant history.

PAST HISTORY

The patient had been subject to recurrent attacks of inflammation of the eyes for the past fifteen years; local treatment always cleared up the condition satisfactorily.

PRESENT ILLNESS

Two years before admission, when doing up her hair, her right arm became unaccountably fixed in abduction and was accompanied by pins and needles in the fingers. Within two minutes she could lower the arm, but it was weak. However, this weakness passed away within two to three hours, but the pins and needles remained unchanged.

Seven months before admission she had difficulty in selecting the correct word when speaking and since that time she had shown a variable defect of speech, which tended to worsen with each subsequent episode. Three months ago reading became difficult and about four weeks later her friends noticed that her right face had dropped, although there was no worsening of her other symptoms.

Eight days before admission she complained of being unable to read, i.e., to understand the meaning

of the words she read. Next morning she was aphasic and could only utter "Yes" or "No" and had a severe weakness of her right arm. During the last six weeks of her illness she had experienced mild bifrontal headaches each morning.

#### EXAMINATION

The speech defect was so severe that it was not possible to test the intellectual functions. She had no understanding of written speech, but appeared to appreciate some simple commands and would answer "Yes" or "No" inappropriately.

#### Cranial nerves

Visual acuity was not tested.

The right fundus was obscured by a corneal opacity.

The left fundus showed slight swelling of the nasal side of the optic disc.

The retinal vessels appeared to be healthy.

There was a well-marked right central facial weakness and the jaw tended to deviate to the right.

No other abnormality was discovered in the other cranial nerves.

#### Motor

A severe right hemiplegia was present. No movement was possible in the arm, and only feeble movements were possible at the hip and knee. Tone was slightly increased in both arm and leg.

Tendon reflexes in the right extremities were markedly exaggerated with a right-sided extensor plantar response.

The abdominal reflexes were absent.

### Sensation

This patient was a poor sensory witness but appeared to have diminished appreciation of painful stimuli over the right face, arm and leg, and possibly over the right side of the trunk.

It was impossible to test other forms of sensation.

### General examination

No abnormality was discovered, and in particular the peripheral vessels appeared to be healthy.

The right carotid artery was pulsating in the neck, the left was not felt.

Blood pressure was 135/90.

### INVESTIGATIONS

#### X-ray skull and chest

No abnormality was seen.

#### Electro-encephalogram

The right side was nearly normal with a continuous alpha rhythm at 8-9 c/sec. blocked by visual attention, together with some slower low voltage activity.

Over the left side there were continuous 2-7 c/sec. waves of medium voltage and occasional rather sharp waves in the fronto-Sylvian region spreading from there to the whole cortex on the left side. The record showed the presence of an organic lesion in the fronto-Sylvian region which was extensive and involved the cortex.

Left carotid arteriogram

A low puncture in the neck showed complete occlusion of the common carotid artery at the level of the sixth cranial vertebra. The common carotid had a small lumen and appeared hypoplastic. The contrast medium flowed backwards towards the arch of the aorta.



CASE 11 C.P. aged 60 years

OCCUPATION Editor weekly newspaper

FAMILY HISTORY

Nothing relevant.

PAST HISTORY

1914 - appendicectomy

1938 - sinusitis

1948 - shingles

There was a history of questionable glycosuria twenty-five years ago which led to the avoidance of sugar and sweets. Otherwise he had been quite well.

PRESENT ILLNESS

One month before admission he complained of difficulty in manipulating his cuff-links with his right hand. By next day this disability had disappeared.

A week later he again complained that the right hand was "not quite right", and next day he had difficulty in holding a pen; this too disappeared after several hours, although his wife noted the right side of his face twitched intermittently during the course of that evening.

The following day he was unable to use his right hand properly and from then until the time of his admission to hospital he had numerous attacks of tingling and pins and needles in the ulnar border of his forearm and in the third, fourth and fifth fingers of the right hand. Such attacks lasted a few minutes at a time and recurred several times daily.

Occasionally these were accompanied by a similar tingling in the tongue and by twitching of the muscles of the right side of his face.

Five days before admission he was "unable to get his words out" although he could understand what was said to him perfectly. On the day before admission he had an attack of pins and needles in the right face, together with numbness of the right hand.

#### EXAMINATION

He showed a slurred dysarthria and spoke in short unfinished sentences but with correct syntax and grammar.

There was some comprehensional difficulty of spoken speech, but he could understand simple words when written and could read slowly but fairly well.

#### Cranial nerves

Visual acuity 6/12 on the right, 6/18 on the left.

The visual fields were full and the optic discs normal, but the retinal arteries were narrowed.

Apart from a well-marked right central facial weakness with preservation of emotional movements, the rest of the cranial nerves were normal.

#### Motor

There was a moderate weakness of the right arm which was more marked peripherally; tone was slightly decreased.

Both legs were normal.

Tendon reflexes were slightly increased in the right

arm but were normal in the legs with bilateral flexor plantar responses.

Sensation

No abnormality was discovered.

General examination

The peripheral arteries were hard and tense, but both carotid arteries were pulsating equally in the neck.

Blood pressure was 220/140.

INVESTIGATIONS

Blood coagulation time: 7 minutes 30 seconds (Normal)

Fasting blood sugar: 115 mgms.%

Blood urea: 27 mgms.%

X-ray of chest.

No abnormality seen.

X-ray of skull.

There were a few ill-defined flecks of calcification seen in the plane of the pituitary fossa which could be in the carotid syphon, but they could not be identified in the antero-posterior views.

Cerebrospinal fluid

Pressure 130 mm. with a free rise and fall on jugular compression.

Cells: 1 lymphocyte per c.mm.

Protein: 75 mgms.%

Lange curve: 0001121100

Wassermann reaction: negative.



Electro-encephalogram.

The alpha rhythm of 8-10 c/sec. was better distributed on the right side than the left. There was a continuous irregular slow wave activity of medium or high voltage whose distribution and phase relationships indicated a focus low in the left temporal region, slightly posterior to the centre of the lobe. The record was compatible with a cerebral thrombosis.

Left carotid arteriogram.

An irregular filling defect was seen on the posterior wall of the internal carotid artery extending from the bifurcation upwards for  $1\frac{1}{2}$  cms. The circulation was slowed but both anterior and middle cerebral arteries were filled. Unfortunately the blood in the needle lumen clotted, and repuncture was necessary. A further injection was made and on this occasion the appearances were similar, but the anterior cerebral artery failed to fill.

PROGRESS

Within a few hours of arteriography he was barely conscious, and had a right hemiplegia with many short-lived motor focal fits affecting the left leg.

Within three days he developed signs of a tentorial pressure cone and died.



POST MORTEM EXAMINATION

Heart. Both ventricles were dilated and the left one slightly hypertrophied. The coronary vessels were atheromatous.

The aorta was healthy in its thoracic part, but was atheromatous throughout its abdominal extent.

The other main arteries in the body appeared healthy with the exception of the carotid arteries. At the commencement of the left internal carotid artery there was a large, partly calcified, atheromatous plaque which extended upwards for 7 mms. It had caused considerable narrowing of the lumen which at this level was completely occluded by recent ante mortem thrombus. This was continued upwards for 15 mms. as a loosely attached tongue of tissue (Fig. 1). Above this area the artery appeared healthy, but in both carotid arteries the intracavernous part of each vessel was slightly atheromatous and the short intradural part of each was concentrically narrowed by atherosclerosis. The right internal carotid artery at its commencement was healthy.

To the inner surface of the arteriographic puncture wound in the left common carotid artery a small clot of fibrin was attached.

The circle of Willis was complete. A large patch of yellowish atheroma lay in the internal carotid artery where it bifurcated into the anterior and middle



Fig. 1.

cerebral arteries. Fluid blood could be squeezed past this obstruction into the anterior and middle cerebral arteries.

Histologically the left internal carotid artery at its commencement was almost completely occluded by thickening of the intima by fibrous tissue scattered throughout which were areas containing

abundant calcium and cholesterol deposits (Fig. 2). Many foreign body giant cells surrounded these deposits, and throughout the tissue generally were numerous small round cells. The media and adventitia of the vessel appeared to be relatively healthy.



Fig. 2. LP view obstructed carotid artery.

The left cerebral hemisphere was swollen and the cortex around the lateral fissure was slightly blood-stained. There were scattered infarcts of varying ages intermingled in its substance. In the mid-frontal region nearly all the infarction in the cortex and subjacent white matter was recent. In its middle part the infarction extended as far down as and involved the corpus striatum. Above this area

the cortex was pale and ill-defined and small cysts were present in the white matter. This older type of infarction extended backwards to involve the pre-central gyrus.

There were also very recent areas of haemorrhagic infarction in the cortex of the posterior end of the frontal lobe in its lower part, in the mid-part of the post-central gyrus and around the insular region. Smaller foci of about the same age lay deep in the superior temporal sulcus. The left caudate, putamen and globus pallidus showed extensive haemorrhagic infarction which spared those areas supplied by the anterior choroidal and anterior cerebral arteries (Fig. 3).

In the upper part of the middle cerebral arterial supply were older infarcts lying in the posterior part of the superior frontal convolution, the precentral gyrus, the supramarginal gyrus and the lower part of the occipital convexity. In these areas the destruction of brain tissue varied, but on the whole there was a complete dissolution of nervous elements with infiltration of these areas by fat filled phagocytes. These lesions were bounded by glial scarring and vacuolation of the white matter. In one area there was an old ischaemic infarct with complete breakdown of cerebral tissue, and in a nearby sulcus lay a small arteriole whose lumen was obstructed by cellular and cholesterol crystals (Figs. 4 and 5).

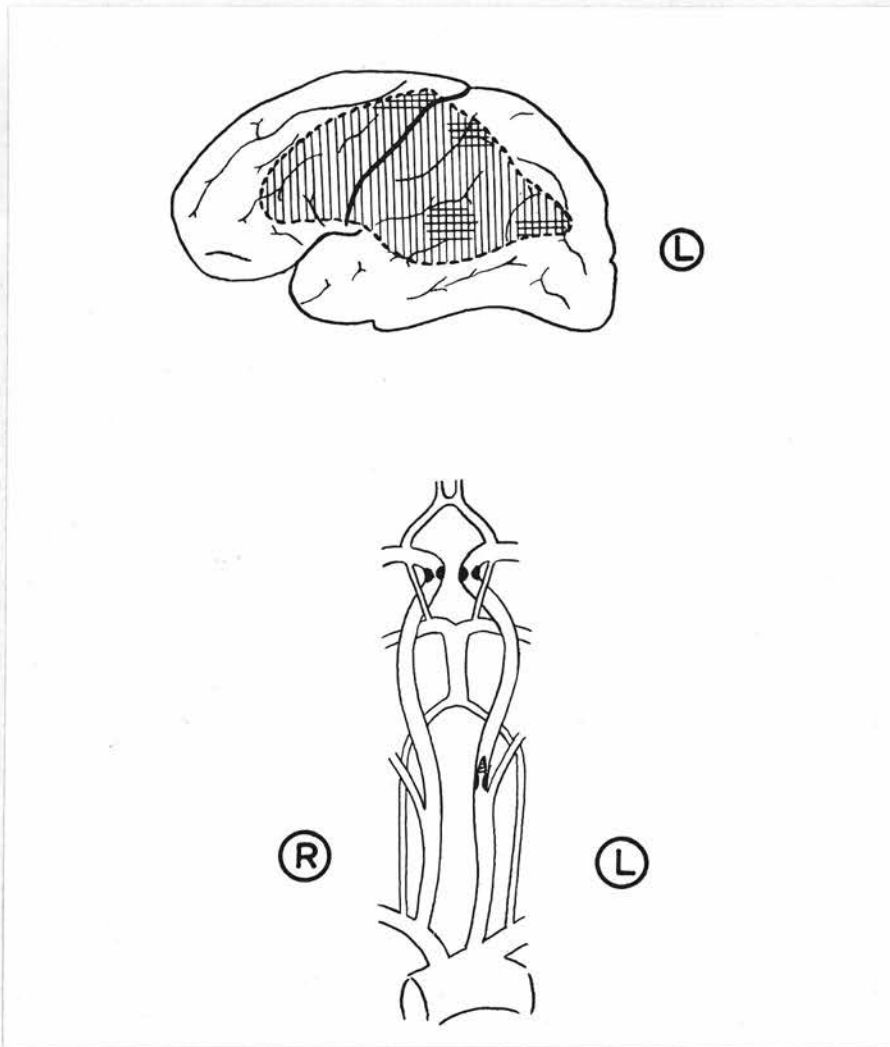


Fig. 3. Diagram of extent of thrombus and cerebral infarction.

■ Atheroma

≡ Thrombus

At the junction of the middle and posterior parts of the middle cerebral arterial supply lay areas of recent infarction (Fig. 6), containing regions of perivascular haemorrhages which were surrounded by

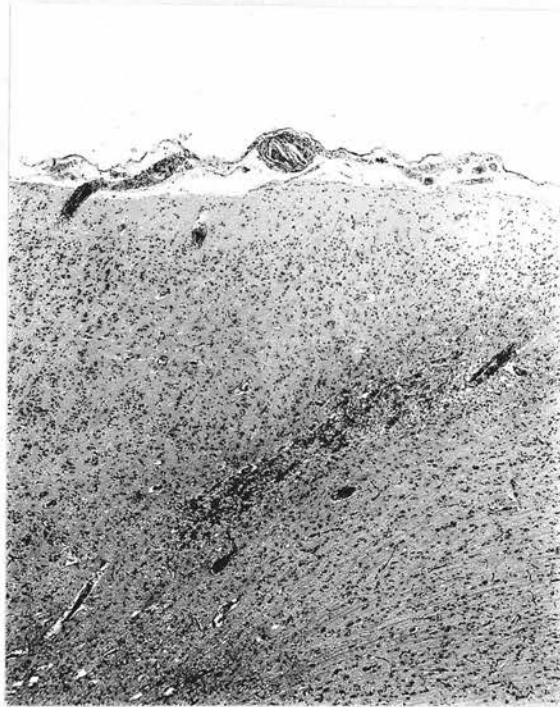


Fig. 4. LP view cortical vessel containing cholesterol clefts.

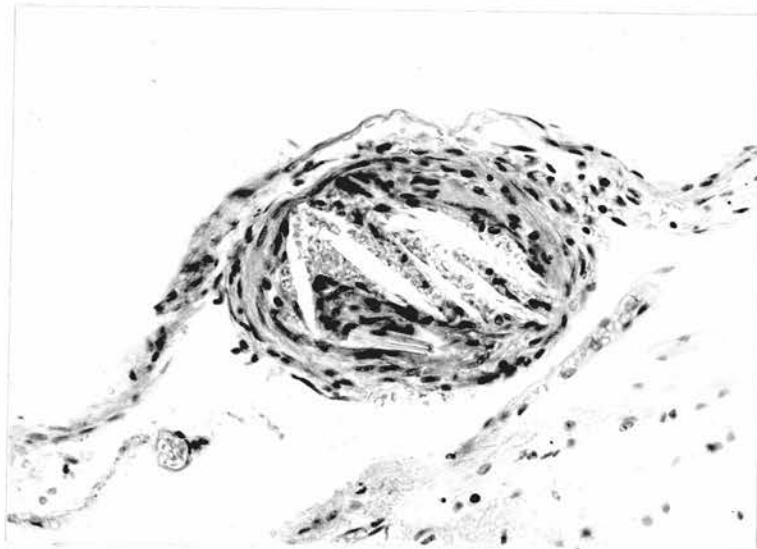


Fig. 5. HP view of same artery.



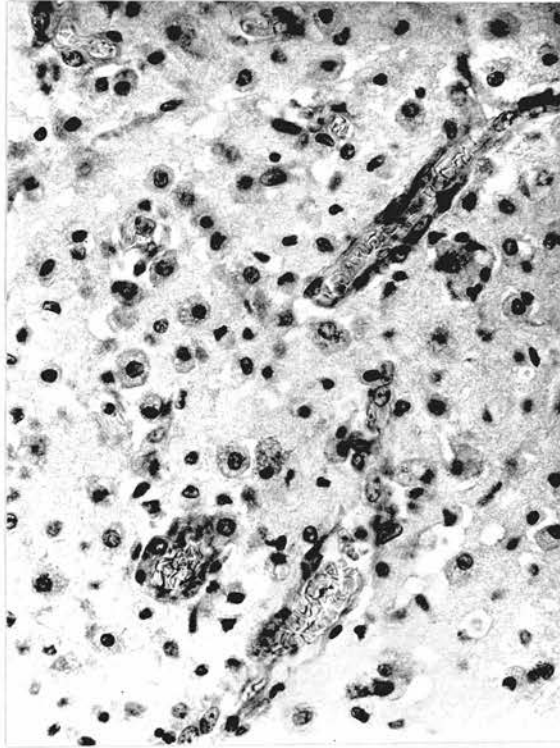


Fig. 6

polymorph leucocytes which had emigrated from the dilated capillaries (Fig. 7).

Many of the adjacent vessels contained organising thrombi within their lumina (Fig. 8). These were intermingled with areas of infarction of longer duration containing irregularly outlined nerve cells with shrunken nuclei and pale cytoplasm; astrocytic nuclei were also present together with fat filled phagocytes. A vessel in a nearby sulcus contained well organised and recanalised clot. Lying within a large branch of the middle cerebral artery near the mid-part of the hemisphere lay a coiled up embolus (Fig. 9).

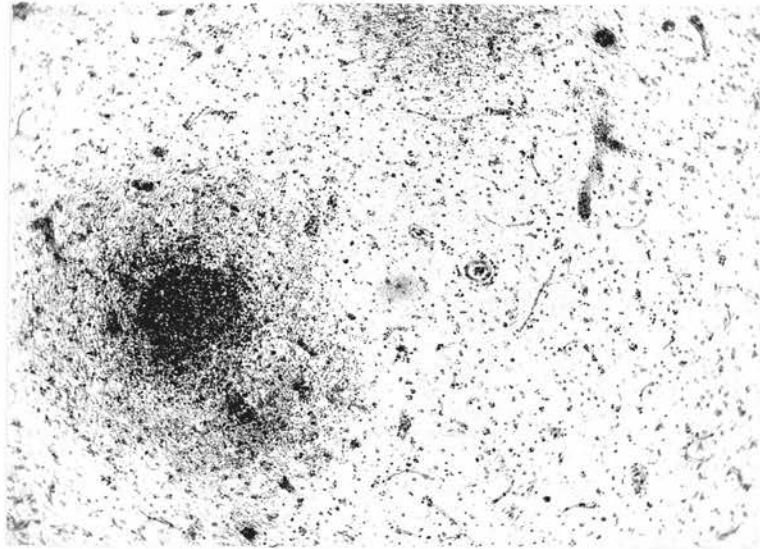


Fig. 7.

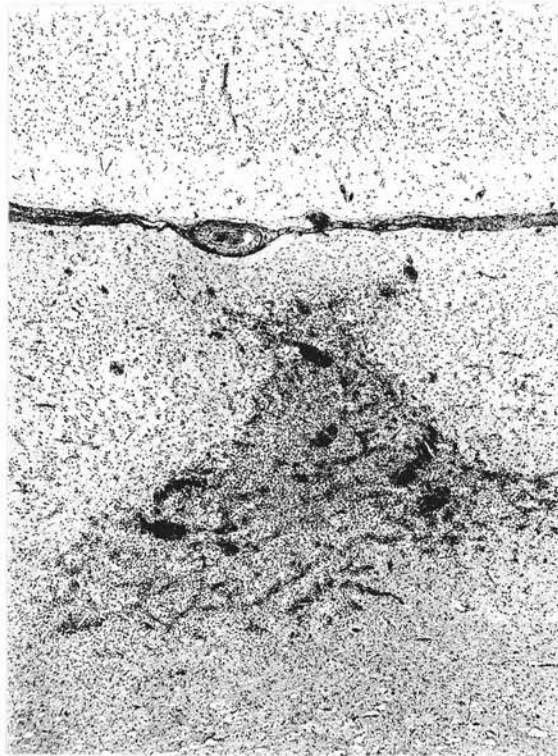


Fig. 8. LP view of small vessel containing organising thrombus with an area of recent haemorrhagic infarction.

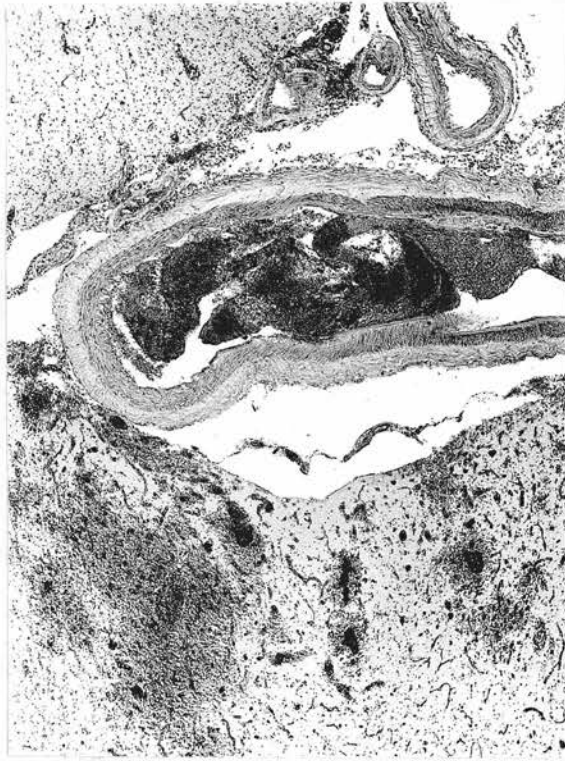


Fig. 9

CASE 12    W.B. aged 58 years

OCCUPATION    King's Counsel

FAMILY HISTORY

No relevant history.

PAST HISTORY

In 1931 he had a pulmonary infarct.

Some years ago he had an attack of jaundice from which he made a good recovery.

PRESENT ILLNESS

Two years before admission, when picking fruit, he suddenly lost consciousness and slumped on to the ground. For the next week he remained in coma and on recovering consciousness was found to have a left hemiplegia and hemianopia. At first his speech was dysarthric but this gradually cleared up, as did much of the lost function of his left extremities. However, he had painful cramps in the affected limbs from time to time.

During the past six months he had several generalised convulsive seizures, the abnormal movements being more marked in the left arm and leg.

EXAMINATION

The intellectual functions were normal.

Cranial nerves

Visual acuity was 6/9 in both eyes.

The optic discs were normal, but the vessels in both fundi showed arteriosclerotic changes. There was a left congruous homonymous hemianopia.

Apart from a left central facial weakness, and some loss of power in the left sternomastoid and trapezius muscles, as part of his left hemiplegia, the rest of the cranial nerves were normal.

#### Motor

There was a severe spastic left hemiplegia more marked in the arm than the leg. All the tendon reflexes in the left extremities were brisk with a left extensor plantar response.

#### Sensation

There was a left hemihypalgesia and hemianaesthesia including the face. Sense of passive movement was impaired in all the left fingers and two-point discrimination faulty over these finger pads.

#### General examination

No abnormality was discovered, with the exception of thickened peripheral vessels. The carotid arteries were pulsating equally in the neck.

Blood pressure was 110/65.

#### INVESTIGATIONS

##### X-ray of skull

Apart from loss of translucency of the left antrum, no other abnormality was seen.

##### Electro-encephalogram

The records showed an asymmetry consisting of smoothing out of normal activity and reduction of wave amplitude on the right side; there were some moderate slow voltage

waves at 4-6 c/sec. in the same area. After over-breathing ceased there was a suggestion of slow waves occurring as sharp pointed transients over the right side.

Right carotid arteriogram

The films showed complete occlusion of the internal carotid artery at its origin. The external carotid and its branches were well filled.

The appearances were similar to those seen in Case 19.

CASE 13 A.H. aged 40 years

OCCUPATION Lieutenant Commander, Royal Navy.

FAMILY HISTORY

Not known.

PAST HISTORY

Sinusitis - no other details available.

PRESENT ILLNESS

During the past few months he had tended to become more irritable and to get his words mixed up. Three weeks prior to admission to hospital he suddenly experienced double vision on looking to his right side. This diplopia lasted for ten minutes, then disappeared. Two days later, when sitting in a chair, his right hand suddenly became numb and useless, and on attempting to stand up he fell to the ground as his right leg was so weak. Within a minute or two he lost consciousness and remained in this state for an unknown period, but probably no longer than one or two hours. On regaining consciousness full power had returned to his right limbs but he had some difficulty in writing and in speaking.

Over the next ten days he experienced recurrent episodes of mild dysphasia and right-sided hemiparesis lasting a quarter-of-an-hour at a time; in the intervals between each attack he remained well.

Twelve days after the onset of this illness he had a severe attack resulting in total aphasia and right-sided hemiplegia.

### EXAMINATION

He was aphasic and could only say "Yes".  
Comprehension of speech was probably impaired as he could only carry out simple commands, but not those of a more complex variety. No apraxia was demonstrated.

Intellectual testing was impossible to carry out.

### Cranial nerves

Visual acuity was probably normal as judged by his ability to see and pick up small objects.  
Both optic discs showed blurring of their nasal margins with slight swelling of the veins.

The visual fields were full to confrontation testing.

The right pupil was larger than the left, but both reacted equally and adequately to light and on convergence

No other abnormality was discovered in the cranial nerves.

### Motor

There was a right-sided hemiplegia.

The right arm was completely powerless, but in the leg feeble movement was present at the hip and knee.

Tone was increased in the right arm and leg.

Tendon reflexes were increased in the right extremities; the right abdominal reflexes were absent with a right-sided extensor plantar response.

### Sensation

As far as could be judged sensation was normal throughout, with the exception of the sense of passive movement which appeared to be impaired in the right fingers.



General examination

No abnormality was detected and in particular both carotid arteries were pulsating equally in the neck.

Blood pressure was 120/80.

INVESTIGATIONS

X-ray of skull

No abnormality seen.

Electro-encephalogram

The only alpha rhythm was of small voltage confined to the right occipital region. In the left occipital area there was a considerable amount of rhythmic activity slower than the alpha rhythm and blocking to visual attention. This rhythmic activity of the left hemisphere was widespread and also occurred in the frontal region. High voltage very irregular slow waves at less than 1 c/sec. occurred over the left hemisphere over a wide area, but tended to leave the left temporal region as an equipotential area.

Left carotid arteriogram

There was a complete block of the internal carotid artery 1 cm. above its origin in the neck. The external carotid, ophthalmic and anterior choroidal vessels were well filled.

Right carotid arteriogram

There was good filling of the right and left anterior cerebral arteries, but none of the left middle cerebral artery.

Blood count

Red blood cells	5.46 million per c.mm.
Haemoglobin	110%
White blood cells	8,400 per c.mm.
Polymorphs	70%
Lymphocytes	29%
Eosinophils	1%

CASE 14 S.F. aged 41 years

OCCUPATION Housewife

FAMILY HISTORY

No relevant history.

PAST HISTORY

Fourteen years ago she was found to be suffering from a well compensated rheumatic heart disease, and during the ensuing years had suffered three embolic accidents, none of which involved the central nervous system. Five years ago subtotal thyroidectomy was carried out.

PRESENT ILLNESS

Twenty-four hours before admission to hospital she suddenly got up from her chair and said, "Oh, no". Her husband saw that her face was pulled over to the left side. Within a quarter of an hour her right arm was paralysed and she became rather drowsy and vomited occasionally. A few hours before admission her right face, arm and leg were completely useless and she could barely utter an occasional "No", although she was able to recognise her relatives.

EXAMINATION

She was mildly drowsy, but could be roused to carry out simple commands correctly. There was a profound expressive dysphasia, although she appeared to understand everything that was said to her quite well.

Cranial nerves

Visual acuity was not tested.

Both optic discs and retinae were normal.

There was a right congruous hemianopia, and a moderate right central facial weakness.

The right trapezius was weak as part of the profound right hemiplegia.

The tongue was protruded to the right side.

Motor

There was a complete flaccid paralysis of the right limbs.

The tendon reflexes were increased on the right side with an extensor plantar response; the abdominal reflexes were absent.

Sensation

No form of sensation was appreciated over the right side of the body or extremities or face.

General examination

No abnormality was detected apart from the cardiovascular system.

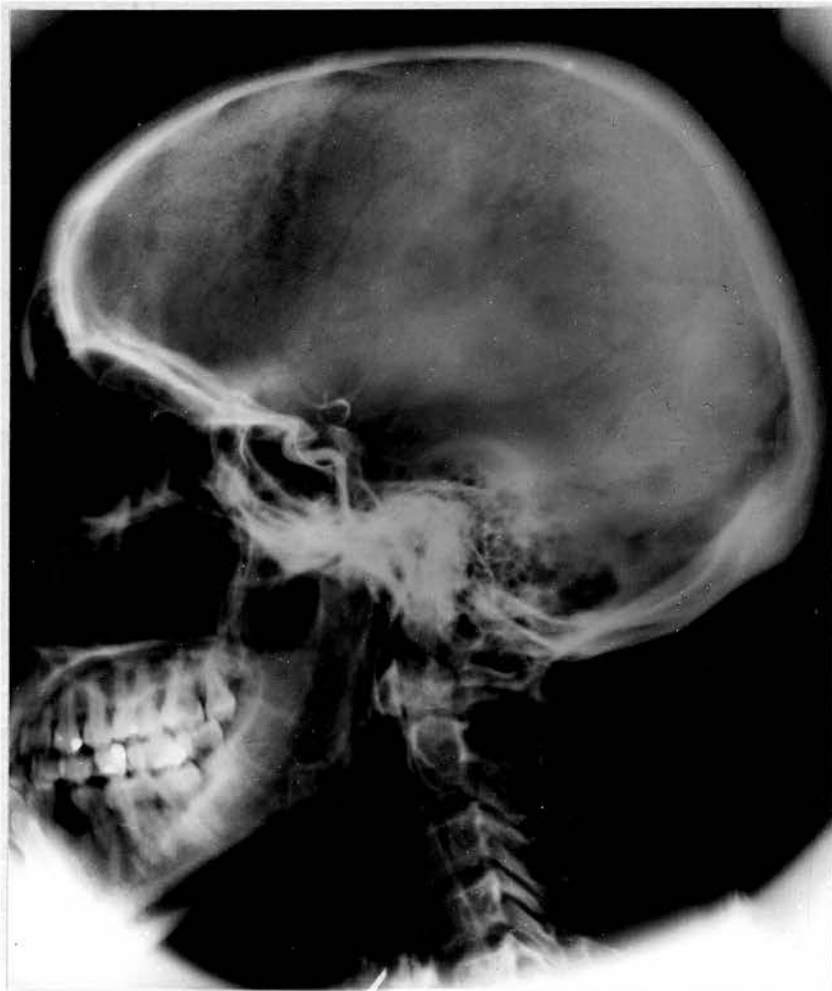
The pulse was irregular in time and force (auricular fibrillation) but the vessel wall was healthy.

Blood pressure was 125/80.

The heart was not enlarged: internal to the apex there was a low pitched diastolic murmur succeeding the first sound.

INVESTIGATIONSLeft carotid arteriogram

Good filling of the external carotid artery and branches was obtained. The internal carotid artery was visualised to the syphon. A small amount of contrast was seen in the left anterior cerebral artery and a few fine branches of the left Sylvian vessels. Contrast was still present in the internal carotid artery six seconds after the injection of contrast medium. The appearances were consistent with a partial occlusion of the internal carotid artery in the region of the carotid bifurcation with an almost complete obstruction of the two main branches of this vessel.



CASE 15 E.B. aged 73 years

OCCUPATION Housewife

FAMILY HISTORY

Her son aged fifty years had suffered a coronary artery occlusion one year before; he made a good recovery.

PAST HISTORY

She had suffered from headaches for the past forty-six years. Thirteen years ago she developed intermittent attacks of pain in her chest and throat and was told that her "arteries were hardened". After taking trinitrin tablets she had no further pain, although from time to time she was subject to palipitations.

For the past seven to ten years her right index finger had tended to become white whenever the hand was immersed in cold water.

PRESENT ILLNESS

For several years her right foot had tended to move in an abnormal fashion when she was knitting. After an operation for rectal prolapse seven months before admission to hospital, she could hardly walk on account of the violence of these movements. However, after several weeks they gradually improved, but became worse again one month before admission, when the right arm became similarly involved. She had a constant dull pain "like a bruise" in her right

shoulder, arm, hand, and to a lesser extent in the leg, for the past month.

For the past five weeks she had experienced occasional difficulty in finding her words, together with slight numbness of the right hand.

Her memory for names had been impaired in recent months.

#### EXAMINATION

A pleasant old lady with a mild defect of memory compatible with her age.

There was no evidence of dysphasia.

#### Cranial nerves

Visual acuity was J 16 in both eyes.

The visual fields were full.

Both eyes showed moderately advanced cataract with normal optic discs, but some "silver wiring" of the retinal arteries.

There were a few beats of nystagmus on looking upwards and to the left.

The rest of the cranial nerves showed no abnormality.

#### Motor

No abnormality detected, apart from moderate hemiballistic movements of the right arm and leg.

Tendon reflexes in the arms were present and equal; the right knee jerk was slightly brisker than the left, but both ankle jerks were equal, with bilateral flexor plantar responses.

Sensation

Sensation was normal throughout with the exception of the sense of passive movement which was slightly impaired in the toes on both sides, and vibration sense which was slightly decreased at both ankles.

General examination

There was a naevus flammeus over the posterior aspect of the right upper arm.

All the peripheral vessels were tortuous and thickened, with a blood pressure of 210/98.

The heart was slightly enlarged, but there were no signs of cardiac failure.

INVESTIGATIONSX-ray of skull.

A small patch of calcification was seen overlying the pituitary fossa in the lateral views, but was not visible in the antero-posterior films.

Electro-encephalogram

The patient would not relax and much of the record was obscured by muscle action potentials. When the record was seen without interference it was of low voltage, but showed traces of alpha rhythm and possibly some slower waves. The record was symmetrical.

PROGRESS

Eighteen days after admission she suddenly developed a right hemiplegia with abolition of the hemiballistic movements, together with a profound



dysphasia limiting her utterances to "yes" and "no".  
Understanding of spoken speech was imperfect. Her  
condition deteriorated and four days later she became  
unconscious with fixed dilated pupils and died later  
the same day.

POST MORTEM EXAMINATION

Heart. The left ventricle was hypertrophied and the myocardium firm, with occasional fibrous scars showing in its substance.

Both coronary vessels were tortuous and atheromatous.

The aorta showed well-marked atheroma in its abdominal part with slight saccular aneurysmal formation.

The kidneys were of normal size and the capsules stripped easily, leaving a granular surface; on section the surfaces were deeply congested and the small vessels were slightly prominent.

In the neck the right internal carotid artery was slightly atheromatous at its commencement. The left internal carotid artery showed atheromatous thickening at its point of origin. Partly organised blood clot filled the lumen almost as high as the commencement of the ophthalmic artery which was free from clot (Fig. 1).

Histology. The left internal carotid artery below the syphon was almost completely occluded by very recent and old organised recanalised thrombus. The intima was markedly thickened and deposited in it were numerous areas of calcification around which were foreign body giant cells together with some small round cells. The internal elastic lamina was reduplicated. The lumen of the left carotid syphon



Fig. 1. Clot in the commencement of the internal carotid artery.

was chiefly obstructed by old organised thrombus but in a small area recent thrombus was seen.

Brain. The basal vessels were all markedly atheromatous. The circle of Willis was symmetrical.

The brain showed a moderately diffuse fronto-parietal gyral atrophy. The medial aspect of the left frontal lobe in the middle part of the cortex showed haemorrhagic infarction, and some haemorrhagic stippling was present in the cortex of the insula (Fig. 2). The corpora Luysii and basal ganglia appeared healthy.

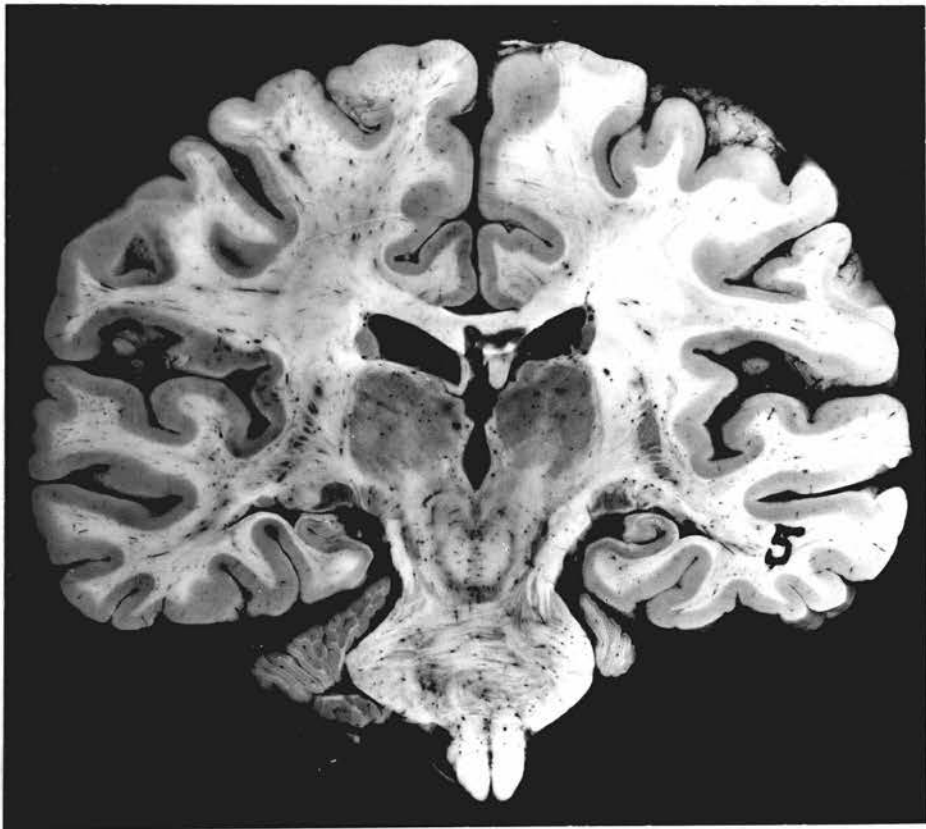


Fig. 2.

There was a small 2 mm. zone of reddish discolouration in the internal capsule lateral to the thalamus on the left side.

Histologically gross atheroma affected the larger branches of the posterior cerebral artery. In one area the lumen of a large branch of the middle cerebral artery showed eccentric narrowing by subintimal fibrous tissue in which were enmeshed a few round cells. It was uncertain whether this represented gross atheroma or an old organised thrombus. No recent thrombus was seen in any of the arteries examined. In the left hemisphere the changes were mainly confined to the cortical and subcortical regions. The overlying meninges were infiltrated with numerous round cells together with polymorphs and a few compound granular corpuscles. Within the distribution of the anterior cerebral artery in the medial superior frontal gyrus there was an area of very recent haemorrhagic infarction with necrosis of all the tissues and polymorph infiltration. The pial arteries were thickened and showed adventitial fibrosis. Several small foci of older ischaemic degeneration of the cortex were seen bordering on the superior frontal gyrus and underlying white matter. In the superior part of the precentral cortex there were numerous scattered foci of cortical and white matter necrosis, some recent and some older with breakdown of tissue and fat filled

phagocytes. The capillary endothelium in these areas was hyperplastic. The remaining cortex in the distribution of the middle cerebral artery showed ischaemic changes mainly in layers 2 and 3 where the neurones were shrunken.

No significant abnormality was seen in the basal ganglia, thalami or corpus Luysii. The right cerebral hemisphere was healthy apart from slight subpial astrocytic gliosis.

These changes were compatible with old peri-arteriolar necrosis of the cortex and white matter in the areas supplied by the more peripheral parts of the middle cerebral artery supply, with more recent infarction in the rest of the middle cerebral and anterior cerebral artery distribution.

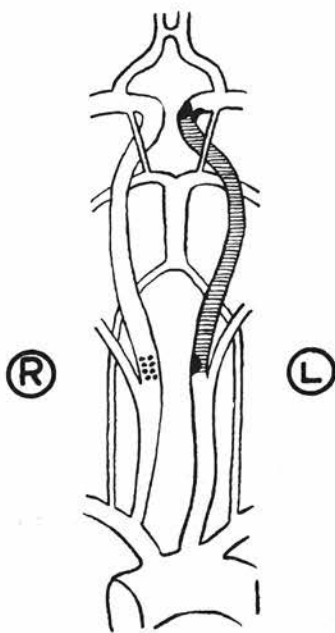
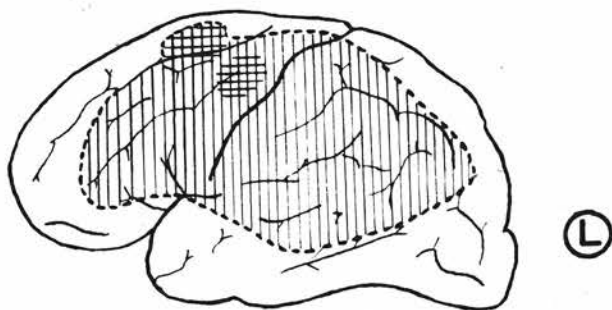


Diagram of carotid artery  
obstruction and area of  
cerebral infarction

■ Atheroma

▨ Thrombus

CASE 16 S.H. aged 62 years

OCCUPATION Retired

FAMILY HISTORY. Nothing of note.

PAST HISTORY

Six years ago following a severe tonsillitis he was found to have a "cancer of the throat" which responded well to local radium treatment; there had been no recurrence.

PRESENT ILLNESS

Two years before admission to hospital he suddenly lost consciousness and recovered after several minutes to find himself flat on his face and unable to move the left arm or leg. Thereafter he made a gradual but incomplete recovery, so that at the end of one year he could walk around unaided, but had little use in his left arm. During this year he had a phantom left arm "like a talon" attached to his shoulder.

Three weeks before admission his left leg suddenly went into spasm and he fell to the ground without losing consciousness. Since then his leg has remained useless and his memory poor.

EXAMINATION

The patient was tense, demanding and critical, as well as being vague and evasive. There was no other evidence of organic intellectual deterioration.



Cranial nerves

Visual acuity was 6/6 in both eyes.

The fields were full and both fundi normal in appearance.

The right pupil was slightly larger than the left, but both reacted adequately to light and on convergence.

Except for a slight left central facial weakness no abnormality was found in the cranial nerves.

Motor

There was a left spastic hemiparesis: little movement was possible in the left arm, but in the leg slight flexion was possible at the knee, with moderately good power at the hip.

The tendon reflexes were increased in the left extremities with a left-sided extensor plantar response.

Sensation

A left hemihypalgesia and hypaesthesia more marked over the limbs than the trunk was present.

General examination

No abnormality was discovered, and in particular the peripheral vessels appeared healthy and both carotid arteries were pulsating equally in the neck.

Blood pressure was 150/90.

PROGRESS

Shortly after admission this patient developed bronchopneumonia and died within six days of the onset.

POST MORTEM EXAMINATION

Both lungs showed patchy bronchopneumonia.

The heart was enlarged and flabby and ante mortem thrombus was present in the right auricle. Both coronary vessels were atheromatous and calcified. In the posterior wall of the left ventricle and interventricular septum was an area of recent infarction.

Both carotid arteries showed ring calcification and atheroma at their bifurcations, resulting in gross narrowing of the lumen of both vessels. The right internal carotid was extremely atheromatous and about one inch above the bifurcation a large yellow plaque almost obliterated the lumen. Below this there was recent red thrombus extending downwards for half an inch into the common carotid artery (Fig. 1).

Histologically the right internal carotid artery near its commencement showed almost complete occlusion by fibrous tissue and organised thrombus which in some areas had become recanalised by numerous fine channels. Lying within progressively more organised thrombus were deposits of calcium and cholesterol with related foreign body giant cells and round celled infiltration. The internal elastic lamina was crenated, reduplicated and in some areas thinned. The media and adventitia appeared to be healthy.

Both vertebral arteries were fairly healthy, although the right one showed slight atheromatous change.

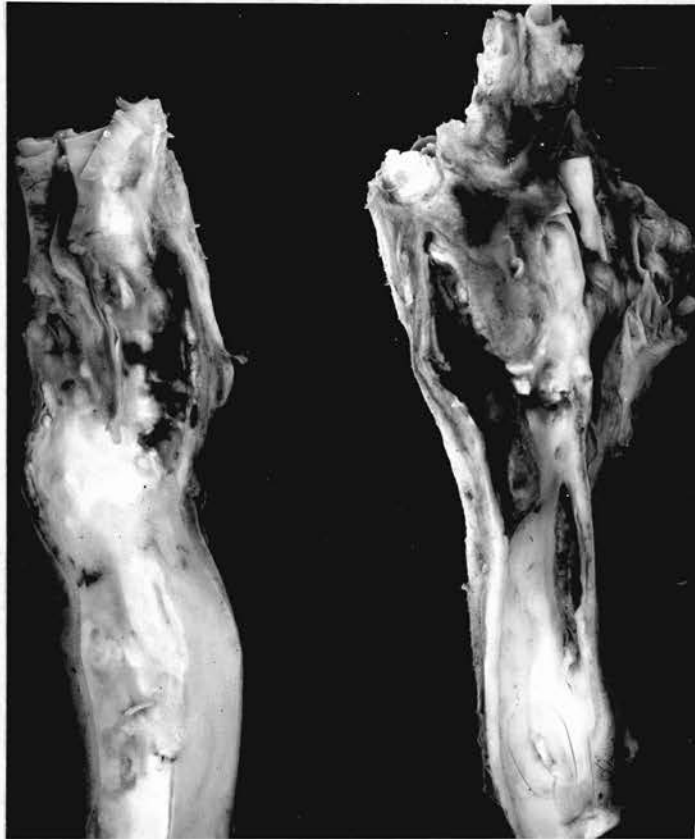


Fig. 1. Thrombus in the lumen of the internal carotid artery near its commencement.

The basal vessels were atheromatous and on the right side at the commencement of the intracranial portion of the internal carotid artery there was old thrombus which almost occluded the lumen.

The right middle cerebral artery, although atheromatous, did not appear to be blocked. Recent ante mortem thrombus was present in the right anterior cerebral artery at the splenium of the corpus callosum.

Externally the right hemisphere showed depression and yellowish colouration over much of the parietal and occipital cortex. There was an extensive



There was also destruction of the upper half of the corpus striatum and the lateral two-thirds of the putamen. Much of the infarct was cystic and pale (Fig. 3), and medially approached the ventricular wall. There was a small area of cortical necrosis on the medial aspect of the upper part of the parietal lobe posterior to the paracentral lobule. Both lateral ventricles were dilated.

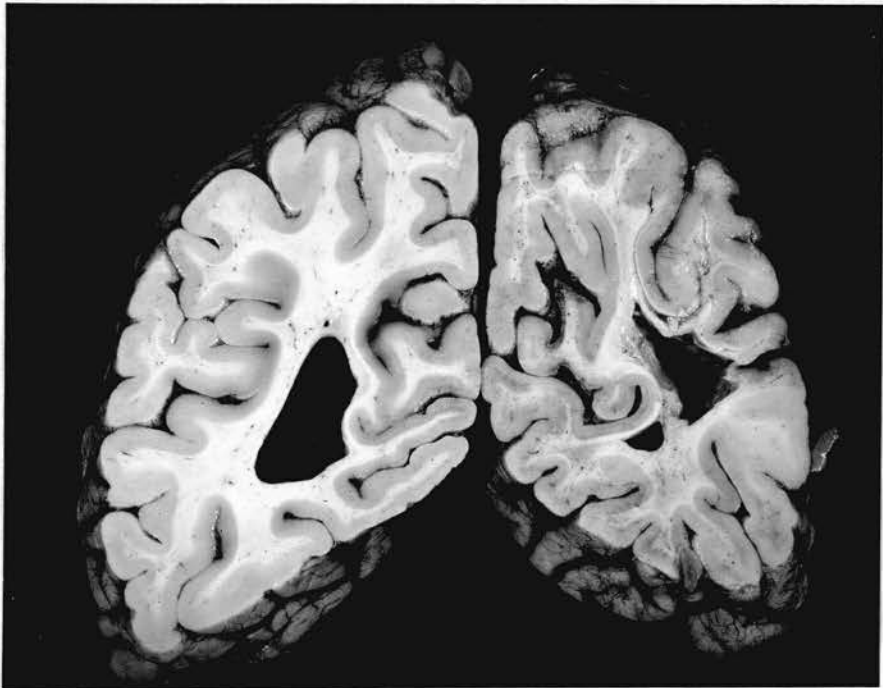


Fig. 3. Old infarct of left cerebral hemisphere.

Histologically the right hemisphere presented infarcts of differing ages which were mostly situated in the cortex and subjacent white matter.

In the superior frontal convolution in the distribution of the anterior cerebral artery there was an area of recent infarction with destruction of neurones and glia together with perivascular haemorrhage and polymorph infiltration.

Around the second frontal and pre-central gyri were small areas of ischaemic necrosis mixed up with smaller infarcts of varying ages frequently laden with fat filled phagocytes. In the underlying white matter a few small isolated infarcts were seen. Several older foci of ischaemic degeneration were present in the cortex bordering on the superior frontal sulcus and underlying white matter, i.e., in the more peripheral parts of the middle cerebral artery territory.

The remaining part of the cortex supplied by the middle cerebral artery showed ischaemic cell damage which was most apparent in the insula and pre-central cortex.

The basal ganglia, thalamus and corpus Luysii appeared healthy.

The smaller vessels throughout the right hemisphere showed arteriolar thickening with some adventitial fibrosis. The larger cerebral blood vessels presented changes consistent with atheroma.

However, in a few of the smaller branches of the middle cerebral artery the lumen was narrowed by marked subintimal eccentric fibrosis. It was difficult to say whether this appearance was due to atheromatous degeneration or an old organised thrombus, but in all probability it represented the latter, as these vessels were not usually of a type affected by atherosclerosis.

The left cerebral hemisphere appeared to be healthy with the exception of mild subpial astrocytic gliosis.

CASE 17 J. O'B. aged 37 years

OCCUPATION Gardener

FAMILY HISTORY

Nothing of note.

PAST HISTORY

About ten years ago he was concussed for a short time, but made an excellent recovery. Six years before he suffered a "nervous breakdown" but after several weeks' treatment at home he regained his usual health and had remained well until the start of this present illness.

PRESENT ILLNESS

Three months before admission to hospital he suddenly developed weakness of the right side of his face together with some indistinctness of speech. Within a few hours this speech defect had become a well-marked nominal dysphasia. The facial weakness cleared in a few days, but his speech defect took a little longer to recover.

One week later he had "an attack" in which his eyes wandered from side to side together with some expressive dysphasia and severe weakness of the right arm and leg. There was no loss of senses and within a few hours he was able to stand upright, although the right limbs remained weak.

At this juncture he was admitted to another hospital where a ventriculogram was carried out, on the



suspicion that he was harbouring a cerebral tumour. The films showed a moderate degree of cortical atrophy but no evidence of any space occupying lesion.

One week after this investigation he suddenly developed pain in the right arm and leg which thereafter remained virtually useless. The right side of his face was also weak, but his speech remained unchanged.

After three days some power had returned to the right limbs, so that he could walk around in a halting fashion. He then noted that he was unable to read as his vision was blurred. Although he had difficulty in expressing his thoughts in words, he could understand everything that was said to him.

#### EXAMINATION

There was no evidence of any gross intellectual deficit. He showed a well-marked expressive dysphasia, although understanding of spoken speech was unimpaired. A mild degree of dyslexia was present with acalculia, slight right-left confusion, and slight finger agnosia.

#### Cranial nerves

Visual acuity was 6/9 in both eyes.

Both optic discs and retinae appeared normal.

There was a right inattention field defect to simultaneous stimuli presented in both visual fields.

Apart from a right central facial weakness no other abnormality was discovered in the cranial nerves.

#### Motor

There was a moderate right spastic hemiparesis involving the arm more than the leg.

He was able to walk about unaided, but the right arm was weak and clumsy and useful only in gross movements. Tendon reflexes in the right arm and leg were exaggerated with a right-sided extensor plantar response; the right abdominal reflexes were depressed.

#### Sensation

Light touch was not appreciated over the right arm. The sense of passive movement and two-point discrimination was impaired in the right fingers. Elsewhere sensation appeared to be unimpaired.

#### General examination

No abnormality was found, and in particular the peripheral vessels were healthy and both carotid arteries were pulsating equally in the neck. Blood pressure was 145/90.

#### INVESTIGATIONS

##### X-ray of skull

No abnormality was seen except for biparietal burrholes.

##### Electro-encephalogram

Little normal activity of low voltage was seen in the record. On the left side, reaching a maximum in the low frontal and fronto-temporal region, there was irregular moderate to low voltage slow activity from 1-5 c/sec., the asymmetry being increased slightly by overbreathing.

The record was consistent with an expanding or other destructive lesion in the frontal lobe.

Left carotid arteriogram

The internal carotid artery was completely blocked 1 cm. from its origin in the neck. The external carotid artery and its branches were well filled.

The appearances were similar to those seen in Case 6.

CASE 18 L.C. aged 46 years

FAMILY HISTORY

His father suffered from diabetes in later life.

PAST HISTORY

The patient had always enjoyed excellent health.

PRESENT ILLNESS

Twenty-four hours before admission to hospital he awoke unable to speak clearly and was noted to have a paralysis of the left side of his face. Towards that same evening he began to drop objects from his left hand, and complained of dull headache radiating from the right frontal region through to the occiput. He fell asleep quite easily that evening, but at 3.30 a.m. awoke with a severe right-sided headache and numbness of the left side of his body. He found that his left arm and leg were virtually paralysed.

EXAMINATION

He was fully conscious but slightly dreamy and apathetic.

Cranial nerves

Visual acuity was not tested.

Both optic discs and retinae were normal.

There was a slight bilateral ptosis and a marked left central facial weakness.

The left corneal reflex was diminished as part of the hemihypalgesia present.

No other abnormality was discovered in the cranial nerves.

### Motor

The left arm was completely paralysed and only feeble movements were possible in the left leg. Tendon reflexes in the left extremities were very brisk with a left-sided extensor plantar response; the left abdominal reflexes were diminished.

### Sensation

All forms were diminished over the left half of the body and left limbs including the face.

Sense of passive movement was absent at the left fingers, wrist and elbow, and two-point discrimination was not appreciated at all over the left fingers.

### General examination

No abnormality was discovered, and in particular the peripheral vessels were healthy.

Blood pressure was 142/90.

### INVESTIGATIONS

#### Blood count

Haemoglobin	77%
White blood cells	14,600 per c.mm.
Polymorphs	81%
Lymphocytes	14%
Monocytes	3%
Eosinophils	2%

Cerebrospinal fluid

Pressure 180 mm. with a free rise and fall on  
jugular compression

Cells; 1 per c.mm.

Protein: 35 mgms.%

Lange curve: No change.

Wassermann reaction: Negative

PROGRESS

Whilst in hospital he developed a pulmonary embolus originating in the veins of the right calf, but made an excellent recovery from this complication and was discharged home after one month.

Three months later he had an attack of unconsciousness preceded by involuntary movements of the left hand. Unfortunately no other details of this episode were available.

He was readmitted to hospital where his physical status was found to be practically the same as on his previous admission.

A right carotid arteriogram showed the internal carotid artery to be blocked at its origin. In this area the vessel wall was a little irregular. The external carotid artery and its branches were well filled.

The appearances were similar to those seen in Case 19.

CASE 19 P.S. aged 49 years

OCCUPATION Caterer

FAMILY HISTORY

Nothing of note.

PAST HISTORY

Following an herniotomy four years ago he suffered a pulmonary infarct from an embolus originating in the veins of the left calf. He recovered fully within a few weeks.

Two years ago, after appendicectomy, he developed a thrombosis of some of the veins in the right leg; after several weeks the condition subsided completely.

PRESENT ILLNESS

Six weeks before admission to hospital both arms and legs suddenly became weak, and he found himself unable to speak.

Full use returned to the left limbs within half to one hour, but four hours elapsed before the right extremities had recovered completely. Speech returned after six hours, but he still had difficulty in finding the correct words to express himself. Immediately prior to this episode a patch of numbness about two inches square had appeared over the outer border of the left eye together with numbness of the right arm and leg, the latter remaining until full power had been regained in his extremities.

Since that time he had had several attacks of right-sided weakness and increased difficulty with his speech lasting a few minutes at a time.

On several occasions before the stroke he had experienced gnawing pains in the left temple lasting half-an-hour at a time. He has had them since with the above-mentioned attacks of weakness of the right extremities.

Two weeks before admission he had had two episodes in which he lost consciousness for ten minutes without warning.

He had difficulty in working out the correct change for his customers and at times his memory seemed to be poor. His speech was "jumbled up" and he frequently used wrong words in ordinary conversation.

#### EXAMINATION

He showed a nominal dysphasia with slight dyslexia, dyscalculia and dysgraphia.

#### Cranial nerves

Visual acuity was 6/9 in both eyes.

Both optic discs and retinae were normal, and there was no visual field defect.

Apart from a slight right central facial weakness no other abnormality was discovered in the cranial nerves.

#### Motor

A slight pyramidal weakness of the right arm was present with some increase in tone.



Tendon reflexes in the right arm were slightly increased, and in both legs were equal with bilateral flexor plantar responses.

#### Sensation

Sensation was normal throughout.

#### General examination

No abnormality was discovered with the exception of the carotid arteries in the neck; the right pulsated strongly, the left pulsated feebly.

Blood pressure was 140/70.

#### INVESTIGATIONS

##### Blood count

Red blood cells	4.5 million per c.mm.
Haemoglobin	94%
White blood cells	5,200 per c.mm.
Polymorphs	57%
Lymphocytes	35%
Eosinophils	4%
Monocytes	4%

##### X-ray of skull

No abnormality was seen.

##### Electro-encephalogram

The record was of low voltage and showed traces of symmetrical alpha rhythm. In the left anterior temporal area there was a focus of 4 c/sec. slow waves also of low voltage, which occurred in runs of 2-3 c/sec. waves; there was no change on overbreathing.

The focal abnormality agreed with the clinical siting of the lesion. It would appear that the brain was unusually inactive so that both normal and abnormal activity was depressed.

Left carotid arteriogram

There was a thrombosis of the left internal carotid artery at its origin. The external carotid artery was well filled.



CASE 20 R.K. aged 58 years

FAMILY HISTORY

His father died following a stroke: one brother died of a post-operative pulmonary embolus.

PAST HISTORY

Thirty-six years ago he was discharged from the Army with the diagnosis of "neurasthenia". His symptoms then consisted of weakness and trembling of the right leg which came on four months after a severe attack of typhoid fever; this disability gradually disappeared over the next five years.

Four years ago he suffered from a perianal abscess.

PRESENT ILLNESS

One year before admission to hospital he began to have attacks of giddiness in which objects within his gaze appeared to rotate. They occurred every two weeks and lasted no more than a few seconds at a time.

Within a few weeks of their onset his right index finger became numbed and the right side of his face occasionally twitched. This numbness disappeared after two weeks but the shortlived attacks of twitching of the face continued for the next three months.

When they ceased he began to experience sudden attacks of transient weakness of the right leg which would cause him to fall. There was never any loss of senses and he was always able to pick himself up

immediately without help.

Six months before admission his right leg became suddenly numbed and weak from the knee downwards, and although over the succeeding months there has been some improvement, the foot remained numbed and the leg felt slightly weak.

Two months later he had several attacks of uselessness of the right hand lasting approximately one minute at a time. These occurred once per day and were accompanied by transient numbness of the right side of his face. Such attacks were often precipitated by coughing or sneezing, and with each succeeding episode the right arm had gradually become weaker. Recently he had had several short-lived attacks of expressive dysphasia.

For the past three months he had complained of dull occipital headache.

#### EXAMINATION

He was mentally alert and at the time of examination did not show any evidence of dysphasia.

#### Cranial nerves

Visual acuity was 6/6 in both eyes and the fundi appeared to be normal.

The visual fields were full.

Apart from a slight right-sided central facial weakness on both voluntary and emotional movement the rest of the cranial nerves showed no abnormality.

### Motor

A minimal pyramidal weakness of the right arm and leg was present: the weakness was more apparent towards the periphery of the affected extremities. Tone in the arm and leg was slightly increased and spastic in type.

All the tendon reflexes were brisker in the right extremities; both plantar responses were flexor.

### Sensation

Light touch was less well appreciated over the right foot and the sense of passive movement was defective in the right great toe.

Elsewhere all sensory stimuli were normally appreciated.

### General examination

No abnormality was discovered.

Blood pressure was 160/98.

### INVESTIGATIONS

#### X-ray of skull and chest

No abnormality was seen.

#### Electro-encephalogram

The only significant activity was a regular alpha rhythm with normal distribution and behaviour. There was nothing in the record to suggest an hemisphere lesion.

#### Left carotid arteriogram

The internal carotid artery was occluded  $\frac{1}{2}$  cm. from its origin, but beyond this a thin stream of contrast could be seen in its lumen. The syphon and middle

cerebral arteries were well filled.

The external carotid artery filled and the maxillary branch was hypertrophied and supplied several large arteries in the orbital region.



MADE IN GREAT BRITAIN

CASE 21 C.C. aged 41 years

FAMILY HISTORY

Nothing of relevance.

PAST HISTORY

He had always enjoyed excellent health until the commencement of this illness.

PRESENT ILLNESS

Five days before admission to hospital he experienced sudden severe headache after lunch, which persisted until the same evening. No other details are available as to its site, intensity or other characteristics. That evening he began to have difficulty in finding the correct words to express himself. He slept well and awoke next morning feeling distinctly better, but still complained of headache and it was noted that he had increased difficulty in expressing himself and that the right side of his face drooped. Next day he complained of pain in the left side of his face and his wife noted that the left eyelid had drooped. He remained in much the same state until twenty-four hours later, when he suddenly became paralysed down the right side and unable to speak; consciousness was retained. He was thereupon admitted to hospital.

EXAMINATION

He was drowsy but could be aroused. He was unable to speak but was able to obey simple commands, although he tended to perseverate.

### Cranial nerves

Visual acuity was not tested.

Both optic discs and retinae appeared to be normal. The visual fields were difficult to assess even to confrontation, and the results obtained were not reliable.

Both pupils were strongly contracted (? due to the morphia given before admission).

The left eye was deviated upwards and outwards.

The left eyelid was partially ptosed.

There was a complete right central facial paralysis with some weakness of the upper facial muscles also.

No other abnormality was discovered in the cranial nerves.

### Motor

The right extremities showed a flaccid paralysis.

The tendon reflexes were slightly increased in the right extremities with a doubtful right extensor plantar response.

### Sensation

All forms of sensation were completely absent over the right side except for an occasional recognition of pinprick over the right lower leg.

### General examination

No abnormality was discovered and in particular all the peripheral vessels appeared healthy.

Blood pressure was 120/70.

### INVESTIGATIONS

#### X-ray of skull

No abnormality seen.



Left carotid arteriogram

There was a complete occlusion of the internal carotid artery 3.5 cms. from its origin in the neck, but towards this point there was a steady narrowing of the lumen.

PROGRESS

He became deeply comatose after arteriography, and died two days after admission.



POST MORTEM EXAMINATION

The heart appeared healthy.

The aorta and coronary arteries showed only mild degenerative changes.

At the bifurcation of the right common carotid artery there was a moderately large plaque of atheroma. One-and-a-half cms. from the origin of the left internal carotid artery was adherent thrombus which extended upwards into the left middle and anterior cerebral arteries but not into the anterior communicating or Heubner's artery. Small atheromatous plaques were seen at the origin of the left internal carotid artery and extended a little way down into the common carotid on the same side (Fig. 1). The right carotid artery was healthy.

Histologically in the left internal carotid artery the intima had been stripped up from the media by recent haemorrhage. This intimal separation by haemorrhage extended to above the carotid syphon. The appearances were consistent with a dissecting aneurysm although the actual point of rupture could not be determined.

In the brain the left cerebral hemisphere was swollen and the area supplied by the left middle cerebral artery was softened.

The left cerebellar tonsil and hippocampus showed evidence of herniation.



Fig. 1. Internal carotid artery showing atherosclerotic plaques at commencement with blood clot above.

On section the infarct of the left hemisphere extended on the lateral surface from the level of the genu of the corpus callosum posteriorly to the anterolateral part of the occipital lobe. The infarct involved cortex and white matter of the **infero-lateral**

part of the frontal lobe, inferior part of the parietal lobe and the island of Reil, the upper two temporal gyri and the antero-lateral occipital lobe.

Anteriorly the infarct also involved the superior part of the corpus striatum, the claustrum, putamen and outer two-thirds of the globus pallidus and the upper part of the internal capsule (Fig. 2).

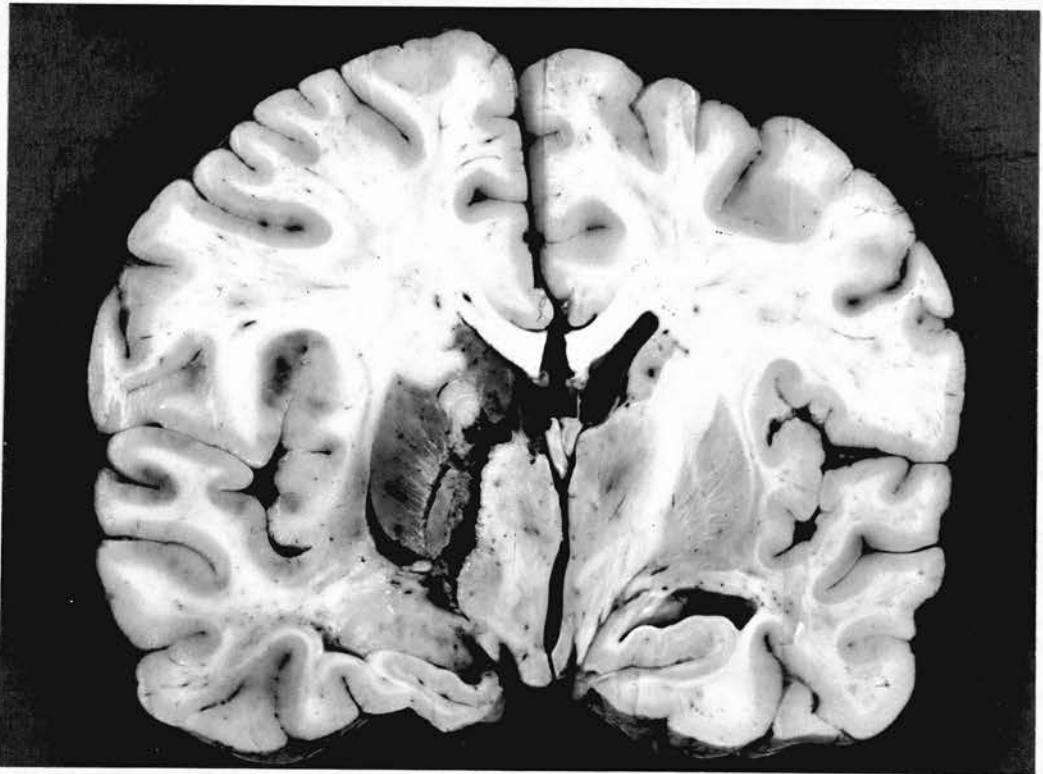


Fig. 2. Infarcted area of left hemisphere.

The corpus luyssii and thalamus were not involved. The midbrain presented elongated haemorrhages between the red nuclei. Small haemorrhages were also present in the tegumentum and ventral part of the pons.

Histologically the infarcted cortex presented degeneration and loss of nerve cells with numerous dilated capillaries filled with red blood cells and leucocytes. There were numerous perivascular ring haemorrhages with migration of leucocytes into the cerebral substance. The margins of the infarct were sharply defined by vacuolated areas. Throughout the white matter the capillaries were widely dilated.

In the second and third frontal convolutions and the lateral part of the convexity of the parieto-temporal region the cerebral tissue presented demyelination and infarction. Similar changes were present in the occipital lobe where the capillaries showed endothelial proliferation. Compound granular corpuscles lay in the leptomeninges overlying the infarcted area. The claustrum, outer putamen and lentiform nucleus had all undergone softening together with the first and second temporal convolutions and the tip of the temporal lobe.

The cerebral infarct was approximately the same age in all areas.

Although the vessels were dilated and packed with red blood cells no thrombi or emboli were seen.

CASE 22 W.W. aged 52 years

OCCUPATION Clerk.

FAMILY HISTORY

No relevant history obtained.

PAST HISTORY

For several years he had suffered from attacks of precordial pain which were relieved by trinitrin tablets.

PRESENT ILLNESS

Five months before admission to hospital he found his right hand clumsy and was unable to guide a pen correctly when writing. He had difficulty in speaking and wept a great deal. Next day the right side of his face was twisted, but this weakness cleared up within the next few days, although his right hand remained clumsy and he had considerable difficulty in finding the correct words to express his meaning.

Shortly after the commencement of this illness he had episodes of numbness of the right hand and fingers, occurring twice per day and lasting ten minutes at a time.

Six weeks later he began to have intermittent short-lived attacks of weakness of the right leg quite independently of the episodes of numbness in the right hand. He had had six attacks in all up to the time of his admission.

EXAMINATION

He showed a nominal dysphasia, but understanding of the spoken and written word was unimpaired. Spontaneous writing and writing to dictation was excellent.

Cranial nerves

Visual acuity was 6/6 in both eyes.

No abnormality of optic discs or retinae was seen.

The visual fields were full.

Apart from a minimal right central facial weakness there was no other abnormality found in the cranial nerves.

Motor

No abnormality was discovered.

Sensation

Sensation was normal throughout.

General examination

No abnormality was present and in particular the peripheral vessels were all healthy.

Blood pressure was 150/90.

INVESTIGATIONS

X-ray of skull and chest.

No abnormality was seen.

Electro-encephalogram

A 9 c/sec. alpha rhythm was present which blocked on eye opening. A moderate amount of 4-7 c/sec. activity was fairly widely distributed. Intermittent very slow waves occurred in the left temporal region

and some runs of 4-6 c/sec. were seen in the left fronto-temporal region. The left-sided slow activity increased on overbreathing and runs of 4 c/sec. activity appeared in the occipital region. The left-sided slow activity was greatest temporally, but was not a sharply defined focus.

#### Cerebrospinal fluid

Pressure 125 mm. with a free rise and fall on jugular compression

Cells: 2 per c.mm.

Protein: 45 mgms.%

Lange curve: No change

Wassermann reaction: Negative

#### Left carotid arteriogram

The external carotid artery was well filled and there was a trace of contrast in the basilar artery.

At the site of origin of the internal carotid artery there was a marked irregularity of the wall but no contrast was seen in the artery. The appearances were similar to those seen in Case 19.

#### PROGRESS

After the arteriogram he complained of an inability to see out of the lower part of his left eye. A lower altitudinal field defect was present. The optic disc appeared healthy, but the upper branch of the central retinal artery was greyish-white and had three spots of pigment on it. The retina between the



temporal disc margin to a short distance beyond the macula was oedematous above the horizontal line. The appearances were those of a superior temporal artery occlusion.

CASE 23 E.B. aged 37 years

OCCUPATION Agricultural worker

FAMILY HISTORY

His mother died of an heart attack in her late sixties.

PAST HISTORY

He had always enjoyed excellent health except for his present illness.

PRESENT ILLNESS

At the age of eighteen years he had a "bilious attack" with severe headache which lasted more than a week. During this time his right eye turned inwards, and for the next eight years the condition of his eye remained stationary.

Ten years before admission to hospital he experienced a curious sensation over the right shoulder radiating over the right side of his head to the forehead. It was likened to boiling water trickling over the skin and followed by a cold feeling in the same area. It lasted a few seconds and was accompanied by stiffness of the right side of his face.

Three years later he developed aching pain over the right side of his head in the same distribution, which lasted a day or two and was accompanied by tenderness of the scalp. Coughing caused momentary aggravation of the pain and at such times he would vomit.

Over the past seven years he had had seven such attacks, occurring approximately once yearly.

Six months ago during the last attack of pain and vomiting, he consulted his doctor who found wasting of the right masseter muscle and advised his admission to hospital.

Recently the right side of his face had been constantly stiff. He had also had some right-sided deafness with slight aural discharge.

#### EXAMINATION

##### Cranial nerves

Visual acuity in the left eye was 6/6.

In the right eye hand movements only were appreciated.

The left fundus was normal; the right disc showed primary optic atrophy.

The left visual field was full and as far as could be judged the right temporal field was within normal limits. (Further testing was impossible on account of strong adduction of the right eye.)

There was a slight right proptosis: the right eye was fully adducted and moved outwards, upwards and downwards very slightly.

Movements of the left eye were full and free.

Cutaneous sensation to pain and light touch was diminished over the first and second divisions of the right trigeminal nerve; the right temporal and masseter muscles were moderately wasted and weak.

Hearing was normal and both drums appeared to be healthy. No other abnormality was discovered in the cranial nerves.

Motor

Power, tone, co-ordination and posture of the upper and lower extremities was normal.

The reflexes in the arms were absent but were present and equal in the legs. Both plantar responses were flexor.

Sensation

Sensation was normal throughout.

General examination

No abnormality was discovered and in particular the peripheral vessels were healthy.

Blood pressure was 125/80.

INVESTIGATIONS

X-ray of chest

No abnormality was seen.

X-ray of skull

The vault and sella were normal. Most of the orbital portion of the greater wing of the sphenoid was destroyed, with some erosion of the floor of the middle fossa and the right petrous apex. A curved linear calcification was seen laterally and inferiorly behind the right orbit outlining an oval the size of an hen's egg. The appearances were compatible with calcification in the wall of an aneurysm.

Right carotid arteriogram

The internal carotid artery was completely occluded

1.5 cms. from its origin. The external carotid artery was well filled and its branches appeared to be hypertrophied. No cerebral circulation was seen.

Left carotid arteriogram

The internal carotid artery appeared to be hypertrophied. Both anterior and middle cerebral arteries were filled. The contrast was seen to pass to the opposite side but filling of the right internal carotid artery could not be established.





CASE 24 H.H.-J. aged 51 years

FAMILY HISTORY

No history of note.

PAST HISTORY

Twenty-five and twenty-two years ago he had had blackwater fever from which he made a good recovery. One year ago he developed a scrotal swelling due to an hydrocoele. Apart from these illnesses his health had been excellent.

PRESENT ILLNESS

Fourteen months before admission to hospital he had difficulty with his vision for five days. During this time objects appeared brighter than they really were.

Nine months ago he had some difficulty in finding words to express his meaning, and later the same month was unable to speak at all, although he could write fairly well.

About this time he had difficulty in concentrating, calculation and in understanding verbal or written instructions, and did not know his right from his left side.

The following month he had three attacks of short-lived violent occipital headache, each occurring after an emotional upset. Thereafter his speech and concentration improved, although he still had a

tendency to stutter over some words. The difficulty in calculating, reading, and distinguishing his left from his right side remained. He also had difficulty in identifying coins in his left trouser pocket. He continued to suffer from mild occipital headaches, which gradually disappeared one month before admission.

#### EXAMINATION

He was depressed and anxious, retaining complete insight into his illness.

He showed a mild expressive dysphasia with a superadded nominal defect and a tendency to word transposition. There was a mild dyslexia with severe dyscalculia, and a mild degree of constructional apraxia.

#### Cranial nerves

Visual acuity was J6 in the right, J14 in the left eye. The optic discs were normal in appearance, but the retinal veins were full and the arteries presented slight arteriosclerotic changes.

There was an incomplete right homonymous hemianopia. No other abnormality was discovered in the cranial nerves.

#### Motor

A mild degree of right hemiparesis was present, more marked in the arm than the leg.

On sustained posture a fine rhythmical pronation-supination tremor affected the right hand, which persisted throughout movement.



Sensation

Two-point discrimination was impaired over the right fingers, but otherwise sensation was normal throughout.

General examination

Over the outer aspect of the right upper arm lay a small lipoma. Several café au lait spots were present over the skin of the abdomen and lower back. The peripheral vessels were healthy and the blood pressure was 130/85.

INVESTIGATIONS

X-rays of skull and chest

No abnormality was seen.

Left carotid arteriogram

There was an occlusion of the internal carotid artery at the syphon with an anomalous carotid-basilar anastomosis. The terminal part of the basilar and right posterior cerebral arteries were filled. The left anterior and middle cerebral arteries contained a small amount of contrast which appeared to reach them through the right posterior communicating artery.

PROGRESS

During the last intracarotid injection of diodone he became drowsy and within a few minutes lapsed into unconsciousness. When he recovered consciousness an hour later he had a complete right flaccid hemiplegia with aphasia.

Procaine stellate ganglion blocks did not improve his condition.

The cerebrospinal fluid examined ten days after this incident contained 1800 red blood cells, 9 lymphocytes and 1 polymorph, with a protein of 120 mgms.%. The Lange curve was 5555532100, and the Wassermann reaction was negative.

An air encephalogram showed changes consistent with a slight degree of left cortical atrophy.

Three months later power in his right arm and leg had improved slightly but he could not understand what was said to him, and speech was restricted to an occasional "Yes", or more colourful expletive often inappropriately uttered.



CASE 25 R.N. aged 53 years

OCCUPATION Engineer

FAMILY HISTORY

No details were available.

PAST HISTORY

Three years ago he was found to be suffering from diabetes mellitus which was adequately controlled by dieting.

PRESENT ILLNESS

Two months before admission he suddenly complained of generalised aching headache and was unable to find his words or to write correctly. His letters contained many grammatical errors and the individual letters were poorly formed. Within a few days his speech became worse and he appeared to have difficulty in remembering day-to-day events. About this time he had two attacks in which his right arm became involuntarily abducted, the right side of his face twitched, and the right leg became useless. They lasted for a few seconds at a time. Soon his speech became disjointed in English and he was unable to speak in French or Italian, in which languages he was normally fluent. His reading was incorrect and his writing worse than before. He complained of difficulty with his memory, was depressed and cried easily.

About six weeks before admission he complained of almost continuous pain and numbness in the right

hand and leg, and of mild generalised headaches from time to time.

#### EXAMINATION

When speaking in English he was often lost for a word and his grammar was imperfect. In French and Italian he was more obviously dysphasic.

Complicated commands in English were not understood, and simple written commands were imperfectly appreciated.

Although he only made an occasional error when reading, his voice was monotonous.

He also showed slight dyscalculia, but no apraxia was present.

#### Cranial nerves

Visual acuity was normal in both eyes.

The optic discs and retinae appeared healthy.

Apart from a minimal right central facial weakness no other abnormality was discovered in the cranial nerves.

#### Motor

The sole abnormality lay in the tendon reflexes, which in the left arm were slightly brisker than those in the right. The knee and ankle jerks were present and equal with bilateral flexor plantar responses.

#### Sensation

Sensation was normal throughout.

#### General examination

No abnormality was detected and in particular all the peripheral vessels appeared healthy.

Blood pressure was 145/85.

### INVESTIGATIONS

#### Blood count

Red blood cells	5.02 million per c.mm.
Haemoglobin	88%
White blood cells	8,400 per c.mm.

#### Blood sugar curve

Fasting	275 mgms.%
½-hour	300 mgms.%
1 hour	360 mgms.%
1½ hours	370 mgms.%
2 hours	320 mgms.%

#### Cerebrospinal fluid

Pressure was not recorded.

Cells: 0 per c.mm.

Protein: 70 mgms.%

Lange curve: No change

Wassermann reaction: Negative

#### X-ray of skull and chest

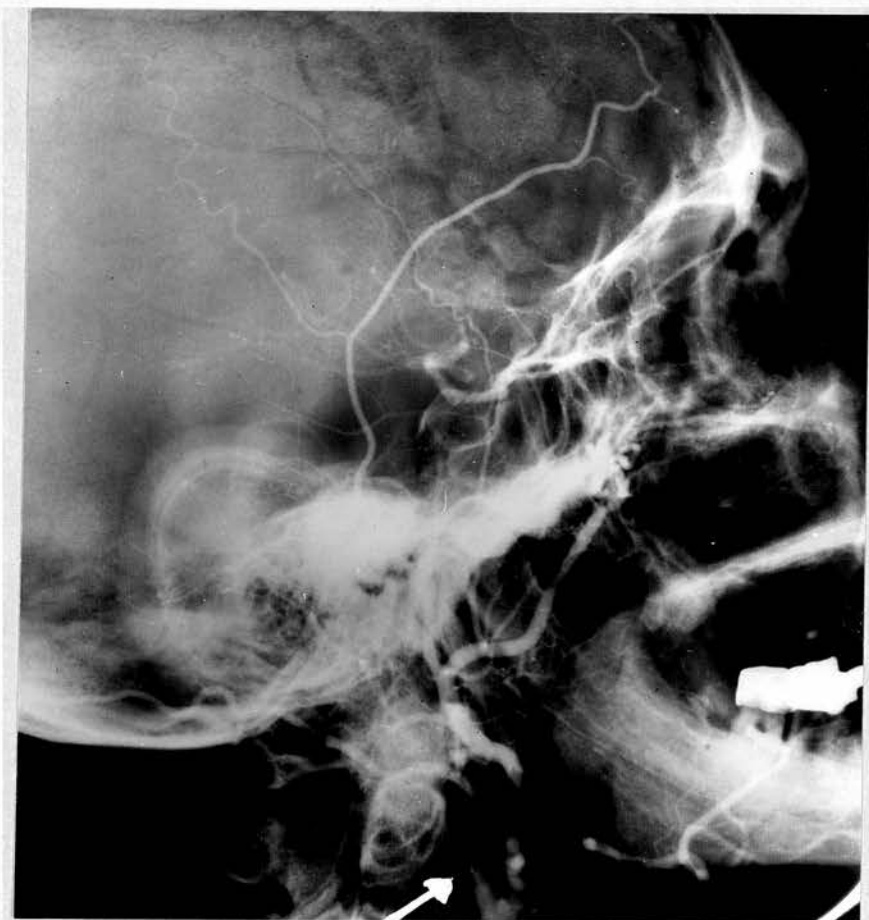
No abnormality was seen.

#### Electro-encephalogram

There was a suppression of all normal rhythm over the left hemisphere with continuous medium voltage 1-2 c/sec. waves in the left Sylvian region. These findings were more in keeping with a neoplasm in this area than with a cerebral thrombotic episode.

Left carotid arteriogram

The internal carotid artery was completely occluded 1 cm. from its origin. The terminal part of the carotid syphon and the middle cerebral artery were partially filled with contrast, presumably indicating some anastomosis between the external and internal carotid circulations, although this was not demonstrated.



CASE 26 E.C. aged 66 years

FAMILY HISTORY

His father died at fifty-nine years of nephritis and his mother died at sixty-nine years of arteriosclerosis.

PAST HISTORY

Eleven and four years ago he had had "heart attacks" characterised by precordial pain lasting several hours. Between these times he had suffered from "cardiac pain" on exertion.

PRESENT ILLNESS

Nine months before admission to hospital he began to suffer from severe frontal headaches occurring each morning which were aggravated by stooping but disappeared as the day wore on. These headaches were occasionally accompanied by partial blindness which lasted for a quarter-of-an-hour, i.e., there were blank scotomata over the visual field. He often complained of vertical diplopia during an attack. After a few months they were replaced by a constant neuralgic aching above the eyes.

He then complained of difficulty with his memory, and was unable to dress himself or to calculate correctly.

Six months ago his left hand became progressively clumsy, weak and numb, and within the past

two months the left side of his face weakened and he had considerable difficulty in swallowing and in using his tongue.

For three weeks before admission the left side of his mouth was numbed and he was unable to pronounce words correctly.

Throughout this illness he had occasional mild dizziness, but had never experienced true vertigo.

#### EXAMINATION

He showed a non-specific intellectual deterioration with some tendency to perseveration in thought and speech.

There was no dysphasia or dyscalculia, but he did have an apractic dysarthria. There was no evidence of visual spatial disability, but he tended to neglect objects in his left visual field and from time to time neglected his left hand.

#### Cranial nerves

Visual acuity was 6/12 in the right and 6/18 in the left eye.

The optic discs were normal, but the vessels showed mild arteriosclerotic changes.

There was a homonymous left hemianopia sparing the macula. The left pupil was slightly larger than the right but both reacted adequately to light and on convergence.

There was a left central facial weakness and movements of the tongue were clumsy (apraxia of tongue).



Motor

All movements of the left arm were clumsy but not weak and he occasionally had some difficulty in placing it correctly in space (apraxia).

The tendon reflexes were slightly increased in this extremity.

The reflexes in the lower extremities were present and equal and both plantar responses were flexor.

Sensation

The appreciation of light touch, pain and temperature were diminished over the left face and arm and to simultaneous stimuli there was a tendency to neglect the left side of his body.

The sense of passive movement was grossly impaired at the left fingers and wrist.

Two-point discrimination was grossly defective over the left fingers.

Elsewhere all sensory stimuli were normally appreciated.

General examination

No abnormality was detected except for the peripheral arteries which were slightly thickened.

Blood pressure was 130/70.

INVESTIGATIONS

X-ray of skull and chest

No abnormality was seen.

Electro-encephalogram

The left side was normal showing only low voltage alpha rhythm and a little fast rhythm. On the right

side in the parieto-temporal region there was continuous moderate low voltage slow activity from 2-6 c/sec., many of the waves having a sharp outline.

The record was consistent with structural damage in the right parieto-temporal region and the local character and waves suggested a chronic lesion.

#### Cerebrospinal fluid

Pressure was not recorded.

Cells: 3 per c.mm.

Protein: 60 mgms.%

Lange curve: 0012521000

Wassermann reaction: Negative

#### Right carotid arteriogram

There was a marked delay in the passage of the contrast in the carotid system and a constant clear area was seen in the horizontal loop of the internal carotid syphon measuring  $\frac{1}{2}$  cm. in length. The anterior cerebral and middle cerebral arteries were well filled.

The appearances suggested a mural thrombus.

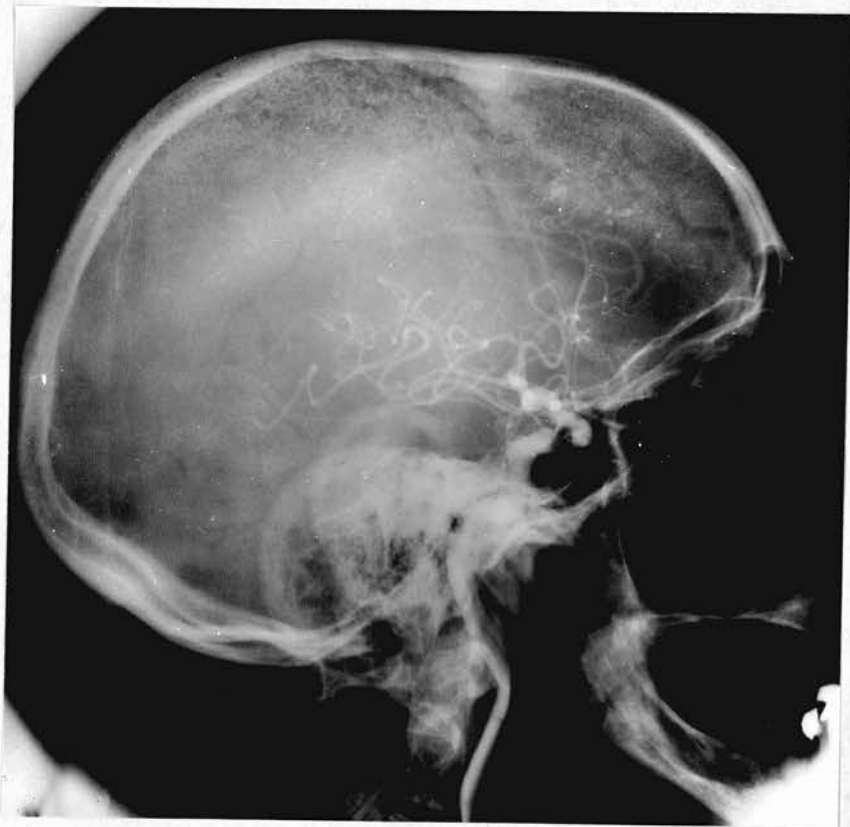
#### PROGRESS

After one month he was discharged from hospital in much the same state as on admission. He remained thus for nine months, then became progressively worse. An accurate account of this deterioration could not be obtained from him, but his relatives thought that he had shown a progressive lack of interest in his appearance and surroundings, with aggravation of his headache. Recently the right arm and leg had weakened,

but whether this feature was sudden or gradual in onset they were unable to say.

Examination on this occasion showed further intellectual deterioration together with a mild expressive dysphasia. The left hemianopia remained. In place of the mild left-sided weakness he now had a severe spastic hemiparesis, more marked in the arm than the leg.

The right carotid arteriogram was repeated and on this occasion the internal carotid artery was occluded just distal to its origin.



CASE 27 L.W. aged 58 years

OCCUPATION Bicycle engineer

FAMILY HISTORY

His father died of a "broken" blood vessel in his fiftieth year.

His wife suffers from general paralysis of the insane and is confined to a mental institution.

PAST HISTORY

He had become gradually deaf over the past ten years, otherwise his health had been good.

PRESENT ILLNESS

Seventeen years before admission he had an attack of "influenza" during which he had severe pain in and watering of the left eye. His friends remarked that this eye was bulging and squinted and he himself saw double. The squint improved with orthoptic exercises but vision remained blurred in this eye.

Eight years ago he had another bout of "influenza" with acute pain in the eye for three to four days. The eye did not bulge further forwards but he recovered from this episode with a blind left eye.

Four months ago he had two attacks of malaise with vomiting, and pain recurred in the eye. After six weeks it subsided, but he has since experienced intermittent attacks of pins and needles in the left eye, cheek and lip.

EXAMINATION

Although moderately deaf he was alert, co-operative and intelligent.

Cranial nerves

Visual acuity was 6/18 in the right eye; light perception only in the left eye.

The right disc was normal; the left showed a primary optic atrophy. The left eye was moderately proptosed with a complete paralysis of abduction and a partial paralysis of other movements, i.e., complete VI nerve and incomplete III and IV nerve palsies.

Both pupils were equal, but slightly irregular in outline. The right pupil reacted briskly to light and convergence, the left reacted hardly at all to direct light, but briskly to consensual light stimuli.

The left corneal reflex was depressed with hypalgesia over the first and second divisions of the left trigeminal nerve.

Apart from a bilateral nerve deafness, no other abnormality was discovered in the cranial nerves.

Motor

No abnormality was present.

Sensation

Sensation was normal throughout.

General examination

No abnormality was discovered and in particular the

peripheral vessels were healthy.

Blood pressure was 120/85.

### INVESTIGATIONS

#### X-ray of chest

There was some fibrosis of the right apex probably indicating an old healed tuberculous infection.

#### X-ray of skull

There was a calcified ring to the left of the sella measuring 4.5 cms. in length and 3 cms. in diameter. The left sphenoid wing and anterior clinoid process was decalcified.

#### Cerebrospinal fluid

Pressure was 90 mm. with a free rise and fall on jugular compression

Cells: 2 per c.mm.

Protein: 55 mgms.%

Nource Apelt and Pandy: Slightly positive

Lange curve: 0112210000

Wassermann reaction: Negative

#### Left carotid arteriogram

The internal carotid artery was occluded just distal to its origin.

#### Right carotid arteriogram

In the lateral films both anterior cerebral arteries filled and were apparently displaced forwards, but in the antero-posterior views they were not filled.

CASE 28 M.F. aged 61 years

OCCUPATION Housewife.

FAMILY HISTORY

Her mother died of a stroke in late middle life.

PAST HISTORY

She had suffered from rheumatic fever during childhood but apparently she made a good recovery, although within recent months she had had some effort dyspnoea and slight swelling of the ankles.

Thirty years ago a cyst was removed from one ovary.

Twelve years ago she had an attack of right-sided sciatica which subsided spontaneously after several weeks and had not recurred.

PRESENT ILLNESS

Eight months before admission to hospital she developed severe pain in the middle of her back which persisted for a few weeks, then radiated into both thighs and gradually extended down the front and back of both legs toward the ankles. Within two months of the onset of pain both legs became progressively weak and stiff and she had considerable difficulty in holding her water.

EXAMINATION

No abnormality was discovered in the cranial nerves or upper extremities.

The spines of L2, 3 and 4 were tender to pressure and in D8-10 dermatome distribution on both sides there were several pigmented naevi and café-au-lait patches. Both legs were moderately weak and spastic. Appreciation of painful stimuli was slightly diminished over D10 to L1 segments on both sides: vibration sense was diminished at both ankles.

### INVESTIGATIONS

#### X-ray of spine

No significant abnormality was seen.

#### Cerebrospinal fluid

Initial pressure 100 mm. with a free rise on jugular compression, but a slow fall indicating the presence of a partial fluid block.

Cells: 0 per c.mm.

Protein: 60 mgms.%

Lange curve: 0001110000

Wassermann reaction: negative.

### PROGRESS

She was regarded as suffering from spinal compression caused by a neoplasm. Under general anaesthesia an endothelioma was removed from the region of D1. Her condition remained "satisfactory" throughout the operation and on recovery from the anaesthetic two hours later she was given three grains of luminal intramuscularly on account of restlessness. After several hours, when the effects of the sedative



have usually worn off, she was noted to be excessively drowsy. Further examination revealed a complete flaccid left hemiplegia. She died within eight hours.

POST MORTEM EXAMINATION

There was a depression over the dorsal surface of the cord at the level of T 3 from which the endothelioma had been removed.

In the territory of the right middle cerebral artery there was congestion and softening of the white and grey matter. In the upper part of the carotid artery in the cavernous sinus was recent thrombus which extended into the middle cerebral artery. The right heart chambers were full of agonal clot, but the left auricle was healthy. The heart valves were normal: a small patent foramen ovale was present.

Unfortunately the histological sections of this case were lost and could not be replaced.

CASE 29 K.W. aged 48 years

OCCUPATION Housewife

FAMILY HISTORY

No relevant facts obtained.

PAST HISTORY

Seven years before admission to hospital she complained of attacks of numbness which momentarily "seemed to go through her", ending up in the particular part of the body which she happened to be using at the time. She attended the National Hospital for Nervous Diseases, Queen Square, where these attacks were thought to be hysterical in nature. She was given phenobarbitone gr.  $\frac{1}{2}$  thrice daily and after six months the attacks ceased.

Thereafter she remained well until four years later when she had one isolated attack similar to those described above.

PRESENT ILLNESS

One year before admission she suddenly became "numb all over" and felt dazed, as though about to faint. A few minutes later her legs suddenly gave way and she fell to the ground unconscious. Within a few minutes she had recovered completely. Since then she had had two similar episodes lasting for a few minutes, consisting of clouding of consciousness and weakness of the limb she happened to be using at the time, i.e., her so-called "numbness".

Three days ago she awoke with a severe thumping pain in her right temple which lasted several hours then settled down to a steady aching around the eye. When the thumping headache ceased vision in the right eye became misty.

#### EXAMINATION

She was slightly confused, but even allowing for this there appeared to be a marked organic intellectual deterioration.

#### Cranial nerves

The right eye was completely blind; visual acuity in the left eye was 6/9.

The right optic disc was slightly swollen and grey in colour; the appearances of the left disc were normal.

The right pupil was ovoid and reacted poorly to direct light; the left pupil reacted briskly to light and on convergence.

Apart from a slight left central facial weakness no other abnormality was discovered in the cranial nerves.

#### Motor

There was slight pyramidal weakness of both left extremities more marked peripherally.

The tendon reflexes in the left arm and leg were slightly increased but both plantar responses were flexor.

#### Sensation

All modalities were correctly perceived everywhere, with the exception of the left finger pads, where two-point discrimination was slightly defective.

General examination

No abnormality was discovered, and in particular all the peripheral vessels appeared healthy.

Blood pressure was 130/80.

INVESTIGATIONS

X-rays of skull

No abnormality was seen.

Cerebrospinal fluid

Pressure: 70 mm.

Cells: 0 per c.mm.

Protein: 40 mgms.%

Lange curve: No change

Wassermann reaction: negative

Electro-encephalogram

Alpha rhythm was present in both occipital and temporal regions but was more irregular in frequency and amplitude in the right posterior temporal region. Low down in this region was a focus of small waves at 2-3 c/sec. of fair voltage associated with sharp waves; this focus was extensive and surrounded by irregular activity at 6 c/sec. Theta activity occasionally spread across from the other hemisphere.

Right carotid arteriogram.

The internal carotid artery was completely occluded  $\frac{1}{2}$  cm. above its origin.

CASE 30 A.T. aged 55 years

OCCUPATION Housewife

FAMILY HISTORY

Her father died of a cerebral haemorrhage at the age of fifty-nine, and her mother died at sixty following an illness with alternating weakness of the extremities and aphasia. One sibling died in early middle life of a "cerebral thrombosis".

PAST HISTORY

Nothing of note.

PRESENT ILLNESS

Two years before admission to hospital her left leg began to tire easily and gradually became progressively weak and stiff. Some six months ago she began to have intermittent weakness of the left hand and arm lasting five minutes at a time and recurring several times daily. Between these attacks her left arm and hand recovered completely. The attacks ceased after two months.

One month before admission she complained of right-sided headaches together with some deterioration in her vision. Her left arm had become practically useless and she was inclined to weep profusely with little reason.

EXAMINATION

Her mood was labile and there was evidence of marked intellectual deterioration with some dyscalculia.

Cranial nerves

Visual acuity in the right eye was 6/18, in the left 6/9. Both optic discs were blurred in outline and the retinal veins were full.

There was a left homonymous hemianopia sparing the macula. Except for a mild degree of left central facial weakness and a tendency for the tongue to be protruded to the left the cranial nerves were normal.

Motor

She showed a severe left hemiplegia: the left arm was completely paralysed and movements in the leg very weak. Tone was increased in both these extremities and spastic in type.

All tendon reflexes in the left arm and leg were exaggerated with a left-sided extensor plantar response.

Sensation

Appreciation of light touch was slightly diminished below the level of C2 on the left side, but pain and temperature sensibility was unimpaired.

The sense of passive movement, vibration and two-point discrimination was grossly impaired in the left fingers and toes.

General examination

No abnormality was discovered.

Blood pressure was 180/105.

INVESTIGATIONS

X-ray of skull

The pineal gland was calcified and displaced 0.3 cm. to the left of the midline.

Cerebrospinal fluid

Pressure was not recorded

Cells; 7 per c.mm.	Lymphocytes	2
	Polymorphs	5
	Red blood cells	4,200

Protein: 25 mgms.%

Electro-encephalogram

Due to lack of co-operation the record was unsatisfactory and no conclusions could be drawn from it.

Right carotid arteriogram

The common carotid artery was difficult to puncture and only faint filling of the internal carotid and cerebral vessels was seen.

PROGRESS

Following arteriography the patient became progressively more drowsy and within a few hours lapsed into unconsciousness; the right pupil was dilated and fixed. She died six hours later.

POST MORTEM EXAMINATION

Heart. The heart was generally dilated and the left ventricle slightly hypertrophied.

Both coronary arteries were atheromatous.

The aorta was markedly atheromatous in the descending thoracic and abdominal parts, and the left renal artery presented similar changes.



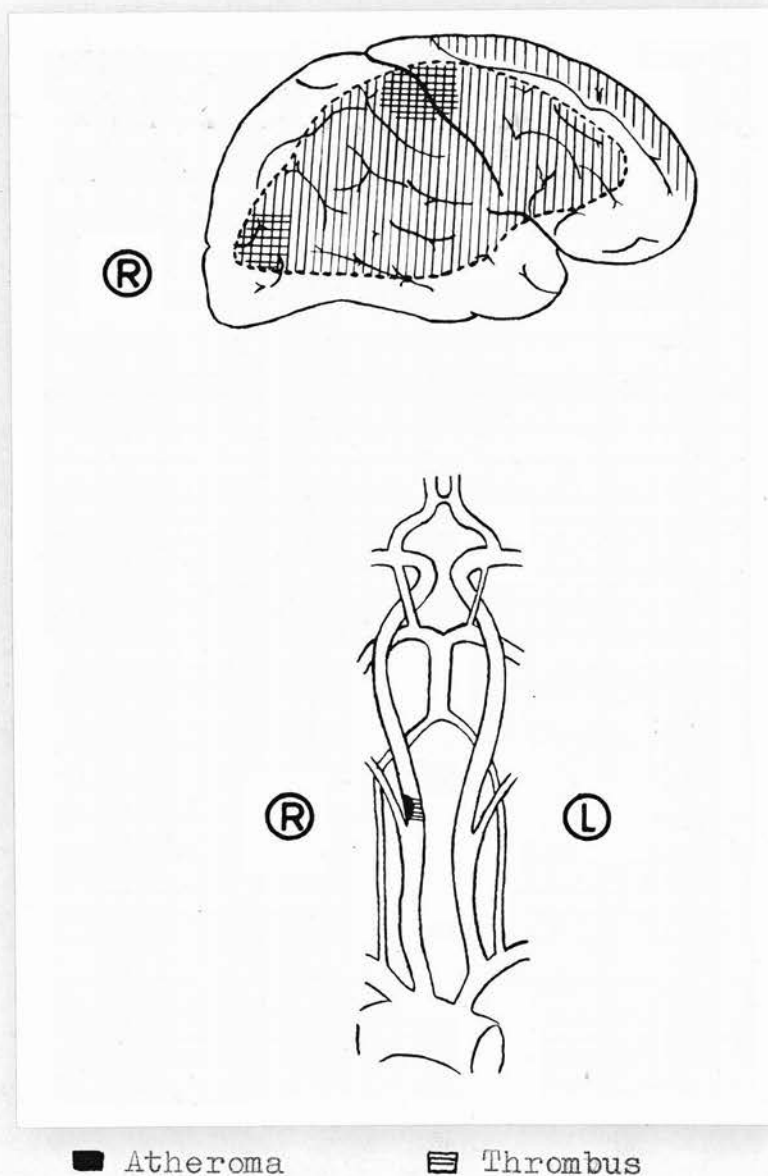
In the right side of the neck the soft tissues around the carotid bifurcation were bruised and haemorrhagic. The internal carotid artery was extensively narrowed by atherosclerosis in the region of the sinus and was almost occluded by a 4 mm. long recent thrombus which was adherent to the site of the arterial puncture.

Histologically the lumen of the artery was narrowed by progressive layers of subintimal fibrous tissue, in the depths of which lay calcified plaques surrounded by round cells and an occasional giant cell. Judging from the cellular reaction in the recent thrombus it was similar in age to the site of the needle puncture. The left carotid artery was unfortunately not examined.

Both cerebral hemispheres were swollen and that on the right side showed a moderate degree of hippocampal herniation. The dura overlying the right hemisphere was covered by recent, thin subdural haemorrhage and the leptomeninges overlying the convexity were oedematous and blood-stained.

The greater part of the right hemisphere, especially in the distribution of the middle cerebral artery, was the site of recent infarction. The cortex showed scattered haemorrhagic mottling and the underlying white matter was pale and swollen. However, around the upper part of the central sulcus the cortex was shrunken and orange coloured, indicating an

infarction of some duration. A similar infarct with yellowish discolouration was present over the convexity of the occipital lobe (Fig. 1).



The basal vessels were atheromatous. The left posterior communicating artery was thin and thread-like; the right posterior communicating artery was hypertrophied. No blood clot was visible to the naked eye in the larger cerebral arteries.

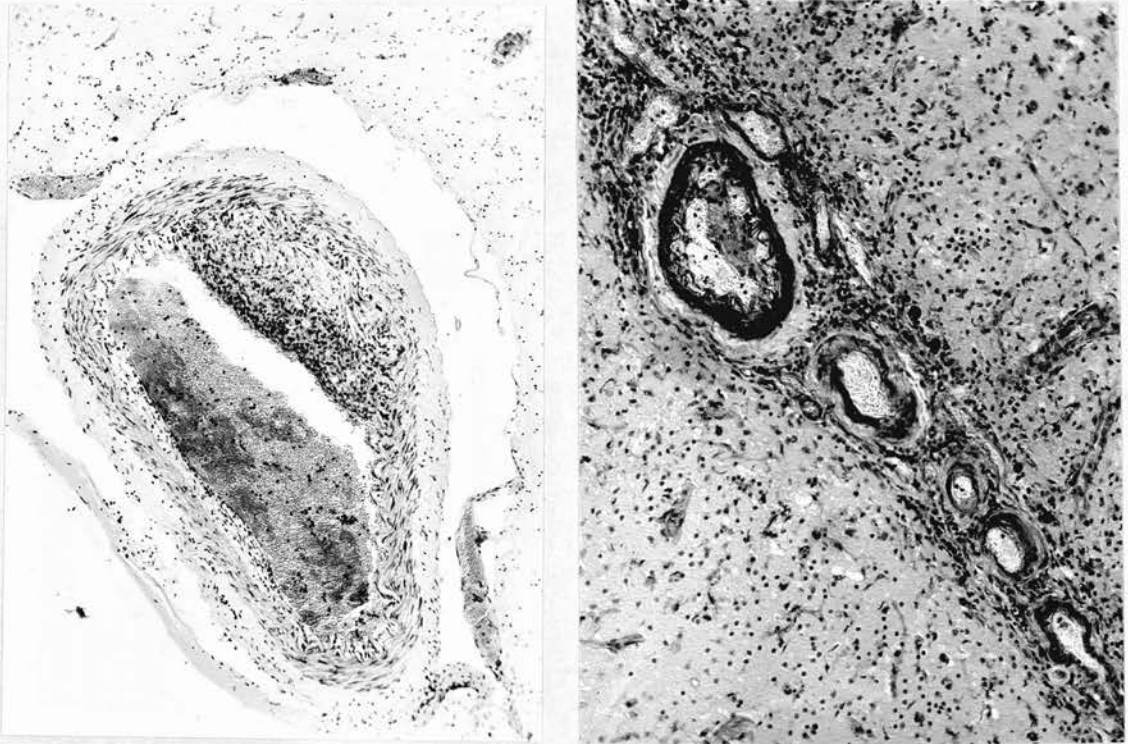
Histologically, the right hemisphere showed scattered infarcts of varying ages both in the cortex and underlying white matter. In the frontal lobe there were small focal lesions of recent ischaemic change in both the anterior and middle cerebral artery distributions. These varied in severity from slight ischaemic change in the nerve cells to active foci of destruction which were largely periarteriolar in distribution. Occasionally older lesions of several weeks' duration were also seen.

In the central part of the middle cerebral arterial territory there was patchy haemorrhagic infarction which was largely periarteriolar in type and lay scattered throughout the cortex and white matter. In these areas all the nervous elements were destroyed with little or no accompanying round cell infiltration or phagocytic reaction. The overlying leptomeninges contained numerous red cells, polymorphs, lymphocytes, large mononuclear cells and fat-filled phagocytes.

In the upper part of the precentral gyrus and in the occipital convexity the lesions were of long standing. They again varied in severity from total ischaemic destruction of all the tissues to a sparsely cellular necrosis which involved both the cortex and white matter. In these areas there was either a predominance of polymorphs or fat granules with astrocytic scarring.

In the cornu Ammonis there was a marked cellular loss with rod cell microglial change and

astrocytic hyperplasia. In the putamen were older lesions with breakdown of the cerebral tissues which were infiltrated by numerous compound granular corpuscles.



Many of the cortical vessels, especially in the peripheral branches of the middle cerebral artery, showed eccentric encroachment of the lumen by cellular masses containing cholesterol crystals and multinucleated giant cells. Other vessels of a similar calibre lying in the same area contained organising blood clot of varying ages, some of which had become recanalised (Figs. 2 and 3). Occasionally occluded vessels were seen lying in the sulci near areas of recent infarction when they were surrounded by a marked

cellular exudate including polymorphs, small round cells and compound granular corpuscles (Fig. 4). It was thought that this cellular exudate was the result of the recent cerebral infarction.

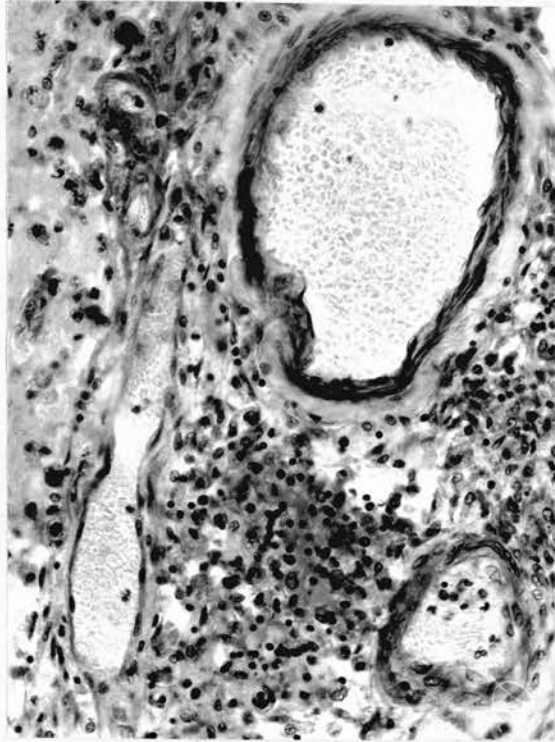


Fig. 4.