has an appreciable incidence and in which early diagnosis and surgical intervention may be life-saving.⁵⁰

At the moment one cannot differentiate between small localized intracerebral haematoma and ischaemic disease on clinical grounds but many physicians are now prepared cautiously to treat patients with a diastolic blood pressure of 110 mm or more who first present with symptoms of cerebral ischaemia. The benefits of such treatment seem to be established.^{12 51 52}

Miscellaneous Disease

The Wassermann reaction should be examined in every patient, young or old, with cerebral ischaemia. Twenty years ago this statement would be regarded as a statement of the obvious; it still is, but the infrequency of neurosyphilis is tending to a neglect of this precaution. In the elderly giant-cell arteritis is an important cause of cerebral ischaemia for, though its classical presentation is headache over one or other superficial cranial arteries, intracerebral ischaemia may be the first sign. The importance of recognizing the condition is that 20% of the patients may become blind as a result of the process.

In the younger patient the development of a stroke may indicate a wide variety of pathological conditions. Bickerstaff⁵³ has emphasized the importance of infection of the tonsillar bed in causing carotid artery disease and infarction of the cerebral hemispheres in childhood. In youth and early middle age systemic lupus erythematosus and polyarteritis nodosa need to be considered since they may present as typical

cerebral vascular disease. Takashay's syndrome with progressive encroachment on the major vessels of the aortic arch needs to be mentioned but is rare in the Western world.⁵⁴

Blood dyscrasias may rarely present with cerebral haemorrhage—usually because of thrombocytopenia.⁵⁵ "Acute blastic leukaemia" and subacute or chronic myeloid leukaemia head the list of the blood dyscrasias responsible. Haemophilia rarely presents with intracranial haemorrhage but such a case has been reported by Adeloey *et al.*⁵⁶ Even the otherwise relatively benign conditions of infectious mononucleosis has been known to cause cerebral haemorrhage with an associated reduction in platelets.⁵⁷

Conclusions

The recognition of the importance of thromboembolism from extracranial vascular sites in both cerebral infarction and transient cerebral ischaemia has prompted both physicians and surgeons to adopt a more dynamic approach to the problems of cerebral ischaemia. Even more fruitful may be the recognition of a separate pathological entity—namely, vascular brain lesions due directly to hypertension. The published results of treatment of hypertension in patients with cerebrovascular disease encourage the hope that these latter changes may be reversible.

It remains for clinicians to determine how one may distinguish on clinical grounds, or with ancillary aids, the essential differences between these two major processes in cerebrovascular disease.

Investigation of Stroke

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A realistic plan for the investigation of a patient with stroke must start with an honest estimate of the chances that it will lead to decisions about treatment that could not be taken otherwise. The natural history of this multiform disease is so variable that prognosis without treatment is unpredictable and such specific therapeutic procedures as are available—and they are few—have limited application. They may even carry a degree of risk and forms of investigation itself are not devoid of complication. Hence the question of "how to investigate" is generally less of a problem than "whom to investigate," and in this article a practical approach will be adopted with a constant eye on possible therapeutic implications.

Classification

Strokes have traditionally been classified as thrombotic, haemorrhagic, or embolic, but this strictly pathological division is scarcely adequate at the bedside. Though the distinction might seem easy, failure to make it correctly is commonplace. Furthermore, this classification deals in static pathological concepts and does not comprehend the subtler dynamic clinical phenomena of insufficiency and transient ischaemia, wherein the main therapeutic possibilities lie. The

usual practice now is to base our classification on readily observable clinical fact without presuming to divine the pathology: to describe the episode in terms of its temporal pattern using the expressions "completed stroke," "advancing stroke," and "impending stroke," as suggested by Millikan *et al.*⁵⁸ By "impending stroke" these authors meant the brief episodes of neurological dysfunction, usually lasting only seconds or minutes and leaving no residual deficit, that we now call "transient ischaemic attacks." The latter term is preferable because such episodes do not necessarily herald a major stroke.

The other change that affects nomenclature stems from a recognition of the role of the extracranial vessels in causing cerebrovascular symptoms. Whereas once we referred to thrombosis in small named intracranial arteries, now we attempt little more than a distinction between carotid and vertebrobasilar territories as sites from which symptoms arise. Thus at the bedside the tendency now is to categorize strokes according to this broad anatomical division coupled with an evaluation of its evolution in time, and the problems of investigation will be considered within the framework of this simple but practical system of classification.

The Completed Stroke

This is much the commonest clinical presentation of cerebrovascular disease. Though a few of those affected will be in the younger age groups, most will be over 60. The clinical picture will vary according to the site of the infarct or haemorrhage but many patients will have classical hemiplegia with or without dysphasia according to the side of the

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lesion. The severity will also vary. About 15% will die in the acute illness but among survivors the outcome may be anything from complete restoration of function within a week to total and permanent disablement. Many of the survivors will later suffer further strokes or other vascular accidents.

INVESTIGATION

Investigation of the completed stroke has one of two principal objectives, which may be combined. The first, and probably the more important, is to confirm that a stroke-like presentation is not due to some lesion other than cerebrovascular disease; the second is to determine the precise nature of the vascular lesion in true stroke cases. Nearly every well-documented "stroke" series includes the occasional patient who turns out unexpectedly to have a tumour, and such an occurrence is relatively common clinical experience. Probably in many instances the patient does have a cerebral infarct, but this is secondary to the tumour, perhaps on the basis of venous occlusion.

Apart from tumours, and these may be of any sort, other conditions may masquerade as strokes. Subdural haematoma, though strictly speaking a cerebrovascular disease, is not generally included in the category of stroke and indeed usually presents rather differently. Nevertheless, confusion may arise, and as subdural haematoma is so often curable by surgery it is vital that it should not be missed. The "stroke" victim whose level of consciousness fluctuates and is depressed disproportionately to his neurological deficit is the one in whom to suspect a subdural collection. Occasionally an abscess may present like a stroke and even the coma of severe meningitis or drug overdose, particularly in the elderly, may easily be ascribed to a cerebrovascular accident.

Clinical History

Other conditions may also mimic stroke, but these examples illustrate some of the diagnostic pitfalls and emphasize the need for special investigation in selected cases. It is, of course, neither necessary nor desirable that every case of stroke should be investigated and undoubtedly the single most useful item in the detection of those that need further study is the history. A good history will usually go a long way in eliminating non-vascular pathology, and it may provide strong supportive evidence in favour of stroke and sometimes a clue as to its precise nature. Thus a history of angina or intermittent claudication, rheumatic heart disease or hypertension, a family history of diabetes or myocardial infarction may be useful pieces of evidence. After the history, clinical examination of the nervous system can do little more than indicate the anatomical site of the lesion, but again general aspects of the case may give helpful pointers to the aetiology. An arcus senilis, diminished peripheral pulses, and a carotid bruit strongly suggest atherosclerotic occlusive disease as a cause for a brain syndrome, while an enlarged heart, grade IV retinopathy, and albuminuria would suggest a diagnosis of cerebral haemorrhage in a patient who had suddenly become comatose.

Obviously very many findings from the general examination may be of paramount importance. So may those from routine laboratory tests and ideally a full blood count including sedimentation rate, blood urea and electrolytes, cholesterol and glucose tolerance curve, and a serological test for syphilis should be carried out in all cases; also an electrocardiogram with particular reference to the heart rhythm and signs of ischaemia.

A careful clinical evaluation backed up by a few routine tests will thus in most cases go a good way towards confirm-

ing that a true stroke has occurred and also establishing something of its nature. There is a wide range of conditions, many of them rare, that may present as a cerebrovascular accident. Cerebral infarction can occur on an embolic basis in rheumatic heart disease, bacterial and "marantic" endocarditis, atrial myxoma, and air or fat embolism. Non-embolic infarction is encountered in several haematological disorders such as macroglobulinaemia, thrombotic thrombocytopenic purpura, myeloproliferative disorders (such as polycythaemia vera), and haemoglobinopathies—for example, sickle cell anaemia. It also occurs in inflammatory arterial diseases such as meningovascular syphilis, Takayasu's arteriopathy, giant-cell arteritis, polyarteritis nodosa, and other collagen disorders. Migraine and oral contraceptives must be included in this whole group of which the above list is only a sample. Levine and Swanson⁵⁴ have reviewed in detail the "nonatherosclerotic causes of stroke." Many of these disorders occur in the younger age groups and many are treatable. Uncommon though most of them are, it is nevertheless essential not to miss them. It is reassuring, however, that almost invariably the ordinary clinical procedures and routine tests already discussed will provide a clue, if not to the exact diagnosis, at least to the fact that we are dealing with something out of the ordinary.

Investigation beyond the point so far considered becomes necessary where doubt still exists about the basic pathology or where, particularly in younger people, it is felt necessary to define the nature of a vascular accident precisely. Unfortunately the latter seldom leads to specific treatment. Except in embolic infarction anticoagulants are contraindicated in the completed stroke and surgery has only a very limited place. It was hoped that patients with an acute stroke due to thrombus occluding an internal carotid artery might benefit from its immediate removal, but, while this operation still has a few advocates, most surgeons have now abandoned it. Urgent evacuation of clot as a routine procedure in cases of cerebral haemorrhage is profitless,⁵⁵ though in the rare case of haemorrhage into the cerebellum it may be life-saving.⁵⁶

Radiography

Further investigation, when it is necessary, should start with straight radiography. A skull x-ray film may show clinoid erosion or other evidence of raised intracranial pressure in cases of tumour, and shift away from the mid-line of a calcified pineal gland will indicate a space-occupying lesion. Abnormal areas of calcification may be due to neoplasms, arteriovenous malformations, or chronic haematomas and thin lines of calcification sometimes betray degenerative disease in the carotid siphon or in the distal segment of the basilar artery. A chest x-ray film should never be omitted as it may immediately indicate the nature of the cerebral lesion by showing a primary lung tumour.

Echo-encephalography

In cases where the pineal remains uncalcified, shift of mid-line structures may be demonstrated by echo-encephalography, and in experienced hands this safe and inexpensive procedure may also help in the detection of subdural haematomas.⁶⁰ Echo-encephalography does not, of course, distinguish between shifts due to tumour and those due to infarction or haemorrhage except that with serial measurements the vascular shifts will diminish. Achar *et al.*⁶¹ showed that a shift appearing very shortly after the onset of an acute stroke was strongly suggestive of haemorrhage rather than infarction.

Brain Scans

A cerebral hemisphere lesion, be it vascular or neoplastic, is likely to be accompanied by an abnormality in the electroencephalogram, but unfortunately there are no characteristic features that reliably distinguish the two causes. Serial records that show improvement obviously favour a vascular lesion.⁶² Another investigation where serial examination may be helpful is the isotope brain scan. It too is devoid of complication or discomfort for the patient but unfortunately cerebral infarcts and haemorrhages as well as tumours may give positive results.⁶³ The scan is not therefore the ideal discriminator but in most patients with a stroke it takes a week or so to become positive and after about six weeks the capacity for uptake is diminished. Hence repeated scanning for these characteristics may be of diagnostic help.⁶⁵

Lumbar Puncture and Angiography

One investigation that is useful in distinguishing between haemorrhagic strokes and infarcts (but that must be avoided with possible tumours because of its dangers) is lumbar puncture. The presence of blood in the cerebrospinal fluid, even in microscopic amounts, is strongly indicative of intracranial haemorrhage. Otherwise there are no special characteristics of the spinal fluid that help in the diagnosis of vascular cases and a striking increase in cells or protein (for example, over 100 mg/100 ml) must raise doubts about other lesions.

The definitive investigation in this context is, of course, cerebral angiography. It will usually demonstrate a tumour when present by the displacement of vessels and possibly too by a pathological circulation. It will show stenoses and occlusions of vessels and also kinks and atheromatous ulcers. In occlusion of the internal carotid artery it will show if the hemisphere in question is adequately supplied from the vessels on the other side and if collateral circulation has developed. It will be particularly useful in demonstrating aneurysms and angiomas. General aspects of angiography are discussed by du Boulay,⁵ and its role in cerebrovascular disease, including its hazards, by Marshall.⁶⁶

The Advancing Stroke

Though less important numerically, the advancing or progressing stroke has special therapeutic implications. The difficulty is that at any one time the doctor cannot establish whether or not the deficit is still advancing and hence must rely on personal observation or accurate historical information over a short period. Most strokes in this category are due to infarction and when in the vertebrobasilar territory the clinical picture is striking. Nevertheless, some are due to haemorrhage. Nearly all the points discussed in relation to the investigation of the completed stroke apply to the advancing stroke and the general approach is exactly the same. Here, too, it is extremely easy to be misled by the patient with a rapidly growing tumour associated with oedema who presents with a stroke-like picture.

The importance of the advancing stroke is that it may respond to anticoagulant therapy.⁶⁷ Clearly, if this treatment

is to be worthwhile it must be instituted without delay and the extent of preliminary investigation is a matter of debate. Because of the many diagnostic pitfalls, including the difficulty of recognizing haemorrhage, it is probably wise to carry out angiography as well as lumbar puncture as a preliminary where carotid territory is involved. But in advancing vertebrobasilar infarcts, whose clinical pattern is so characteristic, angiography can usually be omitted.

Transient Ischaemic Attacks

It is in this category that the investigation of stroke illness assumes the greatest importance for herein lie the main therapeutic possibilities. Again, the first stages of investigation are largely clinical to distinguish transient ischaemic attacks from other paroxysmal disorders such as migraine, epilepsy, carotid sinus syncope, and Ménière's syndrome. Most patients with transient ischaemic attacks have no neurological deficit and the detection of bruits in the neck is one of the most important parts of clinical examination. Another is careful fundoscopy in the search for retinal microemboli. The radial pulses and brachial blood pressures in the two arms should always be compared to detect subclavian stenoses. These may be associated with vertebrobasilar transient ischaemic attacks, where the stenosis is proximal to the take-off of the vertebral artery, the circumstance in which the "subclavian-steal syndrome" may be encountered.⁶⁸ X-ray films of the cervical spine should be included in the investigation of these vertebrobasilar attacks because of their association with cervical spondylosis.⁶⁹

Many patients with transient ischaemic attacks will be treated with anticoagulants but investigation is directed particularly towards finding atherosclerotic lesions in extracranial vessels that may be amenable to surgery.⁷⁰ Various ancillary investigations have been described which may help the detection of carotid stenosis. These include ophthalmodynamometry⁷¹ and thermography,⁷² but the definitive investigation is cerebral angiography. As it is obviously desirable to see the state of all the neck vessels, including their origins, when surgery is a possibility, some form of aortography is the method of choice. The variety of techniques available have been reviewed by Wood and Hilal,⁷³ and individual radiologists have their personal preferences.

Hypertension and Atherosclerosis

Thus far we have considered mainly the different categories of stroke illness, and little attention has been given to the investigation of patients from the point of view of the basic pathologies of cerebrovascular disease—hypertension and atherosclerosis. Probably the most important therapeutic measure of all in this field is the proper control of blood pressure in those with significant hypertension and a necessary preliminary to this is the investigation of its cause.⁷⁴ The possibility of influencing the cause of the atherosclerosis is at present more speculative, but (while the findings have doubtful relevance to treatment) it is nevertheless worthwhile investigating for lipoprotein abnormalities in cerebrovascular disease.⁷⁵