Vertebro-basilar Ischaemia*

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The transient reversible disturbances of neural function so often seen in older patients can be very perplexing, for at the time they are happening there may be no evidence of the cause and nothing upon which to base rational treatment or prognosis. As in these circumstances the patient recovers, often quickly and generally completely, the pathologist has been as bewildered about the nature of the disturbance of cerebral function as has the clinician. We have all seen patients who awaken aphasic or monoplegic or perhaps with a brain-stem syndrome of vertigo, ataxia, and diplopia, who improve in a few hours and entirely recover. In these circumstances the experienced physician defers judgment, for on the evidence available at the time he cannot tell if the disorder will advance to justify the diagnosis of thrombotic occlusion or whether rapid recovery may finally preclude diagnosis.

Little Strokes

These small strokes have been the subject of much speculation and have led to dispute on the existence of a state of vascular spasm. Pickering (1955) has been foremost in opposing this view, but local spasm of cerebral vessels has been seen during surgical manipulation of vessels (Pool, 1957) and at arteriographic puncture (Fletcher *et al.*, 1959), and it has been produced by experimental hypertension (Byrom, 1954).

The idea that local spasm may cause these episodes has finally been rejected, and in the past few years interest has been focused upon the effects of reduction in central blood flow. As occlusion of large intracranial vessels is associated with demonstrable infarct of the brain or brain-stem, and as it has been customary to relate what is happening in a patient with the structural changes seen in a pathological specimen, the smaller and transient disturbances were often considered in the same way, as due to occlusion of very small vessels, the degree of disability and its duration being related to vessel-size. It is now realized that intense but reversible disorder of function may result from ischaemia without any persisting disturbance of structure, and the whole approach to the problem of "little strokes" has taken on a more dynamic aspect. Clinicians are thinking in terms of rate of blood flow, and the height of the blood-pressure is being regarded as only one of the factors involved, although it has for so long dominated their interest and determined their approach to management of the patient.

Blood Flow

The physiology of local blood flow, involving cardiac output, blood volume, and both general and local peripheral resistance, has been very fully reviewed by MacDonald (1960), who outlines the many physical and physiological variables upon which it depends. We no longer consider an ischaemic portion of nervous tissue to be immediately distal to an occluded vessel, as in a pathological specimen; for pontine ischaemia, for instance, may be directly due to atheromatous stenosis of one vertebral artery in the thorax while all the distal portion of that long vessel is of normal calibre. Indeed, the ischaemic

event may not in time be directly due to the atheromatous stenosis ultimately responsible for it, because it may have supervened through fall of systemic blood-pressure due to several coincident causes, or have been caused by progressive narrowing of the more healthy contralateral vertebral artery or of a carotid artery which until that time had been providing adequate collateral flow (Fields *et al.*, 1961).

Once flow is held to be responsible for disorders of this kind a whole dynamic series of physical factors must be considered which do not operate in the static situation of ischaemic tissue distal to a thrombosed end-artery.

Angiography

The most important single reason for this advance in understanding of the complex factors underlying central ischaemia has been the demonstration of the nature and site of causal vascular lesions by angiography. It has shown that severe stenosis or even complete occlusion of great vessels may produce fluctuating, recurring, and reversible symptoms, so long as collateral flow is adequate—that occlusion may exist without infarct. Indeed, many instances have been described of patients surviving and experiencing only minor symptoms, with total occlusion of two of the great vessels in the neck (Groch *et al.*, 1960). Next, it has shown that narrowing of the appropriate artery is often remote from the resultant ischaemic area, to invoke the idea that alterations in the rate of flow in any vessel will depend upon many factors related to the state of the vessel itself, to its anastomotic connexions, and to systemic blood-pressure.

Thirdly, angiography showed that ischaemic episodes may happen without a gross vascular lesion, and it is now realized that in the ageing patient hypotension relative to the subject's needs is potent in causing central ischaemia. The tendency to think of a theoretically ideal normal blood-pressure has been replaced by the idea that many patients need a higher blood-pressure than is usual in order to maintain health, particularly of the central nervous system. While the general physician may wish to reduce blood-pressure to safeguard the heart and kidneys, the neurological physician may be equally concerned to keep it higher to ensure adequate central blood flow, and so safeguard the brain. Some of the so-called toxic effects of hypotensive drugs are the symptoms of central ischaemia.

Finally, angiography has demonstrated the extraordinary efficacy of collateral flow in the head, not just through the circle of Willis, but in the anastomoses which exist in the small vessels in the posterior fossa and between the internal and external cranial circulations. The advances in vascular surgery, based upon hypotensive and hypothermic techniques, have quickened interest, and the debate upon the use of anticoagulants has helped to focus it upon the subject of the management of cerebrovascular disorders, which has been neglected for so long.

Hutchinson and Yates (1956) made a great advance when they showed that morbid-anatomical examination of the vessels in the neck and thorax was essential to the understanding of strokes, for previously it had been usual to confine examination to the intracranial circulation. Following up their work, Sheehan *et al.* (1960) found that in about a third of their patients with cerebrovascular catastrophes there was disease of

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the vertebro-basilar system, in a third there was disease of the carotid arteries, and in the last third there was disease in smaller vessels within the cranium. Denny-Brown (1951, 1953) referred to a state of carotid insufficiency and later to vertebro-basilar insufficiency in order to emphasize that in many of the ischaemic disorders in the territories of these vessels the cause was reduction in the rate of flow in distinction from its causation through thrombosis. Brain (1957), Wells (1960), and Hutchinson (1962) have reviewed the very important and variable role of the circle of Willis and other collateral mechanisms within the head and neck in maintaining blood-flow when one or more of the large vessels is stenosed or occluded, thus making possible the maintenance of function in brain-stem and hemispheres. Alpers *et al.* (1959) and Alpers and Berry (1963) have found that while there are "normal" circles of Willis in 52% of subjects with normal brains, such a state is found in only 33% of the subjects with cerebral softening. Riggs and Rupp (1963) found hypoplasia of one or more components of the circle in 79% of 994 subjects with evidence of "neural dysfunction."

Causes of Vertebro-basilar Ischaemia

In addition to atheromatous stenosis of the vertebral or basilar arteries within the thorax, neck, or head—see Williams (1961) and Williams and Wilson (1962)—many ancillary causes for diminished flow in this system must be considered. The vessels are very vulnerable to the effects of neck movements (Sheehan *et al.*, 1960), particularly at the atlanto-occipital joint (Brain, 1963), and extreme rotations, as in backing a car, may be disastrous. Therapeutic manipulations of the neck have initiated a similar sequence (Hallberg, 1957), especially with cervical arthritis (Sheehan *et al.*, 1960), and many of us have experienced the subjective effects of compressing the vertebral arteries in full extension, which, for instance, prevents admiration of cathedral vaultings. It is best to recline on a pew for this purpose, for from middle age onwards any but the most natural movement of the neck is folly. The effects of reduction in systemic blood-pressure from any normal or abnormal cause, including ischaemic heart disease, have already been mentioned, and the responsibility of anaemia is easily overlooked.

Syndromes of Vertebro-basilar Ischaemia

We are not here concerned with the effects of massive brain-stem infarction which causes a syndrome, including coma with spastic tetraplegia; but it is well to recall that Kubik and Adams (1946) described the necropsy findings in 18 patients with this syndrome and then gave the histories of four patients, still living, with similar syndromes, and so opened the way for our present discussion. Biernond (1951), Denny-Brown (1953), and Millikan and Siekert (1955) followed this with accounts of the symptoms which may be due to reduction of flow in the basilar system; the whole matter of the diagnosis of these vertebro-basilar syndromes has been reviewed by Williams and Wilson (1962) on the basis of 20 confirmed cases and of 65 patients with minor degrees of the same disorder.

The diagnosis of basilar insufficiency depends upon the association of sets of symptoms which recur or fluctuate in patients whose general condition suggests the possibility of one of the responsible mechanisms—atherosclerosis, cervical arthritis, relative hypotension, or coronary heart disease, with particular precipitating factors such as sudden change in posture or neck movement, or with the factors, such as fatigue, which may cause temporary arterial hypotension.

The most common combination of symptoms met in these circumstances is that of visual disorders with vertigo, and perhaps faintness and evidence of local brain-stem dysfunction such as diplopia. There are usually black or white spots before the eyes (attributed to "liver") or other patterns of obscuration

of vision (hemianopic or central, yellow patterns, fortification spectra, or organized hallucinations) associated with vertigo related to neck movement, occipital headache and tenderness, faintness, and many other less common symptoms. The frequency of the main symptoms in order is: visual changes, including diplopia in two-thirds; vertigo in nearly two-thirds; vasomotor, thoracic, or abdominal disturbances with nausea in one-quarter; ataxia, weakness of the legs, or drop attacks in one-third; lowering of consciousness in one-third; other uncommon symptoms—sensory, hemiplegic, trigeminal, or auditory; occipital headaches often. If the vertebral artery is also involved there may be sensory changes in an arm at the same time.

The most common initial symptoms in the attacks are vertigo, visual hallucinations, lowering of consciousness, nausea, ataxia, diplopia, and drop attacks, in that order.

The natural history is that of brief recurring minor episodes over months or years, to which the patient may have become accustomed, and which are described only after a more severe episode has brought the disorder to a physician's notice. These small attacks usually carry a good prognosis at the time and in time, the outlook being better when they are related to fluctuating hypotension or to neck movement, and more grave when there are no evident precipitating causes for the episodes of ischaemia. They are common over 60 and their relationship to transient reduction in blood flow will offer an explanation for a miscellany of inexplicable symptoms encountered so often by the family doctor.

Investigation and Management

Early in management a distinction must be made between the young generally healthy patient experiencing distressing and ominous attacks due to gross local stenosis for which reparative vascular surgery might be indicated, and the older arteriopathic or hypotensive subject in whom arteriography should not be undertaken. Retrograde panarteriography via the brachial or femoral artery, or direct vertebral puncture, may be used, but they should be undertaken only when there is likelihood of the presence of a surgically amenable lesion, and they carry risks in the arteriopathic.

The first medical decision is whether or not to use anti-coagulants, and though most of the evidence is contrary, as Shaw (1962) has concluded in his review of the subject, "their use should be limited to the treatment and prevention of cerebral embolism, actively progressing neurological deficit, particularly in the vertebro-basilar territory, and transient ischaemic attacks involving either the carotid or vertebro-basilar system." Certainly intermittent disturbances due to stenosis proximal to the circle of Willis constitute a situation like that in the coronary circulation, in which, given time, a collateral circulation may become established and anticoagulants may prevent thrombus extension during that time.

More important is attention to the patient's pattern of living, to increasing his daily exercise and reducing his daily strains, and so often to efforts to raise his blood-pressure. A therapeutic method of maintaining a higher blood-pressure may well give greater benefit to more elderly patients than have hypotensive substances. We must remember that a moderate sustained increase in systemic blood-pressure will greatly affect the blood flow at end branches of one of the long tenuous pontine arteries, through the mediation of collateral circulation, which can change it from an inadequate to an adequate level. At present that can only be achieved temporarily with amphetamine, ephedrine, or ergotamine, but this, with early mobilization, exercise (keeping the neck still), and a new curriculum vitae, may ensure many more years of healthy life.

Though the great advances in surgical and medical techniques have not yet fulfilled the promises we expected, the present convergence of interest in central blood flow has altered our

whole approach to these disorders, so that lively and prospective management has replaced inertia and the chronic ward, and that in itself is worth while.

Summary

In opening a discussion on vertebro-basilar ischaemia, transient and reversible disturbances of cerebral and brain-stem function—"little strokes"—are attributed to reduction in the speed of blood flow, while both vascular spasm and thrombotic occlusion of small vessels are rejected as causal. Angiography shows that stenosis or occlusion of a large vessel may be remote from the resulting neural lesion, and that the haemodynamic properties of collateral flow may determine the pattern of disordered function and modify it in time. Precipitating factors, especially transient reduction in general or local blood-pressure, with preceding stenosis or occlusion, are largely causal. Many related changes in cardiovascular function may decide whether local flow is sufficiently reduced to cause transient symptoms.

The diagnosis of vertebro-basilar ischaemia depends on the association at any one time and from time to time of a number of apparently unrelated symptoms. The most common association is that of obscurity or other disorder of vision, with vertigo, ataxia, nausea, sensory changes, drop attacks, or loss of consciousness.

Investigation by angiography is reserved for special cases in the young; the results of treatment by vascular surgery have so far been disappointing; there is a place for the use

of anticoagulants, but usually treatment is by general medical management.

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Proteins of Serum and Oedema Fluid in Rheumatoid Arthritis

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Oedema occurs in many conditions and can usually be explained on the basis of sodium retention, increased filtration pressure, lymphatic insufficiency, reduced plasma osmotic pressure, or increased capillary permeability. The cause of the oedema which occurs quite often in rheumatoid arthritis has not yet been established.

Crockett (1956) measured the protein levels of oedema fluid in several diseases and on the basis of his results he was able to classify the causes of oedema into three distinct categories. This is shown in Table I. The third class of oedema, which is that due to increased permeability of the

in rheumatoid arthritis have not previously been reported. This information, together with a knowledge of the relative sizes of the different protein fractions, should make it possible to decide whether or not the oedema is due to increased capillary permeability.

In the subacute and chronic phases of rheumatoid arthritis, oedema is most prominent in the region of the feet and ankles.

Material

Specimens of oedema fluid were obtained from the subcutaneous tissues by acupuncture. In order to avoid dilution of the fluid a local anaesthetic was not used, and the discomfort was only slight. There was difficulty in obtaining specimens which were uncontaminated with blood, and it was usually impossible to do more than introduce the tip of a Southey tube under the skin. Any attempt to pass the tubes full length, in the usual way, nearly always provoked bleeding. Since attempts at acupuncture were limited to two per patient the number of specimens obtained was restricted. A further difficulty was the slow rate of flow from the tubes; even after 15 to 20 minutes' collection the samples were small, usually 0.5 to 1 ml.

TABLE I.—Classification of Oedema According to Protein Level (Crockett, 1956)

Cause of Oedema	Protein Level of Oedema Fluid (g./100 ml.)
1. Disturbed balance of the capillary filtration-absorption equilibrium	0.1-0.9
2. Impaired lymphatic clearance of tissue-fluid protein	1.0-4.0
3. Increased capillary permeability	4.0-6.0

capillary endothelium, occurs in inflammatory conditions, including burns and scalds, and in allergic reactions. It was thought possible that the oedema of rheumatoid arthritis might also be caused by increased capillary permeability, resulting either from the inflammatory nature of the underlying disease or from tissue responses of an allergic type. The protein levels and electrophoretic pattern of oedema fluid

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