Progress Review

Evolution and Testing of the Lacunar Hypothesis

John M. Bamford, MD, MRCP, and Charles P. Warlow, MD, FRCP

Since Fisher’s detailed observations in the 1960s, the term lacunar infarction has become established in the cerebrovascular literature. To some extent, users of the term implicitly accept the bipartite hypothesis that, among patients with cerebral infarction of diverse cause, there exists, first, a small number of distinct clinical syndromes that are associated with small deep infarcts or lacunes and, second, that these are the result of occlusion of single perforating arteries by characteristic vascular lesions. Several studies have suggested that lacunar infarcts may constitute up to 20% of all cases of cerebral infarction—though less is known about the specificity of the underlying arteriopathy. Despite their relative frequency, there have not been any trials of specific treatments, and furthermore, few treatment trials of cerebral infarction in general have taken this important subgroup into account, perhaps resulting in the inappropriate discarding of therapeutic measures that might benefit other subgroups.

To decide whether this is due to some basic flaw in the hypothesis, to inadequate testing, or to poor communication of its clinical implications to other physicians, two questions need to be answered: are the clinically recognizable lacunar syndromes usually caused by lacunes and, if they are, are these lacunes usually caused by a specific disorder of the small perforating arteries at the base of the brain, which differs qualitatively from the more widely studied atheroma of extracranial arteries.

Over a period of 150 years reports have come from clinical, pathological, and, more recently, radiological sources. These disciplines identify cases of “lacunar infarction” in different ways, and each places, often implicitly, its own interpretation on terminology common to them all. To use all available data to test the hypothesis, one has to examine the relations between findings from each discipline. Since in clinical practice patients are likely to come to medical attention because of clinically apparent strokes rather than because of pathological or radiological findings, we have considered the clinical features to be the primary way of delineating this group of patients.

Evolution of the Hypothesis

Lacunes

The first pertinent observations were made in the French literature of the mid-to-late 19th century and have been reviewed in detail. Lacune was simply a descriptive pathological term, first attributed to Dechambre. The uncritical and therefore confusing use of the term lacune lead Poirier and others to distinguish three types: Type I, small areas of cerebral infarction; Type II, the cystic scars that are the residua of small hemorrhages; and Type III, areas of perivascular dilatation not associated with infarction. A further division might be made between those patients with many lacunes and those with either a single or very few lacunes. Multiple Type III lacunes were described as l’état crible by Durand-Fardel. They are seen frequently at autopsies, and various mechanical theories have been proposed for their genesis though no definite association has been made with any clinical syndrome. In contrast, l’état lacunaire or the lacunar state, first described by Marie, consists of multiple Type I lacunes. It has been associated with chronic, progressive neurological deterioration, often without any clear-cut strokes, culminating in a variable combination of dementia, pseudobulbar palsy, incontinence, and gait disorder (marche à petits pas). The further investigation of these pathological findings represents an important independent area of research, but in this review we are primarily concerned with the lacunes that present as strokes.

Though it has been suggested that the lacunar state is rare in modern clinical practice, it is important to distinguish it from single lacunes presenting as strokes when examining the lacunar hypothesis. In autopsied cases in which a stroke has been attributed to a particular lacune, very few other lacunes have been found despite several years elapsing between the stroke and the autopsy. While one has to accept that there may well be a
Clinicopathological Correlation

Following the recognition of lacunes at autopsy, reports appeared correlating them with specific clinical deficits. In 1885 Bennett and Campbell reported a patient with brachiofacial weakness resulting from a capsular lacune. Marie and Ferrand recognized that capsular or pontine infarction could give a hemiplegia without persisting sensory loss, visual field defect, or aphasia, and other workers reported variations in the extent and pattern of the hemiplegia. Interest then waned until the seminal papers of Fisher and his colleagues in the 1960s reporting a total of 97 patients with strokes. They drew attention to a number of distinctive syndromes that might be caused by small lesions in the basal ganglia and pons, where fiber tracts are densely packed, but that would not be expected to occur as a result of cortical lesions without evidence of higher cerebral dysfunction or hemianopia. This first part of the hypothesis was generated by autopsy evidence of lacunes in nine cases of pure motor hemiplegia (six in the basal ganglia and three in the pons) and in a single case of homolateral ataxia and crural paresis (capsular lacune) and dysarthria-clumsy hand syndrome (pontine lacune). The single autopsy case reported as pure sensory stroke from a thalamic lacune had had only transient ischemic attacks clinically. Since then, a small number of other autopsied cases have been reported. Pure motor stroke has been associated with lacunes in the basal ganglia, the medullary pyramid, the cerebral peduncle, and the pons. Fisher and his colleagues and Weisberg reported cases of pure sensory stroke associated with thalamic lacunes, and three cases of ataxic hemiparesis have been associated with pontine lacunes. Undoubtedly this relative paucity of autopsied cases reflects the very low early case-fatality rate of patients with this type of stroke, but it does serve to emphasize that these reports expanded rather than proved the first part of the hypothesis.

Fisher and Curry considered pure motor stroke (or hemiplegia) to be a complete or incomplete paralysis of the ipsilateral face, arm, and leg accompanied by sensory signs (though symptoms might be present), visual field deficit, evidence of higher cerebral dysfunction, or signs that clearly localized the lesion to the brainstem. They emphasized that the definition depended on observations made during the acute phase of the stroke, a fact that is either overlooked or not detailed in many reports, particularly those describing apparent exceptions to the hypothesis. The definition of pure sensory stroke was similar, with a sensory deficit rather than paralysis, though Fisher noted that “a more limited sensory involvement might represent a partial syndrome.” Indeed, in a later pathological study one case had convincing symptoms and signs only in a brachiofacial distribution. We shall return to the question of partial syndromes later though La不再是le and Haguenau have discussed topographical sensory disturbances from thalamic lesions. The syndromes of homolateral ataxia and crural paresis, dysarthria-clumsy hand syndrome, and ataxic hemiparesis are generally thought to represent broadly similar processes in which a disturbance of corticospinal or corticobulbar function is combined with ipsilateral incoordination of a cerebellar type, and this group as a whole will be referred to as ataxic hemiparesis.

The Underlying Vascular Lesion

The second and most important part of the hypothesis, in terms of defining an etiologically distinct subgroup of cerebral infarction, is that ischemic lacunes are caused by a specific disease of a single perforating vessel. The amount of time it takes to demonstrate such pathology no doubt accounts for the small number of detailed reports in the literature. In a 1969 paper, Fisher reported the vascular pathology underlying 50 lacunes. In 40 lacunes there was occlusion of the supplying artery by segmental disorganization of the wall (called lipohyalinosis, a term that emphasizes that the lesions stain readily for fat) when the normal vessel diameter was between 40 and 200 μm. In three other lacunes segmental disorganization was suspected. The microscopic features of lipohyalinosis are the replacement of the muscle and elastic laminae by collagen and a generalized increase in subintimal hyaline material, which in places is sufficient to cause vessel occlusion. This does not always occur at sites of arterial bifurcation. Lipohyalinosis is also associated with areas of focal dilatation and may be the underlying cause of Charcot-Bouchard aneurysms, though thrombosis within or emboli from these areas of dilatation might equally occlude the vessel. The vessels supplying three larger lacunes (in the internal capsule, the caudate, and the thalamus) were found to be occluded more proximally (normal vessel diameter between 300 and 500 μm) by plaques of foam cells subsequently termed microatheroma. In one of these three lacunes the arterial wall was almost destroyed, and Fisher speculated about a possible connection between the two apparently distinct processes. Two other lacunes appeared to be related to thrombosis of fusiform aneurysms on cortical penetrating arteries, one lacune was attributed to pressure from an adjacent microaneurysm, and in one lacune no lesion was found.
is important to note that 36 of the 40 lacunes associated with lipohyalinosis came from a single patient who had the clinical features of the lacunar state, whereas the three lacunes related to microatheroma came from a patient who had had three discrete strokes, at least one of which was a pure motor stroke.

Ten years later, Fisher21 described the vascular pathology underlying capsular lacunes. The vessels supplying six lacunes were occluded by proximal microatheroma, often at a site of acute change in vessel direction, and in another vessel there was a hemorrhagic area of lipohyalinosis. The vessels supplying two other lacunes were patent 1 month and 6 years after the stroke. Fisher suggested that embolism was the most likely mechanism, though no obvious embolic source was found. Six patients had presented with a pure motor stroke. The final, large lacune appeared to have been caused by an atherosclerotic plaque in the middle cerebral artery at the origin of two perforating arteries, but in addition to a motor deficit the patient had a disorder of higher cerebral function. The vascular lesion underlying single, symptomatic lacunes has been confirmed in two additional cases in which lipohyalinosis was associated with thalamic lacunes. A lacune in the cerebral peduncle, which had caused a pure motor stroke, had hyalinized arterioles close to the infarct, and in an additional case a basilar branch was occluded by a plaque in the parent artery.

From the limited pathological evidence available, microatheroma seems to be the most frequent cause of single symptomatic lacunes. However, the exact relations between microatheroma and lipohyalinosis and between these small-vessel arteriopathies and large-vessel atheromatous plaques remains uncertain. Are they independent arterial disorders, or do they always occur together in the same individual, the small-vessel disease merely becoming symptomatic first? Could the small-vessel pathology even be the consequence of embolism from proximal sites? Microatheroma and lipohyalinosis have been considered to be the reactions of different parts of the arterial system to different grades or durations of hypertension, though the association with hypertension is less convincing in cases of single symptomatic lacunes than in cases with the lacunar state. Fisher commented that “in general the degree of atherosclerosis paralleled the number of lacunes.”10 There are morphological similarities between microatheroma and the early stages of a typical extracranial atheromatous plaque, but autopsy studies undertaken years after the first symptomatic event would not necessarily give an accurate view of the state of the arteries at the time of the stroke. This should not detract from the clear need for further detailed studies of the underlying vascular pathology.

Other Lacunar Syndromes

Pure motor stroke, pure sensory stroke, and ataxic hemiparesis were the prototype lacunar syndromes, but should other clinical deficits be included? If the potential value of the hypothesis depends on the group remaining as etiologically homogeneous as possible, then it seems reasonable to suggest that, if other patterns of neurological deficit are to be considered as lacunar syndromes, there should be evidence that they are usually caused by ischemic lacunes. Ideally, one should also demonstrate that the lacunes are caused by small-vessel disease, but this council of perfection is unlikely to be attained, and one may have to assume this after the exclusion of other causes. Thus, although many of the traditional brainstem syndromes have been associated with small areas of infarction, they seem to be caused most frequently by occlusion of the mouth of a basilar branch artery, either by embolism or atherosclerosis in the parent artery. To include such cases limits the utility of the original clinicopathological observations, and we would agree that it is confusing to call these lacunar syndromes. Similarly, areas of striatocapsular infarction that often give disorders of language or mentation, though confined to the “deep” structures, are usually caused by occlusion of the mouths of several perforating arteries by thrombosis or embolism in the stem of the middle cerebral artery.

There has been a reluctance to accept sensorimotor stroke as a lacunar syndrome partly because of the limited pathological confirmation and partly because of the anatomical argument that the lenticulocapsular region, where most lacunes causing pure motor stroke are found, obtains its blood supply from the lenticostrate branches of the middle cerebral artery while the ventral postero-lateral (VPL) nucleus of the thalamus, the site of most lacunes causing pure sensory stroke, is supplied by the thalamogeniculate arteries arising from the posterior cerebral artery. Nevertheless, it would seem unlikely that cortical infarction sufficiently extensive to cause this sensorimotor deficit would do so without also causing higher cerebral dysfunction or hemianopia. The term sensorimotor stroke was first used to denote a lacunar syndrome by Mohr et al, whose case had an area of infarction in the VPL nucleus, though a zone of myelin loss was seen to involve the posterior limb of the capsule. Previously, three reports had described both motor and sensory disturbance (among other symptoms) from lacunes predominantly in the thalamic nuclei. The vessel supplying the lacune in one case with motor and sensory loss described by Fisher was patent 1 month after the stroke, and embolism was suggested as a possible mechanism. Robinson et al reported a case with an infarct in the posterolateral nucleus of the thalamus, with some extension to the postero medial nucleus. Fur-
thermore, some cases reported as pure motor stroke had objective sensory loss for >24 hours. Many cases of pure motor stroke have initial sensory symptoms, and this may reflect ischemia of the VPL nucleus, perhaps related to edema, though infarction might not occur due to the independent vascular supply. It seems quite likely that the classification of any individual case will depend on the timing, extent, and competence of the sensory examination. Interobserver variation in such testing is well documented, and neurophysiological techniques can show evidence of involvement of the lemniscal pathways in cases of apparent pure motor stroke. Thus, the distinction of sensorimotor stroke from pure motor stroke is somewhat arbitrary and would be important only if they were shown to have different etiologies. The presence or absence of an objective sensory deficit at the time of examination has been suggested as a way of distinguishing them.

A number of abnormal movement syndromes have been associated with lacunes at autopsy, and it has been suggested that hemichorea should be considered as a lacunar syndrome. Such cases appear to be relatively rare, and the acceptance of them as lacunar syndromes should probably await further reports.

The pathological studies in a small number of patients described above generated the hypothesis linking the four lacunar syndromes with ischemic lacunes and they in turn, more or less convincingly, with arteriopathies of single perforating vessels. However, to assess the utility of the concept of lacunar infarction, it is imperative to investigate the specificity of these associations on large, unselected groups of patients with stroke. While not detracting from the need for further detailed pathological studies, the role of this discipline will be limited since most patients will not die from their stroke, and even if an autopsy is eventually obtained, one is then faced with the problems of interpreting pathological findings in patients who may have had multiple clinical events. Thus, different ways of testing the hypothesis have to be explored.

Testing the Hypothesis

Small Deep Infarcts

The advent of computed tomography (CT scanning) resulted in a large number of reports of its use in lacunar stroke and a natural tendency to regard CT as the in vivo equivalent of an autopsy examination. However, when using CT reports to test the lacunar hypothesis, one has to make assumptions: first, that a small area of reduced attenuation seen on CT in a patient with a lacunar syndrome represents an ischemic lacune (hence the view that the term lacune should be reserved for the lesion seen at autopsy), and second, that the underlying vascular pathology is a small-vessel arteriopathy similar to the few pathologically examined cases. These assumptions will apply equally to lesions visualized with magnetic resonance imaging (MRI). There are a few pathoradiological studies that report both high false-positive and high false-negative results, but further pathoradiological correlation studies would help to clarify whether we are usually correct in making these assumptions. On the other hand, smaller lacunes (<1 cm in diameter), especially in the posterior fossa, are unlikely to be visualized by CT with any regularity at the present time. Using serial and slow scanning techniques, Donnan et al reported that among patients with lacunar syndromes an “appropriate” CT abnormality was seen eventually in 69%. However, in large studies <35% of patients with lacunar syndromes have had lesions on CT. Kappelle and van Gijn have pointed out that it is not always possible to infer the origin of the involved artery from the position of small deep infarcts on CT as the branching pattern of the penetrating arteries is not uniform. Similarly, though autopsy reports have described the size of lacunes, there is no clear evidence that the maximum size of an infarct attributable to occlusion of a single perforating artery has been established, nor is there any evidence that measuring the volumes of infarcts on CT and applying the autopsy-derived values is useful in distinguishing cases with a small-vessel arteriopathy. Nevertheless, if we accept these limitations, there is now a considerable amount of data that can be used to test the lacunar hypothesis.

Lacunar Syndromes and Nonischemic Pathology

It is worth stressing that lacunar syndromes should represent the maximum neurological deficit occurring from a single vascular event and, therefore, the reports of similar clinical deficits resulting from nonvascular pathologies have not been considered further. In larger hospital series of patients with lacunar syndromes, between 7% and 14% were caused by intracerebral hemorrhage, though they constituted only 3% of a community-based series. Huang et al noted that the degree of motor or sensory deficit in cases due to hemorrhage was generally severe, a factor that has been shown to increase the chances of hospital admission. Each lacunar syndrome has been reported to have been caused by intracerebral hemorrhage. Early CT scanning is necessary to exclude hemorrhage since in these cases there is rarely intraventricular extension and, therefore, hemorrhage cannot be distinguished reliably from infarction on clinical grounds.

Lacunar Syndromes and Cortical Infarcts

It is more difficult to determine the frequency with which cortical infarction presents as a lacunar syndrome, and it is likely to be very dependent on the clinical definitions that are used; the more anatomically restricted the neurological deficit the more likely it is to occur from a cortical lesion in the absence of a hemianopia or higher cerebral dys-
function. An example of this would be two of the three cases of Pullicino et al in which large cortical lesions were reported to have caused pure motor deficits. In one case only the face and hand were involved, and the other patient had weakness of the leg alone, progressing to a hemiparesis only at a later date. This also demonstrates the difficulty of diagnosing lacunar syndromes in patients who have had previous strokes. While equally restricted deficits have been reported in association with small deep infarcts, investigators must show that such patterns usually occur with small deep infarcts rather than with cortical infarction before including them as lacunar syndromes. Nelson et al reported five of 26 cases of pure motor stroke who had large superficial infarcts. Although their reasons for selecting patients for CT and the timing of the clinical examinations are not given, their report raises the question of whether the routine clinical examination of nondominant hemisphere higher cerebral function is sufficiently sensitive since all five patients had right hemisphere infarcts.

A number of studies do provide support for the inclusion among lacunar syndromes of patients with clinical deficits that are less extensive than those described in the original pathological papers. Rascol et al noted that among 30 cases of pure motor stroke, of whom 29 had appropriate small deep infarcts on CT, 16 had classical pure motor hemiplegia as described by Fisher and Curry, while 13 had only brachiofacial weakness. Donnan et al reported a series of 69 CT-positive cases, of whom 32% had incomplete syndromes, most frequently brachiofacial. Such lesions tended to occur in the corona radiata or the junctional zone between this and the internal capsule and on average had a smaller volume than cases with the complete facio-brachiofacial syndrome. A recent study of sensorimotor stroke supports the inclusion of brachiofacial and brachiofacial deficits as lacunar syndromes, and in a community series using these anatomical definitions, only 3% of patients with lacunar syndromes had infarcts on CT that were not compatible with occlusion of a single perforating vessel. There will always be exceptions to any method of classification, but the inclusion of these partial syndromes seems likely to increase the sensitivity of the clinical classification without substantially lowering the specificity.

**Lacunar Syndromes and a “Normal” Computed Tomogram**

The CT scan is often “normal” in patients with a lacunar syndrome; this could be a failure to visualize either a cortical infarct or a small deep infarct. However, in a large prospective series the clinical features and risk factor profile showed better correlation with CT-positive small deep infarcts than with CT-positive cortical infarcts. The report of the use of cerebrospinal fluid enzymes to distinguish these groups is interesting but requires further confirmation. There are several reports of the use of electroencephalograms in lacunar stroke, but the discriminant value of this technique is likely to be low. However, the recent report of Rothrock et al comparing CT and MRI in patients with a clinical diagnosis of lacunar stroke (assessed within 72 hours after onset) supports the lacunar hypothesis. Among nine patients examined with both techniques within 120 hours after onset, MRI showed appropriate new areas of infarction in all cases, none of which were seen on CT. In five cases the area of infarction was in the pons. When performed later MRI remained more sensitive, and among 29 patients with lacunar syndromes no acute cortical infarcts were demonstrated.

**Lacunar Syndromes and Small Deep Infarcts**

Cases with pure motor stroke have been reported most frequently, and the majority of those that were CT-positive had infarcts in the capsular region. Using computerized superimposition, Allen et al demonstrated that such lesions most frequently overlapped in the posterior half of the internal capsule. Infarcts have also been visualized in the pons in keeping with the pathological studies. There are very few reports of the CT appearances in pure sensory stroke though small deep infaracts have been visualized in the thalamocapsular region in keeping with pathological studies. Superficial infarcts have been reported to give pure sensory stroke, but usually, insufficient clinical details are available to assess them. In one case the clinical deficit was anatomically restricted and involved only cortical sensory modalities.

A number of authors have described the CT appearances in patients with ataxic hemiparesis (or its variants). Lesions have been most frequent in the posterior limb of the internal capsule and the adjacent corona radiata, more in keeping with the autopsied case of dysarthria-clumsy hand syndrome than the cases of pure ataxic hemiparesis that had pontine lacunes, though these have also been visualized on CT.

CT studies support the inclusion of sensorimotor stroke as a lacunar syndrome. The most detailed study is that of Huang et al who reported 45 patients, 30 of whom had deep infarcts most frequently in the thalamocapsular-corona radiata region. Allen described 12 cases of sensorimotor stroke examined soon after onset, 11 of whom had areas of low attenuation that were, on average, larger than those in patients with pure motor stroke. When superimposed, they extended more medially, abutting the posterolateral aspect of the thalamus. This would be in keeping with the pathologically studied cases, though cases with initial sensory symptoms do not always have infarcts closer to the thalamus.
Lacunar Syndromes and Angiography

It is much more difficult to test the second part of the hypothesis, that the small deep infarcts associated with these syndromes are usually caused by a specific small-vessel arteriopathy. No radiological technique will show us reliably the site of occlusion in the perforating arteries, let alone the changes in the vessel wall. Therefore, we are left trying to exclude other possible causes of infarction. As we mentioned earlier, the question of coexistent extracranial atherosclerosis is of considerable importance. Some angiographic data are available, though the reasons for selecting patients for angiography are usually not stated and, therefore, there may be bias. In the original series of pure motor strokes, none of the five cases undergoing angiography had marked extracranial or intracranial stenoses, though in two there was possibly poor filling of the lenticulostriate vessels. Similarly, all 10 angiograms performed in patients with pure sensory stroke were normal. Rascol et al noted that no carotid or vertebral stenosis was found in 21 patients with pure motor stroke who underwent angiography. Mohr et al reported that among patients undergoing angiography, 63% of those with lacunar syndromes were normal compared with only 4% among those with "cerebral thrombosis." In the series of Loeb et al, 41% of lacunar cases and 69% of other ischemic cases had significant carotid stenosis or occlusion, and Donnan et al reported ipsilateral carotid abnormalities in 35% of their lacunar infarcts.

Small Deep Infarcts and Angiography

A number of studies have described the angiographic findings in patients with small deep infarcts on CT. While one cannot be certain of their relevance to patients presenting with lacunar syndromes, it seems pertinent to review these data in view of the rather limited number of studies that have provided clinical details. Olsen et al reported 73 consecutive and relatively unselected patients with nonhemorrhagic stroke, all of whom had angiograms and CT within 2 days after admission. Virtually all cases with small deep infarcts on CT had minimal changes in their carotid arteries and had significantly less internal carotid disease than those with larger infarcts involving the cortex. These results are in accord with the earlier findings of Prineas and Marshall and Pullicino et al. Ringelstein et al reported stenosing lesions in the extracranial vessels in 22% of patients with small deep infarcts compared with 71% in other types of cerebral infarction, and other studies have reported a frequency of ipsilateral carotid stenosis of between 30% and 60%. Kappelle and van Gijn noted the great difficulty in comparing angiographic studies but felt that approximately 26% of small deep infarcts were associated with significant internal carotid artery disease. Doppler studies have also shown a lower proportion of hemodynamically significant extracranial carotid lesions in cases with small deep infarcts.

Risk Factor Analysis

An alternative approach has been to see if the risk factor profile differs between patients with lacunar infarcts and those with cortical infarcts. A significantly lower prevalence of potential cardioembolic sources has been found in patients with lacunar infarcts in both a hospital-based and a community-based series, though most other risk factors seem more or less evenly distributed. Santamaria et al reported 12% of cases with small deep infarcts as having potential cardioembolic sources, similar to the 10% in the Harvard study, though there were no such cases in Weisberg’s study. Santamaria et al reported a series of patients with basal ganglia infarcts and a variety of cardiac conditions that frequently cause embolism. They noted that the clinical abnormalities were usually more extensive than the described lacunar syndromes, though three cases appear to have had sensorimotor strokes. Interestingly, all three involved the right hemisphere, again raising the question of the sensitivity of routine testing of nondominant hemisphere cognitive function. Overall, about 13% of lacunar infarcts will have a potential cardioembolic source. As with angiographic abnormalities, potential cardioembolic sources may be coincidental and must not be assumed to have caused the small deep infarcts.

Conclusions

The validity of the lacunar hypothesis and its use in clinical research and practice to distinguish an important subgroup of cerebral infarction should be considered in two parts. The first concerns the quantitative aspects of the hypothesis. It seems that if a patient is assessed as soon as possible after the stroke and if a pure motor stroke, pure sensory stroke, ataxic hemiparesis, or sensorimotor stroke is diagnosed according to the criteria discussed above, then the likelihood of the stroke being caused by a small deep infarct is extremely high. The inclusion of brachiofacial and brachiocrural deficits is likely to increase the sensitivity of the criteria without significantly decreasing the specificity. Special care should be taken when examining patients with nondominant hemisphere symptoms and when patients have had previous strokes with residual deficits. Early CT scanning will exclude the 5-10% of cases due to cerebral hemorrhage as well as the very infrequent nonvascular causes of the syndromes. The assumption that small deep infarcts seen on CT scans represent lacunes requires further pathological confirmation, and more information is also required about CT-negative cases.

The validity of the second part of the hypothesis, which concerns the relation between a qualitatively distinct small-vessel arteriopathy and lacunar strokes, remains uncertain due to lack of data rather than to evidence refuting it. Indirect methods do
suggest that significant extracranial atherosclerosis and cardioembolic sources are less frequent among lacunar infarcts, a fact that should encourage further research in this field. If the vascular pathology underlying lacunar infarcts really is qualitatively distinct, then it would appear to develop in a rather similar atherogenic milieu as large-vessel atherosclerosis, and the reasons for this would bear further inquiry.

A strong case can be made for using the presenting clinical features, which can be recorded in virtually all clinical and research settings worldwide, as the primary way of distinguishing lacunar strokes. This seems to have considerable practical value in identifying a quantitatively distinct subgroup of cerebral infarction. Imaging techniques of varying and ever-changing sophistication and availability can then be used to refine rather than define the criteria in individual series. While current evidence does not permit us to conclude that these infarcts are usually due to a qualitatively distinct arteriopathy, this issue is of such potential importance that investigators should be alert to any possibility of extending our understanding in this area. In the 20 years since C.M. Fisher reported the findings that form the basis of the lacunar hypothesis, much has been written on the subject. Some contributions, in attempting to define or expand the limits of its application to clinical practice, have caused the whole hypothesis to be questioned, yet it seems to us that the central tenets remain valid though still incompletely tested.

References

11. Poirier J, Detrouesné C: Le concept de lacune cérébrale de 1838 à nos jours. Rev Neurol (Paris) 1985;141:3—17
25. Bennett AH, Campbell CM: Case of brachial monoplegia due to a lesion of the internal capsule. Brain 1885;8:78—84
100. Caplan LR, Young RR: EEG findings in certain lacunar

103. Allen CMC: The accurate diagnosis and prognosis of acute
100. Caplan LR, Young RR: EEG findings in certain lacunar

109. Derouesn6 C, Yelnik A, Castaigne P: Deficit sensitif isole
108. Landi G, Anzalone N, Vaccari U: CT scan evidence of
107. Stiller J, Shanzer S, Yang W: Brainstem lesions with pure
106. Allen CMC, Hoare RD, Fowler CJ, Harrison MJG: Clini-
105. Schneider R, Korber N, Zeumer H, Kiesewetter H, Ring-

113. De Renzi E, Nichelli P, Crisi G: Hemiataxia and crural
112. Sage JI, Lepore PE: Ataxic hemiparesis from lesions of the
111. D. De Renzi E, Nichelli P, Crisi G: Hemiataxia and crural
hemiparesis following capsular infarct. J Neurol Neurosurg
Psychiatry 1983;46:561-563

114. Perman GP, Racy A: Homolateral ataxia and crural paresis:
113. Gorsehink EL, Fechter PHM, Lodder J: Causes of small
depth infarcts detected by CT. Clin Neurol Neurosurg 1984;
86:271-273
112. Araki G: Small infarctions of the basal ganglia with special
reference to transient ischaemic attacks. Recent Adv Gerontol
1978;469:161-162
111. Forbert A, Zeumer H, Ringelstein EB: Dopplersonographi-
sche Befunde beim ischamischen Hirinfarkt unterschiedlicher
Evolution and testing of the lacunar hypothesis.
J M Bamford and C P Warlow

Stroke. 1988;19:1074-1082
doi: 10.1161/01.STR.19.9.1074

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/19/9/1074.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org/subscriptions/