

# Risk Factors and Clinical Manifestations of Pathologically Verified Lacunar Infarctions

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**Review of 2,859 autopsy reports disclosed lacunar infarctions in 169 patients (6%). Review of the charts of 167 of these patients revealed hypertension in 64%, diabetes in 34%, smoking in 46%, and no known risk factor for cerebrovascular disease in 18%. As many as 81% of the patients with lacunes were asymptomatic. Symptomatic lacunes presented most commonly as pure motor hemiparesis (31%), aphasia plus right hemiparesis (20%), or sensorimotor dysfunction (11%); none presented as pure sensory stroke. These results suggest that the spectrum of lacunar infarction is more heterogeneous than previously thought. Most lacunes are asymptomatic, and the majority of symptomatic patients do not present with "classical" lacunar syndromes. (*Stroke* 1989;20:990-999)**

**S**ubcortical infarcts are common causes of stroke and represent up to 19% of all cerebral infarcts.<sup>1</sup> Lacunar infarcts, the most common form of subcortical infarcts, have been defined by Fisher as small, deep cerebral infarcts resulting from occlusion of small penetrating cerebral arteries.<sup>2</sup> The etiology of lacunes is varied and includes microvascular disease (lipohyalinosis and microatheromata)<sup>3</sup> as well as microemboli, microaneurysms, and arteritis.<sup>4-6</sup> Hypertension is a risk factor for lacunar infarction in approximately two thirds of the patients with lacunes.<sup>1,7-9</sup>

A number of clinical syndromes have been described in patients with lacunes. These syndromes include pure motor hemiparesis or hemisensory dysfunction, clumsy-hand dysarthria, ataxic hemiparesis, movement disorders, and others.<sup>2,4,5,10</sup> The relative frequency of these diverse clinical presentations have not, however, been determined in a large series of patients with pathologically confirmed lacunes. Therefore, we reviewed the clinical and postmortem records of all patients with pathologically verified lacunar infarcts to examine risk factors that may predispose to the development of lacunes and the type and relative frequency of

the associated clinical dysfunction. Preliminary results and a case report have been published.<sup>11,12</sup>

## Subjects and Methods

Autopsy records at The New York Hospital from 1975 to 1985 were reviewed for reports of lacunes or small subcortical infarcts sparing the overlying cortex. Infarcts that involved the cerebral cortex or extensive areas of the subcortical white matter or that were >2 cm in greatest diameter were excluded. At the time of autopsy, the brain and spinal cord were placed in formalin; after 2 weeks they were serially sectioned at 1-cm intervals. After being embedded in paraffin and stained with hematoxylin and eosin, routine microscopic sections of the cerebral cortex, basal ganglia, hippocampus, cerebellum, brainstem, and spinal cord were examined. Microscopic sections of a lacune were examined in nearly all patients in whom such infarction was suspected. The final autopsy report provided information about the cause of death, the size and location of lacunes if present, and atherosclerosis in the circle of Willis.

Etiologic mechanisms underlying lacunes were evaluated by extensive pathologic investigation in a subset of consecutive patients with lacunar infarcts autopsied during the first 5 years of our study. The microscopic brain slides of the basal ganglia were reexamined for the presence of mild, moderate, or severe medial hypertrophy, hyalinization, and dilatation in the intraparenchymal arteries and arterioles. Lipohyalinosis and Charcot-Bouchard aneurysms were classified as severe changes. The final autopsy reports in this subset of patients were reviewed for diagnoses of hypertension, atherosclerotic cardiovascular disease (ASCVD) in the absence

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**TABLE 1. Locations of 327 Pathologically Verified Lacunes in 169 Patients**

Location	Lacunes	
	n	%
Basal ganglia	204	62
Internal capsule	37	11
Pons	36	11
Thalamus	35	11
Centrum semiovale	11	3
Clastrum	2	0.6
Midbrain	1	0.3
Hypothalamus	1	0.3

of ulcerative plaques in the aorta or major vessels in the neck or of mural thrombi in the left side of the heart, ASCVD with ulcerative plaques in the aorta or major vessels in the neck or with mural thrombi in the left side of the heart, valvular heart disease, embolic disease characterized by multiple systemic and brain infarcts in the absence of hypertension and ASCVD, and atherosclerosis in the circle of Willis. The carotid bifurcation was not studied, and only the intracranial portions of the internal carotid and vertebral arteries were examined.

Clinical information for the patients with pathologically verified lacunes was obtained by chart review and included age, sex, family history, smoking history, presence of diabetes, hypertension, myocardial dysfunction, and neurologic signs and symptoms. Information from neurologists was noted separately. The clinical signs were compared with the pathologic findings. The patients were divided into five groups. Group A comprised patients with symptoms and signs clearly attributable to a lacunar infarct alone (for example, a hemiparesis contralateral to a lacune in the motor system with no appropriately located cortical lesion). Group B consisted of patients with symptoms and signs clearly attributable to cortical lesions (for example, hemiparesis associated with a contralateral cortical lesion of the motor system but no contralateral lacune). Group C patients had clinical symptoms that could be attributed to either lacunes or cortical infarcts in the same hemisphere. Group D contained patients whose clinical symptoms had no apparent pathologic correlate (e.g., hemiparesis without contralateral lacunes or cortical or brainstem infarcts). Finally, group E consisted of asymptomatic patients (no history of focal symptoms and nonfocal neurologic examinations) with lacunes at autopsy.

### Results

Of 2,859 adult autopsies, 169 patients (6%) had 327 lacunes, an average of 1.9 lacunes per patient. A single lacune was present in 46% of the patients, two lacunes in 16%, and three or more lacunes in 38%. The anterior circulation contained 78% of the lacunes and the posterior circulation 22% (Table 1). Ninety-one percent of the infarcts for which size

**TABLE 2. Correlation Between Systemic Disease and Pathology of Intraparenchymal Brain Vessels in 56 Patients With Lacunes Verified at Autopsy**

Systemic disease	Pathologic changes of brain vessels		
	Normal to mild (n=27)	Moderate (n=21)	Severe* (n=8)
Hypertension	12	13	8
Alone	3	3	1
ASCVD	5	1	2
ASCVD+embolic source	4	9	5
Normotension	15	8	0
ASCVD	6	2	0
ASCVD+embolic source	5	4	0
Rheumatic heart disease	2	1	0
Embolic infarcts (? source)	2	1	0

ASCVD, atherosclerotic cardiovascular disease; embolic sources include ulcerative plaques in ascending aorta or proximal neck vessels, or mural thrombi in left side of heart.

\*Hypertensive and normotensive patients differ significantly ( $\chi^2$ ,  $p<0.05$ ) with respect to distribution of vascular pathology but differences are not significant if those with severe pathologic changes are omitted.

was specified were  $<1$  cm in greatest diameter. Coexistent but noncontiguous infarctions of the cerebral cortex were present in 39% of the patients. Atherosclerosis of the circle of Willis was moderate to severe in 51% of the patients, mild in 27%, and absent in 22%. Evidence at autopsy of acute or remote myocardial infarction was found in 52% of patients.

The subset of 56 consecutive patients with lacunar infarcts diagnosed at autopsy examination from 1975 through 1979 underwent more extensive evaluation of pathogenic mechanisms. Hypertension was present in 59% of these patients and was usually associated with ASCVD. The relative number of hypertensive patients with normal intraparenchymal vessels or with mild to moderate hyalinization or dilatation did not differ significantly from that seen in normotensive patients with ASCVD ( $p>0.05$ ); however, severe cerebral intraparenchymal vascular disease was significantly more common in hypertensive than in normotensive patients with lacunes ( $p<0.05$ ; Table 2). All eight patients with severe cerebral intraparenchymal vascular disease among this subset of 56 patients were hypertensive and had marked hyalinization of the small parenchymal arteries and arterioles; Charcot-Bouchard aneurysms were seen in three and lipohyalinosis in one. Since only one of the eight had hypertension alone, the data suggest that the concurrence of hypertension with atherosclerosis may predispose a cerebral vessel to develop severe arterial and arteriolar pathology. At least 41% of the 56 patients in this subset may have had diseases other than hypertension as the cause of their lacunes. Rheumatic heart disease was the sole apparent etiology in three patients, and embolic disease (from

**TABLE 3. Risk Factors for Lacunes Verified at Autopsy in 167 Patients With Clinical Data**

Risk factor	%
Hypertension	64
Diabetes	34
Smoker at time of stroke or death	46
Coronary artery disease	47
Family history of stroke	17
Family history of myocardial infarction	35
Hypertension, smoking, or diabetes	82
No risk factor	18

Hypertension, blood pressure of >160/95 mm Hg or clinical treatment for hypertension.

possible nonbacterial thrombotic endocarditis not persisting at autopsy) was the etiology in another three patients with multiple systemic and brain infarcts but without ASCVD or hypertension. In 17 patients, ASCVD was the sole etiology of lacunar infarcts, secondary either to emboli from the aorta, the proximal neck vessels, the unexamined portions of the carotid or vertebral arteries, or secondary to occlusive disease in the penetrating arteries at the base of the brain. Nine of the 17 patients had either ulcerative plaques in the aorta or its major proximal branches in the neck or had mural thrombi overlying old myocardial infarcts as potential sources of emboli. None of the 17 had occlusive ASCVD in the appropriate artery at the base of the brain according to the final autopsy descriptions.

Clinical data for the 10-year study period was available for 167 (99%) of the 169 patients with lacunes; the 167 patients had a total of 324 lacunes. Neurologists evaluated 108 of the 167 patients (65%) for symptoms referable to stroke or for other disorders including metabolic encephalopathy (18 patients), senile dementia of the Alzheimer's type or parkinsonism (six patients), central nervous system metastases (five patients), and head trauma (four patients). Hypertension was the most commonly noted risk factor among the 167 patients, followed by coronary artery disease, cigarette smoking, and diabetes mellitus (Table 3). A family history of myocardial infarction (35%) was reported more commonly than a family history of stroke (17%). However, nearly one patient in five (18%) lacked risk factors for cerebrovascular disease. Eighty-four clinically evident ischemic cerebrovascular episodes occurred in 74 of these 167 patients (44%), whereas the other 93 patients (56%) were asymptomatic. Coexistent but noncontiguous cortical infarctions were present in 36 of the 74 symptomatic patients (49%). The sex ratio was 1.3:1 (male:female) and the mean age was 73.5 years. The most frequent cause of death was acute myocardial infarction, present in 22% of these 167 patients; other forms of heart disease accounted for another 5% of the deaths. Acute cerebrovascular events caused 12% of the deaths, but most of these

**TABLE 4. 35 Lacunar Presentations in 32 Patients With Ischemic Events Attributable Solely to Lacunes**

Symptoms/signs	Total (N=35)		Seen by neurologists (N=23)	
	n	%	n	%
Pure motor hemiparesis	11	31	8	35
Aphasia/right hemiparesis	7	20	5	22
Hemiparesis plus		17		22
Dysarthria	2		2	
Change in LOC	2		2	
Mutism	1		1	
Unknown	1		0	
Sensorimotor dysfunction		11		17
Alone	3		3	
Plus dysarthria	1		1	
Extrapyramidal disease	1	3	1	4
Other	6	17	0	0
Total presentations	35		23	

N, number of patients; n, number of presentations; LOC, level of consciousness; Other, only lacunes present at autopsy with clinical history of "stroke."

were cortical strokes. Other leading causes of death were cancer (20%), infection (17%), and gastrointestinal disease (8%).

Correlation of clinical symptoms and signs with pathologic findings in these 167 patients with 324 lacunes revealed that 35 ischemic events occurred in the 32 patients (19%) in Group A, 11 events occurred in the 11 patients (7%) in Group B, 27 events occurred in the 26 patients (16%) in Group C, and 11 events occurred in the 11 patients (7%) in Group D. The remaining 87 patients (52%) were in Group E. Thus, at least 19% of the patients with lacunes were symptomatic (Group A), and as many as 41% may have been symptomatic due to lacunar infarcts (Groups A plus C plus D). Analyzed on the basis of the number of lacunes, at least 11% were symptomatic (Group A), and as many as 23% may have been symptomatic (Groups A plus C plus D).

Similar analysis of a subset of patients with only a single lacune at autopsy revealed that a range of 15–26% of such patients may have been symptomatic from their lacunes.

Among the 32 Group A patients with 35 ischemic events attributable solely to lacunes (Table 4), pure motor hemiparesis was the most common clinical presentation (31%) and was followed in frequency by aphasia plus right hemiparesis (20%), hemiparesis plus other symptoms (17%), and sensorimotor dysfunction (11%); parkinsonism was infrequent (3%), and pure sensory stroke was not seen. Since patients examined by neurologists represent a more reliable and detailed subset, the presenting signs of 23 lacunes in 21 such patients in Group A are presented below in more depth (see also Table 4).

Eight Group A patients examined by neurologists had pure motor hemiparesis. Lesions were found in

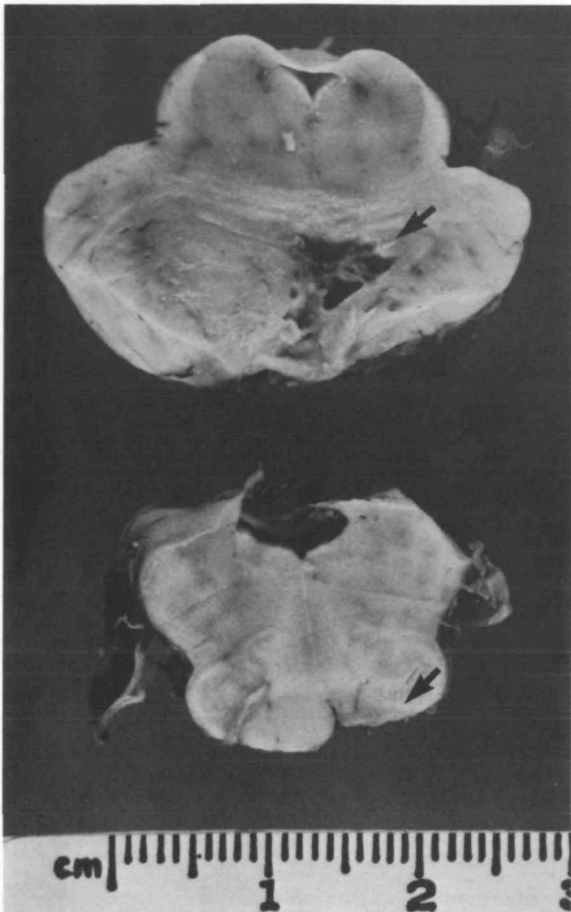


FIGURE 1. Transverse sections of brainstem showing (top) 0.7×1.0-cm cystic infarct of medial rostral basis pontis (arrow) with (bottom) Wallerian degeneration of ipsilateral medullary pyramid (arrow).

the posterior limb of the internal capsule in five and in the basis pontis in two (Figure 1). The eighth patient, with weakness restricted to the face and arm, had a single 2×3×4-mm lacune in the left caudate nucleus and anterior limb of the internal capsule.

Five Group A patients examined by neurologists had aphasia plus right hemiparesis. One had an ischemic infarction of the left thalamus (Figure 2), two had lesions of the left anterior internal capsule and caudate or putamen, one had a left anterior capsular lesion as well as a noncontiguous left thalamic lesion, and the fifth patient had a small left caudate lacune and "small infarcts of both basal ganglia." Three of the five lacunes in these five patients were  $\geq 1$  cm in size. Two of these five patients had subsequent brainstem lacunes, associated with left hemiparesis and mutism in one (Figure 3) and with left sensorimotor dysfunction and dysarthria in the other (see below). Clinical and pathologic findings in these five patients with hemiparesis and aphasia are summarized in Appendix 1.

Four Group A patients examined by neurologists presented with mixed sensorimotor deficits, one of

whom also had dysarthria and a previous episode of right hemiparesis and aphasia (see above). One patient had a 1.7-cm cystic infarct of the right posterior limb of the internal capsule, with extension to the adjacent thalamus and putamen (Figure 4), one had multiple 2-mm lesions bilaterally in the basal ganglia and internal capsules; one had only a lesion in the right putamen; and the fourth (with dysarthria) had multiple 1-mm cystic pontine lesions.

Two Group A patients examined by neurologists presented with left hemiparesis plus dysarthria. One had a 0.5×0.5×1.5-cm lesion in the anterior limb of the right internal capsule and the other had a 1-cm lesion of the right basis pontis. No cortical infarcts were seen. Two other Group A patients, aged 77 and 89 years, presented with left hemiplegia plus altered level of consciousness. Both were hypotensive on admission, and one was septic; the causes of death were sepsis and acute myocardial infarction, respectively. Although the initial clinical diagnosis at the time of admission in both patients was vertebrobasilar insufficiency, autopsy revealed several 2–3-mm infarcts in the right thalamus, internal capsule, and left basal ganglia in one patient and a single subacute 3-mm infarct in the right posterior limb of the internal capsule in the other patient. Basilar artery thrombosis or severe stenosis was not present.

Lastly, an 83-year-old man presented with a 5-year history of tremor, rigidity, and a short-stepped, shuffling, unsteady gait. Examination revealed increased tone, cogwheeling, hyperreflexia, and bilateral extensor plantar responses. Two neurologists diagnosed "extrapyramidal disease." The patient died at home of appendicitis. Autopsy showed a 2-mm cystic infarct of the left lateral thalamus and multiple bilateral microscopic infarcts of the globus pallidus and pons. Marked vascular changes of lipohyalinosis were noted, but neither hydrocephalus nor pathologic changes of Parkinson's disease were present.

Additional Group A patients not examined by neurologists were said to have had basilar insufficiency, right hemiparesis plus other deficits, a "left MCA stroke," a "right CVA," a "left CVA," and a "stroke." However, only lacunes were present at autopsy.

### Discussion

The limitations of a retrospective study must not be ignored. Its reliability depends upon the non-standardized examining and charting skills of a number of physicians and upon the thoroughness of pathologic data that is largely unavailable for reexamination. Thus, the frequency of symptomatic lacunes in our study may be underrepresented due to incomplete reporting of symptoms by patients or physicians and because many lacunes are smaller than 1-cm sections used to study these brains anatomically. Similarly, the interpretation of information obtained from symptomatic patients depends

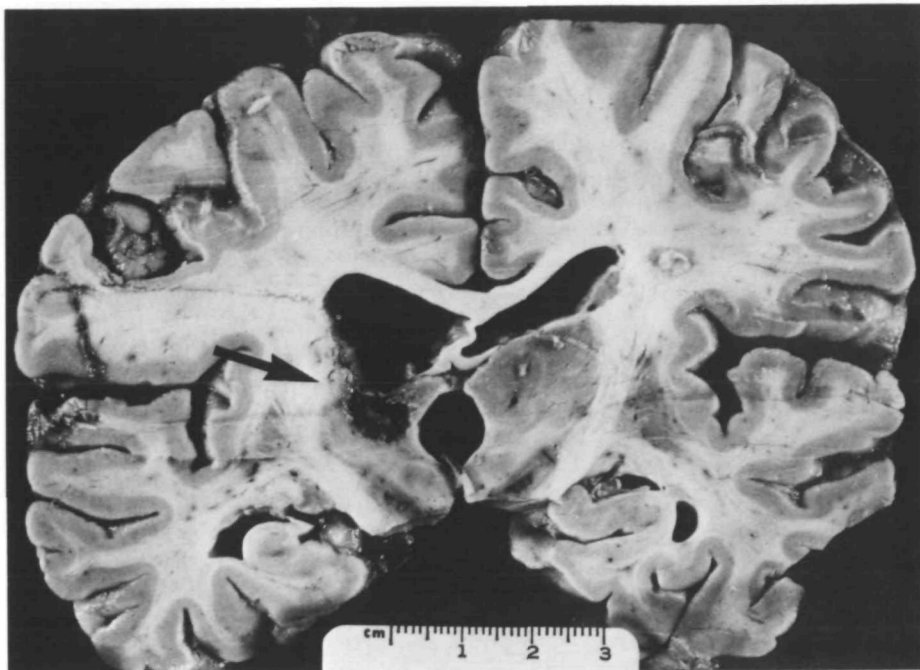


FIGURE 2. Coronal section showing 1-cm cystic lacune (arrow) in left thalamus with ipsilateral hydrocephalus ex vacuo.

upon the assiduousness of the examining physician, the ability of the patient to cooperate in providing a history, and the accuracy of the pathologic data. It is hoped that the large size of our study and our analysis of more detailed subsets of patients in certain instances help to minimize the effects of these potential sources of error. Clear patterns have emerged from our review that merit presentation. Confident verification must await the presentation of correlative prospective data, however.

Lacunar infarctions were common, occurring in 6% of the 2,859 autopsies in our series and in 11%<sup>10</sup> and 10%<sup>13</sup> of the autopsies in Fisher's series. In our study, 91% of the lesions for which size was specified were  $\leq 1$  cm in size. They were usually multiple (average 1.9 per patient) and were most commonly located in the basal ganglia and less often in the internal capsule, pons, and thalamus, a distribution paralleling that described by Fisher.<sup>10</sup>

Coexistent but noncontiguous cortical infarctions were present in 49% of the symptomatic patients in our series compared with 26% observed by Fisher.<sup>10</sup> The high concurrence rate for cortical and subcortical infarction suggests shared risk factors and possibly shared pathogenesis.

Hypertension is the most common risk factor for lacunar infarcts. It was found in 64% of our patients for whom clinical data were available, a figure that correlates well with the range (57–75%) in published series.<sup>1,7–9</sup> The high incidence of 94% reported by Fisher<sup>10</sup> probably results from the fact that he used a threshold for hypertension of  $>140/90$  mm Hg whereas others have generally used a threshold of  $160/95$  mm Hg. Hypertension was also the most common risk factor in our subset of 56 patients with more detailed pathologic examination; hyperten-

sion occurred in 59% of these patients. However, it was the sole risk factor in only 12.5%, although the association of hypertension plus atherosclerosis was frequent (46%). The incidence of normal intracerebral vessels or vessels showing mild to moderate hyalinization among hypertensive patients was similar to that found in normotensive patients with ASCVD. Severe pathologic changes, although infre-

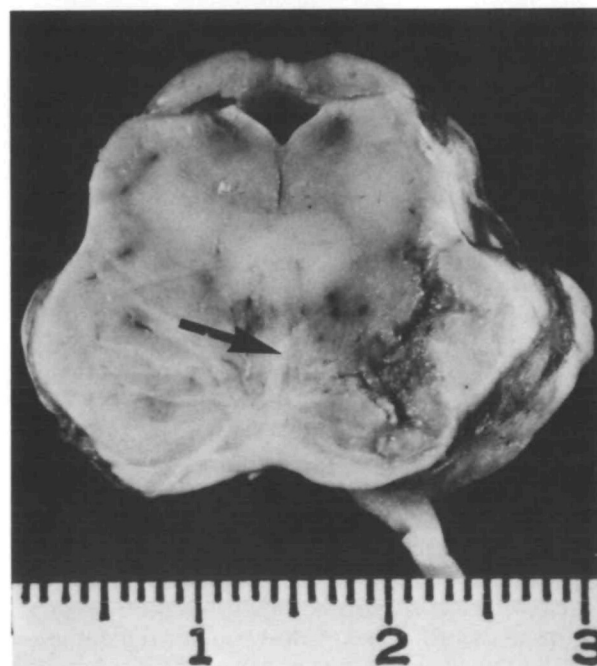


FIGURE 3. Transverse section of rostral pons showing 0.3x1.2-cm cystic infarct (arrow) in right basis pontis. Centimeter scale. (Same patient as in Figure 2.)

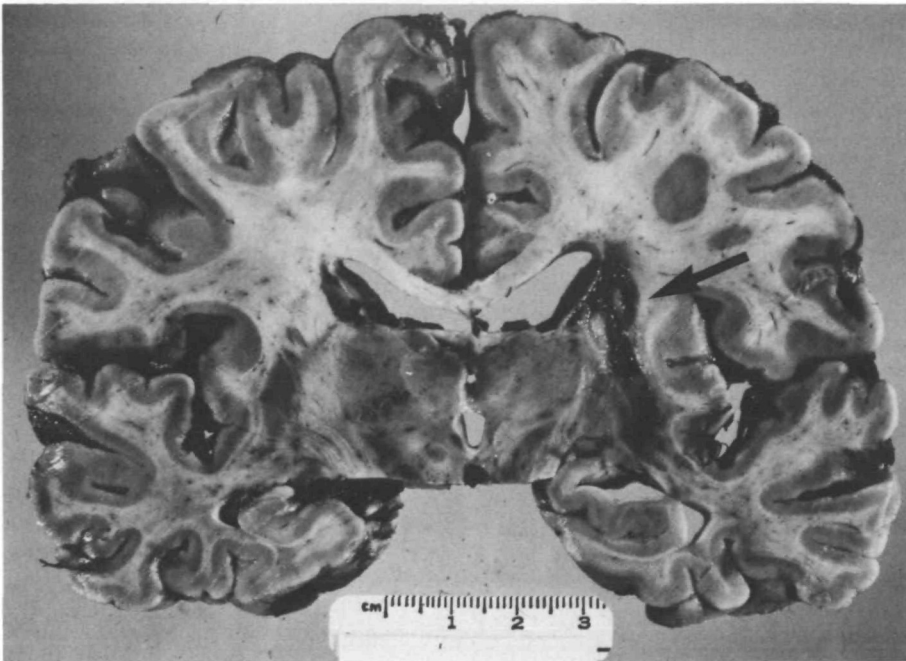


FIGURE 4. Coronal section showing 1.0×1.5-cm cystic infarct (arrow) involving superior aspect of right internal capsule, posterior putamen, and small area of thalamus. Remaining posterior limb of ipsilateral internal capsule is shrunken.

quent (14%), were confined to hypertensive patients and were histologically similar to those changes previously described by Fisher.<sup>3</sup>

Atherosclerosis is an important cause of lacunar infarcts. The established association of ASCVD with transient ischemic attacks<sup>14–16</sup> and stroke<sup>17</sup> can be extended to lacunes. Risk factors associated with atherosclerosis were common among our patients. Diabetes was present in 34%, a figure comparable to previous reports of 27%,<sup>18</sup> 29%,<sup>1</sup> and 11%.<sup>10</sup> A family history of stroke was seen in only 17% of our patients, but 35% had a family history of myocardial infarction. During life, coronary artery disease was diagnosed in 47% of all patients in our series, and at autopsy myocardial infarcts were found in 52%. Forty-six percent of the patients were smokers, a factor of uncertain significance with regard to the risk of cerebrovascular disease.<sup>19–24</sup>

Among the subset of 56 patients with more detailed pathologic data, ASCVD was the sole apparent etiology of the lacunes in 30%. These patients were normotensive and had systemic atherosclerosis with normal or mild to moderate vascular changes in the intraparenchymal brain vessels. Since none of the autopsy reports described occlusive atherosclerotic plaques in the appropriate penetrating arteries of the circle of Willis and since the intraparenchymal changes in the blood vessels were not severe, the data suggest that atherosclerosis may give rise to lacunes primarily via emboli from plaques in the ascending aorta or major vessels in the neck, including the carotid bifurcation, which were not examined. Indeed, slightly more than half of the normotensive atherosclerotic patients had clear sources of emboli as described in the postmortem records. Embolism from the heart valves was the sole etiolo-

gy of the lacunes in 10.7% of the patients and was due to rheumatic heart disease in three and to probable nonbacterial thrombotic endocarditis in three. None of these six patients had either hypertension or ASCVD. While the carotid bifurcation was not studied in these six patients and thus cannot be definitively excluded as a source of embolism, isolated atherosclerosis in the neck is rare in the absence of systemic atherosclerosis at autopsy.

The incidence of asymptomatic patients with lacunar infarcts in our series was high (59–81%). Although this incidence is higher than in previous studies, which have estimated the incidence as roughly 30–33%,<sup>8,9</sup> those studies may have underestimated the frequency of asymptomatic infarcts since only symptomatic patients were studied and since the authors employed computed tomography (CT) rather than autopsy to detect lesions. Fisher has suggested that “the first or only lacune tends to be symptomatic.”<sup>22</sup> However, only 15–26% of our patients with one lacune were symptomatic. This finding indicates that the first or only lacune is not necessarily symptomatic and that patients are more likely to be symptomatic if more than one lacune is present.

Forty-four percent of our patients were symptomatic from all causes of cerebrovascular disease, including cortical strokes. Fisher noted an incidence of 23%,<sup>10</sup> supporting our conclusion that most lacunes are asymptomatic.

The distribution of symptoms and signs of lacunes in our series of patients differs from that in previous reports. Aphasia and mixed sensorimotor deficits were relatively frequent, and pure sensory stroke was not reported. In agreement with other reports,

pure motor hemiparesis was the most common presenting symptom, occurring in 31% of the patients compared with reports of 21–60% in the literature.<sup>8,25</sup> Most lesions causing pure motor hemiparesis were located in the posterior limb of the internal capsule or basis pontis, corresponding to previous descriptions.<sup>3,26,27</sup>

Aphasia plus right hemiparesis was the second most common presentation, occurring in 20% of our patients. Language deficits were either mixed or predominantly expressive, with sparing of repetition in some cases, and all lesions were left-sided and involved either the thalamus, anterior internal capsule, or basal ganglia. Subcortical aphasia has been well documented by CT studies and by occasional clinicopathologic case reports,<sup>2,28–40</sup> but a frequency as high as 20% has not previously been documented in patients with lacunes. Aphasia with variable expressive and receptive components associated with lesions in the dominant anterior limb of the internal capsule, the head of the caudate, and the putamen has been described in at least six patients by CT scan,<sup>29</sup> and mild fluent aphasia associated with lesions in the posterior limb of the dominant internal capsule was reported in six patients by CT scan.<sup>28,32</sup> Single case reports have documented right hemiparesis plus expressive aphasia with an infarct in the anterior limb and genu of the internal capsule and adjacent inferior corona radiatum<sup>2</sup> and right hemiparesis plus anomia and word-finding difficulty with a dominant posterior capsular infarct.<sup>34</sup> Mutism has also been reported following bilateral capsular lesions.<sup>2</sup> Aphasia resulting from lesions of the basal ganglia<sup>33,35</sup> or thalamus<sup>36–40</sup> has been described in CT-based studies without pathologic confirmation and in three clinicopathologic reports.<sup>41–43</sup>

Several of these reports are subject to doubts regarding the strictly subcortical localization of their lesions, due either to a lack of pathologic confirmation or to the presence of symptoms in addition to aphasia, including altered sensorium and eye movement abnormalities. Nonetheless, taken together the available evidence supports the concept of strictly subcortical aphasia.

Factors that might account for a failure to recognize subcortical aphasia more commonly in the past include: 1) a failure to consider subcortical localization of a language deficit; 2) the prolonged survival of patients with subcortical lesions, making opportunities for clinicopathologic correlations rare; and 3) the unavailability, until recently, of the technology with which to visually localize lesions during life. Of note, most reports of subcortical aphasia have appeared since the availability of high-resolution CT scanning. Furthermore, our study is only the second large series of patients with pathologically verified subcortical infarcts, so there is no clear precedent suggesting that subcortical aphasia is rare. Thus, aphasia should not preclude the diagnosis of lacunar infarction. Although overlap

with cortical syndromes exists, subcortical localization of hemiparesis and aphasia may be suggested if accompanying sensory deficit, neglect, left–right confusion, and other manifestations of cortical dysfunction are not present and if aphasia is transcortical in nature.

Sensorimotor dysfunction was another common presentation of lacunar infarction in our series, affecting 11% of the patients. Lesions were found in the posterior limb of the internal capsule in three patients and in the base and lateral portion of the pons in a fourth. At least 15 cases of sensorimotor dysfunction from lacunar infarction are described in the literature.<sup>7,9,25,44–47</sup> Mohr et al<sup>44</sup> described a pathologically confirmed case caused by a single 4×4×2-mm thalamocapsular lacune. Subcortical infarcts can interrupt projecting thalamocortical sensory fibers<sup>48</sup> as well as motor fibers, without involving thalamic nuclei, to produce sensorimotor deficits.<sup>7,9</sup> Small capsular hemorrhages have also resulted in sensorimotor loss.<sup>49</sup> In addition, reports of “pure” motor hemiparesis often include subjective sensory complaints.<sup>26</sup> Others have reported that sensorimotor dysfunction occurs in 1%,<sup>9</sup> 17%,<sup>8</sup> 33%,<sup>7</sup> and 38%<sup>50</sup> of symptomatic lacunes. Our cases support the assertion that sensorimotor dysfunction may be a common presentation of lacunar infarction. As with hemiparesis plus aphasia, the absence of other cortical signs should lead to suspicion of a subcortical lesion.

Two patients presented with left hemiparesis plus dysarthria. One had a lesion of the anterior limb of the nondominant internal capsule, and the other had lesions in the right basis pontis, right thalamus, and right basal ganglia. Hemiparesis plus dysarthria has been described with lesions of the anterior limb of the nondominant internal capsule,<sup>29</sup> and Fisher<sup>26</sup> noted slurred speech in two thirds of patients with “pure” motor hemiplegia. Thus, lesions of the dominant internal capsule can produce aphasia plus hemiparesis, whereas lesions of the nondominant internal capsule can produce dysarthria plus hemiparesis.<sup>29</sup>

Lacunes can occur with altered levels of consciousness. Two elderly patients in our series had left hemiplegia plus altered mentation with a single infarction in the right internal capsule and with bilateral lacunes, respectively. Both also had concurrent systemic compromise (myocardial infarction, sepsis, and relative hypotension) that presumably accounted for their diminished alertness. Fisher<sup>2</sup> presented a case of “pure motor hemiparesis with confusion” reportedly caused by a 1.2-cm lacune in the anterior limb and anterior part of the posterior limb of the right internal capsule, presumably interrupting thalamofrontal connections. Lacunes can therefore directly or indirectly alter the level of consciousness, although coma has not been reported with lacunes.

Finally, one patient presented with progressive rigidity, tremor, and short-stepped, shuffling,

unsteady gait, the "lacunar state" of Marie.<sup>51</sup> Marie attributed this progressive decline to the cumulative effect of multiple lacunes. Given the relatively small number of lacunes and the presence of ventricular dilatation in many similar cases in the literature, Fisher<sup>2</sup> attributed the lacunar state to occult normal pressure hydrocephalus. The absence of ventricular dilatation at autopsy in our present case tends to support the first view.

Pure sensory stroke was not described in the patients in our series. Fisher<sup>2</sup> stated that pure sensory stroke is the most common lacunar presentation, whereas Donnan et al<sup>9</sup> and Pullicino et al<sup>8</sup> had no pure sensory lacunar strokes in their series and Weisberg<sup>7</sup> noted pure sensory strokes in approximately 8% of the presentations. Similarly, patients with ataxic hemiparesis plus clumsy-hand dysarthria were not present among Group A patients, although possible examples of these presentations occurred in Group C patients. In agreement with previous accounts,<sup>2,4</sup> lacunar infarcts with visual field cuts or apraxias were not encountered.

Although our series suggests a different clinical spectrum from previous series of patients with lacunes, important clinical distinctions still distinguish lacunar from cortical infarcts. Visual field defects, neglect,<sup>52,53</sup> agnosias, apraxias, acalculias,<sup>54</sup> behavioral abnormalities, auditory deficits, and seizures are very rare with lacunes that spare the thalamus. In contrast, pure motor hemiparesis, the most common clinical finding with lacunes, occurs rarely with cortical stroke.<sup>55–58</sup> Lacunar strokes that are more difficult to distinguish from cortical infarcts (e.g., aphasic/hemiparetic presentations) may be suspected when deficits are confined to one or two modalities (e.g., motor and language) rather than to several modalities. Thus, the entity of lacunar infarction, albeit more heterogeneous pathogenetically, epidemiologically, and clinically than previously believed, remains. Attempts at recognition are important since lacunar strokes usually have a favorable prognosis.<sup>2,6,50</sup>

#### Appendix 1: Case Reports of Aphasic Patients

A 77-year-old hypertensive, diabetic, right-handed man presented with the abrupt onset of a moderately severe right hemiparesis and aphasia. Language testing showed mild comprehension impairment, anomia, diminished fluency, occasional paraphasic errors, intermittent verbal preservation, and intact repetition. The deficits gradually improved, but he was readmitted with the abrupt onset of left hemiplegia and mutism 38 days later. Minimal improvement occurred, and he died 71 days later of pneumonia. Autopsy revealed a 1×2-cm cystic infarct in the left lateral thalamus, extending to the adjacent posterior limb of the internal capsule (Figure 2), and a second 0.3×1.2-cm cystic infarct in the right basis pontis (Figure 3). No cortical lesions were present.

A 66-year-old hypertensive, diabetic, right-handed woman developed left hemiparesis and dysarthria that improved over several days. One year later, right hemiparesis and dysarthria occurred with a gradual onset and progressed over the next 12 hours to right hemiplegia and expressive language dysfunction characterized by frequent paraphasic errors, diminished fluency, and normal comprehension. The patient regained fluency the next day but remained dysarthric and hemiplegic on the right. The patient died 1 month later of pneumonia and sepsis. Autopsy revealed a 1-cm cystic infarct of the anterior limb of the left internal capsule and caudate nucleus, a 1-cm cystic infarct of the ventral half of the right basis pontis, and several 2-mm cystic infarcts in the right thalamus and basal ganglia. No cortical infarcts were present.

A 78-year-old hypertensive right-handed woman presented with the abrupt onset of right hemiparesis and dysphasia characterized by paraphasic errors. She improved little and died 2 years later of aspiration pneumonia. Autopsy revealed multiple small cystic infarcts bilaterally in the anterior internal capsules, putamina, and thalami. No other lesions were present grossly or microscopically.

A normotensive 57-year-old right-handed woman in chronic atrial fibrillation suffered the abrupt onset of right hemiparesis and expressive language difficulties that resolved over 6 months. Seven years later she developed left-sided weakness and dysarthria, then became septic and died. Autopsy revealed three infarctions: a 1-cm cystic lesion in the left putamen and globus pallidus with extension into the anterior internal capsule, a subacute embolic 2×2-cm right lateral occipital infarction, and a subacute embolic 1×1-cm right frontal infarction.

Lastly, a 52-year-old right-handed man with a long-standing history of poorly controlled hypertension and previous myocardial infarction presented with a right thalamic hemorrhage. Initial stupor and left hemiparesis improved over several months to a mild residual left hemiparesis. Two years later he noted recurrent episodes of right-sided numbness and expressive language difficulty lasting minutes, culminating 1 week later in the progression over 13 hours of right hemiplegia, right hemisensory deficit to pin-prick only, and language difficulties. Comprehension and naming were intact, but word-finding difficulty was present. One week later the deficits had improved considerably, and 2½ weeks after admission function had returned to baseline. He died of myocardial infarction 5 years later. Autopsy revealed a 2×7-mm cystic infarction of the left caudate nucleus, several additional 1–2-mm cystic infarctions in both basal ganglia, and an old 1.1×1.5-cm previously hemorrhagic lesion of the right thalamus and caudate nucleus. No cortical infarctions were present.

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KEY WORDS • lacunar infarction • risk factors • pathology

## **Risk factors and clinical manifestations of pathologically verified lacunar infarctions.**

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