Previous studies have shown that about 80% of all first-ever strokes are due to cerebral infarction. However, cerebral infarction is not a pathologically homogeneous condition since the underlying vascular lesions vary. One distinct form is lacunar infarction. Though the term lacune has been associated with small holes in the deep cerebral tissue for almost 150 years, it was Fisher who demonstrated that such lesions could be the result of occlusion of a single perforating artery, and that they might be manifest clinically as a number of specific syndromes. Stroke patients with lacunar syndromes have been reported to contribute between 13 and 23% of all cerebral infarcts, yet in the 20 years since Fisher's first observation, no study has described the natural history of this group in an unselected series. Since computer tomographic (CT) scanning became widely available, there have been many reports of individual cases or small series, but their very number and frequent lack of attention to the details of the original clinical descriptions have meant that "the utility of the original (clinico-pathological) correlations has been called into question, threatening to overturn the entire concept." It is important to examine the concept of lacunar infarction since the risk factors, natural history, and rational treatment may differ significantly from infarction due to the more widely studied atherothromboembolism affecting the cervical and larger cerebral arteries. Consequently, when considering the prevention of stroke (either primary or secondary) or limiting the extent of infarction in the acute phase, treatments that might be appropriate to one group but not the other may fail to show any benefit in trials if the subgroups of cerebral infarction are not distinguished. Furthermore, trials of treatment specifically for lacunar infarction can be planned rationally only when the natural history of the condition is known. One must be aware of the problem of making assumptions about the underlying vascular pathology in an individual case based on the clinical and radiologic features, but these are investigations that are applicable to all patients in life. We report the results of such a study, which used a community-based register of first-ever stroke and combined prompt neurologic assessment with the widespread use of CT scanning.

Subjects and Methods

The detailed methodology of the Oxfordshire Community Stroke Project (OCSP) has been reported elsewhere. In brief, it is a prospective study of first-ever stroke, based in the community, which combines complete case ascertainment, irrespective of hospital admission, with prompt assessment by a study neurologist and CT or autopsy examination in 90% of all cases. Extensive details of prestroke risk factors have been collected and will be reported separately. All patients are being followed up prospectively by research nurses using a standard questionnaire designed to detect recurrent cerebrovascular events and to assess residual disability and handicap. For the purposes of this communication, patients will be described as capable of living independently or dependent on other persons in some way. Patients who were thought to have had a recurrent stroke were reassessed by a study neurologist. In the event of death, all available records were reviewed, and the cause of death was determined. The following causes were recognized: those due to the direct neurologic sequelae of the stroke (e.g., transtentorial herniation), but also those due to cardiac or other nonstroke causes.
torial herniation), those due to cardiac disease, those due to conditions related to immobility (e.g., pneumonia, pulmonary embolism), and those due to totally unrelated conditions. Thus, the OCSP provided a well-documented group of patients with first-ever stroke, unbiased by hospital admission, ideal for a natural history study.

Stroke was defined as rapidly developing clinical symptoms and/or signs of focal, and at times global (applied to patients in deep coma and to those with subarachnoid hemorrhage), loss of cerebral function, with symptoms lasting > 24 hours or leading to death, with no apparent cause other than that of vascular origin (after Hatano). We feel that the high rate of CT scanning and autopsy examination combined with complete, prospective follow-up makes it unlikely that nonvascular lesions were mistakenly included in our series.

The pathologic type of stroke was classified as definite cerebral infarction if 1) a CT scan performed within 28 days of onset showed either an area of low attenuation in a region compatible with the clinical signs and symptoms or no specific abnormality, or 2) an autopsy examination showed an area of infarction in a region compatible with the signs and symptoms. If the above examinations were lacking, the Allen diagnostic score was applied. This is a CT-verified clinical scoring system that allows the probability of a stroke being due to infarction or hemorrhage to be calculated from a number of clinical variables and is more accurate than unstructured clinical diagnosis. We considered that strokes were due to probable cerebral infarction if they had a score of < 4, indicating a > 90% probability that the stroke was due to cerebral infarction.

A lacunar syndrome was defined as a constellation of clinical symptoms and signs at the time of maximum deficit, caused by a single vascular event, which has been associated with restricted areas of infarction due to primary disease of a single perforating artery of the brain in autopsy studies. The following 4 syndromes were recognized: pure motor stroke, pure sensory stroke, sensorimotor stroke, and ataxic hemiparesis. The complete definitions of these syndromes are given in Appendix 1.

Lacunar infarction was defined as a case of stroke with one of the recognized lacunar syndromes in whom the CT or autopsy data were compatible with cerebral infarction due to primary disease of a single perforating artery of the brain.

Odds ratios were calculated according to Armitage. The confidence limits (CL) of proportions were calculated according to Miettinen. Pooled odds ratios were calculated according to Yusuf et al.

Results

Between 1 November, 1981 and 31 October, 1984, 515 patients with a first-ever stroke were registered with the OCSP from a total population of 104,221 persons. One hundred eight patients (21%) had a lacunar syndrome. A single set of CT scans without contrast enhancement was performed in a total of 104 (96%), within 28 days of onset in 93 (86%). During the first 2 years, scans were performed on a modified EMI 1007 machine with a 160 × 160 matrix taking 1-cm slices and in the third year on a Siemens Somaton DR1 taking 0.8-cm slices. The other 15 cases (14%) had an Allen score of < 4 (indicating a > 90% probability that the stroke was due to cerebral infarction). In the 11 patients who had CT scans performed > 28 days from onset, areas of low attenuation were considered due to cerebral infarction in the following analyses. The CT findings according to the presenting lacunar syndrome are presented in Table 1. Six cases were excluded from further analysis: 3 due to primary intracerebral hemorrhage and 3 with areas of infarction that could account for the symptoms and signs but that were not compatible with occlusion of a single perforating artery. The remainder of this report describes the 102 cases of lacunar infarction, representing 19.8% (95% CL, 16.4%-23.2%) of all first-ever strokes and 24.6% (95% CL, 20.5%-28.7%) of all cases of cerebral infarction.

A study neurologist assessed 101 of 102 patients (99%) with lacunar infarction, the median time to as-

Table 1. Pathologic Type of Stroke in Patients With a Lacunar Syndrome

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Appropriate infarct*</th>
<th>No relevant lesion</th>
<th>Probable infarct†</th>
<th>Inappropriate infarct‡</th>
<th>PICH</th>
<th>TOTAL n</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMS</td>
<td>10</td>
<td>20</td>
<td>28</td>
<td>57</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td>SMS</td>
<td>13</td>
<td>30</td>
<td>24</td>
<td>56</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>PSS</td>
<td>1</td>
<td>17</td>
<td>3</td>
<td>50</td>
<td>2</td>
<td>33</td>
</tr>
<tr>
<td>AH</td>
<td>5</td>
<td>50</td>
<td>3</td>
<td>30</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>TOTAL</td>
<td>29</td>
<td>58</td>
<td>15</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

PMS, pure motor stroke; SMS, sensorimotor stroke; PSS, pure sensory stroke; AH, ataxic hemiparesis; PICH, primary intracerebral hemorrhage.

*Area of infarction compatible with occlusion of a single perforating artery.
†Of 15 cases categorized as cerebral infarction by the Allen score, 11 had computed tomography (CT) scans > 28 days from onset; 6 had PMS (in 2, CT showed no lesion and in 4, an appropriate low density), 1 had SMS (no lesion on CT), 2 had PSS (no lesion on CT), 2 had AH (1 had no lesion on CT and 1 had an appropriate low density).
‡12 cases had multiple areas of cortical infarction despite only 1 clinically apparent stroke; 1 case had an infarct in the territory of the pericallosal artery.
assessment being 4 days. The other patient, whose presenting syndrome was determined by review of the hospital notes, died suddenly from a presumed cardiac dysrhythmia. A CT scan was performed in 98 of 102 (96%), the median time to scan being 10 days. Figure 1 shows the cumulative time to assessment and CT scanning.

The presenting clinical syndromes were pure motor stroke in 47 (46%), sensorimotor stroke in 39 (38%), pure sensory stroke in 6 (6%), and ataxic hemiparesis in 10 (10%). The mean age for all patients with lacunar infarcts was 71.8 (SD, 11.8) years. The mean age for patients with pure motor stroke was 70.7 (SD, 11.9) years, for sensorimotor stroke 74.7 (SD, 9.6) years, for pure sensory stroke 55.8 (SD, 14.9) years, and for ataxic hemiparesis 75.6 (SD, 10.3) years. There were 60 women and 42 men. There was no significant difference between the risk of women sustaining a lacunar infarct and that of men (pooled odds ratio, 1.02; 95% CL, 0.68–1.53).

The crude annual incidence rate was 0.33/1,000 (95% CL, 0.26–0.39), and the age- and sex-specific incidence rates are shown in Figure 2.

Of the 98 patients with lacunar infarction who had CT scans performed, areas of low attenuation in an area compatible with occlusion of a single perforating artery were seen in 34 (34.7%). There was no significant difference in the proportion of "positive" scans between pure motor stroke (14 of 45, 31.1%) and sensorimotor stroke (13 of 38, 34.2%) (odds ratio, 0.87; 95% CL, 0.01–6.04).

The 1-month case fatality rate was 1% (1 of 102). In the first year after stroke, 10 of the 102 patients died, a 1-year case fatality rate of 9.8% (95% CL, 4.0%–15.6%). The timing and cause of death are shown in Table 2. No deaths were caused by the direct neurologic sequelae of the infarct. The mean age of those patients dying in the first year was 83.3 (SD, 7.74) years.

Twelve patients suffered a recurrent stroke within a year of the initial event, a 1-year recurrence rate of 11.8% (95% CL, 5.5%–18.0%). One had occurred within 3 months, 6 within 6 months, and 10 within 9 months of the first stroke. While these patients clearly had a recurrent stroke, many were becoming increasingly disabled and were reluctant to have further CT scans. Therefore, we cannot comment about the pathologic type of the recurrences.

The proportion of patients capable of independent existence before their stroke and at 1 month and 1 year afterwards are shown in Table 3 according to their presenting clinical syndrome. Significantly fewer patients who presented with sensorimotor stroke were independent before their stroke than those presenting with pure motor stroke (odds ratio, 5.8; 95% CL, 1.04–32.45). This may explain the difference between the proportions who were independent at 1 month (odds ratio, 5.02; 95% CL, 2.13–11.85) and at 1 year (odds ratio, 1.5; 95% CL, 0.4–5.7) after stroke.

**Discussion**

The enormous social and economic burden of stroke in Western countries has been recognized for many years. Despite this, advances in the treatment of stroke have been few and, in general, applicable to only a small number of highly selected patients. While one might try to link this lack of progress with the relative underfunding of stroke research, others have argued that it may be due, in part, to a failure to distinguish pathologically homogeneous groups of stroke patients. Previous studies have suggested that
lacunar infarcts have a different underlying vascular pathology than thromboembolic cortical infarction, and may represent a subgroup of sufficient size that, if included in trials of treatments to which they do not respond, their tendency to support the null hypothesis might mean that effective treatments for other groups of patients are discarded due to the apparently negative results of such trials. Therefore, it is important to be able to distinguish lacunar infarction and to determine its natural history so that likely therapeutic interventions can be assessed.

There is considerable variation in the use of terms relating to lacunar stroke in the literature, broadly dependent on whether a clinical, radiologic, or pathologic point of view is taken. The aim of this study was to distinguish a group of strokes that were likely to have a relatively homogeneous underlying vascular pathology and to describe the natural history of the group. As frequently occurs in epidemiologic studies, one has to strike a balance between including as many patients as possible to reduce bias and excluding patients because of over-rigorous pathologic criteria that might introduce bias. Since one is dealing with an essentially nonlethal form of stroke and the demonstration of the proposed underlying vascular pathology is so labor-intensive, the requirement of postmortem evidence of primary disease of the perforating artery in every case has no useful place when studying the natural history of the group, nor indeed in treatment trials. On the other hand, to include patients with clinical syndromes that have only occasionally been reported to be associated with small areas of low attenuation on CT scans, but where the underlying vascular pathology has never been shown to be due to primary disease of a single perforating artery, would seem likely to reduce the pathologic homogeneity of the group. Thus, to minimize selection bias, our definitions of lacunar syndromes and lacunar infarction are based on clinical features that are easily assessed and can be applied to all patients with stroke. However, in the past each syndrome has been associated, more or less convincingly, with primary disease of a single perforating artery at autopsy, though we recognize that the number of fully documented cases is small and that further work in this important area is required. Therefore, we have used CT and autopsy data to refine these definitions and, in view of the high proportion of patients having such examinations in our series, have increased the likelihood that our cases had a relatively uniform underlying vascular pathology.

The underlying vascular pathology has been demonstrated most conclusively for cases with capsular infarcts clinically manifesting as pure motor stroke. The most frequent lesion in the perforating arteries was microatheroma, though as Fisher commented, "the term is hardly appropriate," and terms such as lipid macrophage plaque might be better. Two cases of pure sensory stroke associated with thalamic infarcts showed lipohyalinotic changes in the perforating vessel supplying the infarct.

There has been considerable debate as to whether sensorimotor stroke should be considered a lacunar syndrome. The pathologic support for its inclusion stems from 3 reports in which clinically relevant capsular infarcts were demonstrated at autopsy, though the perforating artery was not examined in any case. However, cases in the literature (for example that of Englander et al) that were reported as pure motor stroke had objective sensory deficits and would be included as sensorimotor strokes by our definition. Similarly, in Fisher's report, Case 8 had objective sensory loss and was shown to have a microatheromatous lesion in the perforating artery. CT evidence supports the inclusion of sensorimotor stroke as a lacunar syndrome. The distinction between pure motor, pure sensory, and sensorimotor strokes would be important only if they were shown to have different underlying vascular pathologies. It is noteworthy that sensory signs are frequently the source of substantial interobserver variation, and it has been demonstrated that the detection of a sensory abnormality in cases of pure motor stroke may depend on the sophistication of the examination.

In line with the views of others, we have used the term ataxic hemiparesis to encompass those clinical features that have been described separately as homolateral ataxia and crural paresis, dysarthria-clumsy hand syndrome, and ataxic hemiparesis. While the data relating to underlying vascular pathology are not as clear as in pure motor and pure sensory stroke, the cases reported by Fisher each had a pontine lacune associated with a patent basilar artery. He concluded that the responsible vascular lesion was likely to be a primary occlusion of the perforating artery.

In their original descriptions of pure motor stroke, Fisher and Curry refer to cases with involvement of the face, arm, and leg. There are, however, a substantial number of CT reports associating lesions compatible with lacunar infarction with the "partial" syndromes of brachioocular or facioobrachial weakness. Even more restricted deficits have been associated with lesions compatible with lacunar infarction, isolated crural weakness, and isolated facial weakness, but it seems likely that such deficits more often occur

<table>
<thead>
<tr>
<th>Time</th>
<th>PMS</th>
<th>SMS</th>
<th>PSS</th>
<th>AH</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before stroke</td>
<td>45/47 (95.7%)</td>
<td>31/39 (79.5%)</td>
<td>6/6 (100%)</td>
<td>8/10 (80.0%)</td>
<td>90/102 (88.2%)</td>
</tr>
<tr>
<td>1 month after stroke</td>
<td>34/46 (73.9%)</td>
<td>22/39 (56.4%)</td>
<td>5/6 (83.3%)</td>
<td>7/10 (70.0%)</td>
<td>68/101 (67.3%)</td>
</tr>
<tr>
<td>1 year after stroke</td>
<td>31/44 (70.5%)</td>
<td>21/34 (61.8%)</td>
<td>3/5 (60.0%)</td>
<td>6/9 (66.7%)</td>
<td>61/92 (66.3%)</td>
</tr>
</tbody>
</table>

PMS, pure motor stroke; SMS, sensorimotor stroke; PSS, pure sensory stroke; AH, ataxic hemiparesis.

---

**Table 3. Proportion of Patients Capable of Independent Existence**
from cortical lesions. There is pathologic confirmation that partial syndromes of pure sensory stroke can be caused by lacunar infarcts. We concur with Fisher's view that if 2 of the 3 areas are involved, "the odds favour a thalamic rather than a cortical site," and we have also applied this same 2-of-3-areas criterion to the deficits in pure motor strokes. We have also emphasized that the whole limb and not just the digits should be involved, thereby excluding cases with a "pseudoradicular" distribution, which are more likely to be cortical in origin. Also, since there are no cases in the literature with documented lesions compatible with lacunar infarction where the sensory deficit was purely proprioceptive and since there are good anatomic reasons why proprioception should be considered a cortical modality, such cases were also excluded.

The high proportion of patients having a CT scan in our study allows the single case reports of CT findings to be put into perspective. A review of the English-language literature suggests that up to 25% of published reports of lacunar strokes have been related to the presence of primary intracerebral hemorrhage. While it is possible that a few of our patients with later scans may have had small hemorrhages that had resolved, the overall impression is that it is extremely unusual for primary intracerebral hemorrhage to present as a lacunar syndrome. The fact that only 3 patients had CT evidence of infarction that could not be explained by occlusion of a single perforating artery suggests that our definitions of the lacunar syndromes, especially with respect to the extent of the clinical deficit, are clinically useful. The early assessment by a neurologically trained physician may also be important. It seems unlikely that cortical infarcts of sufficient size to cause such an anatomic deficit would not have been visible on any significant number of scans. Our data also provide good supportive evidence for the inclusion of sensorimotor stroke as a lacunar syndrome.

The finding that lacunar infarction represented 24.6% of all cases of cerebral infarction confirms the numeric importance of this group. In any study of natural history, it is important to have complete case ascertainment to avoid bias. Hospital-based studies of stroke must be considered suspect since there is little evidence to support claims that all patients with stroke are admitted to a hospital in any country. We have shown that any impairment of consciousness level, impairment of higher mental function, or a hemorrhagic stroke all increase the likelihood of hospital admission. These features are absent in cases of lacunar infarction and mean that identification of cases that remain in the community is extremely important. The methods of the OCSP allow such cases to be identified, and the lower proportions reported from hospital-based studies (14% in the Stroke Data Bank and 22.6% in the Harvard Cooperative Stroke Registry) may be due to failure to identify these cases. On the other hand, these studies reported on all strokes occurring during the study period rather than first-ever stroke. If a patient has a recurrent stroke, it is our experience that it is very difficult to be sure which features are new and which are residua from a previous event. Consequently, one is less likely to diagnose a lacunar syndrome.

With other groups of stroke patients, the incidence of lacunar infarction rises steeply with increasing age and continues to rise even among the most elderly. The finding of no substantial sex difference in the risk of lacunar infarction is of interest in view of the overall excess risk of stroke among men (28% in the OCSP and between 18 and 66% in other Western studies when calculated in a similar manner). The confidence limits were quite wide due to relatively small numbers, but if this were to be confirmed in other prospective studies, then the result would justify further attention.

Among patients with lacunar infarction, only 34.7% had "positive" scans. This is a proportion similar to that reported by Gross et al and demonstrates the limitations of using purely radiologic findings as a basis for diagnosis and classification. Even with repeated CT scanning, less than 70% of patients with lacunar syndromes might be expected to have "positive" scans. While magnetic resonance imaging (MRI) may increase this yield, its generally restricted availability and current difficulties in distinguishing infarction and hemorrhage mean that its role in epidemiologic and treatment studies of lacunar infarction will be limited. The similar "positivity" rates in patients with pure motor and sensorimotor stroke suggest that the clinical features may have more to do with the site than the size of the lesion. Further details of these findings will be reported later.

As expected, the case fatality rate for lacunar infarction was extremely low, and no patients died due to the direct neurologic sequelae of their stroke, a point of considerable importance when planning trials in acute stroke. Such patients are, however, as vulnerable to the complications of immobility, such as pneumonia and pulmonary embolism, and the complications of cardiac disease as other patients with stroke. Any relative failure to detect cases of lacunar infarction that remain out of a hospital will tend to raise case fatality rates in other studies. The high mean age of patients dying reflects the known increase in case fatality rate with age.

The overall 1-year recurrence rate among cases of lacunar infarction is similar to that reported in other groups of patients with stroke. There was no evidence that a recurrence was more likely to occur soon after the original stroke. This would support the notion that lacunar infarcts occur as a result of occlusion of a single perforating artery, and thus any recurrent event would require the occlusion of another artery. It suggests that an active source of embolism that might give rise to a series of events close together is a less likely mechanism. It is important to try to determine what type of stroke the recurrent event is, but for practical reasons this study was unable to provide such information.

While patients with lacunar infarction are likely to survive their stroke, 1 year later about one-third will
still be dependent on other persons to some extent. This is a proportion similar to survivors of other types of stroke in our study,46 merely serving to emphasize that lacunar infarcts occur in strategically important areas and that this is a clinically important group to identify and treat appropriately.

Appendix 1. Definition of Lacunar Syndromes

A constellation of clinical symptoms and signs present at the time of maximal deficit following a single cerebrovascular event. The presence of a visual field defect, evidence of higher cerebral dysfunction (e.g., dysphasia, visuospatial disturbance, predominantly proprioceptive sensory loss) on standard clinical testing, or features that clearly localize the lesion in the vertebrobasilar distribution (e.g., gaze palsies or crossed deficits, though not nystagmus or dysarthria) exclude the diagnosis of lacunar syndrome.

Pure Motor Stroke. A unilateral, pure motor deficit involving at least 2 of 3 areas (face, arm, leg) and in patients with faciobrachial or brachiocural weakness, affecting the whole limb. Sensory symptoms may be present at the time of onset, but there should not be any objective sensory loss on standard clinical testing.

Pure Sensory Stroke. A sensory deficit (which may be diagnosed even when there is no objective sensory loss on standard clinical testing) involving at least 2 of 3 areas (face, arm, leg). In patients with faciobrachial and brachiocural symptoms, the whole limb should be affected. The sensory deficit may include all modalities equally or may spare proprioception.

Ataxic Hemiparesis. A syndrome of ipsilateral corticospinal and cerebellar-like dysfunction without other features that clearly localize to the posterior circulation. This includes cases with predominantly dysarthria and clumsiness of the hand.

Sensorimotor Stroke. A syndrome of ipsilateral motor and objective sensory loss, involving at least 2 of 3 areas (face, arm, leg). In patients with brachiofascial or brachiocural deficit, the whole limb must be involved. The sensory deficit may involve all modalities equally or may spare proprioception.

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J Bamford, P Sandercock, L Jones and C Warlow

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