SUMMARY The advent of EC/IC Bypass surgery has focused attention on selected patients who might benefit from this innovative procedure. There is a poverty of natural history data pertaining to all such lesions. Two centres (Memphis, Tennessee and London, Ontario) pooled their resources to carry out a retrospective review of 58 patients with angiographically-proven intracranial internal carotid artery stenosis. Only 33% of the patients were alive and free from subsequent cerebral vascular events at the end of the mean follow-up of 30 months. Forty-three percent of the patients died during follow-up: 36% due to stroke and 44% because of cardiac disease. Forty-three percent of the patients suffered cerebral vascular events during the follow-up period: there were 17 strokes (29%) including 9 fatal strokes. The incidence of ipsilateral stroke was 19%; 65% of the strokes were appropriate to the stenotic intracranial carotid lesion under study. The annual ipsilateral stroke rate for patients with this lesion was 7.6% per year. This lesion detected on angiography is indicative of severe atheroma, and carries a serious risk of death due to ischemic heart disease or stroke.

Intracranial Internal Carotid Artery Stenosis

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ATHEROSCLEROTIC STENOSIS OF THE INTERNAL CAROTID ARTERY (ICA) is a common lesion, most frequently found in the cervical portion of the internal carotid artery just beyond its origin. Carotid endarterectomy is often performed in the management of patients with atheromatous irregularity, ulcerative disease and stenosis of this portion of the artery. Severe intracranial ICA stenosis is not as common and is usually found in the surgically inaccessible part of the artery between the carotid canal and the origin of the ophthalmic artery.¹ The advent of extracranial to intracranial (EC/IC) bypass surgery has focused attention on this lesion as one that might benefit from the innovative procedure. Review of this literature reveals a poverty of data on the natural history of such lesions.

The natural history of 21 patients with symptomatic intracranial ICA stenosis from London, Ontario was reviewed and reported in an earlier communication.² Subsequently resources were pooled with Memphis, Tennessee to carry out a retrospective review and analysis of this lesion.

Patients and Methods

Patients were seen at University Hospital, London, Ontario between 1972 and 1980 and at the VA Hospital, Memphis, Tennessee between 1975 and 1981. Seventy-four patients formed the initial data base as judged by angiographic findings. Patients were included who had a stenosis reducing the arterial lumen by at least one-third of its diameter in one or both intracranial portions of the internal carotid arteries. Asymptomatic as well as symptomatic lesions were studied. Several patients had an ipsilateral lesion in the extracranial part of the artery (tandem lesion) and these were included. Also included were patients who had a cervical carotid endarterectomy. Patients were not included in this natural history review for the following reasons: an EC/IC bypass was performed within the Collaborative Study (5 patients); ipsilateral MCA stenosis was associated (6 patients); death occurred from the presenting stroke (2 patients); fatal stroke followed the angiography which identified the lesions (1 patient); nonfatal stroke followed endarterectomy (1 patient); death followed endarterectomy (1 patient). Three of the 21 patients reported in our earlier communication were among those excluded for these reasons. Fifty-eight patients remained for further follow-up study, 40 from Memphis and 18 from London.

Follow-up had been carried out by clinic visits in the majority but in a few instances a telephone interview provided the necessary data. The end-points for the study were stroke, death and subsequent randomization in the Collaborative EC/IC Bypass Study.

Results

There were 13 female and 45 male patients. The age range was 43 to 86 years with a mean of 62.4. Forty-seven of the patients (81%) presented with symptoms appropriate to the lesion under study (see table 1). Sixteen patients (28%) presented with TIA. Thirty-one (53%) presented with stroke: reversible ischemic neurological deficit in 9 (15%), partial nonprogressing stroke (PNS) in 7 (12%), major disabling stroke in 15 (26%).

In the asymptomatic group of patients angiography had been performed for the following reasons: asymptomatic bruit (4 patients), stroke in other vascular territory (4 patients), confusional state due to metabolic encephalopathy (2 patients), investigation prior to major vascular surgery (1 patient).

Associated medical conditions were identified and were common. Hypertension was found in 40 patients (68%), diabetes mellitus in 23 patients (39%), and ischemic heart disease presenting by previous myocardial infarction, prior coronary artery bypass surgery, or history of angina occurred in 28 (48%). Most patients had at least two of the above conditions.

Angiographic Features

The cavernous segment was the most common site of disease found in 42 patients (72%). Nine had steno-
sis of the petrous portion and 7 had stenosis of the supraclinoid portion. Four patients had lesions in two contiguous arterial segments, for example, petrous and cavernous segments. The severity of the lesions as estimated from the angiograms were as follows: 35 (60%) were greater than or equal to 50%, 23 (40%) were less than 50% but more than 30%. Additional significant findings were: 13 patients (22%) had bilateral intracranial ICA stenosis; 7 (12%) had occlusion and 6 (10%) stenosis of the opposite ICA at its origin; 6 (10%) had extracranial stenosis; an extracranial, (carotid sinus) tandem stenosis of 33% to 70% was found in 6 (10%) patients. In 90% of the patients the intracranial ICA stenosis was the only identified ipsilateral carotid lesion (table 2).

Five patients had repeat angiography after periods ranging from 8 months to 4 years (see fig. 1). All the lesions had progressed, 1 of them to an occlusion.

Follow-up Data
Patients were followed for a mean of 30 months (range 2–78 months). Most of the patients whose angiographic lesions were initially symptomatic had been treated with antiplatelet agents although four were treated with anticoagulants.

At the end of follow-up only 19 of 58 patients (33%) were alive and free from subsequent cerebral vascular events. Only 47% of the patients were functioning well. Twenty-five of the patients (43%) suffered cerebral vascular events: 17 (29%) suffered a stroke and 11 (65%) of these were appropriate to the intracranial internal carotid artery stenosis (table 3). None of these cerebral vascular events occurred in the 6 patients with "tandem" lesions. The incidence of ipsilateral stroke during follow-up was 19%. There were 9 fatal strokes: 5 appropriate to the intracranial ICA stenosis, 3 in the opposite internal carotid territory, and 1 in the vertebral basilar territory. Eight patients suffered TIAs of which 25% were appropriate to the lesion under study.

Twenty-five of the patients (43%) died during the follow-up period. Eleven of the deaths (44%) were due to cardiac disease and 9 of the deaths (36%) were due to stroke. Fatal strokes were included in the analysis of subsequent cerebral vascular events and deaths. The causes of death are listed in table 4.

When one considers the symptomatic and asymptomatic groups separately, the incidence of cerebral vascular events was 36% and 45% respectively. In the asymptomatic group 3 out of the 4 subsequent cerebral vascular events (75%) were appropriate to the intracranial ICA stenosis (table 5). In the symptomatic group of patients 9 of the 21 subsequent cerebral vascular events (43%) were appropriate to the intracranial ICA stenosis. The patients with a stenosis of greater than or equal to 50% had a 45% incidence of subsequent cerebral vascular events compared with 39% in those with lesions less than 50% (table 5). There was no major effect of sex on the prognosis: 40% of the male patients and 54% of the female patients died during the follow-up; 49% of the males had subsequent vascular events as compared to 23% of the females. The small number of patients made statistical analyses of the effects on prognosis of degree of stenosis, presence of symptoms or sex of no value.

Discussion
This study confirms our early study and that of Marzewski et al.1 that intracranial ICA stenosis is a highly significant lesion in terms of subsequent cerebral vascular events and death. Only 33% of our patients remained alive and free from subsequent cerebral vascular events over a relatively short follow-up period of 30 months. There was a high incidence of subsequent cerebral vascular events (43%) most of which were stroke and two-thirds of which were in the territory of the intracranial ICA stenosis. There was a high incidence of significant bilateral carotid disease (44%) in this group of patients so that a substantial number (one-third) of strokes in other cerebral vascular territories is not surprising.

The asymptomatic patients had as poor a prognosis as the symptomatic ones, nor did the degree of stenosis appear to have any effect on the prognosis. Recent studies of patients threatened with cerebral vascular events have shown a better prognosis for women than men.4 This was apparent in the London-Memphis se-

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**Table 1 Clinical Presentation (58 Patients)**

<table>
<thead>
<tr>
<th>Symptomatic</th>
<th>Asymptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIA………………..16 (28%)</td>
<td>Stroke-other territory………………..4</td>
</tr>
<tr>
<td>Stroke: Rand………………9 (15%)</td>
<td>Asymptomatic bruit………………..4</td>
</tr>
<tr>
<td>PNS………………7 (12%)</td>
<td>Confusional (metabolic) encephalopathy………………..2</td>
</tr>
<tr>
<td>Major stroke………………15 (26%)</td>
<td>Pre-op. vascular surgery………………..1</td>
</tr>
<tr>
<td>Total: 47 (81%)</td>
<td>11 (19%)</td>
</tr>
</tbody>
</table>

---

**Table 2 Associated Angiographic Features**

| Bilateral intracranial ICA disease 13 (22%) |
| Opposite ICA occlusion at origin 7 (12%) |
| Opposite ICA stenosis at origin 6 (10%) |
| Proximal ipsilateral carotid sinus stenosis (tandem) 33–70% 6 (10%)* |

*Two patients subsequently had carotid endarterectomy.

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**Table 3 Vascular Events in 25 Patients**

<table>
<thead>
<tr>
<th>Ipsilateral</th>
<th>Others</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIA 2</td>
<td>6</td>
<td>8 (14%)</td>
</tr>
<tr>
<td>Stroke 11 (65%)*</td>
<td>6 (35%)</td>
<td>17 (29%)*</td>
</tr>
<tr>
<td>Total 25 (43%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*19% ipsilateral stroke incidence.
†Includes 9 fatal strokes.
ries as the incidence of vascular events was twice as great in men as in women. The numbers of deaths however were similar.

Epidemiologic studies have shown that of the patients who survive the initial stroke, more will die of cardiac disease than recurrent stroke. This phenomenon was found to be the case in this study of patients with intracranial ICA stenosis.

The fate of 50 patients with intracranial ICA stenoses from the records of the Cleveland Clinic has been reported. The criteria for entry to their follow-up required an intracranial stenosis equal to or greater than 50%. Their review included more patients with tandem lesions (36% of the patients had a cervical ICA stenosis equal to or greater than 50%, c.f. the present author’s series with only 10% having this type of tandem lesion). At entry the Cleveland series contained more patients (48% c.f. 19%) who had no symptoms related to the intracranial ICA stenosis at the time of its identification by cerebral angiography. Nevertheless, their finding of an ipsilateral stroke rate of 18% after 44 months of mean follow-up was reasonably comparable to the London-Memphis rate of 19% after a mean follow-up of 30 months. The death-rates for the two groups were 46% and 43% for Cleveland and for London-Memphis respectively. Cardiac deaths accounted for 61% and 44% respectively. Of the first 577 patients randomized into the Collaborative EC/IC Bypass Study, 17% were admitted because of inaccessible ICA stenosis. By comparison 10% have had middle cerebral artery (MCA) occlusion, 12% MCA stenosis, while 61% of the patients were admitted as a sequel to symptomatic internal carotid artery occlusion. In Caucasians intracranial ICA stenosis may prove to be of special importance for bypass surgery if this procedure proves to be beneficial. Available data do not indicate, however, that patients with ICA occlusion represent a substantially lower risk category if one is considering ipsilateral stroke as the end-point which might be preventable by bypass surgery. A large retrospective study involving 138 patients from the Mayo Clinic records has reported a 2% annual rate of ipsilateral stroke in the first four years of follow-up. A smaller prospective study of 47 patients from the University Hospital, London has revealed a 5% annual ipsilateral

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac</td>
<td>11</td>
<td>(44%)</td>
</tr>
<tr>
<td>Stroke</td>
<td>9</td>
<td>(36%)</td>
</tr>
<tr>
<td>Carcinoma lung</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Uremia</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td></td>
</tr>
</tbody>
</table>

Table 4: Cause of Death
stroke rate in a mean follow-up of 2.9 years. In the patients from the London-Memphis and Cleveland groups respectively, the annual ipsilateral stroke rate was 7.6% and 4.9%.**

In terms of survival, the ICA intracranial stenosis patients are a high risk group: the London-Memphis mortality of 43% in 30 months and the Cleveland mortality of 46% in 44 months, with cardiac disease the most common cause of death, indicates that intracranial carotid artery stenosis, whether symptomatic or asymptomatic is indicative of widespread arteriosclerosis. Whether bypass surgery will have an impact on the stroke-rate or on the mortality of this group of patients remains to be established.

Editor’s Note: In accordance with Stroke policy, this article was guest edited by Dr. J. P. Mohr.

References
Intracranial internal carotid artery stenosis.
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Stroke. 1982;13:825-828
doi: 10.1161/01.STR.13.6.825

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