THE READERS OF STROKE are offered in this issue the results of a series of studies and some critical observations relating to the performance of carotid endarterectomy on either asymptomatic or, more importantly, symptomatic patients. Some neurologists, neurosurgeons and vascular surgeons will undoubtedly disagree with the comments made or with the conclusions reached by several, or even by all, of the authors who have submitted these papers. Nevertheless, none can be lightly dismissed.

During the professional lifetime of the present generation of neurologists, cerebral angiography has become widely accepted and practiced, the symptoms of impending ischemic stroke have been delineated, and putative prophylaxis either by anticoagulant therapy or by carotid endarterectomy have been widely utilized for the potential stroke victims identified because of these advances.

Many practitioners have been unhappy with both anticoagulant therapy and carotid endarterectomy because the risk of producing stroke, including even fatal stroke, can be associated with either or both. Convincing studies clearly demonstrating reduced risk of stroke achieved with either treatment have not been forthcoming. Nevertheless, with varying degrees of enthusiasm, most practitioners concerned with stroke prevention have practiced or recommended either, or both, of these strategies.

Recent developments provide a number of compelling reasons for reassessing efforts to prevent stroke by any established or innovative procedure which carries a high risk. The following comments could be applied equally to medical or surgical treatment but our observations below concentrate upon the results of endarterectomy:

1. The mortality and even the morbidity from stroke has been declining steadily for 25 years. Evidence is lacking that this decline relates to the practice of endarterectomy or any other form of secondary prevention. However, the numbers submitted to this surgical procedure may be too few to permit an accurate detection of its influence against the larger population of stroke victims.

2. The prognosis in individuals afflicted with transient ischemic attacks and/or minor strokes has been much better defined. The outlook in particular age groups, with precisely identified specific arterial lesions and with a variety of associated risk factors has been reported. From these studies more credible prognostic data have emerged for selected populations but major differences between all such groups deny their utility as controls for any therapeutic trials.

3. Biostatistics and the methodology of clinical trials have matured, making the evaluation of new treatment strategies more credible. It has become imperative that healthy skepticism be directed towards older treatments that have not been submitted to the scrutiny demanded by modern epidemiologic principles. The evaluation of reports concerning the results from carotid endarterectomy fares badly when submitted to such critical appraisal.

4. Awareness of the importance of the heart in the pathogenesis of cerebral ischemia has increased. Better methods of cardiac monitoring and cardiac imaging have focussed attention on disorders, in all age groups, which once were commonly overlooked or unrecognized. As a result, in keeping with the evidence from post-mortem studies, stroke data banks and stroke registries are reporting that among hospitalized patients 15 to 25% of ischemic events are occurring in patients whose hearts might be a source of thrombo-embolism. Many patients are now found to have both vascular and cardiac lesions which could produce cerebral ischemic symptoms. Patients experiencing transient ischemic events or minor strokes are at risk for major and fatal stroke but in the ensuing years are known to be at equal or greater risk of fatal and non-fatal myocardial infarction. This need not be regarded as imposing an absolute restraint upon the use of an established or innovative strategy for preventing stroke but it increases the need for prudence and responsible evaluation. Moreover, it underlines the need to identify methods of proven efficacy in the primary prophylaxis of progressive generalized vascular disease.

5. Platelet antiaggregants have been introduced as an alternative form of anti-thrombotic therapy. In randomized trials, where sufficient patients were studied to avoid the likelihood of statistical error, aspirin reduced stroke and stroke-death during the period of follow-up of the Canadian (26 months) and the French (36 months) studies. Two other studies including insufficient patients for conclusive analysis suggested a positive benefit and two suggested no benefit. More trials of this type are needed here and it is hoped
that the very large ongoing British trial will supply satisfactory answers. In the meantime there have been no studies comparing directly the risk reduction resulting from the administration of aspirin with that achieved by carotid endarterectomy.

6. “Acceptable risk” for the combination of surgery and angiography in asymptomatic patients was calculated to be 2.9% by analyzing the outcome of stroke in the methodologically imperfect Extracranial Arterial Occlusion Joint Study. Some authors claim to have achieved such an allowable morbidity and mortality. Clearly, before recommending a therapeutic procedure one must judge it by the results achieved in widely tested and carefully analyzed nationwide medical practice, not merely by the results published by a few specialized centers. This is especially true in respect to endarterectomy which, at 80,000 operations per year, has become the third most common operation performed in the United States. Illustrating this principle, disturbing figures are presented in this issue of STROKE and others have been published elsewhere, which report between 3 and 4 times the “allowable” morbidity and mortality. The statistics from the compilation by Dyken and Pokras suggest that the recent overall morbidity and mortality resulting from endarterectomy in the United States can be conservatively estimated at 10% per year. Figures published about the risks of angiography are hard to assess because most are based on retrospective studies. One prospective study in patients with vascular disease reports a 4.2% neurological complication rate, with 0.6% experiencing a permanent disability. Asymptomatic carotid artery disease has been identified by seeking bruits in the neck as part of a routine physical examination. Large numbers of these patients have been subjected to arteriography and endarterectomy. The morbidity and the mortality from this surgical procedure and from the arteriographic investigation that precedes it have not been negligible. In some published series it exceeds the “allowable” calculations for symptomatic disease.

8. Noninvasive techniques (such as Doppler ultrasound) which make it easier to detect asymptomatic carotid artery disease, and which allow the physician to follow progressive changes from mildly to severely stenosing lesions are in widespread use. An increasing number of patients are being referred from this pool of asymptomatic individuals for consideration of endarterectomy. Many neurologists, neurosurgeons and vascular surgeons have expressed varying degrees of enthusiasm for this course of action, regrettably without sound biological guidelines to direct their decision-making.

All these new ingredients in the mix of knowledge demand of the practicing neurologist, neurosurgeon and vascular surgeon that the future use of carotid endarterectomy be carefully re-appraised. Alternatives for dealing with asymptomatic carotid disease have emerged:

1. A careful analysis of many patients studied over a long period of time, recruited in a multicenter fashion, could be carried out to determine what the best medical care, including the use of platelet anti-aggregant drugs, offers by way of reducing the incidence of stroke in this population. A randomly selected group not receiving platelet antiaggregants would be acceptable as a control. Ideally this trial would require that the diagnosis be confirmed by good noninvasive studies, standardized throughout the centers. From this, if the study could be made large enough, might emerge the means of detecting a group carrying demonstrably higher risks.

2. A randomized clinical trial involving a nonsurgical and surgical group could be done admitting all patients identified with a bruit and a stenosis of 50-75% or greater, screened first by noninvasive techniques and then delineated by angiography. An assumption would have to be made that asymptomatic patients with this degree of stenosis, with or without ulcerative disease, represent a group carrying a higher risk than normal. Pilot observations such as that reported in this issue by Chambers et al, although identifying a group at higher risk of stroke, failed to pinpoint a group which they judged to be at sufficient risk to justify a clinical trial considering the known risk of the surgical procedure. Questions about the ethics of embarking on such a study are very real. The execution of such a trial, if it were ever done, would prove to be an enormous task: the risk of stroke in the population under study is low and a very large sample-size would be needed.

3. A policy of doing nothing in the way of a trial for asymptomatic patients could be adopted and a clinical decision made to deal with each patient in terms of risk factor management with or without the empirical usage of platelet inhibitors.

At the present time there is not sufficient evidence available to justify the risk of operating on patients with asymptomatic carotid lesions. This constraint applies equally to casually detected lesions, to lesions found on the side opposite to symptomatic stenosis, to lesions found in patients with only vertebral-basilar symptoms, and lesions found in patients about to undergo open heart or aortic surgery.

Acceptable principles to be applied by the physician dealing with the symptomatic patient with an accessible stenosing carotid artery lesion, appropriate to symptoms, emerge as the following:

1. A very demanding clinical approach must be adopted. High standards of diagnostic accuracy and in all aspects of medical or surgical management of these patients must be achieved.

2. Physicians referring patients for endarterectomy must make themselves acquainted with the anticipated morbidity and mortality associated with the procedure in their particular institution. This requires institutional audit. Institutional audit must be carried out, as the word implies, by disinterested individuals prepared to undertake a careful appraisal of the results, and of the morbidity and mortality of arteriography, medical treatment and surgery.

3. When institutional audits determine that the risk
for endarterectomy in a given institution is beyond acceptable levels, the acknowledged narrow gap between the risks of modern medical management and those of surgical management suggests that the procedure be discontinued in that hospital. This surgical embargo would appear to be the only ethical course to follow in any hospital where the figures are of the magnitude of those presented in some published papers including some in this issue of STROKE.

4. A new clinical trial, multicenter in scope and large enough to satisfy the sample size requirements set out in this issue by Taylor et al must be welcomed. The results of such a trial recently launched in Britain and Europe will be watched with great interest.

Those interested in stroke prevention must face the serious responsibility of evaluating the benefits of endarterectomy for symptomatic patients by deploying all the scientific resources at our disposal. We cannot pretend to patients with carotid disease that we yet have any final answers. We must solicit their assistance in achieving this goal. The undersigned neurologists represent different clinical backgrounds, different patterns of socio-economic circumstances governing the practice of medicine, and different ways of looking at technological advances in relation to the quality of life. We share a common concern about the status of endarterectomy in stroke prophylaxis.

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Carotid endarterectomy--an expression of concern.
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