A current advertisement in the glossy magazines shows a picture of an attractive young woman, modishly dressed, with the exultation printed beneath, "You've come a long way, baby." So it is with our understanding of the causes and treatment of cerebrovascular disease commonly called "stroke." Like many advances in medicine, this has happened in our lifetime. Many of the council members attending this meeting today have made significant contributions to current knowledge of the epidemiology, diagnosis, prevention, and treatment of stroke.

It has become a tradition of the Council on Cerebrovascular Disease for the outgoing chairman to provide a personal account of the past, present, and future of cerebrovascular disease. My distinguished predecessors, Dr. Irving Wright and Dr. Clark Millikan, have provided useful accounts of considerable historical as well as therapeutic interest, and the present contribution is an attempt to follow this tradition.

My personal interest in therapy of stroke began in 1948 after completing medical school and beginning postgraduate work at the Montreal Neurological Institute under the guidance of Dr. Wilder Penfield. While working there, word reached me that my father, a surgeon and practitioner in London, England, had suffered the sudden onset of nausea, vomiting and vertigo, had staggered around for several seconds, and collapsed to the floor where he remained incapacitated but not unconscious. After examination by a world-renowned neurologist, he was admitted to a distinguished neurological hospital where the initial diagnostic impression of acute labyrinthitis was abandoned and the correct diagnosis of lateral medullary infarction was established. The cause of the infarct was thought to be due to “posterior inferior cerebellar artery occlusion.” When I visited him in the hospital 22 years ago, as I recall it, the following points were apparent: 1. The initial diagnostic impression was not correct despite examination by a neurologist of unquestioned competence. 2. The final diagnosis of posterior inferior cerebellar artery occlusion was made without any objective proof. Had arteriography been performed, present knowledge indicates that occlusion or stenosis of the vertebral artery would have been established. 3. No therapy was considered—let alone prescribed. Upon questioning, there were no studies then available for establishing the usefulness of anticoagulant...
therapy. The work of Wright, Millikan et al., and Fisher later established the effectiveness of these drugs in treating patients with stroke. The prognosis and natural history of this well-recognized clinical entity had still to be determined. He is still alive 22 years later. There has been little progression of his brain-stem symptoms at the age of 83, in keeping with the published studies of the natural history of this disorder ten years later by Currier et al. Nothing was known of the factors that might have precipitated this catastrophic event. At that time, the association of hypertension, heart disease, diabetes, obesity, smoking, rheumatic fever, and other disorders was not understood. In my father's case, 15 years prior to the occurrence of stroke, he had sustained a fracture of his cervical vertebra in an automobile accident. This may have resulted in compression or trauma to the vertebral artery, which is now known to be a cause of vertebral artery occlusion.

All that was available about stroke at that time were some tables giving autopsy statistics of the relative incidence in hospital populations of cerebral hemorrhage, thrombosis, infarction, and aneurysm. Prospective studies have shown these figures to be biased in favor of cerebral hemorrhage, since this is a common cause of death in the hospital. Current figures from the Framingham, Massachusetts, study show that cerebral infarction due to thrombosis accounts for 62% of strokes, embolism for 19%, subarachnoid hemorrhage for 12%, and intracerebral hemorrhage for 5% to 10%. In addition, there were numerous clinical and pathological studies such as those reported by Foix and Hillemand, who described vascular syndromes, particularly of the brain stem, as though all vessels supplying the brain were end-arteries and thrombosis of them produced neat little round infarcts in their specific areas of supply. No account was made of the importance of the collateral circulation, vascular anomalies, and proximal occlusive disease of the aorticcranial circulation.

Apart from rare reports by Moniz, Walker, and a few neurosurgeons who were doing arteriograms for other reasons, arteriograms simply were not performed in stroke patients in the 1940s. It was common practice at that time to base the diagnosis of stroke on a purely clinical appraisal, often without a lumbar puncture. It was not uncommon to do a pneumoencephalogram to rule out brain tumor. I can remember my instructors at a famous neurological institute telling me that pneumoencephalograms regularly made patients with stroke temporarily worse. Nowadays, we realize that the danger of hypotension in such patients may cause further cerebral thrombosis, although ventriculography is certainly justified in diagnosing hemorrhages in the brain stem and pneumoencephalography in diagnosing hemorrhage of the cerebral hemispheres. As part of my thesis for a master's degree in neurology on the subject of the diencephalon, Dr. Penfield assigned me a patient for study who had suffered a sudden onset of akinetic mutism. On the basis of expert clinical evaluation, Dr. Penfield correctly diagnosed a lesion of the diencephalon and one in the region of the third ventricle. A ventriculogram revealed a round mass in the anterior third ventricle. Arteriography was not performed and a surgical approach to the third ventricle was made by splitting the corpus callosum. I was permitted to assist at the time of surgery, and a hemorrhagic cyst was identified in the anterior hypothalamus and the anterior perforated space. Had an arteriogram been done, as would be routine nowadays, I have no doubt that an aneurysm of the anterior communicating artery would have been revealed.

The most significant contribution to progress in cerebral arteriography was the development in the 1950s of nontoxic contrast media such as sodium diatrizoate, which made it possible to perform arteriograms with a low incidence of complications. These improved contrast media permitted retrograde brachial-subclavian arteriography by the use of pressure injectors and seriograms. This, in turn, made possible correct diagnosis of aortocranial occlusive and intracerebral hemorrhagic processes. In 1958, some physicians carried out arteriographical surveys in the majority of stroke patients, but this was considered to verge on unethical conduct; indeed, some of us were snubbed at professional scientific meetings by our more conservative colleagues. The classical paper of Kubik and Adams on basilar artery thrombosis and the equally classical paper by Fisher on the carotid artery occlusion syndrome described the recognition
of vertebrobasilar insufficiency and carotid insufficiency by their clinical manifestations. The findings of both these investigators were confirmed at autopsy. I cite also the classical paper of Millikan and Siekert, who defined symptoms of vertebrobasilar insufficiency.

During the 1950s, methods of measuring cerebral blood flow and metabolism, such as the Kety-Schmidt technique, were applied to the problems of stroke. Experiments with animals together with studies in man permitted definition of the basis for the reversibility of symptoms of cerebrovascular disease. The role of the collateral circulation in maintaining tissue viability also was recognized during these early investigations.

The first operations for restoration of carotid artery flow were performed by vascular surgeons and neurosurgeons in the early 1950s. Cooperative studies were organized which have confirmed that hypertension is commonly associated with ruptured aneurysm of the cerebral vessels, causing vasospasm and often symptoms of cerebral ischemia. Ligation of the carotid artery for treatment of aneurysms arising from it or from the posterior communicating artery as well as clipping these aneurysms has been found effective in the relief of symptoms. The Joint Study of Extracranial Arterial Occlusion, after a five-year follow-up of stroke patients, has established that control of hypertension reduces the incidence of stroke as well as heart and kidney disease. If control of hypertension is widely practiced, a reduction in morbidity and mortality rates should become evident in the next ten years. Improved surgical techniques are available for the treatment of aneurysms and occlusive lesions of the extracranial vessels and aortic arch which produce symptoms of cerebrovascular disease. In a controlled study following surgical replacement of heart valves, which carries a high risk of cerebral embolization probably from platelet fragments, dipyridamole reduced the incidence to almost zero in the treated group. In the untreated group, all had emboli to the brain.

Inhibition of a hypercoagulable state may be indicated in some patients, while vasodilators are indicated in others. It is only in rare circumstances such as intracerebral hematoma, acute and massive cerebral infarction, as well as brain tumor, that these drugs may be contraindicated. In the vast majority of patients with cerebral ischemia, blood flow to the ischemic zone is improved by cerebral vasodilatation. The rare phenomenon originally called the “intracerebral steal” occurs only during the first few days of cerebral infarction, although quite consistently with brain tumor and intracerebral hematoma. In my opinion, a better term would be the intracerebral displacement or the “intracerebral squeeze” syndrome, since it is now evident that carbon dioxide increases intracranial pressure, further compressing an area of tumor, hemorrhage, or massive infarction and squeezing the blood out of the tissue. Cerebral vasoconstrictors, on the other hand, reduce intracranial pressure, increasing regional flow in the abnormal area. Drugs such as glycerol or mannitol are more effective than hyperventilation in reduction of intracranial pressure. This is clearly an area in which regional cerebral blood flow measurements appear to benefit the patient, not only in establishing a diagnosis when arteriograms are normal but in planning treatment. Control of hypotension when it falls to excessively low levels is crucial in managing the patient with acute stroke and in preventing chronic deterioration of patients with postural hypotension. Clinical trials and cerebral blood and metabolic measurements appear to benefit the patient, not only in establishing a diagnosis when arteriograms are normal but in planning treatment. Control of hypotension when it falls to excessively low levels is crucial in managing the patient with acute stroke and in preventing chronic deterioration of patients with postural hypotension.
lism have provided evidence that in patients with acute stroke due to cerebral thrombosis with ischemia or infarction or both, intravenous administration of low molecular weight dextran for five days increases cerebral blood flow, reduces neurological deficit, and lowers the morbidity and mortality rates.31,32

When contemplating the future, it seems important that epidemiological surveys must be interpreted more thoroughly than heretofore. For example, why should the stroke rate in Akita in northern Japan be 300 per 100,000 population accompanied by an extremely high incidence of intracerebral hemorrhage and hypertension? There must be some explanation such as a high-salt diet, exposure to cold and stress, and other underlying factors for this regional enormously high incidence of stroke. Fat intake and other dietary factors must be analyzed extensively in relation to epidemiological surveys in the United States to determine why we have such a high incidence of atherosclerotic occlusive disease of the extracranial vessels. It seems evident that in the near future the relationship of hypertension to changes in the walls of both the small and large extracranial vessels will be clarified. For instance, it is known that chronic hypertension leads to hypertrophy of the muscularis media of the cerebral arteries, just as it leads to hypertrophy of the muscular coat within the renal arteries.33 Screening devices will be developed which will detect impaired cerebral blood flow in patients while they are still asymptomatic. Inhalation of a radioactive gas in conjunction with the Anger camera for external measurement of regional cerebral blood flow should become a feasible screening method, even though there is about a 15% error due to extracranial contamination. Percutaneous noninvasive methods of measuring arterial and venous blood flow using the percutaneous Doppler ultrasonic flowmeter is another possibility.34

Once the high-risk patient has been identified by clinically measurable data (blood pressure, cholesterol, blood sugar, and other appropriate tests), forms of treatment must be evolved to prevent the occurrence of a stroke. For example, methods of controlling high blood pressure, cholesterol levels by diet and drugs, diabetes, and other associated disorders would presumably reduce the chance of a stroke's developing. Means of attaining these goals will undoubtedly become actualities in the not too distant future.

In all general hospitals, intensive care units will be installed for the medical and surgical treatment of patients suffering from stroke. Those with cerebrovascular symptoms will be looked upon just as urgently as those with symptoms of myocardial ischemia. Therapeutic agents available in the future no doubt will include proteolytic drugs, potent platelet inhibitors, drugs to reduce edema and increased intracranial pressure, and precise knowledge of when to use vasodilators and cerebral vasoconstrictors. Methods for measuring regional cerebral blood flow will be widely used not only in diagnosis but also in the evaluation of treatment of patients with cerebrovascular disease. Last, there is still room for improvement in surgical treatment of stroke patients. No doubt removal of intracerebral hematomas in the brain stem, cerebellum and cerebral hemispheres will become more routine than at present, and bypass procedures from the common carotid artery in the neck to the circle of Willis within the skull will be assessed. New and imaginative rehabilitation measures of speech therapy, occupational therapy, neuropsychological tests, and re-education will all play a part in the treatment of these patients.

Insofar as future research is concerned, electron microscopy studies will be undertaken to determine the mechanisms of cerebral edema and diapedesis; and routine methods for combined measurement of regional cerebral blood flow, regional blood volume, intracranial pressure, and intracranial venous pressure should all become possible. More sophisticated methods for isotope measurement of regional cerebral blood flow and consumption of glucose, amino acids and fats as well as oxygen consumption will be developed, and our understanding of the biochemical abnormalities of the brain following ischemia and infarction will be enhanced so that appropriate correction of disorders of oxidative glucose, fatty acid, and amino acid metabolism will be possible.

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