Cerebrovascular Research: The Opportunity Has Never Been Better

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IN LESS THAN FIFTY YEARS, cerebrovascular research has changed from a predominantly morphological and clinical descriptive science to one characterized by the use of the tools of modern cellular biology and clinical investigation. In addition, the brain and its blood supply in health and in disease are now recognized as a unique biological entity for which vascular models in other parts of the body such as heart and kidney can be utilized only rarely. For the cerebrovascular biologist, studies of cellular perfusion have reinforced those of hemispheric blood flow, investigations of focal metabolism have joined those of regional electrical activity, and the evaluation of rapid and dynamic changes in autoregulation has replaced measures of hemispheric ischemia. In clinical studies, the CT scan and more recently MRI have provided tools which are challenging our comfortable concepts of the use of differential symptomatology as a basis for clinical diagnosis. The duration of neurological prodroma and the severity and persistence of neurological deficit continue to be prime indicators of the pathophysiology of a clinical cerebrovascular event, but the clinical differentiations are less specific between hemorrhagic and occlusive disease and between temporary ischemic events and irreversible cellular damage. Reinforced by epidemiological studies on the natural history of the several specific cerebrovascular diseases, clinical case reports of therapy have been replaced by case series and now science demands controlled clinical trials to evaluate both time honored methods of therapy and newer clinical interventions. The clinical trial protocol has itself become a very specialized methodology demanding combinations of finely integrated clinical, statistical and administrative skills. What then have advances in methodology taught us about the clinical aspects of the cerebrovascular diseases? We now recognize that:

— the natural history of stroke is not the result of a single event; the term stroke embodies a wide variety of cerebrovascular pathologies each of which is influenced by a host of variables including genetics, life style, other illness, and selective interventions;
— for reasons yet unknown, there has been a continuing decline in both incidence and mortality of stroke since 1950;
— in the period 1970–1980, there has been an increase in the rate of decline in both stroke incidence and mortality due to cerebral occlusive or hemorrhagic disease; this is probably due to improved methods of hypertension control and to improvements in medical supportive therapies. A similar decline in the incidence and mortality of subarachnoid hemorrhage has not occurred;
— most patients who die following a cerebrovascular episode do so because of intracerebral events during the acute period and cardiac events during the later period, the latter perhaps because of cerebral effects on cardiac rhythm;
— diastolic hypertension is a major risk factor for stroke; isolated systolic hypertension is thought to be an important risk factor but the safety and benefits of systolic pressure reduction for stroke prevention are still uncertain;
— platelet aggregation factors at cellular and subcellular levels are recognized as important factors in both stroke prevention and therapy. Improvements in chemical intervention are being sought that are specific to biochemical systems in blood and in the brain's blood vessels.

The funding of cerebrovascular research continues to increase with substantial support from the NIH complemented by assistance from the private sector such as the American Heart Association and the Easter Seal Foundation. An example of this is support for stroke research from the NIH National Institute of Neurological and Communicative Disorders and Stroke during the period 1966–1986; $4M was invested in stroke research in 1966; $10M in 1976 and $27M in 1986.

What are the research areas of immediate relevance?

Prevention is still the key to an important impact on stroke incidence, morbidity and mortality. Although hypertension is a key risk factor, nearly half the persons who have a stroke have no previous history of hypertension. What are the other risk factors which...
need attention? Are they controllable? The period of acute hypoxia is critical in determining the eventual extent of cellular damage. There are still very few methods of medical-surgical intervention that have been demonstrated to influence the immediate course of the evolving neuronal pathology. One of the major issues is the timing of intervention. Does increasing cerebral blood flow during the period of hypoxia and the related deficit in autoregulation have beneficial or deleterious consequences? Do the medical and surgical therapies that are presently widely used have significant impact on the acute course of the disease or on its long-term consequences? Restitution of function is the goal for those who recover from the acute episode. Do methods to enhance neuronal sprouting and axonal regeneration offer promises to reestablish or circumvent destroyed pathways? Can neuronal implants influence return of function in sensory or motor tracts? Do neural prostheses offer practical methods for electronic substitution of injured biological pathways? Each of these questions of clinical significance is surrounded by a host of questions that require information obtainable only from the basic science laboratory.

Answerable questions can now be posed by the cerebrovascular investigator both in basic and clinical areas. Research tools have been developed that provide the methodologies for addressing these questions. Competition for research funds is intense, but funds are available for high quality research. In many ways, the opportunity for important advances lies in our understanding of the forces that regulate cerebral circulation and neuronal metabolism. The outlook for the development of improved methods of diagnosis and therapy has never been greater.

"A leader is a person who can place himself at a time in the future and from that position govern his actions accordingly."

Philip H. Frohman, Architect, Washington National Cathedral

So it is with stroke research.

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Early Management of the Patient with Recent Aneurysmal Subarachnoid Hemorrhage

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Annually, more than 26,000 people in North America suffer an acute aneurysmal subarachnoid hemorrhage (SAH). At least half of the persons die or become disabled as a result of the illness. If we are going to improve these dismal statistics, we must improve our early diagnosis and management of SAH; the first few days are critical.

Diagnosis

One of the major problems in early management of SAH is delayed diagnosis. Approximately 25% of the patients with SAH are initially treated for another disease. SAH is commonly missed among less seriously ill appearing persons; those that walk into an emergency room or a physician’s office complaining of an unusually severe headache, often of sudden onset. These are the persons who are most likely to benefit from early medical or surgical treatment. As a consequence of misdiagnosis, critical early treatment for SAH is lost. Computed tomography of the brain (CT) is now readily available in most hospitals in North America. We should not be reluctant to use this highly sensitive technology in our evaluation of patients displaying symptoms that possibly represent SAH. Besides aiding the initial diagnosis of SAH, CT provides information about complications such as intracerebral hematoma, cerebral infarction or hydrocephalus. CT also facilitates prediction of overall outcome, survival and the development of vasospasm.

Consequences

Patients are at risk for a number of complications during the first days after SAH; they should be treated in a facility that has special expertise. The leading causes of death during the first few days after SAH are: 1) acute, often irreversible effects of the initial hemorrhage, 2) recurrent hemorrhage, and 3) cerebral vasospasm and infarction. Unfortunately, some patients are so severely injured that no medical or surgical therapy will improve outcome. However, some acute complications such as hydrocephalus, convulsions, intracranial hemorrhage, cardiac arrhythmias or electrolyte disturbances can be treated.

Medical Management

Definite advances in the treatment of SAH have appeared during the last decade. During this time, the standard management has been early medical treatment followed by intracranial operation at 7-14 days after the ictus. New data about medical therapies have
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