Nihilism and Stroke Therapy

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In spite of recent advances in supportive management and prevention of stroke, it is not uncommon to hear nonneurologists as well as neurologists express the opinion that "nothing can be done for a patient with a stroke." These individuals are expressing an attitude of therapeutic nihilism. The word nihilism is derived from the Latin nihil, meaning "nothing." A therapeutic nihilist is one who shows skepticism regarding the therapeutic value of drugs. Since ancient times, therapeutic nihilism has been accepted in relation to diseases of the nervous system, particularly stroke.

To trace the roots of nihilistic attitudes toward stroke, one must begin by analyzing the definition of apoplexy or stroke. Apoplexy means "struck with violence" in Greek and "being thunderstruck" in Latin. Stroke was not seen as an affliction from within the body, but the result of a force from outside the body, perhaps even celestial. This view is reflected best by the definition of stroke in the 1599 Oxford English Dictionary as a "stroke of God's hands." The logical deduction was that if the disease were caused by divine intervention, no human intervention such as drug therapy could possibly alter the outcome. Often, stroke has been referred to as a "cerebrovascular accident," a term that supports the concept of stroke as a random, unpredictable catastrophe. The term "cerebrovascular accident" should be banished from our vocabulary.

Historical writings about stroke provide some insight into the evaluation of therapeutic nihilism. Hippocrates wrote that "to get over a strong attack of apoplexy is impossible, over a weak one, not easy." An indication of early thoughts about the prognosis of stroke is contained in the writings of Aretaeus of Cappadocia during the second century AD. He wrote that "should indeed the apoplexy be severe, they cannot survive the greatness of the illness combined with the misery of advanced life." Paul of Aegina expressed that, "in some patients, the power of speech was lost and if it did not return in 14 days, the physician should do something about it." In 1892, Osler stated that in cases of hemiplegia "the friends should at the outset be frankly told that the chances of full recovery are slight." He also wrote that "when hemiplegia has persisted for more than 3 months and contractures have developed, it is the duty of the physician to explain to the patient or to his friends, that the condition is past relief, that medicines and electricity will do no good, and that there is no possible hope of cure." The lack of urgency for intervention after a stroke has been a theme for many years. Attempts to alter the course of cerebral infarction have led to the development of some peculiar remedies, some of which continue to be used in some locales. These unusual treatments include purgatives, bleeding with leeches, and "opening of the bowels." From this historical perspective, one senses that a recurring theme in stroke therapy has been an attitude of hopelessness, with a tendency to view stroke as a disease rather than as a disorder with many different etiologies. The lack of urgency in the diagnosis and management of stroke on the part of physicians has fostered a nihilistic attitude, and many of the misconceptions of our predecessors have been carried into the present age of stroke therapy. The nihilistic attitudes of physicians have resulted in an equally misinformed public.

Although there have been no definitive breakthroughs in the treatment of stroke, striking progress in that direction has been made during the past several decades. We are much more knowledgeable about stroke epidemiology and prevention, diagnosis of stroke, and pharmacological therapy after stroke. Until the early 1980s, a decline in the incidence of stroke over the preceding 30 years had been observed. This decline was attributed primarily to better management of hypertension. The exact cause for the recent reversal of this trend is not known. Recent estimates of the incidence of acute cerebrovascular disease indicate that 150 such events occur per 100,000 population per year. Close follow-up of these trends provides important information about therapeutic efforts.

Diagnosis of stroke continues to rely primarily on clinical features. However, advances in neuroimaging techniques allow early documentation of stroke and differentiation between hemorrhagic and bland infarcts. More detailed information about cerebral arterial thromboembolism can be obtained with visualization of a hyperdense cerebral artery on noncontrast computed tomography or with the absence of a flow-void phenomenon on magnetic resonance imag-
ing (MRI). Exciting breakthroughs have been made in the technique of MRI angiography, which provides a noninvasive method of visualizing the cerebral circulation. Progress has been made in diagnosing hematological and cardiac sources of stroke. These advances have made "garden-variety" stroke a repugnant term. On the contrary, stroke is a heterogeneous condition with varied etiologies. There is no place for investigative nihilism.

Over the last three decades, medical and surgical therapy for cerebrovascular disease has undergone intense evaluation. While modernists think that anticoagulation is a relatively new intervention, this therapy has been used since ancient times. Leeches were used for their anticoagulant properties due to the presence of hirudin in their heads. Beginning in the 1930s, the use of anticoagulants such as heparin and warfarin was gaining popularity for the treatment of cerebrovascular disease. In spite of little definitive evidence to support their use, anticoagulants became widely used.

There have been few trials evaluating the efficacy of anticoagulants and, as a result, their use is governed in many instances by emotions. One area where there is more conclusive evidence for the use of anticoagulants is for the primary prevention of cardiogenic cerebral embolism. Three important primary prevention studies — the Copenhagen AFASAK Study, the Stroke Prevention in Atrial Fibrillation (SPAF) Study, and the Boston Area Anticoagulation Trial for Atrial Fibrillation — have supported the efficacy of warfarin in nonvalvular atrial fibrillation. The efficacy of warfarin compared to aspirin for that indication is being investigated in SPAF II.

Surgical therapy for carotid artery disease emerged in the mid-1950s. At the peak of its popularity, more than 100,000 carotid endarterectomies were performed annually. During the past few years, several new advances have been made in the understanding of cerebral revascularization in the treatment of selected patients with cerebral ischemia. The Extracranial-to-Intracranial Bypass Study demonstrated that the addition of surgery to medical therapy did not improve outcome for symptomatic patients with distal internal carotid artery stenosis, internal carotid artery occlusion, or middle cerebral artery stenosis or occlusion. The North American Symptomatic Carotid Endarterectomy Trial recently reported that carotid endarterectomy is more beneficial than the best medical care, including antiplatelet therapy, for patients with carotid artery territory transient ischemic attacks or nondisabling strokes and ipsilateral 70-99% narrowing of the carotid luminal diameter. Likewise, the European Carotid Surgery Trial (ECST) demonstrated that the operation was effective in preventing fatal and disabling strokes among high-risk patients who had recent ischemic symptoms and ≥70% carotid artery stenosis. In contrast, the ECST demonstrated that surgery did not provide additional benefit among patients with <30% carotid artery stenosis. Studies are under way to evaluate the possible benefits of carotid endarterectomy for symptomatic patients with moderate (30-69%) stenosis.

Intense research is under way for the medical management of acute cerebral ischemia. Evidence from several studies favors the use of platelet antiaggregants (aspirin and ticlopidine) as first-line agents for patients with threatened stroke, and other antithrombotic agents such as low-molecular-weight heparinoids are being investigated. Novel approaches to the alteration of cellular events after stroke are receiving focused attention. Cerebral protection with calcium channel blockers and excitatory amino acid antagonists are currently under intense investigation. The safety and potential efficacy of therapy with tissue plasminogen activator is being evaluated in cerebral infarction, subarachnoid hemorrhage, and intracerebral hemorrhage. The advent of thrombolysis has brought about an awareness of the potential importance of hyperacute therapy for stroke. Finally, while hemorrhological therapy in general has not been successful, trials evaluating the efficacy of ancrd are in progress.

As these and other therapies are being tested, several important concepts about stroke management are emerging. First, it is likely that there is a narrow therapeutic window for pharmacological intervention after stroke, probably less than 6-12 hours for most agents. This will place further emphasis on the importance of viewing stroke as a neurological emergency in order to preserve vulnerable brain tissue. Second, it has become clear that the best way to evaluate therapies is with randomized, double-blind, placebo-controlled, multicenter studies. This mechanism of critical evaluation provides many important advantages for the assessment of stroke prevention and treatment. Finally, it may be that a combination of drugs, each affecting a different cellular mechanism or process, initiated acutely after stroke will be the therapy of choice.

This review of recent advances in the evaluation of stroke-prone patients and therapeutic strategies to alter cellular mechanisms early after stroke elevates us from an age of therapeutic nihilism to one of cautious optimism. It is hoped that a successful drug therapy for stroke will emerge that will reverse the trend of nihilism. This feeling of optimism should be conveyed to the public, especially in light of the importance of early therapy. The symptoms of stroke should be as well known to the nonphysician as are the symptoms of myocardial infarction, and the treatment of stroke should be considered just as urgent.

References


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