Contributions of Epidemiology to the Prevention of Stroke

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Epidemiological study and clinical trial research has flourished during the past 40 years. During this period the decline in death rates from stroke in the United States has accelerated. Since 1970 the US stroke mortality rate has declined nearly 60%. There is reason to believe the declining death rate is related to improvements in the risk factor status of the US population.

Some of the data presented is derived from the Framingham Study and has been collected by many investigators during the past 40 years. I specifically acknowledge the contributions of William B. Kannel, Ralph B. D’Agostino, Margaret Kelly-Hayes, Carlos S. Kase, Thomas R. Dawber, and William B. Castelli to this effort.

Stroke is the third leading cause of death in the United States, accounting for 147,470 deaths in 1989. Stroke is more often disabling than lethal and is the No. 1 cause of neurological disability in adults. Mortality statistics fail to convey the toll of stroke. One must also take into account the extraordinary degree of human suffering experienced by stroke survivors and their families, whose lives are irreversibly altered by this catastrophic illness. To the functionally independent elderly person, stroke often represents a situation worse than death itself. It is estimated that 30% of stroke survivors need assistance in their daily activities, and in the elderly, the attendant loss of function and independence often signals the end of an active life. Many of the estimated 2,980,000 stroke survivors require chronic health care, including institutionalization. Not all stroke occurs in the elderly: one third of stroke victims are younger than 65 years of age, and most of them will never be able to work again.

Nevertheless, the remarkable decline in stroke mortality clearly shows that stroke is preventable. Stroke is not an inevitable consequence of aging but rather the consequence of a chain of events set in motion many years before. Furthermore, risk for stroke is predictible. After 36 years of follow-up of the Framingham Study cohort there were 693 strokes and transient ischemic attacks (TIAs). Since 1967, most cases were seen either by me or by another Framingham Study neurologist at the time of the acute stroke soon after admission to the hospital. Before the advent of the computed tomography scan, acute evaluation by a neurologist specializing in stroke was important to determine that a stroke had occurred and to categorize it according to subtype, because laboratory tests such as an electrocardiogram or enzyme assay for stroke did not exist. Since 1978, more than 85% of stroke patients in Framingham have had at least one computed tomography scan; in recent years magnetic resonance scans have also been done frequently.

Unlike myocardial infarction, stroke is a heterogeneous condition, although the subtypes occur with similar frequency in men and women. More than half of all stroke events were secondary to atherothrombotic brain infarction, the most frequent stroke type and the cerebral disease analogous to myocardial infarction. As a minimal estimate, 20% of atherothrombotic brain infarctions resulted from cardiogenic embolism and 13% were due to hemorrhage.

Most precursors of coronary heart disease (CHD) also predispose an individual to stroke; however, there are some important differences. The most important risk factors for stroke are age and hypertension. These two risk factors also clearly predispose persons to CHD, as do diabetes and cigarette smoking. Blood lipids are powerful risk factors for CHD but have only a minimal effect on stroke in general and atherothrombotic brain infarction in particular. For stroke, cardiac conditions are important predisposing factors; in the presence of CHD, cardiac failure, or atrial fibrillation, stroke incidence is increased approximately fivefold.

Incidence of atherothrombotic brain infarction, like that of myocardial infarction, increases with age, doubling every 10 years of life after age 45. However, unlike incidence of myocardial infarction there is no 20-year lag in incidence of atherothrombotic brain infarction in women (Fig 1). Women develop atherothrombotic brain infarction and stroke at nearly the same rate as men. Unlike myocardial infarction, for which incidence in men is four times that in women, atherothrombotic brain infarction is only 25% more common in men.

Over the years a great deal has been learned about the epidemiology of stroke and the importance of hypertension as the preeminent risk factor. However, much of what appeared in the 1955 edition of Cecil and Loeb’s Textbook of Medicine, which I used as a third-year medical student, has been supplanted by data collected in prospective epidemiologic studies. It may be instructive to review certain passages from this author-
enerative text, now more than 35 years old, to see how far we have come and to reflect on some residual notions that persist despite strong evidence to the contrary. Vestiges of these old teachings linger on, particularly those concerning hypertension and stroke in the elderly.

Hypertension has long been recognized as a key factor in cerebral hemorrhage and hypertensive encephalopathy. However, in 1955 the link between hypertension and brain infarction was less clearly noted and the relation of brain infarction to specific blood pressure levels was unclear: “There is little or no correlation between the height of the blood pressure and symptoms, rate of progression, and development of complications.”2 It is now clear that the incidence of stroke and atherothrombotic brain infarction is directly related to blood pressure. This effect persists powerfully in the oldest age groups, in which stroke incidence is highest. In terms of risk for stroke, there is no evidence that women tolerate hypertension better than men do. Furthermore, systolic blood pressure level is directly related to incidence of brain infarction in both men and women and in all age groups, including persons 75-84 years old.

A key factor in shaping opinions on treatment of elevated blood pressure in persons at risk of stroke was the understanding of the mechanism of brief episodes of neurological dysfunction, TIAs. In 1951, the prominent and influential Boston neurologist Dr. Derek E. Denny-Brown reflected on the mechanism of TIAs.3 He rejected vasospasm as the mechanism and hypothesized that “[t]he repeated transient disorders reflect the sensitivity of the tissue, thus indirectly supplied by collateral vessels, to fluctuations in systemic blood pressure.” He concluded, “[i]t would therefore appear logical to adopt measures designed to raise systemic blood pressure.”3

However, since 1970 trials of drug treatment of hypertension have incontrovertibly shown that for stroke prevention, the benefits of that treatment clearly outweigh the hazards, first for severe diastolic hypertension, and later for moderate and mild diastolic hypertension. In a meta-analysis of 14 trials it was estimated that treatment reduced incidence of stroke by 42%, although the durations of the trials were no longer than 5 years and for many subjects far shorter.4,5 This remarkable effect of antihypertensive treatment on occurrence of both fatal and nonfatal stroke was not seen for coronary heart disease, for which there was a 14% reduction of incidence. The stroke reduction was consonant with that predicted from prospective observational studies such as the Framingham Study, but the effect on incidence of CHD was far less than predicted. As a result of these trials, treatment of severe, moderate, and mild diastolic hypertension to prevent stroke and other complications has been widely accepted for young and middle-aged patients.

However, the reluctance to lower elevated pressure in the elderly, as expressed by Denny-Brown in 1951, persists in 1993. The effectiveness and safety of treatment of hypertension in the elderly, in whom incidence of stroke is highest, has been clearly demonstrated in a number of trials in recent years; one is the recently published Swedish Trial in Old Patients with Hypertension, or the “STOP Hypertension Trial.”6 After 25 months of follow-up of 1627 men and women aged 70 to 84 years (mean age, 76), the group randomly assigned to treatment in this prospective, double-blind trial had significantly fewer primary end points (fatal or nonfatal stroke or death) than the placebo group (Fig 2). These elderly subjects had definite diastolic hypertension: At entry, subjects had either a systolic pressure between 180 and 230 mm Hg and a diastolic pressure of at least 90 mm Hg or between 105 and 120 mm Hg (irrespective of systolic pressure). The mean entry blood pressure was 195/102 mm Hg. Benefits of treatment extended over the age span of the study group. What is particularly striking is the rapidity with which blood pressure reduction was followed by reduced incidence of stroke in these elderly men and women with diastolic hypertension. Although it is likely that subjects had been hypertensive for years, within 1 year of treatment the benefit of antihypertensive therapy became apparent (Fig 3). This suggests that elevated blood pressure, in addition to promoting atherosclerosis, acts to precipitate stroke, and this precipitating effect is rapidly reduced by treatment.

In 1955 it was believed that “[t]he physiologically important blood pressure is the mean pressure. Because mean pressure is usually nearer the diastolic than the
systolic value, the diastolic blood pressure is of far greater clinical significance than the systolic.72 However, data from the Framingham Study indicate that diastolic pressure has less of an impact than systolic pressure on incidence of stroke. In fact, at any level of diastolic pressure and in both men and women, stroke incidence rises with systolic pressure (Fig 4). At any particular systolic pressure, there is far less impact of increasing diastolic pressure on incidence of stroke. Even in persons with diastolic pressure less than 95 mm Hg, including the oldest age groups (persons aged 65 to 74 and 75-84 years), incidence of stroke increases with level of systolic pressure (Fig 5). Although systolic blood pressure continues to rise with age, diastolic pressure levels off and then falls. In the Framingham Study, more than 30% of women and 20% of men older than 70 years had systolic pressures of 160 mm Hg or greater and diastolic pressures of less than 95 mm Hg. The most prevalent variety of hypertension in those over 65, isolated systolic hypertension, is associated with approximately twice the incidence of brain infarction in men and 1.7 times the incidence in women. These isolated systolic elevations were believed to be an innocuous consequence of aging. It was thought that elevated systolic pressure, a result of inelasticity of the arteries, would be difficult to reduce and hazardous to control. Furthermore, it was believed that it would be hazardous to reduce systolic pressure because higher pressures were needed to perfuse the narrowed cerebral vessels in these elderly persons. It was also feared that treatment might produce severe side effects, including confusion, depression, syncope, and fractures due to falls.

After a pilot study, 4736 men and women, aged 60 or older with systolic blood pressure 160 mm Hg or greater and diastolic blood pressure less than 90 mm Hg, were randomly assigned to a treatment or placebo group.7 After 4.5 years, the incidences of stroke, myocardial infarction, and cardiac failure were significantly lower in the treatment group (Fig 6). By 2 years of follow-up, incidence of all stroke in the treatment group was lower than in the group taking a placebo (cumulative stroke rates were 2.1% and 3.2%, respectively). There was no excess mortality from active treatment and no excess depression or dementia. There was a reduction in all types of stroke, including subarachnoid hemorrhage.

How far should blood pressure be lowered? This question is the title of a recent examination of trial data to determine the optimal level to which elevated blood pressure should be reduced. Based on an analysis of eight studies, including a meta-analysis, it was suggested that systolic pressure be reduced to below 125 mm Hg and diastolic pressure to below 85 mm Hg (Fig 7).8 However, the issue of target blood pressure levels has yet to be resolved and is still under study.

Despite the accumulated data offering compelling evidence of the advisability of blood pressure reduction to reduce stroke, old concepts die hard. In a textbook published in 1992, a respected geriatrician wrote, “Although advocated as a possible ideal, there is therefore no need to ‘normalize’ the blood pressure to a diastolic below 90 or a systolic below 160 mm Hg in order to produce at least some benefit. A more modest reduction of pressure may constitute a desirable compromise between benefit and adverse effects of treatment for some patients.”9 However, clinical trial data suggest that a somewhat more aggressive approach is indicated.

A number of other risk factors have been identified as increasing incidence of stroke, including diabetes, elevated fibrinogen level, positive family history of stroke, reduced physical activity, and heavy consumption of alcohol. However, it may not be either easy or possible to modify these factors, or there are insufficient data to recommend risk factor modification to prevent stroke. Elevated blood lipids, a key risk factor for coronary heart disease, have little influence on incidence of stroke generally or of brain infarction specifically. Even the total high-density lipoprotein cholesterol ratio is only minimally related to brain infarction in women and is not related in men. Among the other risk factors for stroke, cessation of cigarette smoking and the use of warfarin for atrial fibrillation offer clear opportunities to reduce risk for stroke.

Cigarette smoking has been shown to be an important risk factor, independently increasing the incidence of stroke generally by 40% in men and 60% in women.8 The effect of smoking on risk of brain infarction is even greater. Risk of stroke is related to number of cigarettes smoked, regardless of age. Like that of CHD, risk of stroke in those who quit falls rapidly and returns to the level of someone who never smoked within 5 years.8,10
Although smoking, like hypertension, may promote atherosclerosis, cigarette smoking probably also precipitates stroke in susceptible people. Interestingly, cigarette smoking has been shown to contribute to risk of subarachnoid hemorrhage due to berry aneurysms of the circle of Willis. Although the underlying lesion has long been considered congenital, rupture with bleeding has recently been related to environmental factors, including hypertension, heavy intake of alcohol, and, most powerfully, cigarette smoking.11 The odds ratio of subarachnoid hemorrhage was 11 among persons who smoke heavily. Therefore, quitting smoking may help reduce risk of most stroke types.

A key component in the risk profile for stroke is impaired cardiac function. Persons with prior CHD, cardiac failure, left ventricular hypertrophy on electrocardiogram, or atrial fibrillation have increased stroke risk.12 Cardiac dysfunction and disease predispose a person to stroke through shared risk factors, by impaired cardiac output and pump failure, and, most importantly, as a source of or path for emboli to the brain. Nevertheless, it is difficult to determine the precise mechanism of stroke in persons with cardiac impairments. Demonstrating a cardiac source of embolism, even seeing a clot on an echocardiogram, does not prove that embolism was the mechanism.

Incidence of stroke is increased in people with coronary heart disease, congestive heart failure, non-valvular atrial fibrillation, and hypertension (Fig 8).12 The use of aspirin after myocardial infarction reduces incidence of subsequent stroke.13 Warfarin sodium after myocardial infarction reduced incidence of stroke by a remarkable 55% in one trial.14 The growing number of myocardial infarction survivors, the result of improved management of acute myocardial infarction, is probably at increased risk of stroke. This increased risk can be reduced, at least to some extent, by antithrombotic and antiplatelet agents. Presumably, prevention and more effective treatment of cardiac failure will reduce stroke incidence.

Random allocation clinical trials have provided the methodological basis for a number of major advances in stroke prevention. These include warfarin anticoagulation for atrial fibrillation,15,16 carotid endarterectomy,17 and antithrombotic agents after transient ischemic attack or minor stroke.13

Nonrheumatic atrial fibrillation becomes increasingly frequent with advancing age, the risk doubling with each decade of life after age 55. Atrial fibrillation is present
in 15% of stroke victims in the Framingham Study. At ages 70 to 79, 18.8% of strokes occur in persons with atrial fibrillation, and at ages 80 to 89 the figure is 30.7% (Table 1). In 75% of strokes occurring in people with atrial fibrillation, embolism from a left atrial clot, a consequence of the arrhythmia, is the likely stroke mechanism. Incidence of stroke is increased 4.8 times in people with atrial fibrillation, with a stroke rate of 5% per year. Although not all people with atrial fibrillation sustain a stroke, approximately 35% do so over their lifetimes. The attributable risk provides a measure of the impact of a risk factor on disease in the population, taking the relative risk and the prevalence of the disease into account. Attributable risk is the proportion of disease incidence that would be prevented if the risk factor’s impact could be eliminated. Unlike for CHD, cardiac failure, and hypertension, for which attributable risk declines with age, for atrial fibrillation the attributable risk increases with age. After the age of 80 the attributable risk for atrial fibrillation nearly equals that of hypertension, which is 10 times more prevalent (Table 1).

The last of a remarkable series of clinical trials of the use of warfarin by patients with atrial fibrillation was recently published. Warfarin prevented nearly all stroke events in subjects with atrial fibrillation, with an acceptable level of intracerebral hemorrhage of less than 1% per year. Results seemed equally good with low-intensity anticoagulation (International Normalized Ratio, 2.0 to 3.0 [Prothrombin Time Ratio, 1.2 to 1.5]). These data should settle the question about mechanism of stroke in atrial fibrillation; it is likely due to cardiogenic emboli. Whatever the mechanism, warfarin prevents it and does so safely in a clinical trial setting. Aspirin was ineffective in AFSAK, and in patients older than 75 in the Stroke Prevention in Atrial Fibrillation Study. Eight of 13 strokes occurring in the Boston Area Anticoagulation Trial for Atrial Fibrillation placebo group were not prevented by aspirin.

Identification of persons who have had a TIA, and who are at greatly increased risk of ischemic stroke, has facilitated the study of a variety of measures and agents for stroke prevention. Although initially described as a manifestation of large-artery atherosclerotic disease, TIA is not solely a consequence of large-artery disease and occurs with equal frequency in all infarct types. However, TIA occurred in approximately 21% of embolic, lacunar, and atherothrombotic infarcts and infarct of undetermined cause (Fig 9) in the National Institutes of Neurological Disorders and Stroke data bank of 1254 well-studied cases of infarcts. Infarct of undetermined cause was the most prevalent subtype (34%). Only 12% of all infarcts resulted from large-artery atherosclerosis; half of these were carotid artery and half vertebralbasilar artery.

### Table 1. Prevalence of Various Cardiovascular Conditions and Attributable Risk of Stroke for Hypertension, Coronary Heart Disease, Cardiac Failure, and Atrial Fibrillation, by Age

<table>
<thead>
<tr>
<th>Cardiovascular condition</th>
<th>50-59</th>
<th>60-69</th>
<th>70-79</th>
<th>80-89</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of stroke events</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attributable risk (%)</td>
<td>48.8</td>
<td>53.2</td>
<td>48.6</td>
<td>33.4</td>
</tr>
<tr>
<td>Percentage of events in persons with condition</td>
<td>72.8</td>
<td>80.3</td>
<td>83.9</td>
<td>84.0</td>
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<tr>
<td>Coronary heart disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attributable risk (%)</td>
<td>11.1</td>
<td>12.4</td>
<td>12.6</td>
<td>0.0</td>
</tr>
<tr>
<td>Percentage of events in persons with condition</td>
<td>25.0</td>
<td>32.9</td>
<td>38.0</td>
<td>28.0</td>
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<tr>
<td>Cardiac failure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attributable risk (%)</td>
<td>2.3</td>
<td>3.1</td>
<td>5.6</td>
<td>6.0</td>
</tr>
<tr>
<td>Percentage of events in persons with condition</td>
<td>9.8</td>
<td>11.7</td>
<td>18.2</td>
<td>18.7</td>
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<tr>
<td>Atrial fibrillation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attributable risk (%)*</td>
<td>1.5</td>
<td>2.8</td>
<td>9.9</td>
<td>23.5</td>
</tr>
<tr>
<td>Percentage of events in persons with condition</td>
<td>6.5</td>
<td>8.5</td>
<td>18.8</td>
<td>30.7</td>
</tr>
</tbody>
</table>

*Significant increase with age (P<0.01).
These data contradict the recent view that carotid artery disease is the most frequent basis of cerebral infarction. The number of carotid endarterectomies performed in the United States peaked in 1985 at 107,000. Even after more than a million operations over the past 20 years, the indications for, and effectiveness of, this procedure in stroke prevention had not been demonstrated until recently. Many operations were done for uncertain indications. Only 35% of carotid endarterectomies performed on Medicare patients were definitely appropriate. Regardless of appropriateness of indication, more than 10% were followed by major stroke or death. As awareness of the risk of this procedure grew, the number of operations declined.

To clarify the role of carotid endarterectomy in stroke prevention, two clinical trials, the North American Symptomatic Carotid Endarterectomy Trial and the European Carotid Surgery Trial, were begun in the late 1980s. Because of the substantial power of a well-designed randomized clinical trial, it was only necessary to follow fewer than 2000 patients for less than 3 years to demonstrate the effectiveness of endarterectomy under certain specified conditions. The trial clearly answered in the affirmative the primary question of whether carotid endarterectomy reduces the risk of ipsilateral carotid stroke in patients with recent carotid distribution transient ischemic attack and ipsilateral stenosis. At 24 months, ipsilateral stroke incidence was 9% in the surgical group and 26% in patients randomly assigned to the best medical treatment. The conclusions held only if the degree of linear stenosis was 70% or greater, the complication rate was low, and the TIA had occurred recently. The European Carotid Surgery Trial showed a clear advantage of medical management over surgery for less than 30% stenosis. However, the role of carotid endarterectomy in patients with 30% to 69% stenosis has not been settled, and entry of subjects into the North American trial continues for this group. The role of surgery for asymptomatic stenosis is also under study in randomized trials, and results of the Asymptomatic Carotid Artery Surgery trial are awaited. A recent report was inconclusive.

Nevertheless, carotid artery disease accounts for less than 10% of all stroke (Fig 9). In patients without carotid stenosis, aspirin reduces stroke incidence after TIA or minor stroke by nearly 40%. In the Antiplatelet Trialist meta-analysis of a large number of clinical trials for a variety of cardiovascular conditions, stroke occurrence was reduced by 22% by aspirin. They suggest there is no need to use more than 325 mg per day, although the major aspirin trials in stroke have been done with 975 or 1300 mg of aspirin per day. Some experts have reservations about the 325 mg per day dose, because no single study that demonstrated the efficacy of aspirin used less than 975 mg daily. However, the disadvantages of the larger aspirin doses include gastrointestinal toxicity, which occurs in proportion to aspirin dose and has the theoretical disadvantage of interfering with arterial wall prostacyclin. It is possible that a study may be done to compare a dose of 325 mg or lower with one of 1200 mg/d to settle this important issue.

Ticlopidine, an antiplatelet agent, is more effective than aspirin in patients with TIA and minor stroke and significantly reduces stroke recurrence after completed stroke. Ticlopidine has some benefits and some drawbacks. It is more effective than aspirin and has fewer gastrointestinal side effects. On the other hand, it is substantially more expensive and approximately 1% of those taking it develop leukopenia. White cell counts need to be monitored every 2 weeks during the first 3 months when the leukopenia develops.

Death rates from stroke have declined since 1915. This decline is real and is not an artifact of diagnostic or death certification practices. Between 1915 and 1950 the decline was gradual, approximately 1% per year, accelerating to 2% per year between 1950 and 1972. In 1972 the slope of the decline steepened to an annual rate of 7% annually between 1973 and 1981. In the 1980s the decline leveled off to an annual rate of approximately 3.5%. What is the mechanism of the decline? In the population of Rochester, Minn, incidence of stroke has declined, first in women and then in men. At the same time, there has been improved detection, treatment, and control of hypertension. This control of hypertension may underlie the decline in incidence of stroke. A similar pattern of declining incidence has occurred in Japan, Finland, and other places, while no decline was seen in stroke incidence in Framingham or Göteborg, Sweden. In most studies a substantial decline in stroke severity was seen with improved survival and decreased neurological deficit.

The advent in 1973 of the computed tomography scan increased the diagnostic sensitivity of stroke diagnosis. Computed tomographic scan of the brain facilitated the diagnosis of smaller lesions and milder clinical stroke events. At about that time, incidence of stroke in
Rochester, Minn, leveled off and began to rise\textsuperscript{35} (Fig 10). Increased diagnostic sensitivity afforded by the computed tomography scan might underlie both the increasing incidence and decreasing severity of stroke.

In the community, identification, treatment, and control of hypertension has been steadily improving. In the cities of Minneapolis and St. Paul, Minn, the proportion of people whose hypertension was identified, treated, and controlled increased over a 12-year period. The impact was greater for women, 42.7\% of whom had controlled hypertension, compared with 23.1\% of men. However, on the "flip side," in 77\% of the men and 57\% of the women, hypertension was not controlled.\textsuperscript{36} Similarly, while prevalence of cigarette smoking has declined, 26\% of the population still smokes. This suggests there is considerable benefit yet to be gained in terms of stroke prevention from more diligent application of what has been clearly demonstrated to have an impact on stroke prevention.

Considerable progress has been made in identifying precursors of stroke and in applying these lessons to stroke prevention. A risk profile for stroke has been developed using the Framingham Study data.\textsuperscript{37} The gender-specific Cox proportional hazards model enables a physician to create a quantitative synthesis of a patient's risk factors and compute the probability of stroke within the next 2 to 10 years. Probability of stroke is determined by adding up the points assigned on the basis of risk factor levels readily measured during the course of a routine physical examination: age, gender, history of cigarette smoking, systolic blood pressure, antihypertension treatment, diabetes, prior cardiovascular disease, atrial fibrillation, and left ventricular hypertrophy by electrocardiogram. This probability of stroke can be compared with that of the average probability of persons of the same age and gender to determine whether an increased risk is present. The risk profile should help physicians and their patients appreciate the importance of specific risk factors and observe the benefits to be derived from risk factor modification.

During the past several decades, major strides have been made in the understanding of the incidence and manifestations of cerebrovascular disease and of the factors that predispose a person to it. Much of the increase in understanding has been derived from epidemiologic study and from the application of clinical trial methodology to unresolved clinical problems and predicaments. In addressing these unresolved issues, the superiority of planned systematic observation of populations to casual clinical impression of patients has been repeatedly and convincingly demonstrated. Although written more than 2000 years ago, Hippocrates' observation that "It is impossible to cure a severe attack of apoplexy and no easy matter to cure a mild one" unfortunately still holds true today. To quote Wade Hampton Frost, "No disease has ever been conquered by treatment of every affected individual." Prevention holds the key to control of disease, particularly a devastating and apoplectic disease like stroke.

References


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