# Special Report From the World Health Organization

## Stroke—1989

**Recommendations on Stroke Prevention, Diagnosis, and Therapy**

Report of the WHO Task Force on Stroke and Other Cerebrovascular Disorders

---

### Contents

<table>
<thead>
<tr>
<th>I. Introduction</th>
<th>1408</th>
</tr>
</thead>
<tbody>
<tr>
<td>II. Stroke Risk Factors</td>
<td>1408</td>
</tr>
<tr>
<td>A. Arterial Hypertension</td>
<td>1409</td>
</tr>
<tr>
<td>B. Diabetes Mellitus</td>
<td>1410</td>
</tr>
<tr>
<td>C. Heart Disease</td>
<td>1410</td>
</tr>
<tr>
<td>D. Transient Ischemic Attack (TIA) and Completed Stroke</td>
<td>1410</td>
</tr>
<tr>
<td>E. Obesity</td>
<td>1411</td>
</tr>
<tr>
<td>F. Platelet Hyperaggregability</td>
<td>1411</td>
</tr>
<tr>
<td>G. Alcoholism</td>
<td>1411</td>
</tr>
<tr>
<td>H. Smoking</td>
<td>1411</td>
</tr>
<tr>
<td>I. Elevated Blood Lipid Levels</td>
<td>1412</td>
</tr>
<tr>
<td>J. Hyperuricemia</td>
<td>1412</td>
</tr>
<tr>
<td>K. Infections</td>
<td>1412</td>
</tr>
<tr>
<td>L. Genetic or Familial Factors</td>
<td>1412</td>
</tr>
<tr>
<td>M. Other Factors</td>
<td>1412</td>
</tr>
<tr>
<td>III. Principles of Stroke Diagnosis</td>
<td>1412</td>
</tr>
<tr>
<td>A. Presenting Signs and Symptoms</td>
<td>1413</td>
</tr>
<tr>
<td>1. Temporal profile</td>
<td>1413</td>
</tr>
<tr>
<td>2. Distinction between TIs in carotid and vertebrobasilar regions</td>
<td>1413</td>
</tr>
<tr>
<td>B. &quot;Classical&quot; Types of Focal Cerebral Infarction</td>
<td>1414</td>
</tr>
<tr>
<td>1. Carotid artery region</td>
<td>1414</td>
</tr>
<tr>
<td>2. Vertebrobasilar artery region</td>
<td>1414</td>
</tr>
<tr>
<td>3. Lacunar syndromes</td>
<td>1414</td>
</tr>
<tr>
<td>C. Syndromes of Intracerebral Hemorrhage</td>
<td>1415</td>
</tr>
<tr>
<td>D. Subarachnoid Hemorrhage (SAH)</td>
<td>1415</td>
</tr>
<tr>
<td>E. The Search for Causes</td>
<td>1415</td>
</tr>
<tr>
<td>1. Past history and associated conditions</td>
<td>1415</td>
</tr>
<tr>
<td>2. Risk factors</td>
<td>1415</td>
</tr>
<tr>
<td>F. Laboratory Investigations</td>
<td>1416</td>
</tr>
<tr>
<td>1. Ocular fundus</td>
<td>1416</td>
</tr>
<tr>
<td>2. Doppler sonography</td>
<td>1416</td>
</tr>
<tr>
<td>3. Echocardiography</td>
<td>1416</td>
</tr>
<tr>
<td>4. Holter monitoring</td>
<td>1416</td>
</tr>
<tr>
<td>5. Cerebrospinal fluid (CSF) examination</td>
<td>1416</td>
</tr>
<tr>
<td>6. Neurovascular imaging techniques</td>
<td>1417</td>
</tr>
<tr>
<td>G. Diagnostic Conclusions</td>
<td>1417</td>
</tr>
<tr>
<td>H. Appendix</td>
<td>1418</td>
</tr>
<tr>
<td>IV. Strategies to Prevent and Treat Stroke and SAH</td>
<td>1418</td>
</tr>
<tr>
<td>A. Primary Prevention: Strategies to Prevent Atheroma Development</td>
<td>1418</td>
</tr>
<tr>
<td>B. Secondary Prevention of Threatened Stroke</td>
<td>1418</td>
</tr>
<tr>
<td>1. Risk factor adjustments</td>
<td>1419</td>
</tr>
<tr>
<td>2. Dietary adjustments</td>
<td>1419</td>
</tr>
<tr>
<td>3. Associated conditions and/or risk factors</td>
<td>1419</td>
</tr>
<tr>
<td>C. Antithrombotic Agents</td>
<td>1420</td>
</tr>
<tr>
<td>1. Anticoagulants</td>
<td>1420</td>
</tr>
<tr>
<td>2. Platelet antiaggregants</td>
<td>1421</td>
</tr>
<tr>
<td>3. Other issues in the use of antithrombotics for which imperfect knowledge is available</td>
<td>1422</td>
</tr>
<tr>
<td>4. Antispasmodics, &quot;brain oxygenators,&quot; and &quot;metabolic enhancers&quot;</td>
<td>1423</td>
</tr>
<tr>
<td>D. Treatment of Patients Following Recent Ischemic Stroke</td>
<td>1423</td>
</tr>
<tr>
<td>E. Treatment of Patients Deteriorating With Ischemic Stroke</td>
<td>1424</td>
</tr>
<tr>
<td>F. Medical Management of SAH</td>
<td>1424</td>
</tr>
<tr>
<td>V. Surgical Treatment for Occlusive Cerebrovascular Disease, Intracerebral Hematoma, and SAH</td>
<td>1424</td>
</tr>
<tr>
<td>A. Carotid and Vertebrobasilar Endarterectomy</td>
<td>1424</td>
</tr>
<tr>
<td>1. Present status of indications for carotid endarterectomy</td>
<td>1425</td>
</tr>
<tr>
<td>B. Extracranial–Intracranial (EC/IC) Bypass Surgery</td>
<td>1426</td>
</tr>
<tr>
<td>C. Intracerebral Hematoma</td>
<td>1426</td>
</tr>
<tr>
<td>D. Surgical Management of SAH Arising From Aneurysm and Arteriovenous Malformation (AVM)</td>
<td>1426</td>
</tr>
<tr>
<td>1. Grading patients with SAH from aneurysm</td>
<td>1427</td>
</tr>
<tr>
<td>2. Timing of investigation and operation in cases of aneurysmal SAH</td>
<td>1427</td>
</tr>
<tr>
<td>E. Some Recent Advances in General Management Techniques</td>
<td>1428</td>
</tr>
<tr>
<td>1. Technical surgical changes</td>
<td>1428</td>
</tr>
<tr>
<td>2. Other possible surgical maneuvers in the treatment of intracranial aneurysms</td>
<td>1428</td>
</tr>
<tr>
<td>3. Treatment of SAH from AVM</td>
<td>1428</td>
</tr>
<tr>
<td>VI. Rehabilitation After Stroke</td>
<td>1429</td>
</tr>
<tr>
<td>A. Factors That Influence Recovery of Impaired Functions</td>
<td>1429</td>
</tr>
<tr>
<td>B. Basic Principles of Rehabilitation</td>
<td>1430</td>
</tr>
<tr>
<td>C. Social Consequences of Effectiveness of Rehabilitation Following a Stroke</td>
<td>1431</td>
</tr>
</tbody>
</table>
I. Introduction

Cerebrovascular disease has been shown to be a major cause of death and disability in all societies in which it has been studied. This is true irrespective of the type of community (industrial, agricultural, urban, or rural); it is also true with respect to other characteristics of the population (cultural, economic, or ethnic). Stroke, the major consequence of cerebrovascular disease, afflicts all ages but certainly is more usual in the sixth, seventh, and eighth decades of life. As public health, medical, and social advances continue to extend life expectancy, we can expect an increase in the size of the world community at risk of stroke. Stroke is and predictably will continue to be a major public health problem demanding increased and focused attention.

To enable countries to deal better with this problem, the Mental Health Programme (MNH) of the World Health Organization (WHO) established a Task Force on Stroke and Other Cerebrovascular Disorders. The Task Force was charged with identifying measures to prevent the occurrence of stroke and providing advice on the efficacy and safety of stroke therapies.

"Stroke—1989" is a report of the Task Force's deliberations. The report is aimed principally at the needs of the primary health care worker, the physician not expert in disorders of the nervous system, and the public health worker concerned with community health programs. "Stroke—1989" is the result of an analysis of the world literature and a review of the clinical experience of international scientific and medical leaders. Particular attention was given by the Task Force to a critical review of published data in support of specific diagnostic, preventive, and therapeutic methodologies. Although strategies may be considered by some clinicians as "customary," scientifically acceptable evidence of safety and efficacy had to be available to the Task Force before any strategy was designated as acceptable; where preliminary but as yet inconclusive evidence has accumulated to support a strategy, it was designated as acceptable; where strong evidence has accumulated to deny efficacy, a strategy was designated as unacceptable. The Task Force was well aware of the urgency of clinical practice, the force of patient pressure, and the power of regional custom, but to be designated as acceptable or provisionally acceptable a strategy needed to be supported by scientifically valid evidence. It also should be noted that there are methodologies that are experimental, being developed and evaluated in animal or human populations. These methodologies need to be considered just that, experimental, and should be employed by a clinician only under socially and scientifically acceptable experimental conditions.

In summary, the Task Force's conclusions are 1) effective methods for stroke prevention are available and can be used by individuals and in community-based programs; 2) clinical evaluation reinforced by laboratory studies can separate ischemic and hemorrhagic types of stroke, an important distinction for management; 3) better methods of effective and safe treatment have been developed or are under investigation to diminish the occurrence of severe disability or death in a significant proportion of those affected; 4) application of preventive, diagnostic, and therapeutic methods can reduce the disastrous consequences of stroke for an individual, the family, and society (community-based programs offer an effective method for accomplishing this); and 5) further research is needed to improve preventive and therapeutic interventions. Areas in which research is the most promising have been identified; examples are epidemiology and controlled clinical trials.

WHO/MNH Task Force on Stroke and Other Cerebrovascular Disorders

M. Goldstein, D.O., M.P.H. (chairman), USA
H.J.M. Barnett, M.D., Canada
J.M. Orgogozo, M.D., France
N. Sartorius, M.D. (WHO/MNH), Switzerland
L. Symon, M.D., England
N. Vereshchagin, M.D., USSR

II. Stroke Risk Factors

Stroke prevention is a primary goal of community and personal health programs. Identification of stroke risk factors and implementation of activities to eliminate or diminish their impact are essential to the reduction of stroke morbidity and mortality. For an individual, the presence of any single risk factor or combination of risk factors in itself does not predict that a stroke will occur; conversely, the absence of any known stroke risk factors does not ensure that a stroke will not occur. However, it can be confidently asserted that the probability of a stroke occurring is clearly influenced by the presence of these risk factors. Therefore, risk factor reduction is an important step in preventing stroke and becomes an imperative for clinicians and public health officers to address.

From the World Health Organization, Geneva, Switzerland.

The WHO/MNH Task Force on Stroke and Other Cerebrovascular Disorders wishes to acknowledge with gratitude the contributions made to "Stroke—1989" by the central office and regional staffs of the WHO and by the many scientific and medical consultants who responded to the Task Force's requests for information and critique. Specific recognition needs to be given for their expert advice to H.P. Adams (USA), M.G. Bousser (France), J.P. Castel (France), P.M. Dalai (India), J.D. Easton (USA), R.W. Gunton (Canada), V.C. Hachinski (Canada), Chen Ya Huang (Hong Kong), A.S. Kadykov (USSR), Kyuya Kogure (Japan), H. Lechner (Austria), J.M. Mazaux (France), Shi-chou Li (People's Republic of China), S.J. Peerless (Canada), W.J. Powers (USA), B.S. Schoenberg (deceased) (USA), J. Toole (USA), F.A. Wolf (USA), and to Mrs. Devera G. Schoenberg (USA) for her invaluable editorial assistance.

Address for reprints: Division of Mental Health, World Health Organization, 1211, Geneva, 27, Switzerland.

Received April 11, 1989; accepted May 10, 1989.
Some stroke risk factors are genetic and are difficult or impossible to influence (e.g., age, sex), some are environmental and are more easily preventable (e.g., infections), some are a function of personal lifestyles and are controllable (e.g., cigarette smoking), and some are a combination of familial and environmental factors and are often manageable (e.g., hypertension). An analysis of the world literature reveals that while some stroke risk factors are specifically geographic, most appear to be universal. Even those risk factors that are controlled by a genetic variable can often be influenced by a change in geography, alterations of personal habits, or medical therapy.

Tables 1, 2, and 3 summarize the current world literature. Risk factor studies are reported as being related to all strokes (generally meaning undifferentiated stroke including both ischemic stroke and hemorrhagic stroke), to ischemic stroke (generally meaning cerebral infarction due to thrombosis and/or emboli), and to hemorrhagic stroke (generally meaning SAH and/or intracerebral hemorrhage). For the purposes of this analysis, the world was arbitrarily divided into geographic areas. Within each geographic area, research on the identification of stroke risk factors is usually limited to a few countries. The information available is derived from studies often done in Europe, North America, and Japan, with contributions from China, India, and a few African and Latin American countries. However, many and perhaps most of the stroke risk factors identified appear to be universal and significant irrespective of geographic area.

The conclusions to be drawn from Tables 1, 2, and 3 are:

A. Arterial Hypertension

In all geographic areas in which they have been studied, there is substantial evidence that systolic hypertension, diastolic hypertension, and combined systolic and diastolic hypertension are each risk factors for all strokes, for ischemic stroke, and for hemorrhagic stroke.

**Conclusion:** Arterial hypertension is an important risk factor for all types of stroke. There is strong evidence that control of diastolic hyperten-

---

**Table 1. Risk Factors for All Stroke, 1988**

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>North America</th>
<th>Europe</th>
<th>South America</th>
<th>Japan; Oceania</th>
<th>China</th>
<th>Southeast Asia</th>
<th>India</th>
<th>Sub-Saharan Africa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Systolic</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Diastolic</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Heart disease</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+/-</td>
<td>0</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Obesity</td>
<td>+/-</td>
<td>+/-</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>-</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Platelet hyperaggregability</td>
<td>+/-</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>+/-</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Smoking</td>
<td>+</td>
<td>+/-</td>
<td>0</td>
<td>+/-</td>
<td>+/-</td>
<td>0</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Elevated blood lipid levels</td>
<td>+/-</td>
<td>0</td>
<td>0</td>
<td>+/-</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>+/-</td>
<td>+/-</td>
<td>0</td>
<td>-</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>+/-</td>
<td>+/-</td>
<td>0</td>
<td>-</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Low density lipoproteins</td>
<td>+/-</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>+/-</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hyperuricemia</td>
<td>+/-</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>Infections</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>+/-</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Genetic or familial factors</td>
<td>+/-</td>
<td>+/-</td>
<td>0</td>
<td>0</td>
<td>+/-</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Other**

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Presence/No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migraine</td>
<td>+</td>
</tr>
<tr>
<td>Cold temperature</td>
<td>+/-</td>
</tr>
<tr>
<td>High-estrogen contraceptives</td>
<td>+/-</td>
</tr>
<tr>
<td>Socioeconomic status</td>
<td>+/-</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>+/-</td>
</tr>
</tbody>
</table>

**Note:**

+ , yes; +/- , suggestive; - , no; 0 , insufficient data.
sion and of combined systolic/diastolic hypertension reduces stroke incidence; the effect on stroke incidence of the control of isolated systolic hypertension and the safety of its reduction in aged populations are under study.

B. Diabetes Mellitus

In nearly all North American and European countries in which it has been studied, there is substantial evidence that diabetes mellitus is a risk factor for all strokes and for ischemic stroke; from Europe, there is inconclusive evidence that diabetes mellitus is a risk factor for hemorrhagic stroke; from Japan and China the evidence is that diabetes mellitus is not a risk factor for all strokes, for ischemic stroke, or for hemorrhagic stroke.

Conclusion: Diabetes mellitus is a risk factor for ischemic stroke in large-vessel disease but is of questionable impact in small-vessel disease; the role of this risk factor in hemorrhagic stroke is yet to be clarified. There is no evidence that controlling diabetes mellitus decreases stroke incidence, but control of hyperglycemia can diminish the severity of cerebral damage during the acute stroke period.

C. Heart Disease

In nearly all geographic areas in which it has been studied, there is substantial evidence that heart disease (e.g., rheumatic heart disease, coronary artery disease with myocardial infarction, cardiac arrhythmia) is a risk factor for all strokes and for ischemic stroke. Left ventricular hypertrophy is usually found to be a risk factor for all strokes. Also, cardiac emboli or cardiac standstill can be an etiology for ischemic stroke. With the exception of inconclusive results from studies in Japan and Oceania, there are few studies of heart disease per se as a risk factor for hemorrhagic stroke.

Conclusion: Heart disease is an important risk factor for ischemic stroke; its role as a risk factor in hemorrhagic stroke is yet to be clarified.

D. TIA and Completed Stroke

The pathophysiology of TIA is under review; namely, does a TIA indicate a completed cerebral infarction with no clinically recognizable permanent neurologic deficit, or does it indicate cerebral ischemia without infarction? Despite this uncertainty, studies from North America and Europe report that TIA and completed stroke are each substantial risk factors for all strokes and for ischemic stroke.

Conclusion: TIA and completed stroke are important risk factors for all stroke and for ischemic stroke. TIA is an urgent medical matter demanding...
### TABLE 3. Risk Factors for Hemorrhagic Stroke, 1988

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Geographic area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>North America</td>
</tr>
<tr>
<td>Hypertension</td>
<td>+</td>
</tr>
<tr>
<td>Systolic</td>
<td>+</td>
</tr>
<tr>
<td>Diastolic</td>
<td>+</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0</td>
</tr>
<tr>
<td>Heart disease</td>
<td>0</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>0</td>
</tr>
<tr>
<td>Obesity</td>
<td>0</td>
</tr>
<tr>
<td>Platelet hyperaggregability</td>
<td>0</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>0</td>
</tr>
<tr>
<td>Smoking</td>
<td>0</td>
</tr>
<tr>
<td>Elevated blood lipid levels</td>
<td>0</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>0</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0</td>
</tr>
<tr>
<td>Low density lipoproteins</td>
<td>0</td>
</tr>
<tr>
<td>Hyperuricemia</td>
<td>0</td>
</tr>
<tr>
<td>Infections</td>
<td>0</td>
</tr>
<tr>
<td>Genetic or familial factors</td>
<td>+/−</td>
</tr>
<tr>
<td>Other</td>
<td>Migraine</td>
</tr>
<tr>
<td></td>
<td>Socioeconomic status</td>
</tr>
<tr>
<td></td>
<td>Hematocrit</td>
</tr>
<tr>
<td></td>
<td>Proteinuria</td>
</tr>
<tr>
<td></td>
<td>Sodium intake</td>
</tr>
<tr>
<td></td>
<td>Hepatic disease</td>
</tr>
</tbody>
</table>

+, yes; +/-, suggestive; -, no; 0, insufficient data.

Early evaluation and appropriate intervention to prevent stroke occurrence or recurrence. The more frequent the TIA, the higher the probability of stroke; previous stroke is a greater risk factor for subsequent stroke than is TIA alone.

**E. Obesity**

There are inconclusive results from studies in North America and Europe that obesity per se is a risk factor for all strokes, and from North America and Japan there are inconclusive results that obesity is a risk factor for ischemic stroke. A study from sub-Saharan Africa reports obesity to be a risk factor for all strokes; studies from Japan and Oceania, China, and India indicate that it is not a risk factor for all strokes.

**Conclusion:** The risk factor status of obesity as an independent variable for all strokes or for ischemic stroke is inconclusive.

**F. Platelet Hyperaggregability**

There is inconclusive evidence that platelet hyperaggregability per se is a risk factor for all strokes or for ischemic strokes; there are no data about its role in hemorrhagic stroke.

**Conclusion:** The risk factor status of platelet hyperaggregability as an independent variable for all strokes or for ischemic stroke is inconclusive.

**G. Alcoholism**

There is evidence that an acute alcoholic episode or chronic alcoholism are each important risk factors for all strokes and for ischemic stroke, and perhaps for hemorrhagic stroke. In rural China there is a strong correlation of alcoholism with stroke, but not in urban China.

**Conclusion:** Evidence that an acute alcoholic episode or chronic alcoholism are risk factors is suggestive but still inconclusive. There is no evidence that occasional or modest use of alcohol is a risk factor for stroke.

**H. Smoking**

There is evidence that cigarette smoking is an important risk factor for all strokes and for ischemic stroke; evidence of its role in hemorrhagic stroke and in SAH is compelling in some geographic areas but is less certain in others. The role of tobacco used in other ways (cigars, pipe smoking, chewing) is still unknown.
Conclusion: Evidence of cigarette smoking as a risk factor for all strokes and particularly for ischemic stroke is substantial. There is evidence that cessation of cigarette smoking will eliminate it as a risk factor.

I. Elevated Blood Lipid Levels

The role of elevated blood lipid levels as risk factor(s) remains unclear. There is evidence that hypercholesterolemia and/or increased concentrations of low density lipoprotein (LDL) are risk factors for ischemic stroke in certain populations (e.g., young males in Western societies), but not in others (Asian populations). In Japan and China, a relative increase in blood lipids is not a stroke risk factor when compared with the usual levels present in these populations; however, it must be recognized that the blood lipid levels in these populations are lower than those in other societies.

Conclusion: Evidence of elevated blood lipid levels as a risk factor for ischemic stroke in certain populations is suggestive; in other populations the evidence is not yet clear. Elevated blood lipid levels, particularly levels of LDL, are important as a risk factor for atherosclerosis per se, and correction for the effect on atherosclerosis has been shown to reduce significantly the risk for stroke.

J. Hyperuricemia

North American, European, Japanese, and Indian studies indicate that a high blood uric acid level is a risk factor for all strokes. However, the number of studies is few.

Conclusion: Evidence of hyperuricemia as a risk factor for all strokes is suggestive.

K. Infections

A wide variety of infections with cerebral infestation have been demonstrated as risk factors for all strokes and for ischemic stroke, particularly in parts of the world other than North America and Europe; among these infections are tuberculosis, helminthic infestation, malaria, syphilis, and leptospirosis. Clinicians report that systemic viral or bacterial infection is a risk factor for stroke, but the data are inconclusive.

Conclusion: Cerebral infection is an important risk factor for ischemic stroke in populations exposed to these infections; the status of systemic infection is not yet agreed upon.

L. Genetic or Familial Factors

There are some studies demonstrating familial aggregation of all strokes, ischemic stroke, and hemorrhagic stroke; that genetic factors per se are important risk factors has yet to be demonstrated.

Conclusion: Genetic or familial factors as independent variables in stroke are as yet inconclusive. These factors appear to be important when linked to other variables such as hypertension. The type of stroke (e.g., cerebral hemorrhage) appears to be influenced by genetic or familial factors.

M. Other Factors

A variety of other factors have been studied. Advanced age and male sex are important independent risk factors. Possible stroke risk factors include cold temperature, high-estrogen contraceptive modalities in females, low socioeconomic status, increased hematocrit in males, decreased hematocrit in females, high dietary intake of sodium, low dietary intake of potassium, and systemic infection. In most studies, the problem of whether these are independent variables or are important only when associated with other risk factors has yet to be resolved. However, the use of high-estrogen contraceptive modalities when combined with hypertension and/or cigarette smoking has been shown to be an important stroke risk factor in women of child-bearing age.

Even when no individual risk factor identified above is present, stroke can occur. Thus, other risk factors or combinations of known risk factors must be considered. Community-based and/or case-control studies are needed to identify additional risk factors and to describe the pathophysiologic role of risk factors in stroke. Recent reports on an increased occurrence of stroke in young people associated with drug abuse requires attention from both epidemiologic and pathogenetic viewpoints. Since a large proportion of strokes occurs in normotensive individuals, these studies are particularly important in population-based studies of people without hypertension. There are significant differences in epidemiologic data about different stroke risk factors in different populations that need clarification and further study; examples are the influence of obesity, alcohol use, cigarette smoking, and high density lipoprotein (HDL):LDL ratios. In addition, well-designed controlled clinical trials are needed to clarify the effect of risk factor reduction on the incidence of stroke, particularly by type of stroke.

III. Principles of Stroke Diagnosis

Clinically, a stroke is defined as an acute neurologic dysfunction of vascular origin with sudden (within seconds) or at least rapid (within hours) occurrence of symptoms and signs corresponding to the involvement of focal areas in the brain. Excluded from this definition are syncopees of cardiac or other origin in which no focal cerebral symptoms are present and uncomplicated SAH in which there is no damage to the brain itself. TIAs are a variety of the stroke syndrome, perhaps corresponding to a brief period of cerebral ischemia without cerebral infarction or to a small brain infarction with rapid and complete clinical recovery. However, the clinical distinction between a stroke and a TIA is useful for practical purposes, and the recognition of TIAs is essential for the secondary prevention of severe stroke.
Strokes can be divided into two broad categories according to the nature of the cerebral lesion: infarcts and hemorrhages. A cerebral infarct is the result of temporary or permanent occlusion of a feeding artery, extracranially or intracranially, or (more rarely) of venous thrombosis. A spontaneous cerebral hemorrhage is due to the rupture of an abnormal artery (aneurysm or AVM) or arteriole in the brain parenchyma. Often it is difficult to distinguish clinically between cerebral infarction and cerebral hemorrhage, and their relative occurrence varies from country to country. Cerebral infarction is reported to be more frequent in Europe and the Americas, while cerebral hemorrhage is reported to be more common in some Asian and African countries. This is important because several major therapeutic decisions depend on an early distinction between the two types.

Sensitivity of the clinical diagnosis of stroke (i.e., the proportion of strokes correctly identified) as well as its positive predictive value (i.e., the probability of a diagnosis being correct) is high in a specialized center with neurologic expertise. The use of computed tomography (CT scans) makes a diagnosis more reliable and adds important information about the nature, extent, and location of lesions. The more recently introduced nuclear magnetic resonance imaging (NMR or MRI) technique yields additional information. However, the use of these techniques is largely restricted to the urban areas of technically advanced countries, and therefore these techniques are not available for the early diagnosis of the vast majority of strokes occurring worldwide.

The following presents basic criteria to help a clinician in charge of stroke patients maximize the accuracy of a diagnosis using clinical information and some simple low-cost tests. In general, it is the temporal course of neurologic symptoms and signs that is by far the most important criterion for the differential diagnosis of stroke. The younger the patient, the more useful is the accurate diagnosis of etiology since in many cases etiology significantly influences long-term medical management.

A. Presenting Signs and Symptoms

Strokes result in either transient or permanent focal neurologic deficits that can also result from a host of causes of focal brain dysfunction other than vascular. However, some patterns are more suggestive of a stroke when the grouping of signs corresponds to an arterial area of the brain. In the majority of strokes, these signs are one-sided. Some clinical subtypes correspond to deep small infarcts (i.e., a lesion in the territory of perforating arteries) and are termed lacunar strokes.

1. Temporal Profile

Strokes typically present abruptly, resulting in a maximum deficit within hours at the longest, but usually within seconds or minutes. If the symptoms and signs disappear completely within a few minutes or hours (<24 hours by convention), the event is termed a TIA. If the symptoms and/or signs last for >24 hours, they will most often stabilize or recede partly during the following days; the event is termed a completed stroke. Continuing progression for >24 hours is rare and makes the diagnosis of stroke less likely. The following characteristics should be specified for accurate classification:

a. Mode of onset: sudden (seconds); acute (minutes); stuttering or stepwise; or progressive (hours).

After 24 hours, deterioration may occur in 20–30% of patients due to factors such as increasing cerebral edema and herniation. When another form of brain lesion has been ruled out, progression of stroke may correspond to a variety of mechanisms, among which progressive thrombosis of larger vessels (internal carotid artery [ICA] or basilar artery) and spreading edema around an infarct are the most common. It is unusual that a stroke due to cerebral hemorrhage is clearly progressive during the first 2 days.

b. Course after onset (during the first 2–3 weeks): complete recovery in <24 hours (TIA); complete recovery in >1 day (regressive ischemic neurologic deficit [RIND]), protracted TIAs; partial recovery with persistent sequelae; no recovery or continued worsening; or death. The first two categories (TIA, RIND) usually correspond to ischemic origins, as their names indicate. In the next two categories, hemorrhages are more common. In particular, delayed worsening after the first 3–4 days is usually the result of a cerebral hemorrhage. However, confirmation by brain imaging is mandatory if neurosurgical intervention is considered. TIAs are different from episodes of loss of consciousness (which are not focal symptoms) and from the following focal transient cerebral problems: 1) partial epilepsy, in which symptoms often progress gradually (over several minutes), are “positive” (i.e., limb shaking instead of partial limb paralysis, visual hallucinations instead of loss of vision), and tend to recur in a stereotypical fashion (the distinction may be difficult, especially in older patients, although partial seizures occur at all ages); and 2) classical neurologic migraine with an aura (according to the IMS-WFN classification), in which symptoms (visual or sensory, but sometimes motor or aphasic) develop over some tens of minutes and are usually followed by a headache (classical migraine is more frequent than stroke in adolescents and young adults).

2. Distinction Between TIAs in Carotid and Vertebrobasilar Regions

This distinction is of practical importance for management purposes (i.e., surgical revascularization is considered more frequently for the carotid than for the vertebrobasilar system) and for prognosis (vertebrobasilar TIAs have a less ominous outcome than carotid TIAs). The following applies essentially to TIAs but is also true for completed ischemic strokes:

a. Carotid artery region involved: monocular loss of vision, particularly if accompanying or alternat-
ing with a contralateral partial paralysis of the limbs; unilateral sensory and motor deficit (i.e., face-arm, face only, leg only); difficulties in understanding language and/or in speaking (aphasia); use of wrong or altered words; or face-arm pure sensory or pure motor symptoms.

b. Vertebobasilar artery region involved: acute unsteadiness or ataxia; unilateral* or bilateral (or involving one side after the other) visual, motor, or sensory disturbances; vertigo or dizziness*; double vision; dysarthria or swallowing impairment*; or acute impairment of consciousness or acute confusion*.

B. “Classical” Types of Focal Cerebral Infarction

1. Carotid Artery Region
   a. Superficial middle cerebral artery (MCA) syndrome. This syndrome involves any one or a combination of the following signs: face-arm sensory-motor weakness or hemiparesis (the lower limb may be involved, but less so than the face and arm; intensity of the paresis varies from very mild to complete paralysis); aphasia (language disturbance) when the dominant cerebral hemisphere (usually the left) is involved (can occur without hemiparesis); visual impairment (may be present in the form of either a loss of vision in one half of the visual field or a unilateral visual neglect; in both instances on the side of the hemiparesis. However, visual impairment is difficult to assess in the case of aphasia); eye and head rotation toward the side of the brain lesion (particularly in cases of severe hemiplegia); and/or neglect of the left side of the body in some cases of right-sided cerebral lesions.
   b. Deep MCA syndrome. This syndrome consists of a pure motor hemiparesis or hemiplegia (without sensory or visual impairment) involving the entire side of the body (i.e., face, arm, and leg).
   c. Complete MCA syndrome. This syndrome combines the hemiparesis or hemiplegia of the deep MCA syndrome with the sensory, visual, and language dysfunctions of the superficial MCA syndrome.
   d. Anterior cerebral artery (ACA) syndrome. This syndrome typically features a sensory-motor monoparesis of a lower limb or a more widespread hemiparesis that predominates clearly at the lower limb and at the proximal part of the upper limb. Often found is urinary incontinence, as well as an involuntary grasping reaction of the affected hand (grasp reflex).

2. Vertebobasilar Artery Region
   a. Posterior cerebral artery (PCA) syndrome. This syndrome involves any one or a combination of the following signs: complete loss of vision on one side of the visual field or in only the upper half; widespread hemisensory abnormalities (either troublesome sensations [dysesthesias] or spontaneous pain, or loss of all or several sensory modalities [particularly pain and vibration sensation or both], in an entire side of the body); visual perception difficulties in the absence of, or not explained by, visual field deficits (loss of the ability to recognize visually objects, faces, pictures, colors, or graphic symbols).
   b. Vertebobasilar syndromes of the posterior fossa. These syndromes are characterized by signs or symptoms corresponding to an involvement of the cerebellum and brainstem. The combination of cranial nerve or cerebellar dysfunction on one side with sensory or motor dysfunction on the other side of the body is suggestive of a vertebobasilar stroke. Diagnostic of a vertebobasilar artery localization are oculomotor abnormalities due to a stroke, except for conjugated lateral gaze palsy, which can also occur in carotid artery strokes.
   c. Cerebellar infarction. This is an infrequent type of stroke and is difficult to distinguish clinically from a cerebellar hemorrhage (see below). In addition to possible brainstem signs, the picture in cerebellar infarction is that of an acute cerebellar syndrome with hemiataxia, hypotonia, loss of balance and the inability to stand, intense nystagmus, vertigo, and vomiting but without either headache or decreased consciousness during the first hours. Secondary edema can make the clinical picture identical to that of cerebral hemorrhage.

3. Lacunar Syndromes*
   a. Pure motor hemiparesis. This resembles the deep MCA syndrome to some degree, with a mild-to-moderate hemiparesis, often stuttering or progressive in onset, involving the face, arm, and leg.
   b. Pure sensory stroke. This is defined by sensory symptoms involving an entire side of the body, often transient or preceded by transient episodes if permanent. Most often, the complaint is that of paresthesias and/or dysesthesias, sometimes unpleasant or burning, with little or no objective sensory deficit, so the term “pure paresthetic stroke” might be more appropriate.
   c. Ataxic hemiparesis. This syndrome is less easy to identify, combining cerebellar incoordination and motor deficit on the same side of the body. Two types of ataxic hemiparesis sometimes described separately are crural hemiparesis with homolateral ataxia (partial paralysis in a leg plus incoordination of the ipsilateral arm and hand) and the dysarthria-clumsy hand syndrome (partial paralysis of speech movements plus slight hand incoordination).
   d. Pseudobulbar syndrome and lacunar state. These are due to the accumulation of lacunes in the white matter of the brain, particularly in the pyramidal tracts and basal ganglia, especially of the striatum. The pseudobulbar syndrome consists of spasmodic laughing and crying (emotional inconti-

*Not if it is the sole symptom, but only if it is associated with at least one other symptom on the list.

*The term lacunar syndrome is controversial in that it is used to describe a class of symptoms, or pathology, or both.
ence), primitive reflexes, dysarthria, and swallowing problems with an increased gag reflex. In the lacunar state, the pseudobulbar syndrome is associated with a characteristic short-stepped gait, a generalized akinesia (lack of movement) with a fixed facial expression, and sometimes with urinary incontinence. These syndromes are at times associated with a mental deterioration that can range from minimal to overt vascular dementia. These syndromes have become more rare in communities in which large-scale hypertension detection and treatment programs are implemented.

C. Syndromes of Intracerebral Hemorrhage

Even if it is not possible to distinguish reliably a cerebral hemorrhage from a cerebral infarction on clinical grounds alone, the following features are usually associated with a hemorrhage:

**Headache and/or nausea and vomiting at onset:** When the other symptoms and signs indicate a supratentorial stroke, headache and vomiting during the first hours of onset are strongly in favor of a hemorrhage, especially if there is also a stiff neck.

**Persistent disturbance of consciousness:** When the objective signs unequivocally point to a supratentorial stroke, immediate or early (within hours) decrease in vigilance indicates the presence of an acutely developing intracerebral mass (i.e., a hematoma).

**Nonischemic pattern of stroke:** The following temporal and regional criteria can be used for this distinction: 1) short-lasting transient symptoms are almost always ischemic (hence the name TIA); 2) a proportional (face-leg-arm) motor and sensory deficit is very suggestive of a deep hemispheric hemorrhage, especially if vigilance is altered. When an hemianopsia or visual neglect is added, the resulting syndrome of hemiplegia-hemianesthesia-hemianopsia is much more commonly associated with a deep hemorrhage in the parietotemporal-occipital junction; and 3) an acute cerebellar syndrome with severe headache and/or altered consciousness plus signs of brainstem compression suggest a cerebellar hematoma for which emergency surgical decompression is indicated.

D. Subarachnoid Hemorrhage

SAH is not, strictly speaking, a stroke (in the sense of an acute focal cerebral lesion), at least not in its uncomplicated form. The most frequent complications of SAH are intracerebral hemorrhages and delayed cerebral infarctions (due to vasospasm). The typical presentation of SAH is that of a sudden severe headache, widespread or predominant on one side or at the posterior part of the head, and a stiff neck. Nausea and vomiting occur in most cases within minutes or hours, while the headache does not recede but rather increases. There are no cerebral symptoms or signs in the pure forms of SAH, but ocular nerve motor dysfunction may be present. In more severe cases, the presentation is that of an acute stupor or coma, with a stiff neck and diffuse signs of central nervous system involvement.

E. The Search for Causes

This aspect of stroke diagnosis is the most difficult, even with the assistance of sophisticated laboratory tests. One reason is that stroke can result from a variety of disorders, particularly in the elderly. Despite extensive search, in the young frequently no cause for stroke can be identified. It is the aim of this presentation to help clinicians and investigators systematically look for the various risk factors and mechanisms that can result in a completed stroke.

1. Past History and Associated Conditions

Stroke occurs frequently as a consequence of previous conditions, often long-lasting, which have remained unknown or neglected in many cases. Recognizing these conditions is important because they are major clues to the diagnosis of stroke and its mechanism(s) and because appropriate treatment is essential for the secondary prevention of stroke recurrence (see Sections II and IV).

a. Neurovascular history. Previous TIAS and strokes indicate arterial disease if they have occurred in the same arterial bed and point to cardiac embolism if different regions are involved. It is much rarer for cerebral hemorrhage to recur. Familial occurrence of stroke is frequently reported. Moreover, a family history usually mentions the existence of risk factors such as hypertension or familial arteriosclerosis.

b. Neurovascular signs. Neck bruits suggest arterial disease, especially bruits heard high in the neck, ipsilateral to the stroke. Orbital bruits sometimes can be detected in intracranial artery disease. Asymmetry of wrist pulses and/or of arm blood pressure can reveal a tight stenosis or occlusion of one subclavian artery; this is often asymptomatic but can cause ischemia in the vertebrobasilar system in some patients. Ophthalmoscopic examination demonstrates arterial disease and increased intracranial pressure.

c. Cardiovascular history and signs.

**Definite embolicigenic heart disease:** The most frequent embolicigenic cardiopathies associated with stroke in developed countries are chronic atrial fibrillation, mitral and aortic valvulopathies, myocardial infarction, and congestive cardiomyopathy. Rheumatic heart disease and parasitic cardiomyopathies are common in many parts of the world. Since a stroke may occur as the first manifestation of a heart condition, a thorough cardiac examination is mandatory as part of a stroke evaluation. Systematic electrocardiography (ECG) and chest roentgenography (x-ray) add useful information about rhythm disturbances, myocardial ischemia, and heart size, and more rarely disclose an unsuspected major cardiopathy.

**Other heart conditions:** Following a stroke, cardiac status may be even more important for
long-term prognosis than the risk of stroke recurrence, even when the cause of the stroke was not cardiac. Angina pectoris, cardiac insufficiency, and rhythm disturbances (other than chronic atrial fibrillation) are much less likely to produce emboli than the definite embolic conditions listed above, but occasionally they do so. ECG and chest x-ray are valuable for the diagnosis of these other heart conditions.

Peripheral arteriopathy: This condition does not directly cause a stroke, but its extent and severity often parallel that of cervicocerebral atheroma. Peripheral arteriopathy is, therefore, a clue to the diagnosis of an atherothrombotic mechanism of brain ischemia.

2. Risk Factors
The presence of risk factors contributes to stroke diagnosis in the following ways:

a. Hypertension. When chronic, hypertension is a risk factor for all types of strokes. It accelerates atherosclerosis, hence favoring large-artery occlusion or embolism; it directly causes obstructive atherosclerosis, leading to lacunar infarction; and it produces arteriolar microaneurysms, the major cause of spontaneous intracerebral hemorrhage. Hypertension is also a risk factor for idiopathic chronic atrial fibrillation. Since reactive hypertension is often found after a stroke, evidence of previous hypertension must be looked for in the patient’s history and through its consequences in the ocular fundus (hypertensive retinopathy) and on ECG (left ventricular hypertrophy). In the case of a lacunar syndrome or of a spontaneous cerebral hemorrhage, chronic hypertension, if present, is most likely to be the cause.

b. Diabetes mellitus. This is a major risk factor for large-artery atheroma and as such might predispose to an ischemic stroke. However, in several studies, the frequency of diabetes mellitus was the same in cases of cerebral hemorrhage.

c. Increased hematocrit. This is a minor risk factor for ischemic strokes (both large-vessel and lacunar). Polycythemia vera is a rare but recognized cause of TIA and cerebral infarction.

d. Hypercoagulative states. These states, when found, predispose to an ischemic stroke. Thrombocytosis, disseminated intravascular coagulation (DIC), and nonbacterial endocarditis are more frequently associated with cerebral ischemia.

e. Smoking. This is a major risk factor for ischemia and possibly hemorrhagic strokes.

f. Hyperlipidemia. Hypercholesterolemia, and to a lesser degree hypertriglyceridemia, are more often associated with cerebral infarction than with cerebral hemorrhage.

F. Laboratory Investigations
Some of these tests are not available worldwide, but their moderate cost and the increasing diagnostic accuracy of ultrasound techniques when done by skilled personnel make them of importance in evaluating stroke patients.

1. Ocular Fundus
Examination searches for retinal hypertensive arteriolopathy, which parallels that of the brain. A decrease in retinal arterial pressure as an indicator of obstructive disease of the carotid artery has lost much of its usefulness because of the development of the more sensitive ultrasound techniques.

2. Doppler Sonography
Continuous-wave neck Doppler sonography is a simple and rather inexpensive technique and is of important clinical interest. Continuous-wave Doppler sonography reliably identifies both obstructive cervical carotid artery disease and subclavian artery obstructions. This ability is particularly useful in screening patients considered for surgical revascularization. However, neither the intracranial carotid artery and its branches nor the vertebrobasilar system are accessible with continuous-wave Doppler sonography. Pulsed transcranial Doppler sonography is still under evaluation, and it is thought to complete the previous technique in investigating the ICA in its petrous portion, the carotid siphon, the origin of the MCA and ACA, the communicating arteries, the PCA, the basilar artery, and the intracranial vertebral arteries.

3. Echocardiography
This procedure should be used very selectively after a stroke (except in the young) since its yield is low in the absence of any clinical or ECG abnormalities. When a reasonable suspicion exists, echocardiography is the technique of choice to look for or to document conditions such as valvulopathy, cardiomyopathy, an intracardiac mass or thrombosis, and aneurysm or akinetic segment of the ventricular wall.

4. Holter Monitoring
As with echocardiography, its use should be limited to patients with sufficient indication of a cardiac cause of embolism. Holter monitoring may then document an intermittent atrial fibrillation or a rarer but most ominous sick sinus syndrome, with alternating tachycardia and bradycardia, and risk of recurrent embolism and sudden death.

5. CSF Examination
Lumbar puncture (LP) is easy to perform and will quickly distinguish colorless from bloody CSF, likely to represent ischemia and hemorrhage, respectively. Increased intracranial pressure must be ruled out before LP is performed. A careful examination of the ocular fundus for evidence of increased intracranial pressure is always necessary. Because LP is dangerous when intracranial hypertension is present, a CT scan, if available, is preferred in all circumstances of stroke. LP can give false-positives (because of a vascular puncture) or false-negatives (in case of hemorrhage with strictly intraparenchymal bleeding). CSF studies are sometimes useful to diagnose infectious or inflammatory diseases, which
can be treatable causes of cerebral arteritis, particularly in the young.

6. Neurovascular Imaging Techniques

The following "high-tech" diagnostic techniques are often restricted to large centers in economically developed countries. They comprise neck and cerebral artery imaging techniques, which show stenoses and occlusions, and brain imaging techniques, which describe the type, localization, and extent of vascular damage to the brain. These reliable diagnostic tools for stroke are likely to remain unavailable for a long time in many places throughout the world for economic reasons and are therefore of less practical importance than identifying and managing the primary associated conditions and risk factors previously described. For each technique, reliable results are dependent upon skilled technical personnel.

a. Neck artery echotomography. With rather expensive equipment, this neurovascular imaging technique permits visualization in cross-sectional and longitudinal "slices" of the walls of the arteries going to the brain. Its combination with pulsed Doppler sonography allows assessment of hemodynamics within the diseased vessels. Echotomography is superior to conventional continuous-wave Doppler sonography to diagnose nonobstructive carotid plaques and ulcerations and for vertebral artery obstructions. Echotomography may avoid the necessity for carotid angiography, but it is still being evaluated.

b. Digital subtraction arteriography and conventional angiography. A variety of angiographic techniques are currently available. Arterial catheterization has undoubted risks, but digital subtraction angiography by the intravenous technique gives images that are generally of inadequate quality. Digital subtraction angiography with arterial catheterization may be the methodology of choice in the future because the contrast volume is much lower and the quality of the images is higher. However, unless surgical treatment of an arterial obstruction is being considered, cervical and cerebral angiography has limited practical use in the diagnosis of stroke. Two important indications are 1) ischemic strokes in the young (in search of an arterial dissection or of an arteritis) and 2) intracerebral hemorrhages if cortical or in the lobar white matter or and for vertebral artery obstructions. Echotomography may avoid the necessity for carotid angiography, but it is still being evaluated.

c. CT scan. Immediately following a stroke, CT scans show cerebral hematomas as areas of markedly increased density, usually ovoid or round, with little or no peripheral edema. A CT scan can also document the size and localization of a hematoma. In the case of an infarction, there is a "silent" period of 1–2 days before a focal area of hypodensity appears on CT scan. Only large infarcts with edema will be seen during the first hours after a stroke, but early CT scanning excludes cerebral hemorrhage. Small infarcts, particularly lacunes and brainstem infarcts, will not be visible on CT scans even after a proper delay; a normal CT scan several days after the event is an argument in favor of their diagnosis. After a TIA, the CT scan may be positive for an infarct (usually small) in up to 10% of the cases.

d. MRI or NMR. This technique is not superior to CT in most cases of stroke. However, MRI is better for both early (within the first few hours) localization for lacunar and brainstem infarctions and for the later (after some weeks) differentiation between cerebral infarction and cerebral hemorrhage. When hemorrhage is due to an AVM, the abnormal vessels can often be seen as a tortuous pattern within the parenchyma.

G. Diagnostic Conclusions

The following is a checklist meant to include the more frequent etiopathogenic types of stroke. More precise and detailed classifications are found in the ninth (ICD-9 NA) and tenth (ICD-10) International Classifications of Disease of the WHO.

Cerebrovascular ischemia
- Arterioarterial
- Other cause of thrombosis (specify)
- Cardiac embolism
- Arterioarterial embolism
- Other cause of embolism (specify)
- Lacunar infarction
- Cervical or cerebral arteritis
- Cervicocerebral artery dissection
- Cerebral thrombophlebitis
- Artery trauma
- Other (specify)
- Unknown

Intracerebral hemorrhage
- Primary
  - Includes those associated with hypertension and/or alcoholism
  - Excludes any specified cause listed below:
    - Due to arterial malformation or AVM
    - Due to moyamoya disease or other arterial obstruction
    - Due to amyloid angiopathy
    - Due to trauma
    - Other (specify)
    - Unknown

SAH
- Due to berry aneurysm
- Due to AVM
- Due to trauma
Other (specify)  
Unknown  

In some cases, no cause for a stroke is found even after extensive evaluation. This may mean either that the available diagnostic techniques are not yet sufficient or that some stroke mechanisms remain unknown. Only continuing research effort will solve this problem.

H. Appendix

List of symptoms and signs of stroke:
- Pure motor paresis*†‡
- Pure sensory abnormalities*†‡
- Sensory and motor abnormalities*†‡§
- Motor disturbances other than partial paralysis or hemiplegia*†‡ (ataxia, incoordination, tremor, dystonia)
- Language or speech disturbance‡ (if not due to coma or overt dementia)
- Other higher cortical dysfunction‡ (amnesia, agnosia, apraxia, confusion, delirium, dementia)
- Visual symptoms*‡ (loss of vision, blurring of vision, diplopia)
- Vertigo, dizziness, unsteadiness‡
- Swallowing impairment‡
- Hearing loss, tinnitus*‡
- Convulsions, epileptic seizures*  
- Loss of consciousness‡
- Loss of sphincter control (if not due to seizures or coma)*
- Headache*
- Nausea and vomiting
- Neck stiffness*
- Additional signs found at examination
  - Brisk jerk reflexes,*† Babinski's sign*
  - Decerebration or decortication signs*
  - Nystagmus*

IV. Strategies to Prevent and Treat Stroke and SAH

This section synopsizes therapeutic strategies for the medical management of patients with ischemic events of the brain or retina that can be ascribed to arteriosclerosis of the cervicocerebral arteries, to hematologic abnormalities, to emboli originating from the heart, or to bleeding into the substance of the brain or the subarachnoid space. This section identifies the therapeutic measures that have proven beneficial, the measures that appear to be worthy of continued usage for the time being (although only on the basis of reasonable hypotheses or generally accepted clinical impressions), and finally, those measures shown to be of no value and therefore of 

---

* Determine if right-sided, left-sided, or bilateral.  
† Determine if objective deficit or sign is still present at examination.  
‡ Determine if on ipsilateral or contralateral side.

---

needless expense or harm to stroke-threatened patients and stroke victims.

A. Primary Prevention: Strategies to Prevent Atheroma Development

The first lines of defense in stroke prevention are detecting and adequately treating manageable risk factors. These steps are calculated to prevent the development of atheroma. The current state of knowledge about recognized risk factors has been presented earlier (Section II). To control atheroma it is essential to regulate blood pressure, to reduce dietary intake of saturated fats, and to cease cigarette smoking. Much of the desirable risk factor reduction requires a combination of lifestyle changes, dietary adjustments, and appropriate drug therapy.

Alternate-day therapy with 325 mg aspirin given to 22,000 healthy US physicians reduced the occurrence of myocardial infarction, but there was no detectable reduction in the occurrence of strokes. Whether this cardiac benefit related to the retardation of coronary artery atheroma or to prevention of secondary thrombosis is not known. Longer follow-up and further studies may clarify this. Nevertheless, heart disease (particularly myocardial ischemia) is complicated by ischemic stroke so that the primary prevention of myocardial ischemia is an important goal in stroke prevention. Unless contraindicated by peptic ulcer disease, by bleeding disorders, or by known idiosyncratic response to the drug, alternate-day aspirin is recommended for individuals in the fifth and later decades with a strong family history and other identifiable risk factors for vascular disease. The dosage used in the trial of healthy men of one 325-mg tablet every other day or a similar dose daily is recommended. Individuals should neither initiate nor persist with this usage of aspirin without seeking the advice of health care personnel.

Chelating agents, fish oil supplements, and calcium channel blockers have been reported to inhibit atherogenesis. However, the data are inadequate, and these substances are not recommended at this time. Fish, as opposed to fish oil supplements, is suggested as an alternative to the excessive consumption of red meat.

B. Secondary Prevention of Threatened Stroke

The onset of cerebral or retinal ischemic events signals the progression of arterial or cardiac disease to the point where primary prevention has failed. The presence of these target-organ symptoms frequently indicates the superimposition of thromboembolism on the primary disease process. Secondary prevention measures are now mandatory. Faced with the overt presence of symptoms due to arteriosclerosis, hematologic disorders, or heart disease, any program of secondary prevention demands that specific risk factors be sought and treated. No claim can be made that any other measure directed toward preventing further thrombosis or thromboemb-
bolism are as potent as the normalization of these known and adjustable risk factors.

1. Risk Factor Adjustments
   a. Hypertension. Careful normalization of blood pressure has been shown to reduce the risk of further ischemic or hemorrhagic events. Systolic blood pressure of >160 mm Hg or diastolic blood pressure of >90 mm Hg requires attention. Whether blood pressure will be normalized by some or all of the following must be individually determined for each patient: weight reduction, avoidance of amphetamines and other drugs known to precipitate hypertensive crises, control of sodium and potassium intake, an exercise program, and the use of antihypertensive drugs.
   b. Tobacco use. Cigarette smoking has been established in several studies and in a variety of populations as a risk factor for stroke. There is increasing evidence that stroke risk is reduced with cessation of cigarette smoking. No data are available linking stroke to smoking cigars or pipes or to other non-cigarette tobacco use. Cigarette smoking has been shown to raise blood fibrinogen concentration, to enhance platelet aggregation, and to increase hematocrit; in conjunction with an increased fibrinogen concentration, an elevated hematocrit increases blood viscosity. Cessation of cigarette smoking in any patient who presents with cerebral or retinal ischemic events is mandatory.

2. Dietary Adjustments
   a. Obesity. The dietary control of obesity is recommended, particularly because weight reduction enhances the regulation of hypertension and diabetes mellitus.
   b. Alcohol. Avoidance of its excessive use is recommended because alcohol abuse is associated with an increased risk of stroke. Excessive use of alcohol increases blood pressure, triglyceride levels, paroxysmal atrial fibrillation, and cardiomyopathy (with ventricular thrombi). Alcohol abuse increases platelet aggregability, activates the coagulation cascade, and results in rebound thrombocytosis.
   c. Hypercholesterolemia. Increased LDL and decreased HDL concentrations, although not linked with stroke per se, are associated with an aggravated risk for coronary artery disease. Since myocardial ischemia is a clear risk factor for stroke, control of hypercholesterolemia is required for stroke-threatened patients. Dietary regulation is the first approach, and if this fails to normalize the lipid levels, consideration of cholesterol-lowering drug therapy is indicated in patients with cerebral or retinal ischemic events.
   d. Sodium and potassium intakes. High sodium intake is accompanied by increased hypertension. Reduction of dietary sodium is recommended but should be modified in hot and humid climates to accommodate for the loss of sodium in such extreme conditions. Low intake of potassium is associated with an increased risk of stroke, possibly due to a concomitant risk of hypertension. A diet containing sufficient potassium is recommended. A moderate daily intake of fresh fruit or vegetables is advisable and is adequate to prevent low potassium levels in the absence of potassium-wasting disorders or diuretic therapy.

3. Associated Conditions and/or Risk Factors
   a. Diabetes mellitus. Although rigid control of diabetes mellitus has not been shown to reduce the risk of stroke, both arterial and venous infarcts are reported to be more extensive in the presence of hyperglycemia. The recognition and control of diabetes mellitus are strongly recommended, particularly in patients experiencing cerebral or retinal ischemic events.
   b. Heart disease. Patients who manifest cerebral and retinal ischemic events should be examined for evidence of rhythm disorders (particularly atrial fibrillation and sick sinus syndrome), valvular lesions (particularly mitral stenosis, mitral valve prolapse [MVP], mitral anular calcification, and subacute bacterial endocarditis), and damage to the myocardium (especially recent infarction, old infarction with aneurysmal dilatation or segmental akinesthesia, and cardiomyopathy). In South America the latter will require consideration of Chagas' disease and in Africa, the entity of dilated cardiomyopathy. Therapy will be specialized according to the lesion detected.
   c. Exercise. Exercise is desirable because it is associated with reduced blood pressure, increased HDL levels, and control of obesity. No data are available that document a reduced risk of stroke in patients who pursue an exercise program after the onset of ischemic events. Nevertheless, there is some evidence that exercise reduces the risk of myocardial infarction and, by inference, reduces embolic stroke associated with this disorder.
   d. Hematocrit. Increased hematocrit is associated with an increased risk of ischemic stroke in some populations. Phlebotomy is recommended, on empirical grounds alone, to reduce and maintain the hematocrit at normal levels in patients in whom it is markedly elevated (>55–60%) and who have evidence of threatening cerebral and retinal ischemic symptoms. Decreased hematocrit is associated with an increased incidence of ischemic stroke in women. The specific cause of the decreased hematocrit must be addressed therapeutically.
   e. Thrombocytosis. In the presence of ischemic symptoms, this condition is to be managed by antiplatelet therapy or appropriate chemotherapy. The decision to use one or another therapeutic strategy should be made after careful hematologic study of the underlying cause of thrombocytosis. A platelet count of >600,000/ml should be treated to reduce the risk of thrombosis.
   f. High-estrogen contraceptives. Associated with an increased risk of vascular thrombotic events similar to that induced by pregnancy, high-estrogen contraceptives should be replaced with low-estrogen compounds or an alternative contraceptive strategy. The
risk imposed by hormonal contraceptive therapy is markedly increased in the presence of hypertension and cigarette smoking. Postmenopausal estrogen use is associated with a reduced risk of stroke and probably with a reduced occurrence of coronary heart disease.

g. Triggered coagulation cascade. Other conditions that increase the likelihood of predictable triggering of the coagulation cascade must be identified (e.g., known or occult cancer, pregnancy, trauma, postoperative and postpartum conditions). Prophylaxis in these situations presents a complex management problem and is specific to each underlying cause. An increase in fibrinogen concentration has been determined to be a risk factor for stroke independent of smoking.

h. Sickle cell disease and sickle cell trait. These conditions are known to be clinically associated with an increased risk of cerebral arterial and venous thrombosis and sinus thrombosis, particularly in children. Individuals with this disorder or this trait are advised to avoid excesses of unaccustomed physical exertion, hypoxia (e.g., high altitude), and exposure to excessive heat.

i. Vasculitis. Vasculitis that develops in association with immunologic suppression must be recognized, as must conditions with immunologic abnormalities such as leptospirosis, Lyme disease, and aspergillosis. Meningovascular syphilis, prevalent in certain geographic areas but rare in others, must be detected and treated.

j. Drug abuse. Vasculitis or hypertensive crises with cerebral infarction or hemorrhage are complications of drug abuse. These risks of stroke must be brought to the attention of those who would be prone to adopt the dangerous habit of using street drugs either casually or regularly. Both types of drug users have fallen victim to disastrous strokes.

C. Antithrombotic Agents

1. Anticoagulants

No trials meeting the demands of modern methodologic design have been conducted to evaluate heparin or warfarin in stroke prevention. Recommendations come from abbreviated, or what now must be considered to have been imperfectly designed studies, the information from which are no better than empirical. Anticoagulants carry sufficient risks so that they can be administered only if the patient and a laboratory are readily accessible and if both are known to be reliable. The patient must understand the risk of hemorrhage and the hazards of trauma occurring during the period of therapy with anticoagulants. Therapy should be administered for no longer than is judged optimum in an individual patient. Anticoagulants are not recommended after a recent large cerebral infarction, nor should they be instituted without either a CT scan or LP to exclude hemorrhage. The finding of a large lesion or the early presence of a hemorrhagic infarct must delay the start of anticoagulant therapy for 72 hours. This is prudent despite the fact that many hemorrhagic lesions are the result of recent thromboemboli of cardiac origin, and that for the first 15 days after the episode there is a 1%/day chance of recurrence. With these caveats, anticoagulants are recommended for use only when cerebral or retinal ischemic events have been recognized in the following circumstances:

a. Recent myocardial infarction. The occurrence of emboli and the recognition of intraventricular thrombi are greatly increased if the infarct is large, if it involves the anterior or septal ventricular wall, or if it is associated with atrial fibrillation or congestive heart failure. Echocardiography is a useful diagnostic procedure in detecting associated thrombi. When these conditions are recognized, and especially if warning cerebral or retinal events have occurred, 3 months of anticoagulation therapy is recommended. Therapy should begin with heparin and warfarin and should be succeeded by warfarin alone when the latter's measurable effectiveness reaches the therapeutic range (monitored by the prothrombin time) for several days. The optimum therapeutic range (1½ times baseline prothrombin time) is recommended to minimize the risk of cerebral hemorrhage. More data about the optimum range of prothrombin times are required.

b. Previous myocardial infarction. This condition, with an identifiable ventricular akinetic segment or aneurysmal dilatation of the ventricular wall, is associated with ischemic events. The duration of therapy cannot be definitively stated. Three months is an arbitrary period, with a recommendation for subsequent long-term aspirin therapy (see below). A return to the use of anticoagulants may be indicated if aspirin fails to prevent recurrences.

c. Other cardiac disorders. Particularly cardiomyopathies, and a variety of congenital heart disorders, are prone to thromboemboli. Individual decisions will be required regarding long-term anticoagulant therapy.

d. Rheumatic heart disease. Now rare in developed countries, rheumatic heart disease remains an important source of embolic strokes in other parts of the world. In patients with mitral stenosis, with or without atrial fibrillation, in whom cerebral or retinal ischemic events have occurred and in whom surgical therapy is to be delayed or in whom it cannot be carried out, long-term anticoagulant therapy is required.

e. Other valvular lesions. If complicated by ischemic events and failing to respond to aspirin therapy, other valvular lesions need to be treated with anticoagulants for 3 months. Occasionally, when recurrences persist after cessation of anticoagulants, long-term warfarin therapy is recommended. Patients with ischemia attributed to MVP, usually recognizable as a cause of emboli in younger subjects, must be studied carefully to exclude other alternative mechanisms. Some of these patients will have thromboembolic complications, but many
embolic lesions are small and many patients afflicted do not appear to require more than aspirin therapy. The embolic material with mitral anulus calcification and aortic sclerosis usually consists of calcific debris rather than thrombotic material. However, thrombus formation and thromboembolic events are possible from these lesions, and it is difficult in an individual patient to be certain which is the offending substance. Thrombogenesis is intermittent in a number of these noninfected valvular lesions. If aspirin, given empirically, fails to alleviate recurrent symptoms, the alternative empirical treatment of warfarin is recommended for an arbitrary period of 3 months. Individuals with cerebral and retinal emboli with infective endocarditis should not receive anticoagulants during the period of active infection. Permanent damage to the valve(s) may lead to a new source of thromboemboli after the infective stage is over, and this phenomenon requires reconsideration of the need for anticoagulants.

f. Septal defects. Patients with cerebral/retinal ischemia in association with patent interarterial or interventricular septal defects (the anatomic subartery for paradoxic emboli), should be given warfarin for 3 months; longer times are required if there is persistent evidence of recurring thrombosis in the pelvic or crural veins or if there is hemodynamic evidence of pulmonary hypertension, which will elevate right heart pressures and will increase the probability of right-to-left shunting of microemboli.

g. Prosthetic heart valve. Bioprosthetic heart valves have reduced substantially the risk of thromboembolism, but no heart valve has been developed that remains totally free of this complication. The recommendations for stroke prevention with implanted valves depend on the type of valve. Prosthetic heart valves of the ball valve or tilty disk type in the mitral position require long-term anticoagulant therapy. With prosthetic heart valves in the aortic position, long-term anticoagulation is less universally administered but is recommended. For patients with tissue or bioprosthetic valves in the aortic or mitral positions, anticoagulants are recommended for the first 3 months. Thereafter, longer-term warfarin therapy is generally considered unnecessary for valves placed in the aortic position. With valves in the mitral position, anticoagulants are recommended in the presence of atrial fibrillation, when there is a large left atrium, or as a sequel to evidence of heart failure. A 1% annual morbidity, including cerebral hemorrhage, occurs in patients who receive long-term warfarin therapy. Whether platelet antiaggregants should be added remains an unsettled question. Aspirin, which increases the bleeding time, is not safe in conjunction with anticoagulants, and if a platelet antiaggregant is to be used with warfarin, dipyridamole may be considered.

h. Pulmonary vein thrombosis. This condition is rarely recognized as a cause of cerebral and retinal ischemia. Pulmonary vein thrombosis should be suspected in some individuals following severe pulmonary trauma or septic pneumonia. Heparin, followed by warfarin for 3 months, is recommended when pulmonary vein thrombosis is suspected as the cause of cerebral thromboembolic ischemic events.

i. Certain rhythm disorders. Certain of these, particularly atrial fibrillation and sick sinus syndrome, which occur with and without other recognizable heart disorders, are prone to thromboemboli. If the rhythm disorders have been associated with cerebral or retinal events, anticoagulants for indefinite periods are indicated, albeit on empirical grounds. Patients with other serious rhythm disorders (particularly complete heart block and serious paroxysmal ventricular rhythm abnormalities) experience loss of consciousness and syncopal events; however, these rhythm disorders are rarely attended by thromboemboli, and treatment does not require antithrombotic agents.

j. Cerebral vein and sinus thrombosis. More readily identifiable with the availability of venous angiography and MRI, cerebral vein and sinus thrombosis is commonly hemorrhagic. Recent evidence supports the use of anticoagulants, even in those patients with CT evidence of hemorrhagic infarction, except in those with evidence of gross blood by CT scan or LP. The use of anticoagulants is recommended for 10 weeks to 3 months.

k. Hypercoagulable states. With or without identifiable alterations in coagulation factors, so-called hypercoagulable states occur with the use of estrogen contraceptives, after trauma, during the postoperative and postpartum states, during pregnancy, in the presence of known cancer, and with a variety of hematologic disorders. All such conditions may be complicated by retinal or cerebral ischemic events. Warfarin for 3 months is recommended in patients with an etiology that indicates risk for a definable period (e.g., postoperative, postpartum, using estrogen contraceptives). No evidence exists to determine the value of antithrombotic drugs in marantic (nonbacterial thrombotic) endocarditis. In patients with DIC, anticoagulants have not proven beneficial.

l. Arterial stenotic-ulcerative lesions. Such lesions in the major cerebral arteries are a common site for thromboembolic events. Patients with arterial stenotic-ulcerative lesions have not been shown convincingly to benefit from long-term anticoagulant therapy. Empirical use of anticoagulants is recommended if angiography has identified a thrombus in a carotid or vertebral artery or if a disturbing number of ischemic events are recurring despite the use of aspirin. In neither instance is the use of anticoagulants recommended for >3 months.

2. Platelet Antiaggregants

Patients threatened with arterial causes of cerebral and retinal ischemia (especially atherosclerosis of the cerebral arteries), with and without infarction, are known to benefit from regular daily aspirin.
therapy in the prevention of stroke, stroke death, and all deaths. The optimum dose of aspirin is not known, and conflicting opinion persists. Benefit has been reported with doses ranging between 900 and 1,200 mg/day in several large trials and with a dose of 300 mg in one large trial in which combined vascular end points were analyzed. There is experimental evidence supporting benefit from a dose of <300 mg/day, but no trial using such a low dose has been concluded, and until these data are available the dosage recommended must be 1–4 tablets (300–1,200 mg) daily. Patients who cannot tolerate the higher amount of aspirin should be advised to use less, down to one tablet (300–325 mg) a day; a patient may tolerate the enteric-coated variety of aspirin when the less expensive uncoated regular variety is irritating to the digestive tract.

The use of aspirin was not shown to be beneficial for women in two of the four large stroke-prevention trials that have been completed; in the two other large trials there was an equally positive benefit of aspirin for men and women. Because the risk of stroke following TIA is less for women than for men, more female subjects will be required to demonstrate a benefit. It is possible that this lower risk for women has masked the benefit in some trials. Tentatively, the advice is to use aspirin for both sexes.

Arterial lesions causing the ischemic events present a continuing threat of thromboembolism. Therefore, once aspirin therapy has been initiated in patients with ischemic events of arterial origin, it is recommended that the therapy be continued indefinitely.

With the exception of ticlopidine, there have been no trials reported to date that have demonstrated convincing benefit in stroke prevention attributable to platelet inhibitors available for general use other than aspirin. Sulfipyrazone and suloclidil can be stated unequivocally to be of no value. So far, no trials reported have indicated positive results from the addition of any other platelet inhibitor to aspirin therapy. The addition of dipyridamole to aspirin is popular, but there is no definitive evidence from three large trials that this expensive adjunct therapy is beneficial. No trials of dipyridamole alone have ever demonstrated benefit (only one trial was conducted, with few patients and a negative result). Thus, there is an unresolved enigma as to what therapy to recommend when patients with recurring ischemic events cannot tolerate aspirin therapy. For the time being, based on experimental data alone, it is suggested that 75 mg dipyridamole t.i.d. or ticlopidine be considered. If neither aspirin, dipyridamole, nor ticlopidine can be tolerated due to side effects, a period of warfarin therapy is recommended.

Ticlopidine has been evaluated in two major trials, and beneficial results have been reported in both men and women. However, this drug has significant side effects (leukopenia, rash, diarrhea), it is expensive, and it is not yet generally available. Precise indications for ticlopidine will require continuing evaluation. There is no information about the efficacy or problems of this drug when combined with aspirin. At this time, ticlopidine is recommended for use in those patients in whom aspirin therapy is not successful.

Platelet inhibitors are not perceived to have value in situations in which red thrombi are known to develop, as in patients with cardiac mural thrombi, in those with venous and sinus thrombosis, or in patients whose thrombi are sufficiently large so as to be visualized by angiography in any artery. Warfarin is recommended until the thrombi have dissipated. No controlled trials have been conducted using platelet inhibitors alone or in cardiac or other nonarterial sources of cerebral or retinal ischemia. On empirical grounds alone, aspirin is recommended for patients with cerebral or retinal symptoms complicating MPV.

Combined warfarin and dipyridamole therapy has been claimed to reduce the incidence of emboli in patients with prosthetic heart valves. Methodologic imperfections in the few randomized studies on this subject make the conclusions uncertain. However, the empirical addition of dipyridamole to warfarin is recommended in these patients while awaiting further evidence. Aspirin is not advised because it prolongs the bleeding time and imposes an extra hazard when combined with warfarin.

3. Other Issues in the Use of Antithrombotics for Which Imperfect Knowledge is Available

Most recommendations about the use of antithrombotic agents are imperfect because of incomplete information. The following studies are among those needed to clarify the potential uses of anticoagulants and platelet inhibitors in stroke prevention:

a. Aspirin vs. warfarin. A trial of sufficient sample size is required to compare aspirin with warfarin in transient and minor ischemia arising from arterial lesions.

b. Warfarin with prosthetic heart valves. A repetition of studies with more subjects and longer follow-up is indicated for patients with prosthetic heart valves using warfarin with and without platelet inhibitors.

c. Warfarin plus aspirin. Such trials are being conducted currently in patients with nonrheumatic atrial fibrillation. Trials under way include one of patients without cerebral/retinal symptoms and another of patients who have already experienced symptoms.

d. Aspirin with TIA. There are insufficient data on aspirin therapy in patients with TIAs and in patients with partial stroke using minimal (40–80 mg/day) dosage compared with 325 or 900–1,200 mg/day. Presently, a large trial is under way in the Netherlands, which within the next few years may provide the necessary data.

e. Aspirin vs. dipyridamole. A trial of patients with TIA or partial stroke, comparing the benefit of
aspirin alone with the effect of dipyridamole alone has not been done. Because of the intolerance for long-term aspirin use exhibited by 15% of patients taking 4 tablets/day, the use of dipyridamole in this population might be tested against placebo in a major trial. The result of the ticlopidine trials may eliminate the need for this difficult study.

f. Aspirin plus ticlopidine. Two major trials using ticlopidine have been completed, and in each a benefit has been reported for both men and women. Careful long-term follow-up of patients with TIA and stroke and controlled trials of combined aspirin and ticlopidine therapy need to be initiated.

g. Heparin with TIA. Heparin therapy requires careful and scientifically credible evaluation in patients with the recent onset of TIA and frequent (crescendo) TIA and in patients who have experienced a recent minor ischemic stroke.

4. Antispasmodics, "Brain Oxygenators," and "Metabolic Enhancers"

There are no scientifically acceptable studies demonstrating that antispasmodics, brain oxygenators, and drugs claimed to increase brain blood flow or metabolism are of value in stroke prevention. Such drugs are expensive, and their use is to be discouraged.

D. Treatment of Patients Following Recent Ischemic Stroke

Considerable research is under way to examine treatments that may reduce the extent of brain damage when prolonged symptoms indicate that ischemia has been succeeded by infarction. Neither surgical nor pharmacologic reports to date can claim that any animal model results can be translated into clinical benefit. No clinical trials on any particular drug have been uniformly successful, and further extensive experimental and clinical observations are required. Meanwhile, the following therapeutic recommendations are suggested:

Fluid and electrolyte balance must be maintained.

Adequate airway, good pulmonary function, and sufficient cardiac output must be maintained. Oxygen therapy should be employed only in the presence of decreased oxygen blood levels, a sequel to ventilatory or cardiac complications.

Appropriate blood pressure: Maintenance is of major consequence. Hypotension in ischemic stroke is rare except when there is coincident manifest or silent myocardial infarction. When hypotension is recognized, volume expanders in the form of plasma or low-molecular-weight dextran may be used to restore and maintain normotension. Acute pulmonary edema is a complication of the administration of volume expanders. Furthermore, such agents are expensive biologicals and are seldom necessary because blood pressure tends to rise after an acute stroke and spontaneously declines gradually thereafter. The routine use of volume expanders after a stroke is not justified by recent hemodilution studies. Emergency treatment of hypertension during the acute stage of ischemic stroke may cause precipitous and dangerous reduction in blood pressure, accompanied by a fall in cerebral perfusion. Hypotensive agents should be used only with great caution when blood pressure reaches >120 mm Hg diastolic, when the diagnosis of hypertensive encephalopathy is reasonably certain (including other end-organ evidence of malignant hypertension), or in the event of dissection of the aorta.

Glucose infusion is to be avoided. Hyperglycemia is associated with increased infarction. Nutrition by mouth or by nasogastric tube is preferable.

Anticonvulsant therapy should be given in the event that a patient experiences repeated seizures. Either 100 mg phenytoin sodium (Dilantin [Parke-Davis, Morris Plains, New Jersey]) t.i.d. or 200 mg carbamazepine t.i.d. is satisfactory. The need to maintain anticonvulsant therapy should be reviewed before the patient is discharged from the hospital; if continued, the anticonvulsant regimen should be evaluated at 4-month intervals.

Antiedema agents: In the presence of increasing drowsiness or evidence of signs of uncal herniation, the judicious usage of a short period of mannitol or glycerol therapy is recommended. This therapy is based largely on anecdotal evidence, and thus its use remains empirical.

There are a number of strategies that are not recommended for routine use in the presence of a recent major cerebral infarction. Ongoing research may change the following recommendations, but for the time being they appear to be the best that can be given:

Steroids are of no value. There is good experimental and clinical evidence that steroids could be more harmful than helpful.

Anticoagulants and platelet inhibitors are not useful, nor has prostacyclin been helpful in reducing the extent of damage produced by acute ischemic lesions.

Fibrinolysins are unproven. Particularly tissue plasminogen activators, these compounds are still in the experimental stages. Except in carefully controlled clinical studies, fibrinolysins should not be administered to patients with cerebral ischemia until careful trials addressing the question of benefit have been concluded.

Vasopressors, vasodilators, "brain oxygenators," and "metabolic enhancers" are of no proven benefit. These agents can be harmful.

Reduction of cerebral metabolism and free radical scavenging have failed to show benefit. Barbiturate coma and hypothermia are not recommended. Carefully controlled clinical observations must be continued in such instances.

Opiate antagonists and pentoxifylline have been shown to be not useful in stroke.

Calcium channel blockers, fluorocarbons, and N-methyl-D-aspartate (NMDA) antagonists are
under investigation but are not recommended, based on current knowledge.

E. Treatment of Patients Deteriorating With Ischemic Stroke

Clinical progression while under close surveillance occurs in 20–30% of stroke victims. It cannot be assumed that deterioration represents the progress of thrombogenesis nor that deterioration is due to further thromboembolism. This may be the case, but many other mechanisms (such as deterioration of pulmonary or cardiac function, hyponatremia with inappropriate antidiuretic hormone secretion, dehydration, hypotension, or a combination of these factors) will cause progression. Progressing stroke is commonly associated with drowsiness and with CT evidence of the development of cerebral edema surrounding the infarct.

Using mannitol or glycerol to reduce putative or proven cerebral edema in the presence of ischemic lesions has not been demonstrated to be beneficial in clinical trials. Therefore, mannitol or glycerol should be administered only with caution in a deteriorating patient, assuring the maintenance of fluids and electrolytes to replace their loss from diuresis. Steroids should not be given.

Anticoagulants have been incompletely tested in progressing stroke. Recent studies including one small randomized trial leave persisting uncertainty about the benefit of anticoagulants. Further trials are indicated and are urgently needed because the hazards of this therapy are real. When the progression of an ischemic stroke proceeds in a step-wise fashion, successive thromboembolism or extending thrombosis may be occurring. Under these circumstances and if it is certain that cerebral hemorrhage is not present, the empirical and cautious use of heparin followed by warfarin is recommended as an empirical therapy.

F. Medical Management of SAH

The early medical management of a patient who has suffered an SAH because of a ruptured aneurysm or a ruptured AVM has not become standardized. There are several reasons for this uncertainty, including the protean nature of the responses to blood in the subarachnoid space and the lack of sufficiently large controlled trials to evaluate properly the various treatment possibilities. Early deaths or disability after aneurysm rupture are due to 1) damage from the initial hemorrhage, 2) recurrence of bleeding, and 3) extension of brain damage by infarction often associated with vasospasm. The recommended goal of all early medical treatment is to assure that the patient will be fit to go to the operating room for definitive eradication of the ruptured aneurysm. The surgeon is faced with uncertainty about the optimum time (early versus late) to surgically clip the aneurysm. No studies have been conducted regarding the optimum time to eradicate AVMs, even if their size and location make this possible. Thus, the physician should attempt to stabilize the patient and, if possible, to prevent rebleeding. The risk of rebleeding is approximately 20% during the first 10 days after an SAH. Medical management should include the following:

**Bed rest and quiet** are conventional recommendations. Although this regimen has not been shown to confer real benefit in terms of rebleeding or vasospasm, it will avoid some exertional and emotional elevations of intracranial and systemic blood pressure. Supervised toilet privileges for bowel evacuation are extended to these patients, and stool softeners are recommended to prevent straining.

**Fluid and electrolyte balance** must be maintained. Inappropriate antidiuretic hormone output must be recognized and treated if it develops. Because these patients also have salt wasting and are already dehydrated, there should be cautious fluid restriction. Dehydration should be avoided because the risk of ischemia increases.

**Hypervolemic hemodilution** and drug-induced hypertension are recommended with careful monitoring in patients exhibiting vasospasm and accompanying signs suggestive of cerebral ischemia. The risk of rebleeding exists with this strategy. This vigorous therapy also is accompanied by the risk of congestive heart failure or cardiac ischemia.

**Calcium channel blockers**: The evidence supporting the use of oral and systemic calcium channel blockers is incomplete. Nimodipine, nicardipine, and similar agents are under study with the possibility of promise in the near future.

**Antifibrinolytic drug therapy**, such as with aminocaproic acid, remains controversial. Such therapy has been shown to reduce the risk of rebleeding during the dangerous first 2 weeks; this therapy is not effective for 2–3 days unless a loading dose is given. Most available data have not employed a loading dose, but rather a continuous infusion. Unfortunately, the reductions in disability and death due to rebleeding are offset by an increase in the number of patients who suffer from cerebral infarction. The combination of antifibrinolytic drugs and calcium channel blockers may prove useful in preventing both rebleeding and ischemia after aneurysmal SAH, but the present evidence is anecdotal. As is common with all other programs of drug treatment in SAH, management methods require further extensive studies.

**Hypertension**, if persisting, should be gently controlled, taking care not to induce hypotension.

V. Surgical Treatment for Occlusive Cerebrovascular Disease, Intracerebral Hematoma, and SAH

A. Carotid and Vertebrobasilar Endarterectomy

Between 1954 and 1988, approximately one million carotid endarterectomies were performed worldwide for patients with obliterator extracranial carotid artery atheroma. The procedure has been
who Stroke Prevention, Diagnosis, and Therapy 1425

Carotid endarterectomy is a prophylactic operation performed with the single goal of preventing cerebral ischemia in the territory of the artery subjected to the procedure. A listing of indications in which carotid endarterectomy has been proven beneficial in this regard is difficult because the only large randomized trial that was carried out in symptomatic patients found the procedure to be no better than the best medical care available. Improved surgical technique and better anesthesia might have been able to swing the balance between the risk of the lesion and the risk of perioperative complications in favor of surgery. However, this negative result has not been unequivocally accepted. As a result, major clinical trials with randomly selected age-matched populations have been initiated in Europe and in North America to evaluate the benefit of carotid endarterectomy in both symptomatic and asymptomatic patients.

While awaiting the results of these large trials, it has become increasingly evident that surgical, medical, anesthetic, and radiologic expertise must all be included when making the decision for carotid endarterectomy. Also, the risks of the operation must not outweigh the probable natural consequences of the pathologic process. Because there will inevitably be an immediate worsening of prognosis as a result of the mortality and morbidity associated with any surgery, the life expectancy of a patient must be sufficiently long to enable the subsequent improvement following carotid endarterectomy to be significantly greater than that of the natural morbidity and mortality of carotid atheroma. Recognizing the empirical nature of the recommendations, the following indications are provided as a working guide to using carotid endarterectomy at the present time for symptomatic patients:

**The patient** should have experienced attack(s) of ischemia, retinal or hemispheric, or have had a partial nondisabling ischemic stroke in the territory of a carotid artery that has been shown by angiography to be the site of stenosis or ulceration or both. **The extracranial disease** must give the appearance of being more significant than that in the intracranial portion of the artery. This will be an arbitrary decision, taking into account the length and degree of the stenosis as well as the amount of irregularity and ulceration.

Every institution in which carotid endarterectomy is performed must have a record of performance of the procedure confirming a 30-day perioperative stroke morbidity and mortality of ≤6%. Even under ideal operating conditions, a patient should not be subjected to even this level of risk if any of the following conditions are present:

- Evidence of serious, irreparable, or progressive renal, hepatic, pulmonary, or cardiac function failure.
- Uncontrolled diabetes mellitus or unregulated arterial hypertension.
- Cancer that confers a low 5-year survival.
- Cardiac condition that can reasonably be expected to have been the source of the cerebral ischemic event(s).

Symptoms are of unknown origin, are contralateral to the artery producing the symptoms, or are in the vertebrobasilar artery territory. **Artery** is known to be occluded. **No surgical therapy** for symptomatic carotid artery disease can be recommended as an exclusive alternative to careful attention to risk factors and the use of antithrombotic measures.

The question of carotid endarterectomy for asymptomatic disease is difficult to endorse without major reservations. A recent survey conducted in North America in the large and most experienced academic centers indicates that the average center experiences a 5% major permanent morbidity and mortality rate when asymptomatic patients undergo carotid endarterectomy. The possibility exists that within this group there are patients who are known, by serial noninvasive studies, to have had progression of stenosis to a severe (≥80%) degree who might, in the hands of experienced and expert surgeons, benefit from carotid endarterectomy. Fortunately, two major trials that are seeking a definitive answer for this type of patient are under way. Consequently, carotid endarterectomy for asymptomatic patients is not recommended at this time except as part of a controlled clinical trial or other scientifically meritorious experimental procedure.

There are no good data to support the use of corrective surgery in the proximal or distal portions of the vertebral artery, even in patients afflicted with continuing vertebrobasilar symptoms. The morbidity and mortality reported to date are unacceptably high. Furthermore, the cervical anastomotic
network provides efficient alternative blood flow in the presence of stenosis or occlusion of the proximal vertebral arteries.

**B. EC/IC Bypass Surgery**

This treatment strategy was introduced in 1967, and many anecdotal reports have since emerged. A multicenter, randomized study was conducted with patients having clinical evidence of transient ischemic events or minor stroke in the territory of a stenosed or occluded MCA or a stenosed or occluded ICA not amenable to or accessible by endarterectomy. EC/IC bypass surgery can no longer be recommended for this type of patient for the following reasons:

*Survival:* The surgical patients survived stroke-free less often than did those in the nonsurgical group.

*Benefit:* No subgroup in the trial was shown to benefit from EC/IC bypass surgery compared with completely comparable control groups.

*PET studies:* Subsequent careful studies by positron emission tomography (PET scanning) of patients with similar radiologic lesions and with definite evidence of hemodynamically compromised circulation have not confirmed the expectation that such patients constitute a subgroup that would benefit from EC/IC bypass surgery.

*Controls:* No series of patients with a control population have been published to contradict the negative conclusions of the Collaborative EC/IC Bypass Study.

With recognition of concerns about the characteristics of patients who were not included in the trial, the conclusion is that EC/IC bypass surgery does not prevent stroke.

Two remaining groups of patients in whom the procedure may be of value need further careful study. First, the performance of EC/IC bypass may be useful as a prelude to the deliberate ligation of a major cerebral artery to deal with a large aneurysm or a basal vascular tumor. Second, the gradual loss of blood flow through the terminal branches of the ICA that occurs in moyamoya disease makes the evaluation of a possible benefit from bypass revascularization a rational project for further careful study.

**C. Intracerebral Hematoma**

Intracerebral hematoma presenting as either an acute hemiplegic episode or a gradually progressive hemiparesis over some 12 hours has been addressed by conservative nonsurgical and surgical methods. No consensus as to the relative success of nonsurgical and surgical treatments has yet been reached.

During the acute period, however, there is no debate. A major requirement is the maintenance of a free airway, usually by intubation and under certain circumstances by tracheostomy. $\text{Paco}_2$ is thereby controlled, cerebral congestion is avoided, and blood gases are stabilized. Prolonged periods of unconsciousness can be expected, and under that circumstance nasogastric tube feeding should be instituted.

The management of arterial blood pressure is less contentious in intracerebral hematoma than in acute ischemic stroke. A moderate reduction of arterial blood pressure in these usually hypertensive patients is advised. Serial electrolyte balance should be carefully maintained; cardiac embarrassment should be controlled with diuretics and by the control of cardiac dysrhythmia. The use of antiedema drugs such as mannitol and glycerol is not advisable. These drugs act on normal brain, and having shrunk normal brain they encourage further expansion of the hematoma.

There is no agreement on the indications for surgical treatment of supratentorial hematoma. For a patient with a large central hematoma in the dominant hemisphere, the outcome (the production of coma and hemiplegia) cannot be improved by any medical or surgical regimen. There is general agreement that a large lobar hematoma with hemispheric shift and tentorial herniation is suitable for urgent evacuation by open operation. The management of deep central hematomas without shift in either hemisphere remains less certain. Most authorities regard such hematomas as best treated conservatively.

The management of cerebellar hematomas has changed in recent years. Patients presenting acutely with signs of brainstem compression and coma demand urgent surgery, although ultimate satisfactory outcome in these cases is uncommon. In the CT scan era, however, it has emerged that ingravescent cerebellar hematomas are not uncommon, such patients presenting with perhaps an initial ictus followed by gradual deterioration. In the absence of hydrocephalus or brainstem compression, these patients may be well-managed conservatively. Where hydrocephalus is present, however, surgical evacuation is usually attended by resolution of signs of compression and encouraging recovery.

Hematomas of the brainstem at the present time remain open to either conservative or surgical management. Case series have demonstrated appreciable recovery following open operation or stereotactic aspiration, but it remains unclear whether conservative management would not have produced the same results in terms of either survival or residual neurologic deficit.

**D. Surgical Management of SAH Arising From Aneurysm and AVM**

Between 5% and 10% of "strokes" are more properly classified as SAH. Two of the main causes of SAH are aneurysms and AVMs, both of which are potentially treatable lesions. In the middle decades of life, aneurysm is the most probable cause of SAH. In the fifth decade (40–49 years of age), the frequency of aneurysm is nearly twice that of other causes and >25 times that of AVM. The frequency of AVM as a cause of SAH equals that of aneurysms during the second decade; in patients older
Table 4. Classification of Patients With Intracranial Aneurysms According to Surgical Risk

<table>
<thead>
<tr>
<th>Grade</th>
<th>Category*</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Asymptomatic or minimal headache; slight nuchal rigidity</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Moderate to severe headache; nuchal rigidity; no neurologic deficit other than cranial nerve palsy</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Drowsiness, confusion, or mild focal deficit</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Stupor; moderate to severe hemiparesis; possible early decerebrate rigidity; vegetative disturbances</td>
<td></td>
</tr>
<tr>
<td>V</td>
<td>Deep coma; decerebrate rigidity; moribund appearance</td>
<td></td>
</tr>
</tbody>
</table>

*Serious systemic disease (such as hypertension, diabetes mellitus, severe arteriosclerosis, chronic pulmonary disease, and severe vasospasm seen on arteriography) results in placement of patient in the next higher grade.

There is general agreement that the risks of surgery in patients with SAH from intracranial aneurysm are closely related to the condition of the patient at the time of surgery. A simple classification has been adopted that enables the comparison of data from one clinic with that from another. If the grade of surgery in relation to the occurrence of SAH is noted, one can then calculate the surgical contribution to survival compared with natural mortality (Table 4). Because of improved surgical techniques, improved anesthesia, and improved patient management, surgical mortality has declined significantly compared with natural mortality in Grades I, II, and III (most particularly in Grade III). Evidence of improvement in relation to surgery is less impressive in Grade IV, and surgery is less frequently undertaken in such patients.

Assessment of the comparative morbidity of conservative and surgical treatment is more difficult, largely because of inadequate information concerning the natural history of SAH and its morbidity. It is regrettable to note that a proportion of surgical survivors are intellectually or physically handicapped. The general surgical experience has been that unsatisfactory results, including death, are common in high-risk cases.

2. Timing of Investigation and Operation in Cases of Aneurysmal SAH

The advent of CT has added a new dimension to the analysis of SAH. When available, CT scanning should be performed immediately when a patient with a working diagnosis of SAH is admitted to the hospital; immediate information as to the presence of hematoma is thus obtained. In addition, a CT scan provides information on the amount and distribution of blood in the subarachnoid space, together with the presence of any low-density regions, suggesting ischemia that may appear within a few days after the SAH. From the distribution of blood, the approximate site of an aneurysm may be defined. The amount of blood in the subarachnoid space correlates well with the development of episodes of reduced perfusion, often referred to as vasospasm.

Operating on intracranial aneurysms following SAH cannot be undertaken in all patients immediately after they present in a clinic. It follows, therefore, that if immediate surgery is not to be undertaken in all patients, one must first decide about the propriety and extent of angiographic investigation. If a patient’s overall condition is appropriate for general anesthesia, early angiography facilitates subsequent discussions of surgery even in poor-grade patients. Careful angiography performed by skilled radiologists early after SAH has not contributed significantly to morbidity or mortality. The question of the extent of angiography must also be determined. Here, CT scan data are of considerable value. If the distribution of blood clearly indicates a supratentorial lesion, then bilateral carotid angiography alone is probably all that is required. It is best, however, to arrange four-vessel angiography in patients younger than age 60 so that a full delineation of other possible sites of aneurysm may be made. In the elderly, vertebral angiography should be omitted if CT scan, clinical evidence, and angiography all point to an accessible supratentorial origin. It is wise in all subjects to perform bilateral carotid angiography to eliminate any possible anomalies in the circulation that might alter management at the time of surgery.

Having established the site and accessibility of the aneurysm responsible for an SAH, the question of the surgery’s timing arises. Surgical intervention should not be undertaken in Grade IV or V patients early after SAH, unless an intracranial hematoma appears to be life-threatening; in this circumstance, a judicious burr hole with evacuation of the clot may improve the patient’s condition sufficiently to warrant further surgery later. However, the mere presence of an intracranial hematoma does not demand its immediate evacuation. Changes in intracranial pressure may provoke further rupture of aneurysms, so if a patient’s life is not threatened by the intracranial hematoma and if the condition appears to be improving, it is best to leave the hematoma alone. The presence of a moderate-sized hematoma may well enhance the accessibility of an aneurysm at the time of definitive surgery and may make the entire procedure technically easier to accomplish. Grade V patients should not be subjected to surgery at all unless a life-threatening hematoma is present. Any surgery after the first week should be undertaken only after due deliberation as, for example, in younger patients with reasonable prospects of a worthwhile long-term neurologic recovery. Patients older than age 60 in Grade V are probably best left unoperated.
In Grade I or II patients, there is little justification for delay since such patients will probably get worse if bleeding recurs. There is little doubt that in skilled hands at this time, mortality from surgery in patients of Grades I and II is appreciably lower than is the risk of recurrent hemorrhage. Grade II patients who are stable over 48 hours or patients who show signs of improvement from Grade III, merit surgery as soon as it can be arranged. Surgery should be delayed in Grade III patients if there is very marked neck stiffness, very heavy blood staining in the CSF, or if there are large quantities of blood visible on the CT scan. These patients are more likely than others to develop extensive vasospasm following surgery.

E. Some Recent Advances in General Management Techniques

1. Technical Surgical Changes

There have been two principal changes in surgical techniques in recent years. The first of these is the development of the torsion bar clip, in which the clip is applied to the neck of the aneurysm, not with the surgeon's musculature under active contraction, but with a relaxing grip. The likelihood of the neck of the aneurysm being torn by the vibration of muscular tremor is markedly reduced by this development. The difference in muscular effect is quite striking and justifies the complete abandonment of clips that are not applied by relaxation of the surgeon's hand.

The second major technical advance is the increased use of an operating microscope. The advantages of the microscope technique are 1) excellent illumination, 2) early recognition of field detail and accurate delineation of blood vessels, 3) increased safety in clip placement because of clear vision and dissecting ease, and 4) minimal retraction necessary to satisfactorily complete the operation. Self-retaining retractors with constant and gentle pressure enable dissection of difficult sites, such as the anterior communicating complex, under direct vision and minimal distortion of neuraxial structures. There is no doubt that the magnification and intensity of illumination enable recognition of blood vessel detail behind the covering arachnoid so that accurate dissection through the arachnoid results, rather than the previous tentative opening, hoping to avoid important underlying vessels.

2. Other Possible Surgical Maneuvers in the Treatment of Intracranial Aneurysms

Previously, carotid ligation was widely practiced, particularly to treat terminal carotid artery aneurysms. However, rebleeding occurred subsequently from aneurysms at the origin of the posterior communicating artery from the ICA. The aneurysms had remained patent through collateral supply from either the vertebrobasilar system or from the opposite ICA. Increasing experience with intracranial surgery has encouraged the majority of medical centers to directly attack these aneurysms. Carotid ligation is reserved only for aneurysms in the region of the terminal carotid artery closely involved with perforating vessels, where there are major technical surgical difficulties and appreciable risks of morbidity.

Other techniques that have been used or are under study include 1) piloinjection (i.e., injection of bristles by a special apparatus) at craniotomy, particularly in treating very large aneurysms; 2) endoaneurysmorrhaphy by fine copper needles; 3) obliteration of the aneurysm by injecting iron filings, the positions of which are maintained by a magnet; 4) endovascular balloon occlusion; and 5) stereotactic clipping of vessels. None of these methods have obtained widespread acceptance, and permanent occlusion of giant aneurysms is not reliable.

3. Treatment of SAH From AVM

Although there is presently no conclusive proof that the surgical management of SAH from an AVM is associated with a lower mortality than the death rate by natural rebleeding, the experience of several large series suggests that this is so. Indeed, it does not appear that complete excision of an AVM is the most satisfactory treatment following the presentation of such a lesion with SAH or intracerebral hemorrhage. Even where AVMs are close to major vessels, so that extensive feeding arteries pass straight into the AVM from major portions (for example, of the MCA), careful dissection under an operating microscope in association with hypotensive anesthesia will result in these lesions being accessible to dissection in an increasing proportion of patients, with an acceptable mortality. This conclusion cannot be applied in all cases since the location of a lesion within or involving the brainstem or its inaccessibility in deep structures make surgical treatment impossible. Careful angiography, however, may demonstrate that even in such infratentorial lesions, which at first sight appear to involve important arteries supplying the brainstem, the AVM may be entirely extracerebral and removable by meticulous dissection under the microscope.

Overall, surgical series tend to divide themselves into those cases that are considered operable by the surgeon and those that are not. It is scarcely fair to compare the two groups to indicate a superior mortality for surgery when selection has already been applied. Generally, it is wise to avoid surgery for an asymptomatic AVM or when the symptoms are those of an occasional convulsion that may be adequately controlled by anticonvulsants. Otherwise, in the case of SAH as a presenting feature surgery should be considered, provided adequate anesthesia and meticulous techniques are used.

There is general agreement in the management of AVMs that, with the rare exception of occasional deep lesions feeding from single vessels, ligation of the feeding vessels is not beneficial. Ligation is almost invariably followed within a short time by refilling of the angioma from feeding vessels that were not
visualized on the original angiogram; similar restrictions apply to the previous practice of carotid ligation. More recently, embolization of portions of AVMs, thermocoagulation by stereotactic techniques, or operative excision after partial obliteration of the lesion by cryosurgery have been suggested. Progressively more refined techniques have enabled the introduction of small emboli deep in AVMs, in both the supratentorial and infratentorial regions, or even the endovascular catheterization of the feeding vessels of such lesions and their obliteration by rapidly setting cyanoacrylate or Silastic compounds. These techniques must be regarded as under investigation and have so far yielded acceptable results, principally in the hands of their developers.

VI. Rehabilitation After Stroke

Rehabilitation of stroke victims is an important medical and social need. The sequelae of stroke present themselves in the form of neurologic, cognitive, and behavioral disorders. These deficits can lead to a considerable degree of physical disability and social maladjustment in patients who are often unable to carry out the activities of daily living without assistance. Within a few hours to a few months after a stroke, a large proportion of stroke victims spontaneously experience partial or, on occasion, complete reversal of neurologic symptoms. However, rehabilitation is intended to assist in and accelerate the recovery of impaired functions. Retraining and the use of prosthetics can help disabled patients better use their personal and environmental resources and increase participation in activities of daily living.

The aims of rehabilitation are 1) improvement of motor, speech, cognitive and other impaired functions; 2) mental and social readaptation of patients to restore functional autonomy, social activity, and interpersonal relationships; and 3) where possible, a return to the activities of daily living. Although most clinicians believe that rehabilitation therapy is beneficial, the relative contributions of spontaneous compared with assisted recovery have yet to be satisfactorily determined. Thus, most rehabilitation strategies and the reports of their role in the improvement of function are based on clinical experience and not on scientific evaluations using controlled trials.

Since rehabilitation can be costly, the development of improved criteria for selecting patients for intensive rehabilitation is of the utmost importance. Such selection should be based on the prognosis of the recovery of function(s) in three groups of patients: 1) patients who spontaneously make good recovery without rehabilitation, 2) patients who can make satisfactory recovery only through intensive rehabilitation, and 3) patients with poor recovery of functions irrespective of the type of rehabilitation. Rehabilitation should address those in the second group above. Selecting patients for rehabilitation and selecting the methods to be used must also take into account contraindications, such as serious systemic diseases (cardiac insufficiency with decompensation, angina pectoris, acute renal insufficiency, an active phase of rheumatism, etc.) and severe mental disorders, that might be present. Additional studies to establish meaningful criteria for selecting patients for intensive programs of rehabilitation are necessary and should receive high priority.

A. Factors That Influence Recovery of Impaired Functions

Most investigators consider the site and size of a brain lesion to be the single most important determinant of both the nature and severity of a functional defect as well as the probability of functional recovery. In research studies, the availability of CT, NMR or MRI, and PET have made it possible to ascertain the location, size, and metabolic status of the stroke lesion; in clinical practice, CT scanning can assist in anatomically defining a lesion and in estimating prognosis. A definite relation has been established between the severity of motor impairments, the location of a cerebral lesion, and the degree and rate of restoration of movement. The most serious impairments, combined with poor recovery, are associated with large lesions and with lesions in the area of the posterior limb of the internal capsule. If a lesion occurs outside the main motor regions and tracts of the brain, improvement of motion is often rapid and sometimes considerable.

Serious speech defects are the result of a cerebral infarct affecting the cortical-subcortical formation of two or three critical areas of the dominant hemisphere, usually the left hemisphere. When a lesion is small, even if it is situated in Broca's area, there is often considerable recovery of speech.

The initial severity of a neurologic deficit is an important predictor of the degree of recovery. If dense hemiplegia occurs during the acute phase of the stroke, recovery will be slower and less complete than if there is only mild hemiparesis. However, in a number of cases, the development of a neurologic deficit occurs not so much from destruction of functionally significant brain sites as from dysfunction in neighboring areas. Under this condition, there can be considerable recovery from even an initially severe deficit.

When added to the motor deficit, other neurologic impairments can adversely affect recovery. For example, a recent study has found that most patients with only a motor deficit can be expected to be independently ambulatory within 14 weeks after the stroke; patients with combined motor and sensory deficits have a 35% probability of independent ambulation within 18 weeks after a stroke, but they have little probability of later independent ambulation if it has not been achieved by 18 weeks; and patients with a combined motor, sensory, and visual field deficit have little probability of independent
ambulation, but they can be expected to walk with assistance within 28 weeks. Most experts agree that the late beginning of return of function (≥3 weeks after the stroke) is a poor prognostic sign.

There is no consensus on the influence of age on the recovery of function. Some consider that recovery of function in the elderly is very limited, whereas others discount the significance of advanced age as a critical factor. Age is certainly significant in the mental and social readaptation of patients; the younger the patient, the better the readaptation. It is generally agreed that there is no difference between males and females in the likelihood of recovery of impaired functions after stroke.

The status of cognition and higher mental function is one of the significant factors affecting the degree and rate of recovery, especially of complex motor functions (e.g., walking and self-care) and the social readaptation of patients. When behavioral syndromes result from large lesions in the right hemisphere or the frontal lobes, the level and rate of recovery of complex motor functions is greatly reduced. Many investigators agree that the depression that develops in 20–40% of stroke victims has no substantial influence on the overall recovery process; this is believed to be true irrespective of whether the depression is a direct result of the cerebral lesion or an emotional reaction to the physical and cognitive incapacity.

Several authors have found that there may be relatively poorer recovery of complex motor functions among patients with a lesion in the right hemisphere. This is because such a lesion can lead to underestimation or denial by the patient of the motor defect (anosognosia) because of damage to the body image and may result more frequently (compared with damage to the left hemisphere) in underutilization of the affected limbs. Left-handedness is a positive factor in the recovery of speech. When the speech centers of a left-handed person are affected, there is either no aphasia or a rapid improvement in speech. It is rare to find speech disorders in a left-handed person who has suffered damage to the right hemisphere.

Other factors that impede recovery of movement, walking, and other motor skills are spasticity and occasionally flaccid muscular hypotonia, loss of muscular and articular sensation leading to arthropathy in paralyzed extremities (such as the shoulder-hand syndrome), loss of bladder control, and hemianopsia. Serious systemic illness (cardiac and/or pulmonary insufficiency, frequent angina attacks, etc.) will hinder therapy and will negatively affect the recovery of motor function and the social readaptation of patients.

There is a lack of convincing evidence about the influence of social status (occupation, level of education, role in the family) on recovery from stroke. A number of authors claim that poor education and living alone hinder recovery of impaired functions, whereas other authors deny this. Occupation and level of education seem to be important only in the recovery of fitness for employment. Additional research is needed in these areas.

The cumulative effect of repeated strokes on physical and mental activity may be disastrous; an example is the dementia that can result from repeated stroke. However, there is no predictably consistent effect of previous stroke on the recovery of impaired function.

B. Basic Principles of Rehabilitation

The basic principles of rehabilitation are 1) carefully select the patient, 2) begin early, 3) be systematic, 4) build up in stages, and 5) include the types of rehabilitation treatment specific to the deficit.

An early start to rehabilitation, such as passive limb motion, is particularly important. Encouraging early activity helps prevent thromboembolic and pulmonary complications.

There is no consensus among authorities as to the duration of rehabilitation therapy. A period of gradual recovery of function can last from 3 months to 2 years. In aggregate, experience indicates that the probability of further improvement of movement in paralyzed extremities and of the ability to walk decreases after 6 months, whereas significant improvement of speech, domestic and working skills, and steadiness (where ataxia occurs after the stroke) can continue for up to 2 years. Thus, careful monitoring of a patient’s progress is the best available index for judging when to discontinue rehabilitation therapy.

Because the course of rehabilitation therapy must be systematic and can be relatively lengthy, the type and intensity of rehabilitation must be instituted in stages. Therapy can be done at home, in community outpatient clinics, in local hospitals, or in specialized rehabilitation units. One example of a national stroke rehabilitation program using many sites is the rehabilitation system developed in the Soviet Union. It consists of a three-stage system of therapy: 1) rehabilitation begins while the patient is in the general neurologic hospital (or in a special ward for the treatment of a cerebrovascular incident) to which the patient has been brought on the day the stroke occurs, 2) 3–6 weeks later, the patient is transferred to an inpatient convalescent ward for stroke victims or to an inpatient rehabilitation center, and 3) those patients who still require rehabilitation services after discharge from the inpatient unit are treated on an outpatient basis in a rehabilitation polyclinic or in the rehabilitation department of a polyclinic; patients who might return to work are treated in a rehabilitation sanatorium. Many patients with speech impairment or ataxia are given additional treatment in rehabilitation hospitals or polyclinics.

Some authorities state that the recovery of function in stroke victims is better when rehabilitation services are provided in specialized wards and in rehabilitation units designed specifically for stroke.
patients. This matter is still under debate among rehabilitation experts. However, as important as specialized rehabilitation facilities are, it must be emphasized that many rehabilitation techniques can be carried out by family members at home. Instruction of the family and the patient by a rehabilitation therapist, with regular monitoring of results, can accomplish a great deal for both the patient and the social situation in the family.

Rehabilitation can include a wide range of measures aimed at stabilizing the defect and restoring impaired function(s). In cases of speech impairment, the involvement of a speech therapist (logopedist-aphasiologist or psychologist) can be important.

For motor disturbances, rehabilitation involves methods designed to improve control, to restore a range of movements, and to regain muscle power. All of the therapies used and listed below are empirical in that rigorous trials have not been conducted to evaluate their usefulness. Therapies may include kinesiotherapy (e.g., gymnastic therapy, training in walking), biofeedback, and electrical stimulation of the nervous and muscular systems. For reduction of spasticity, methods include muscle relaxants, selective gymnastic therapy in conjunction with point massage and autogenous training, cryotherapy, heat therapy, position therapy, alcohol-procaine blockade of the area of the spastic muscles, and acupuncture. Treatment of painful joints of paralyzed limbs (poststroke arthropathy) may include heat treatment, massage, and pain-relieving electrical impulse therapy. Improved function can be anticipated for permanently disabled patients with the use and further development of a variety of biophysical apparatuses and prostheses.

Rehabilitation should also include occupational therapy aimed at readaptation to everyday life and using an individualized selection of occupational and home activities that take into account the functional abilities and skills of a patient.

Psychological therapy can be important in rehabilitation since a variety of behavioral disturbances can develop in stroke victims. Apathy, depression, indifference or opposition to treatment, and incipient neurosis all require attention.

Working with a stroke patient’s family is essential. Family therapy helps establish a beneficial rapport between the patient and his or her relatives, aids in resolving family conflicts, and tries to ensure that in spite of impairment the patient is regarded as being of value to the family. In addition to harmonizing relationships within the family, family therapy involves family members in the rehabilitation process, teaches them how to help the patient to acquire self-help skills, and enables them to carry out exercises designed to assist in the recovery of movement, speech, reading, and writing.

C. Social Consequences of Effectiveness of Rehabilitation Following a Stroke

Stroke can have serious medical and social consequences including motor, speech, and mental impairments of the patient and disruption of the family and social and occupational activities. A considerable proportion of stroke patients experience significant recovery from impaired functions, acquiring self-help skills, the capacity to work, and other social activities. By the end of the first year, approximately 60% of all surviving stroke victims need no assistance for activities of daily living, 20% require help only for complex tasks such as bathing, 15% are more dependent on others for help, and only 5% are totally dependent on others. Also, approximately 30% of stroke survivors of working age are able to return to work within 1 year after their stroke. Thus, recovery of function can be substantial.

All experts agree that specific techniques of rehabilitation for a stroke victim must be considered and initiated and that the results must be carefully monitored if the patient is to be assisted in returning to the activities of daily living. Rehabilitation can be inappropriately continued for extended periods of time, with little probability of future results and at great expense to the patient and the community. To avoid this, rehabilitation therapy must be planned carefully and the patient’s progress must be evaluated regularly.

As stated earlier, most of the methodologies used in rehabilitation are based on clinical experience and have rarely been evaluated in controlled clinical trials. Such trials are essential if the role of rehabilitation, its indications, and its contraindications are to be more adequately understood.

Stroke. 1989;20:1407-1431
doi: 10.1161/01.STR.20.10.1407

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1989 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/20/10/1407.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org/subscriptions/