Progress in Cerebrovascular Disease

Management of Patients with Established ("Completed") Cerebral Infarction

FERDINANDO BUONANNO, M.D. AND JAMES F. TOOLE, M.D.

SUMMARY Management of patients with sudden neurological deficit must be based on complete knowledge of the underlying cause. In about 80% of such patients, a careful history and examination will lead to a precise etiologic and anatomic diagnosis. If the deficit is vascular in etiology, therapy and prognosis depend on its stage of evolution.

Definition of Terms

BY ARBITRARY DEFINITION, focal neurological deficit due to vascular disease which resolves in less than 24 hours is called a transient ischemic attack (TIA); one that exceeds this length of time is attributed to infarction or hemorrhage. Some neurologists distinguish another category, in which a neurological deficit lasting more than 24 hours eventually resolves completely — usually within 3 weeks. This has been termed a reversible ischemic neurological deficit (RIND). It is postulated that this situation results from sustained ischemia not severe enough to produce infarction.

To be considered as established, or completed, an infarction in the brain supplied by the carotid system must be static for at least 24 hours; one in the brain supplied by the vertebrobasilar arterial system, for 72 hours. If new symptoms or signs develop during this period, the original episode is regarded as an evolving (progressing) infarction.

Established or completed refers to the sequence of events and does not imply that a neurological deficit is as severe as it can become, but indicates that infarction has remained unchanged. For example, in a right-handed patient with an established infarction in the distribution of the left middle cerebral artery there may be no asphasia. Because it is still possible for the infarction to extend within this vascular bed, the question is whether prophylaxis following the first episode can prevent this.

These definitions are retrospective and arbitrary but because they form a framework with which to link pathophysiology and clinical events, they are important when one is comparing groups of patients and different types of therapy. TIA and RIND suggest ischemia with preserved viability; established and completed infarction, death of tissue.

Emergency Management

With rare exceptions, patients with an infarction must be admitted to the hospital as emergencies. If the patient is in coma or comatose, management geared towards the maintenance of life must be initiated before he is evaluated for cerebral infarction.

If there are signs of increased intracranial pressure, the head of the bed should be elevated; otherwise, the patient should lie supine or, if he can tolerate it, prone in the Trendelenburg position with his head turned to one side.

Immediate differentiation between cerebral hemorrhage and infarction is mandatory, because the 2 conditions require entirely different types of management and therapy.

Diagnostic Evaluation

In order to complete all essential tests within 12 hours, the following procedure should be adopted. While the patient is still in the emergency room, urine and blood samples are obtained for the laboratory investigations listed in the table. A 12-lead electrocardiogram is done before the patient leaves the emergency room, and, thereafter, the patient is maintained on an ECG monitor for 24 hours or more to assess cardiac rhythm. Electrocardiographic abnormalities are more frequent in patients with intracranial hemorrhage than in thromboembolic disorders. Progressive bradycardia may reflect increasing compression of the brainstem, and dysrhythmias may result in diminished cerebral perfusion.

While in the emergency room, the patient is prepared for an emergency computerized cranial tomographic study (CCT) — the keystone of initial management. If CCT is not available for immediate use, skull radiographs can be obtained to display an unsuspected skull fracture, an enlarged sella turcica,
TABLE. Laboratory Investigation of the Patient With Established Infarction

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<tr>
<th>For All Patients</th>
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<tr>
<td>Multi-profile blood chemistries</td>
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<td>Complete blood count, differential and platelet count</td>
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<td>Treponemal serology</td>
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<td>Urine analysis</td>
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<th>For Selected Patients</th>
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<tr>
<td>Protein electrophoresis</td>
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<td>Blood and serum viscosities</td>
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<td>Platelet adhesion and aggregation studies</td>
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<td>Hemoglobin electrophoresis</td>
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<td>Lipid profile</td>
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...or a shift of the pineal gland. If the pineal is not calcified, echoencephalography can be used to determine whether midline structures have been displaced. A midline shift is demonstrable at the time of admission if the stroke is hemorrhagic. In one series, CCT revealed hemorrhages in 43% of patients with intracranial hemorrhage; but only in 4% of patients with cerebral infarctions and then only after edema has developed 6-24 hours after onset.

CCT, performed both before and after the infusion of contrast material, almost always reveals intracranial blood immediately if the stroke is hemorrhagic. In one series, CCT revealed hemorrhages in 43% of patients with stroke clinically diagnosed as having infarction. CCT may also reveal a subdural hematoma and hemorrhage into a neoplasm as causes of stroke. According to recent estimates, neoplasm is responsible for a significant number of acute "strokes".

Repeated CCT also permits direct evaluation of cerebral infarction. While not detectable for 2 or 3 days after the onset, atherothrombotic and embolic infarcts are thereafter readily visualized on CCT as areas of homogeneous decreased density within a particular vascular distribution. As many as 98% of patients with infarctions have abnormal CCT sometime during the evolution of their disease, but normal CCT 48 hours after the onset of symptoms correlates almost exclusively with TIA.

The results of CCT are central to decisions regarding management. If edema is present, consideration must be given to placement of an intracranial pressure monitor, and to appropriate medical or neurosurgical management. If there is a hemorrhage, arteriography and possible evacuation of clot are the pivotal issues. If the clinical picture and CCT do not reveal the etiology, the cerebral spinal fluid is examined for further clues for diagnosis and always before initiating anticoagulant therapy.

A multitude of non-invasive techniques has been developed to help distinguish between extra- and intracranial arterial disease. These tests are not performed as emergencies but on a sequential basis some days after the patient's clinical state has stabilized.

Although their value has diminished since the advent of CCT, radionuclide techniques retain a place in the evaluation of patients with cerebrovascular disease. On rectilinear scanning, the classic picture of an ischemic infarction is an area of increased radionuclide uptake within a particular vascular distribution. Neoplasms usually have a different appearance but in situations where distinction is not evident differential uptake of diverse isotopes has been used. Studies on small numbers of patients cast doubt on the ability of gallium to differentiate cerebral infarcts from neoplasms. Recent studies, however, yielded more encouraging results. In one study, brain scans with both Tc-pertechnetate and Ga-citrate were performed on 93 patients with cerebral neoplasms and on 70 others with cerebral infarction or hemorrhage. While tumor detection was better with Ga (96%) than with Tc (85%), infarctions either did not concentrate Ga (67%) or revealed a much lower concentration than Tc (27%). In another series, Tc-(SM)-diphosphonate demonstrated 15 of 22 infarcts better, 3 less well, and 3 equally well as pertechnetate, while the latter demonstrated 11 of 12 primary or metastatic tumors better than Tc-(SM)-diphosphonate.

Neoplasms are generally evident on brain scan when neurological deficit begins but cerebral infarction is usually not detectable until 2 to 14 days later. Welch et al. have reported abnormal brain scans 48 hours after infarction in 27% of 162 patients. The abnormality is due to increased vascularity of "luxury perfusion" surrounding an infarct and is more often associated with embolic rather than with occlusive disease.

The diagnostic yield increases if static brain scans are coupled with dynamic studies. In 143 patients with stroke, radionuclide dynamic ("flow") studies were abnormal in more than 80%, but static scans were positive in only 42%. In contrast, the percentage of abnormal CCTs in recent infarctions was 40-55% after 2 or 3 days and reached a maximum of 66% at 3 weeks. While the percentages are roughly equal for both techniques, the results of the 2 studies in a given patient may differ. In one recent series the 2 methods yielded complementary findings in 16 (55%) of 29 patients.

Coupling CCT and radionuclide scans is useful as an aid to making decisions regarding etiology and management. If the CCT shows an abnormality suggestive of infarction, a radionuclide brain scan is performed. If this is normal, we conclude that the blood-brain barrier is intact and that angiography, with a view to reconstructive surgery, can be safely performed at once. If the scan is abnormal, suggesting vascular breakdown, angiography is delayed for at least 3 weeks for gial repair to occur as a prelude to reconstructive surgery. During this time the patient is maintained on anticoagulant therapy.

Arteriography is the definitive diagnostic procedure in patients suspected of having cerebrovascular dis-
order. Indications include: 1) uncertainty of the diagnosis; 2) deterioration in the clinical condition of a patient with a previously stable deficit; and 3) the possibility of performing reconstructive surgery.

Our morbidity with angiography ranges between 1 and 2%, the incidence of permanent neurological deficits being about 0.5% and the mortality about 0.2%. This, coupled with the risk of surgery, make it particularly necessary to pre-select carefully patients for arteriography.

Because emergency arteriography and/or surgery during an ictus carries a higher morbidity and mortality,44 angiography is not performed in the acute stages unless brain scan is negative or the diagnosis is in doubt. If the patient makes a good functional recovery, arteriography performed during convalescence may indicate the need for surgery to prevent recurrence or extension of infarction.

General Principles of Management

Fastidious general management of the patient is an important factor in determining the outcome. Apart from those patients who die before therapy can be instituted, the majority of deaths from stroke are not directly due to the cerebral insult but to the ensuing complications.

The patient’s room should be quiet, and he should be sedated, preferably with barbiturates. Barbiturate-augmented hypothermia has been reported to decrease intracranial pressure and cerebral metabolic rate for oxygen45-48 but its clinical utility is still unproven.

Aggressive treatment of hypertension is indicated for patients with hypertensive encephalopathy or subarachnoid hemorrhage. For patients with thrombotic occlusions, on the other hand, moderate elevations may be necessary to maintain cerebral perfusion, and lowering the blood pressure may increase cerebral ischemia. Dysautoregulation has been demonstrated in hypertensive patients49 and — even without the loss of autoregulation associated with a stroke50 — a reduction of blood pressure can jeopardize perfusion. Hence, hypotensive therapy must be used judiciously, if at all. Some51 have recommended the use of norepinephrine to elevate blood pressure during the acute phase of some ischemic episodes. Aside from the treatment of vasospasm or other neurological deficits related to angiography,52 such therapy has not been fully evaluated in controlled studies in patients with stroke.

Fluids should be restricted enough during the first 4 or 5 days following a stroke to keep the patient slightly dehydrated without significantly increasing blood viscosity and further reducing cerebral blood flow.53 Proper fluid management requires weighing the patient at least every other day, determining serum and urinary electrolytes q.o.d., and maintaining accurate records of fluid intake and output. Daily fluid requirements can be satisfied by the administration of about 1500 ml of 5% glucose in 1/2 N saline containing 20 mEq/L of potassium. If oral liquids are not tolerated, a nasogastric tube is passed and tube feed-

ing formula to maintain metabolic requirements is administered after the first 2 days.

To monitor output, comatose or incontinent patients should be catheterized — men preferably by condom catheter, women with a closed-drainage Foley catheter, passed with aseptic technique. If catheterization is necessary for longer than 3 weeks, suprapubic drainage may carry less risk of infection.

For unconscious patients methylcellulose eye drops should be administered twice daily, and the eyelids should be taped shut. Patients should be turned regularly to prevent pressure ischemia of the skin and pressure areas must be regularly inspected for skin breakdown. Abdominal distention may indicate the development of colonic pseudo-obstruction,54 with progressive dilatation of the proximal colon without mechanical obstruction.

An insidious and life-endangering complication is the development of deep venous thrombosis (DVT) and the accompanying risk of pulmonary thromboembolism. Phlebothrombosis occurs in 33-59% of patients with stroke,55,56 the incidence being greater (by a ratio of 9:1) in the paralyzed leg. Since DVT is not diagnosed at the bedside in a third of patients, bilateral phlebography has been recommended as a means of detecting "silent" thromboses.57 The less invasive125-1 fibrinogen technique has been found to be a more effective method for demonstrating DVT in patients with stroke.58 The reported incidence of pulmonary emboli following stroke ranges from 2.8 to 15.9%.59,60 In one series60 about 91% of these patients were found to have concomitant DVT. To prevent this life-threatening complication, well fitted stockings or elastic bandages and early ambulation — should be complemented by drug therapy. Mini-dose heparin is used for decreasing the incidence of phlebothrombosis and pulmonary embolism in patients with a stroke.61-63 Bedridden patients are maintained on subcutaneous heparin, 3000 units every 6 hours or 5000 units every 8 hours. Coagulation time is not visibly affected by these dosages64,65 and no complications have resulted.

In addition to avoiding the complications of bedrest and inactivity, the goal of treatment is to prevent further neurological damage and, if possible, to restore function. In an effort to preserve or restore the blood supply to the brain, attention is directed to the cardiovascular system (including vessel walls) and the blood components. The goals are to control cardiac dysrhythmias, to prevent emboli, and to maintain cerebral perfusion.

A hemoglobin of 9 gm% or below is an indication for a transfusion of packed red cells. A hematocrit above 50% or hemoglobin above 15 gm% indicate the development of hemoconcentration or erythrocytosis which should be corrected with hydration or phlebotomy depending on the underlying cause.

Medications

Anticoagulants

Whether anticoagulation therapy should be given to a patient with completed infarction has not been resolved after 25 years of discussion. If it is used, should
treatment affect the platelet phase of the coagulative process, in the "cascade" proper, or in the thrombo-
lytic phase? "Full anticoagulation" is desirable and is
initiated with heparin and followed by maintenance
coumarin drugs. No consensus has been reached
regarding the utility of such treatment for patients
with established or completed infarction.** Except
when a condition contraindicates anticoagulant
therapy (e.g., pregnancy, hemorrhagic diatheses, ac-
tive peptic ulcers, uremia, pericarditis, bacterial endo-
carditis, hepatic disease*) intravenous heparin is used
in patients with early infarction. The initial dose (5000
U/500 ml saline) is often begun in the emergency
room, an infusion pump being used to control the rate
of administration. Heparin is continued for at least 72
hours, or until definitive decisions about long-term
management are made. Full anticoagulation generally
should be given for at least 2 months following throm-
bosis because this much time is required for the
thrombus to adhere to the vessel wall and to be
deposited with endothelium.9 The dosage of heparin is
regulated by the clotting time. Whether the Lee-White
method for determining whole-blood clotting time, or
the activated partial thromboplastin time (aPTT) is
used, the clotting time should be kept within a range of
one and a half times that of normal controls. The
patient's own blood cannot be used as the control
because thrombosis may accelerate the clotting time.
The method most frequently used is the Lee-White
cutting time which is less sensitive but has the advan-
tage that it can be performed at the bedside. Advan-
tages of the aPTT are that it can be performed on anti-
coagulated blood at the laboratory's convenience, and
that it has a very rapid end-point.

Platelet Antiaggregants

During hemostasis, platelets undergo adhesion,
release reaction, aggregation, and consolidation.
This process involves various steps, but most of
the "antiplatelet" agents employed interfere with
adhesion or aggregation. Antiaggregant effects have
been demonstrated for non-steroidal anti-inflamma-
tory agents (aspirin, phenoprofen, phenylbutazone,
sudoxicam, sulfinpyrazone) and for the pyrimidopy-
ridine compounds (dipyridamole, papaverine, pyri-
dinolcarbamate); similar actions have been reported
for numerous other compounds (antihistamines, barbi-
turates, clofibrate, cyproheptadine, halofenate, pro-
pranolol, prostaglandin PGE1, tricyclic antidepress-
sants, and antipsychotic drugs).79

A significant increase in platelet adhesiveness has
been observed in 43 patients with ischemic infarction,
88% of whom were below the age of 40.80 Platelet
aggregation is significantly greater in young patients
with stroke than in controls.80,81 This difference is not
so evident in older patients because platelet aggre-
gability is thought to increase with age.82 Some
studies83 have shown that dipyridamole reverses ab-
normalsities of platelet aggregation in patients with
cerebrovascular disease, but it was found that aggre-
gated platelets returned to normal 10-40 days after
acute cerebral ischemia even in the absence of aspirin
or dipyridamole therapy.84

Although the numerous agents listed above have not
been extensively tested, there is no present evidence
that platelet antiaggregants are useful for completed
infarction. One report of the effect of such drugs for
reducing morbidity, mortality, or post-infarction
TIAs in patients with previous strokes,85 showed that
the survival rate was improved by the long-term ad-
ministration of sulfinpyrazone, 600 mg/day.

A double attack on the coagulative mechanisms has
been suggested by Sullivan et al.,86 who conducted a
study in patients with prosthetic heart valves. Those
who were treated with a combination of dipyridamole
and warfarin compounds had fewer embolic episodes
than those treated with warfarin alone. No major
hemostatic problems have been reported in patients
receiving both anticoagulants and antiplatelet drugs,
although the incidence of bleeding disorders should be
theoretically increased by such therapy.

Because abnormalities of the fibrinolytic system
have also been demonstrated in patients with stroke,87
plasmin-pathway activators (acetylcholine, adren-
aline, nicotinic acid, streptokinase, urokinase) have
been suggested or employed by some investigators,
but the data are still inadequate.

Anticonvulsants

Generalized or focal seizures occasionally initiate or
accompany cerebral infarction. Seizures are more
frequent in embolic infarction and in cortical venous
occlusions. Two retrospective studies have been con-
ducted on autopsy-proven cerebral infarcts — and
hence on populations selected for the most severe
lesions. In one, seizures were reported in 12.5%, in the
other 6.6% and in a third,89 the incidence of seizures
was 7.7%. In 33 of these 77 patients with post infarc-
tion seizures, convulsions occurred at the onset of
stroke or within the first 2 weeks; in only two of these
33 patients did recurrent seizures develop. Of the 27
patients whose seizures developed after the second
week, 22 became epileptics. Of interest is the fact that
anticonvulsants were ineffective in the patients whose
seizures developed early, whereas late-onset seizures
were easily controlled.

This study throws doubt on the value of "prophylac-
tic" anticonvulsant therapy for patients with nonem-
bolitic cerebral infarction.

Barbiturates

The potential value of barbiturate sedation for
stroke management has been mentioned. The concept
of using these drugs to provide pharmacologic protec-
tion for the ischemic brain has some experimental sup-
port81-83 but has not been tested clinically.

Blood Gas Therapy

Hypocapnia. It has been suggested that prolonged
hyperventilation might benefit stroke victims by
reducing Pco2, causing vasoconstriction, and shifting
blood to an ischemic area, and by reducing intracranial pressure.\textsuperscript{81-84} but there are numerous reports of adverse effects produced by such therapy. No significant difference was noted between patients with severe infarction treated with hypoxic ventilation and those treated with normocapnic active ventilation.\textsuperscript{85}

**Hypercapnia.** Because it is the most powerful cerebral vasodilator, carbon dioxide in varying concentrations has been administered to patients with evolving infarction. In both animals and patients with brain infarctions, an increase in regional cerebral blood flow (rCBF) has been demonstrated after the addition of 5\% CO\textsubscript{2}.\textsuperscript{99-101} however, no rigorous studies documenting its therapeutic effect on human beings are available.

An objection to its use is that it might induce an intracerebral "steal"; i.e., with the non-reactive vessels in an ischemic brain already maximally dilated, dilatation of the remaining normal vessels might shift (steal) blood from ischemic areas. Two studies, however, have shown that vasodilator response was reduced or impaired in only 25\% of patients with cerebrocortical disturbances.\textsuperscript{97, 98} Mathew et al.\textsuperscript{102} noted, in 6 patients with recent hemispheric infarction, that CBF was increased in all regions after CO\textsubscript{2} inhalation. It is generally agreed that the steal response occurs only during the acute stages of severe and extensive cerebral infarction, and then only rarely.\textsuperscript{92, 99-101, 105}

**Hyperoxia.** The use of hyperbaric oxygen therapy to increase the oxygenation of ischemic brain is an appealing idea. Patients with infarction so treated show clinical improvement initially, but the effects are not sustained when the patient leaves the hyperbaric chamber.\textsuperscript{104, 105} The vasoconstricting effects of O\textsubscript{2} reduce CBF to such an extent that tissue oxygenation may not change. This effect may be circumvented by the concomitant use of decarboxylase or carbonic anhydrase inhibitors,\textsuperscript{106} which cause vasodilatation.

**Vasodilators**

Studies on the effects of vasodilators other than CO\textsubscript{2} are also conflicting and inconclusive. In normal subjects, oral or parenteral papaverine increases CBF and cerebral oxygenation.\textsuperscript{107, 108} Clinical improvement in patients with stroke treated with papaverine has been noted in controlled trials.\textsuperscript{109, 110} but McHenry et al.\textsuperscript{111} found no benefit in 6 patients. Furthermore, although Meyer et al.\textsuperscript{112} reported a slight improvement in 27 patients, the control and treated populations were not comparable and embolic events were grouped with thrombotic infarctions. Data regarding the utility of other vasodilators (e.g., dehydroergonovine, ny lidrin, betahistine, beta-blockers, cyclandelate, hexobendine) — are even less conclusive.

**Dehydrating (Antiedema) Agents**

Cerebral edema accompanying ischemia is both cytotoxic and vasogenic in origin. In the early stages, impairment of cellular metabolism leads to cytotoxic edema. The vasogenic component, which arises later, is presumably secondary to cell death, to loss of integrity of the blood-brain barrier, to the extrusion of osmotically active particles into the extracellular space, with a consequent increase in the extracellular water content. A theory, which has not been proven, is that edema is self-perpetuating because it a) overtaxes the cell's Na-K pump so that an accelerating deficit accrues, and/or b) has undesirable effects on the microcirculation, reducing blood flow further and causing additional cellular damage. Cerebral edema may be sufficient to cause brain herniation and death.

**Hypertonic Solutions.** Urea,\textsuperscript{117} mannitol,\textsuperscript{118} and glycerol\textsuperscript{119} have been used to reduce increased intracranial pressure and, more recently, for cerebrovascular insults. These agents act by increasing osmotic gradients, thus promoting the egress of water from areas of cytotoxic edema and from normal brain. They share the ability to act rapidly and to decrease blood viscosity, but may produce some complications such as severe dehydration with electrolyte imbalance and intracranial hemorrhage. Glycerol does not seem to produce the complications associated with the other 2 compounds, and its effect lasts nearly 48 hours, as compared to 6-8 for urea and mannitol. Another advantage of glycerol is that it acts even in nephrectomized animals and is less toxic to both kidneys and liver than urea and mannitol. Theoretically, glycerol, alone of the 3 agents, provides a metabolic substrate and improves cerebral metabolism\textsuperscript{114} as well as increases in cerebral blood flow.\textsuperscript{118}

Meyer et al.\textsuperscript{113} reported reduction of mortality in 36 patients treated with glycerol during acute cerebral infarctions. Mathew et al.\textsuperscript{114} demonstrated improvement in neurological status 14 days after an acute cerebral infarction in patients treated with intravenously administered glycerol. Gilsanz et al.\textsuperscript{115} confirmed the favorable effect of glycerol and noted that it was more efficacious than dexamethasone. Fritz and Werner\textsuperscript{116} noted no improvement in patients with either a minimal or severe deficit, but did note a significant improvement in the moderately-impaired patients. However, the patients were not followed long enough to determine whether such therapy decreased disability or changed life expectancy.

In a retrospective study of 227 patients with infarction treated with various dehydrating agents, Candelise et al.\textsuperscript{117} found no improvement. Gelmers\textsuperscript{120} evaluated 100 patients and could not demonstrate beneficial effects of glycerol during the 4 weeks after an acute infarction, confirming similar results obtained by Larsson et al.\textsuperscript{118}

Glycerol may theoretically have an adverse effect on normal brain,\textsuperscript{121} but this has not been documented.\textsuperscript{79, 113, 114, 122} The hyperosmolarity produced by glycerol does not begin to approach that found in human hyperosmolar states. It has been suggested that an osmolar gradient of about 30 mOsm is desirable for achieving an adequate dehydrating action,\textsuperscript{79, 113, 122} yet the improvement in hemispheric or regional blood flow is noted at 14-20 mOsm. Dehydrating agents have also been criticized as having
only short-lived efficacy.19,180 but Newkirk et al.187 were able to demonstrate control of intracranial pressure continuously for 3 weeks using oral glycerol. Because of its ease of use, lack of toxicity, and rapidity of action glycerol is the leading agent for the control of brain edema — both massive, life-threatening and peri-infarct edema. Beneficial secondary effects of glycerol derive from the enhancement of metabolism,114,188 increase in blood flow,128 platelet antiaggregation,129 and ADH inhibition.180 If given as a bolus, glycerol produces rebound pressure; hence it must be given slowly.128,129,130 A 10% solution is given by slow intravenous drip over 4 to 6 hours twice daily. If intravenous glycerol is not available, it can be given orally at 2-hour intervals, the total daily dose being 2 gm/kg body weight. Glycerol should be administered for about 4 days and complemented by the use of adrenocorticosteroids. Glycerol minimizes the early cytotoxic component of edema, while the steroid (which has maximum effect after 6–48 hours) should counter the later vasogenic component of edema accompanying brain ischemia. Steroids. No matter how rational such a scheme might seem, there is scant evidence that adrenocorticosteroids affect the sequence of events in patients with cerebral ischemia and infarction. Earlier investigations attributing beneficial effects to steroids were either not controlled or lacked adequate statistical analysis. In the widely misquoted study by Patten et al.184 in which the effect of 220 mg of dexamethasone given over 17 days was evaluated in 31 acute stroke patients, 3 patients in the control group had cerebral hemorrhage. With or without these 3 patients there was significant improvement (p = 0.02) in the group presenting the greatest neurologic deficit. The authors concluded that dexamethasone can be a useful adjunct in the therapy of patients with severe stroke. Studies on the effect of mega-doses of steroids (1000 mg/24 h) in patients with evolving infarction have not been reported. Other reports cast doubt on the efficacy of steroids in the treatment of stroke. Dyken and White186 found that death of patients with acute cerebral infarction occurred as frequently whether or not they were treated with 300 mg of cortisone per day, but the investigators themselves indicated that their data were not statistically significant. Hetzel et al.186 evaluated the effect of cortisone “in the dosage recommended” in a double-blind fashion in only 12 patients. In each group 3 patients died, 2 were better, and one remained the same. The authors concluded that “large doses of cortisone” were of no value in the immediate treatment of stroke. The same conclusions were reported by Bauer and Tellez187 in their double-blind study of the effect of 12 mg of dexamethasone daily for 10 days. However, the treated and control groups were not comparable because the placebo patients were more ill on admission. It was reported that dexamethasone treatment did not alter prospects of discharge home or death rate at 3 months in 247 patients with hemiplegia;188 these patients received either 48 mg of dexamethasone over 3 days, or 112 over 7 days, but many had hemiplegia for 7 days before medication was administered. Because edema is most likely to occur during the first 2 to 4 days after the onset, therapy needs to be initiated earlier, as was done by Norris.185 In his study, 53 patients with acute cerebral infarction were treated with 140 mg dexamethasone or placebo for 12 days and evaluated at intervals for 28 days. Norris concluded that the patients treated with steroids fared slightly worse with 2 of the 5 patients in the placebo group dying of cerebral edema, compared to 3 of 7 in the steroid group, while infections, gastrointestinal hemorrhage, and exacerbation of diabetes mellitus occurred more commonly in the steroid-treated group. This contrasts with the study of Bauer and Tellez187 where 3 patients developed gastrointestinal tract bleeding while on the placebo regimen but there were no complications in the steroid-treated group.

In Norris' study the 2 populations were not comparable since the steroid treated group was more seriously ill and there were different etiologies for stroke. The effect of coupling steroid therapy with other anti-edema agents has not been adequately evaluated. In a double-blind study of 40 patients given 215 mg of dexamethasone over 15 days, plus 7500 ml of low-molecular weight dextran over 3 days starting 24–48 hours after the onset of symptoms, Kaste et al.140 could not find a reduction in mortality or morbidity at the end of a 28-day observation period. The simultaneous administration of steroids and diuretics, a combination effective in animal models, has not been tried in humans.

Surgical Measures

Two major surgical techniques have been used in suitable patients with cerebral infarction. These are: 1) endarterectomy or thrombectomy for lesions in the cervical carotid artery, and 2) extracranial-intracranial anastomosis to bypass inaccessible arterial lesions. Re-establishing flow and pressure during acute carotid occlusion accompanied by neurologic deficits is likely to produce intracerebral hemorrhage.141–143 The dangerous period lasts a minimum of 2 weeks after ischemia. A mortality of 42% in 50 patients has been reported for patients operated upon during this period, as compared to a 20% mortality in nonoperated patients.144 Surgical treatment has been recommended for patients with mild completed stroke and for reversible ischemic episodes.

The 4-year mortality reported in groups of patients with RINDs varies from 17% to 40%; during the same period, up to 55% deteriorate neurologically. Twenty-nine–40% of patients with established infarction will die of another stroke within 3 years.144 Elective thromboendarterectomy is indicated in patients whose carotid is stenosed but not occluded, and for patients with a mild to moderate neurologic deficit. For patients of this type, Bauer144 reported significant improvement in the 42-month survival rate after surgery. In that report, as in others,141–143 patients with established in-
Collateral circulation is inadequate to compensate for carotid or middle cerebral artery, and occlusions inaccessible with previous vascular techniques. Some authors suggest that at least a 25% reduction, focal or generalized, of cerebral blood flow should be present before ST-MC bypass is contemplated.

Reports on the use of this new surgical approach are difficult to evaluate because of the wide variation in the time elapsing between the onset of stroke and surgery (one day to 7 weeks or more), differences in the classification of patients, and short follow up periods.

Rehabilitation

Rehabilitation seeks to help the patient with completed stroke achieve as great a degree of independence as possible despite the amount of neurologic deficit. Rehabilitation should begin as soon as possible after the onset of a stroke. The initial goals are to avoid increased disability from immobility by employing daily passive exercise with all weakened extremities being put through a complete range of motion. This avoids muscle shortening and joint fixation which are difficult to treat when the acute phase of stroke is over and function begins to return.

As function begins to return the patient is educated to strengthen it, use it and use his uninvolved extremities to carry out activities of daily living which make for independence. Programs for this phase of treatment are ideally carried out in specialty hospitals with disability oriented units. In such institutions for those patients not neurologically devastated, partial to complete independence can be expected in 60-80% of patients. Treatment can be successfully carried out in nonspecialty hospitals provided there is interest in the problem of stroke rehabilitation and there is personnel skilled in physical and occupational therapy.

Poor outcome from programs of rehabilitation for patients with stroke may be expected when there is severe paresis, left sided neglect, dementia and global aphasia. Good results can be expected in patients with mild to moderately severe paresis even with expressive-receptive dysphasia. Outcome is also improved when patients have families able to care for them at home despite disability. General function may progressively improve over 12-18 months after the onset of stroke despite lack of improvement of neurologic deficits in the involved extremities. This largely is related to the patient's ability to learn to use his uninvolved extremities for improved function.

References

1. Millikan CH (Chairman): Classification and outline of cerebrovascular diseases II. Stroke 6: 594-616, 1975
16. Lavy S, Yaar I, Melamed E, Stern S: The effect of acute stroke on cardiac functions as observed in an intensive stroke care unit. Stroke 5: 775-780, 1974
24. Pearce JMS: If I had a transient ischemic attack at the age of
44. Toole JF: Diagnosis and Management of Stroke. American Heart Association, 1979
46. Michenfelder JD, Thaye RA: Cerebral protection by thiopental during hypoxia. Anesthesiology 39: 510-517, 1973
63. Mustard JF, Packham MA, Platelets, thrombosis and drugs. Drugs (Basle) 9: 19-76, 1975
75. Enge R, Boyesen S: Long-term anticoagulant therapy in...


82 Couch JR, Hassanein RS: Platelet aggregation, stroke, and transient ischemic attack in middle-aged and elderly patients. Neurology (Minneapolis) 26: 888-895, 1976


97 Dodson RF, Tagashira Y, Wai-Fong Chu L: The effects of...


150. Feigenson JS, Gillow HS, Greenberg SD: Disability oriented stroke unit. A major factor influencing stroke outcome. Stroke 10: 5-8, 1979


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