The Management of Acute Cerebral Infarction

CLARK H. MILLIKAN, M.D.

Professor of Neurology, Mayo Medical School, University of Minnesota, Minneapolis, Minnesota, and Director, Mayo Cerebrovascular Clinical Research Center, Rochester, Minnesota

There is no evidence that we are able to reverse cerebral infarction once it gets underway. The day may come when some form of protection for neuronal activity is available to us, but at present there is no such treatment. Prevention is the most important concept; prevention of transient ischemic attack (TIA) or prevention of progression once the process has started. Progressing stroke is that all too common circumstance where focal ischemia is worsening and the process of infarction is beginning or extending. The patient may be seen in the office, emergency room, or in the hospital, and the patient's classification may be changed on successive examinations. There is nothing unusual about such reclassification. For instance, a patient may be admitted to an intensive cardiac care unit with a tentative diagnosis of myocardial infarction; the diagnosis will be changed if the findings change. Thus we look at a patient entering the hospital with a modest neurological defect in the right arm and reexamine the individual some time later. If the defect is worse, we say that the stroke is progressing; if the patient is the same, it appears that the process is completed; if the defect has disappeared, the diagnosis may be TIA.

It is important to differentiate between the carotid and vertebrobasilar systems. The neurological picture in progressing stroke in the carotid system may range from monoparesis to hemiplegia with or without a homonymous defect in vision, a variety of impairments of speech and language, and a range of partial to full sensory abnormalities on the opposite side of the body.

The combination of defects in vertebrobasilar occlusive events is often more complex. The most common defects include abnormalities of motor function; weakness, clumsiness, or paralysis of any combination of the limbs with appropriate pyramidal tract signs combined with unilateral or sometimes bilateral cranial nerve palsies, particularly oculomotor defects or signs of trigeminal or facial nerve involvement. A so-called "crossed" defect (motor or sensory on one side of the face and opposite side of the body) is evidence of a brain stem lesion until proven otherwise. Bilaterality of motor or sensory abnormalities, or both, coupled with cranial nerve palsies indicates brain stem involvement.

The work-up of a patient with acute progressing stroke, whether in the carotid or vertebrobasilar arterial systems must proceed immediately. Particular emphasis is placed on what we now call the neurovascular examination. Certain items have been grouped together under this term. These include:

1. Inspection of vessels
2. Palpation of vessels
3. Auscultation at cervical and cranial sites
4. Ophthalmoscopy (including inspection of the retinae for emboli, cotton-wool patches, vascular occlusions, hemorrhage, and ischemic retinopathy)
5. Ophthalmodynamometry

1. *Inspection of vessels.* Cranial arteritis is an unusual cause of stroke. However, accurate diagnosis is vital to correct treatment, and significant arterial

Correspondence and reprint requests to Dr. Clark H. Millikan, Professor of Neurology, University of Utah School of Medicine, Salt Lake City, Utah 84112.

change may be detected by viewing the superficial temporal arteries, coupled with palpation.

2. *Palpation* of the cervical cerebral vessels should be done gently. Minor differences in pulse between sides are difficult to interpret and it may be impossible to distinguish a pulse coming from the first portion of the internal carotid artery or from the external carotid artery. Patients suspected of having atherosclerosis of cervical vessels may have ulcerated plaques or early thrombus formation; both are situations where manipulation of the arteries could dislodge emboli.

3. *Auscultation* of the cervical vessels often provides important evidence of the pattern of blood flow. A bell-type stethoscope is most easily applied in the supraclavicular fossa and over the eyes, without using physical pressure which may produce artifactual noise. The bell of the stethoscope is first placed over the aortic valve and then moved (1 cm or less at a time) upwards. This movement of the stethoscope is necessary to distinguish transmitted cardiac sounds from sounds arising in the innominate, subclavian, common carotid, or internal carotid arteries. A neutral position (patient sitting or lying with face straightforward) is less likely to create sounds difficult to interpret than a variety of twisted neck positions. If respiratory (tracheal) sounds obscure auscultation, the patient is requested to "stop" breathing for a few seconds and then instructed to "start" breathing. Bruits should be graded for loudness, the scale being 1 (least) to 6 (loudest); for example 1/6 is barely audible, 6/6 is the loudest. The timing (systolic, diastolic, systolic-diastolic), duration (short, medium, long), and quality (rough, soft, smooth, and so forth) should be described. A bruit of 1/6 loudness is of little significance, while one of 2/6 to 3/6 loudness, long systolic-diastolic duration, and timing of fairly high pitch over the origin of the internal carotid artery means high-grade carotid stenosis until proven otherwise. A soft (1/6 to 2/6) diastolic sound, varying with slight change in neck position, is usually an unimportant venous hum. Soft, sometimes almost continuous, cervical bruits are fairly common in children and ordinarily do not indicate the presence of significant pathology. By carefully recording the description of bruits and correlating this with arteriographical and other findings, the examiner will quickly learn to interpret such sounds correctly.

If the patient's history suggests the presence of a neoplasm or arteriovenous malformation, ausculta-tion over the cranial vault and orbits should be performed. When there is a complaint of a rhythmic head noise, particular attention is directed to auscultation of the site of the sound. It may be necessary to wet the patient's hair to eliminate artifactual noise. Auscultation of the orbit is performed by instructing the patient to close the eyes, placing the bell of the stethoscope over the eye, and having the patient open the eyes to eliminate artifactual muscle sounds. Soft bruits over the cranial vault of children are of little importance. Loud bruits may be caused by angiomas, an arteriovenous shunt, and, rarely, brain neoplasms. A continuous, almost machinery-like murmur or bruit over the orbit is most commonly caused by a carotid cavernous arteriovenous shunt. Noises heard over the orbit have been of little help in establishing the site and severity of lesions of the internal carotid artery.

4. *Ophthalmoscopy* provides an opportunity to inspect small blood vessels directly; these blood vessels are a direct continuation of the internal carotid arterial system. In office and hospital practice relatively little use is made of this simple, safe method of acquiring important data concerning the cervical-cerebral portion of the circulation. The retina should be inspected for arterial or venous occlusion, emboli (cholesterol, platelet-fibrin, calcific, mixed, foreign body), hemorrhages, cotton-wool patches, venous stasis, microaneurysms, changes associated with arterial hypertension, papilledema, and ischemic retinopathy.

In the last two decades the importance of detecting a retinal embolus, or emboli, with the ophthalmoscope has been demonstrated. The most common emboli are made up of cholesterol crystals. These appear as shiny orange-yellow plaques often situated at the bifurcation of retinal arterioles. The plaque may appear to be wider than the arteriole; one sees the outer dimension of the column of red blood cells rather than the wall of the arteriole. Pressure on the eye often changes the position of the embolus slightly; the material may appear to glint or change shade, a characteristic sometimes referred to as a heliographic reflection. The blood flow in the arteriole often seems to be unimpeded by these bright orange-yellow plaques. These emboli may move distally and often disappear in a few days. The presence of one or more cholesterol retinal emboli indicates that there is or has been an ulcerated atheromatous carotid (internal) lesion until proven otherwise.

Another important type of embolus in retinal

vessels consists of gray-white material, thought to consist of blood platelets and fibrin. These emboli may be long and seen to move through an arteriole but are commonly stationary; pressing on the eye does not move the embolus, and there is no heliographic reflection. Blood does not appear to flow past these emboli; there may be infarction of the retina. Special studies show that some of these emboli have a high lipid content. In many instances the source of these emboli is an atheromatous lesion at the origin of the internal carotid artery. Particles of calcium form another type of retinal embolus. These are white, generally short, and stationary. Calcium emboli commonly come from heart valve lesions.

Septic emboli, talc, cornstarch, and other less common emboli may also be seen in the retina.

5. *Ophthalmodynamometry* is a procedure for measuring arterial systolic and diastolic pressures in the main retinal branch or branches of the ophthalmic artery. The convex foot-plate of the instrument is applied to the conjunctiva over the insertion of the lateral rectus muscle in a horizontal manner so that the instrument points directly toward the opposite eye. When measurements are being made in the patient's right eye, the instrument is held in the observer's left hand and the ophthalmoscope is held in the right hand. To measure pressure in the left retinal artery, the observer holds the ophthalmodynamometer in the right hand and the ophthalmoscope in the left. When the instrument is in position, the observer must bring the central artery on the disc into focus through the ophthalmoscope. The instrument is then pressed gradually against the eye to raise the intraocular pressure sufficiently to exceed the diastolic level of the blood pressure in the retinal artery. The diastolic pressure is that level which produces the first collapsing pulsation of the artery. At this point, a finger is applied to the brake on the instrument and the reading is taken from the scale. The ophthalmodynamometer is reapplied and several more readings are taken to insure accuracy. The systolic pressure is obtained by increasing the force of application of the instrument still further. The visible arterial pulsation gradually diminishes as the pressure increases and when pulsation ceases, the reading on the instrument is the systolic blood pressure. Ophthalmodynamometry is usually useless unless the arterial pressures are measured in both eyes. It cannot be performed unless the patient is cooperative. It is helpful to instill a mydriatic, but this should not be done if there is glaucoma. The test should not be per-

formed soon after cataract extraction or recent retinal detachment. The clinical significance of the retinal arterial pressure is dependent on comparing the values in the two eyes. A difference of 15% to 20% is almost always a sign of stenosis or occlusion of the internal carotid artery ipsilateral to the lower pressure. The arterial pressures may be equal or normal or both in the presence of unilateral carotid stenosis or occlusion because of the development of a collateral blood supply. Immediately following acute occlusion of an internal carotid artery, the ipsilateral retinal artery pressure drops. Return of the pressure to that of the contralateral eye depends on the speed with which the collateral circulation develops. A marked decrease in retinal arterial pressure (brachial arterial pressure remaining normal) when the patient moves from the supine position to the upright position (ocular orthostatism) is important evidence of carotid occlusive disease.

A number of laboratory tests should be performed. These include common items such as urinalysis, red blood count, white blood count, differential blood count, blood hemoglobin, sedimentation rate, fasting blood sugar, creatinine or urea, prothrombin time, cholesterol, triglycerides, and uric acid. It is important to make a diagnosis of such items as polycythemia; it has been known for decades that there is a high incidence of focal cerebrovascular disease in individuals who have this disorder. One may do a platelet count although it is extraordinarily unusual for thrombocythemia to be a cause of progressing stoke. When cranial arteritis is present, the sedimentation rate will be elevated; this diagnosis should be made quickly because of the risk of permanent impairment of vision. Diabetes is a part of the risk factor profile for stroke and the fasting blood sugar will assist in detecting individuals with this disorder. Renal function should be screened and the prothrombin time determined for baseline value. In acute progressing stroke, cholesterol and triglycerides are probably not of much significance unless they are excessively raised. The uric acid has been determined mainly as an item for study because of the association of hyperuricemia with atherosclerosis; the value is often elevated in patients with stroke.

It is common to do x-rays of the head although the number of instances where a significant abnormality is detected is small. X-rays of the chest are done and an electrocardiogram is performed. The possibility of a hidden myocardial infarction is always present; other evidence of cardiac abnormality

may also be of importance in the long-range management of the disorder.

Cerebrospinal fluid examination should be performed (when choke is absent due to papilledema) when the clinician has a serious problem in establishing the differential diagnosis of the intracranial pathology—bleeding, focal ischemia or inflammatory disease. The common problem for differential diagnosis in this setting is bleeding; only a small amount of fluid needs to be withdrawn to settle this question.

In the usual stroke patient (in a typical TIA, in most instances of progressing stroke, and in amost all cases of completed stroke) the electroencephalogram adds little significant information and is not necessary in the work-up of the patient. Commonly, in vertebrobasilar disease, the electroencephalogram shows no focal abnormality. It has been said that serial electroencephalograms may very well portray accurately the favorable or unfavorable progression of the brain lesion in stroke. However, the clinician can almost always get this information by spending three or four minutes with the patient one or more times a day. In selected instances, an electroencephalogram may reveal multiple focal abnormalities, thus giving potential evidence concerning the presence of multiple metastatic lesions. Particularly in medical centers where computerized axial tomography (EMI scanner, ACTA scanner, DELTA scanner, and others) is available, there is very little need for the electroencephalogram in the diagnosis of stroke patients. Doppler techniques, including the use of a Doppler flowmeter are under research and may be developed for clinical use. The static isotope brain scan has become an established procedure for the detection of intracranial neoplasms. However, where computerized axial tomography is available, there is now very little need for the static brain scan in the differential diagnosis of focal brain lesions. Likewise, dynamic rapid serial scintigraphy using a gamma camera, which gives a serial display to the images, provides much less precise information of clinical significance than computerized axial tomography or arteriography.

Indications for angiography are:

1. Differential diagnosis of the brain pathology (much less often used in institutions where computerized axial tomography is available).

2. Transient focal ischemic attacks—particularly the carotid system. In such instances, cervical-cerebral angiography should be performed if there is one, or more than one, of: amaurosis fugax, bruit over the beginning of the internal carotid artery, retinal emboli, unilateral decrease in retinal artery pressure, or ischemic retinopathy.

3. Selected instances of vertebrobasilar TIAs. In some instances, it may be difficult to make a clinical distinction between the carotid and the vertebrobasilar system. If the TIAs are characteristic of those coming from the vertebrobasilar system, there is little reason to do extensive angiography.

4. Very early progressing stroke or very frequent TIAs in the carotid system with, as part of the history, amaurosis, an appropriate bruit, retinal emboli, and so forth.

5. Many patients with subarachnoid hemorrhage and some patients with intracerebral hemorrhage.

6. A long systolic or systolic-diastolic carotid bruit, particularly with retinal emboli.

This completes the work-up of the patient.

As the patient with acute progressing stoke is worked up, the physician is interested in prognosis. Little has been written about this, if one starts with patients early in the course of their illness. It is important to understand that mortality statistics will vary, depending upon the type of hospital, nature of the population being hospitalized, availability of intensive care units, and other factors. Recently Jones and Millikan[1] studied the records of 179 consecutive patients with acute carotid system cerebral infarction to describe the clinical events during the first week of the illness. Only those patients admitted to the Cerebrovascular Hospital Service within 36 hours of the onset of the first symptom were included. The neurological status of 39% was stable (unchanged) at the end of seven days; 35% of the patients gradually improved. Nineteen percent had a progressing neurological deficit which stabilized within 48 hours of the onset. Six patients (3%) had a remitting-relapsing course during the first 36 hours and eight patients (4%) had a significant late worsening after 48 hours of stable or improving course. The mortality was 11% for the entire group. However, a "high risk of death" group was identified; the mortality was 41% for those patients who had any degree of decreased level of consciousness and hemiplegia at the time of admission. Of 67 patients having hemiplegia or some similar maximum neurological deficit with normal consciousness when admitted, only one died, a mortality of less than 2%. These percentage values have become a baseline for us to use in our institution in comparing possible new therapy with the results of earlier

treatment. In a hospital where there is a sizable population of patients with acute onset cerebral infarction, it probably would be wise to determine similar percentages; the data could then also be used as a baseline for that particular hospital.

Therapy. The primary objective of therapy in occlusive cerebrovascular disease is to maintain a normal or adequate metabolic substrate by maintaining the quality and quantity of blood delivered and removed from brain tissue. This primary goal may need to be attained by treatment of any mechanism which:

1. Interferes with the cardiac capacity to maintain adequate cerebral perfusion,

2. Alters any property of the blood which may maintain adequate neurometabolic substrate (including thrombus formation, anemia, and so forth),

3. Changes in the arterial wall leading to occlusion or thrombus formation (including atherosclerosis, arteritis, and so forth),

4. Affords transient protection of certain aspects of neuron metabolism (hypothermia, steroids, and so forth).

Treatment will be discussed under the following categories: 1) therapy related to the heart, 2) therapy related to alterations of the blood, 3) management of problems concerning the arterial wall, and 4) treatment concerning protection of brain parenchyma.

1. Heart. When there is any kind of causal relationship between cerebral infarction and a change in cardiac rhythm the cardiac dysrhythmia should be corrected. If there is impaired cardiac output, whether due to primary cardiac failure or to hypertension from some systemic abnormality, the cardiac output should be returned to normal. There is uncertainty about the percentage of occlusive disease strokes caused by embolism (mainly from the heart); it may well be higher than previously suspected. Cerebral embolism may occur at various times after myocardial infarction with mural thrombosis, but it most commonly comes within the first six weeks after the infarction. Anticoagulant therapy has been recommended. The principal reason for using an anticoagulant is to prevent the release of further emboli to the brain and other sites. The use of an anticoagulant continues to be a common recommendation in instances where prosthetic cardiac valves have been implanted. When the cause of cerebral infarction is related to subacute bacterial endocarditis, it continues to appear to be unwise to use anticoagulants.

Rather rarely, progressing stroke is a portion of the substructure of hypertensive encephalopathy. The use of the term "hypertensive encephalopathy" is specifically reserved for a syndrome in which there is a stereotyped sequence of events of serious import and dramatic development; in such instances, treatment consists of immediate control of the hypertension. In the usual progressing cerebral infarction, hypertension should be treated cautiously—the blood pressure not being decreased precipitously. If an anticoagulant is being used, the blood pressure should be brought under control, but this need not be done as emergency therapy.

2. Blood constituents. There are very few reports in the literature in which the term "progressing stroke" is used in relatively uniform fashion and comparison made between a group of patients treated with anticoagulant and a group not receiving such medication. The extraordinary variability in the natural history of acute progressing stroke makes it important that comparison be made of treated and untreated patients of similar type. Over two decades ago, I reported on the natural history of 204 consecutive patients with acute onset of progressing stroke in the carotid system. Fourteen days after the onset, 12% of the patients were normal, 5% (using motor phenomena as a basis for comparisons) had varying degrees of monoparesis, 69% had varying degrees of hemiparesis, and 14% were dead.

The Table summarizes those studies reported in the literature which are relatively comparable. A primary determination was made of the status of the patient at the time of the patient's admission to the study; progression of the neurological deficit had occurred in the preceding few minutes. There was frequent reevaluation of the neurological deficit, and subsequently comparison was made between the maximal deficit developed and the deficit present on entering the study. The percentage of patients showing progression of neurological deficit (after primary assessment) in the control and treated groups of each report is in the right-hand column of the Table. In every instance, the treated group fared better than those not receiving an anticoagulant; thus, in one study,[2] 20% of those treated showed evidence of neurological progression after entry into the study, whereas 52% of patients not receiving an anticoagulant showed progression after initial evaluation. Thus, in a few carefully performed investigations using an anticoagulant for acute progressing stroke, the evidence points to fewer patients having progression when receiving an anticoagulant contrasted to the

TABLE

Study	Number of Patients	Follow-up (Mos.)	Cerebral Infarcts (Lethal)	Cerebral Hemorrhage (Lethal)	Progressive Infarcts	Total Percentage Progressive
Millikan[2]						
Control	60	12	25 (40%)	0	8 (13%)	52%
Treated	181	12	12 (7%)	0	25 (14%)	20%
Carter[3]						
Control	38	6	7 (17%)	0	12 (33%)	50%
Treated	38	6	3 (7%)	0	9 (24%)	32%
Cooperative Study[4]						
Control	67	15	10 (15%)	0	21 (31%)	46%
Treated	61	12	5 (8%)	1 (2%)	8 (13%)	23%
Fisher[5]						
Control	14	?	0	0	9	64%
Treated	14	?	0	0	3	21%
Fisher (National Study)[6]						
Control	49	7.4	7		14 (29%)	20 (40%)
Treated	51	5.7	4	1	7 (14%)	7 (14%)

number having progression and not getting such drugs.

If one considers the use of platelet antiagglutinating agents, there are no current data concerning the effectiveness of such drugs as dipyridamole, aspirin, or sulfinpyrazone in the treatment of acute progressing stroke. Gilroy et al[7] reported the treatment of acute stroke with low molecular weight dextran and were optimistic about the effect of the medication. Apparently, however, no widespread enthusiasm for this method of treatment has developed.

The notion that a fibrinolytic (thrombolytic) agent could lyse a clot obstructing arterial flow to the brain has always been an attractive one. Fletcher et al[8] have recently reported a study of the use of the thrombolytic agent, urokinase, in doses sufficient to produce a twenty- to fortyfold increase of plasma thrombolytic activity. However, hemorrhagic complications occurred in several patients and distinctly favorable therapeutic results were not observed.

No comparative studies have been done to guide treatment of polycythemia, anemia, and hypoglycemia in acute progressing stroke. It is presumed that as soon as feasible these phenomena should be corrected and normal values attained. In a usual acute progressing stroke, hyperlipidemia does not receive special therapeutic attention during the first days of hospital admission.

If hyponatremia, hypernatruria, and increased urine osmolality are present [evidence of inappropriate antidiuretic hormone (ADH) secretion], fluid intake should be restricted to approximately 1000 cc/day until the abnormality has disappeared.

3. Arterial wall. The idea of improving the status of a progressing cerebral infarct by some treatment causing vasodilatation took a practical form in 1938 when Mackey and Scott[9] described the treatment of apoplexy by infiltration of the stellate ganglion with novocaine and reported that marked benefit was produced. A variety of techniques for causing vasodilatation have been invoked including the inhalation of 5% carbon dioxide, and the administration of papaverine, isoxsuprine and acetazolamide. In summary, no general enthusiasm has developed for this type of treatment of progressing cerebral infarction.

The use of hypocarbia has also been studied by Paulson.[10] No therapeutic benefit was found, so there is no reason to pursue this method of therapy.

When cerebral infarction occurs secondary to arterial obstruction associated with any form of arteritis or meningitis, attention must be paid to treatment of the primary disease causing the lesion of the arterial wall. Panarteritis, lupus erythematosis, cranial arteritis, and so forth, ordinarily receive steroid therapy while meningitis is treated with antibiotic or other agents, depending upon the organism producing the inflammation.

There is a difference of opinion concerning emergency surgery for patients with rapidly changing flow in the cervical portion of the carotid artery. Blaisdell[11] believes that individuals with progressing stroke should probably not have arteriographic evaluation because of the high risk of surgery or the small possi-

bility of a favorable result. The Joint Study of Extracranial Arterial Occlusion[12] reported a mortality of 42% in 50 patients operated upon within two weeks following an acute stroke while the mortality was only 20% for patients in the same category not having surgery. Bruetman et al[13] and Wylie et al[14] have reported intracerebral hemorrhage as a complication of carotid surgery. Apparently, the opening of carotid occlusion, reestablishing a normal head of perfusion pressure into an area of acute softening, may be associated with the production of intracerebral bleeding. In contrast, Millikan[15] has reported a group of carefully selected individuals, in whom emergency anticoagulant therapy and surgery appeared to be beneficial. The indications for emergency treatment are: 1) clinical events such as a cluster of frequent severe carotid TIAs (a persisting mild neurological deficit accumulates as evidence of mild progressing stroke); 2) a recent mild cerebral infarction in the carotid system followed by a cluster of TIAs; 3) onset of a focal neurological deficit during or soon after arteriography; or 4) sometimes immediate postoperative thrombosis after carotid thromboendarterectomy, and physical signs such as a) retinal emboli, b) long systolic or systolic-diastolic bruit of grade 2 or 3 over the carotid bifurcation, or c) ipsilateral decrease in the retinal artery pressure. A changing carotid bruit suggesting a change in the morphology of the carotid lesion probably should be added to this list of physical signs—signs which coupled with the clinical profile suggest that emergency surgery should be instituted.

4. *Protection of brain parenchyma—anti-edema.*

A. *Steroids.* Dyken and White[16] found the incidence of death in patients with acute cerebral infarction to be the same whether they were treated with cortisone (300 mg/day) or a placebo. Rubinstein[17] noted that the immediate mortality may be reduced and the level of consciousness may be improved when large doses of dexamethasone are administered early in the course of massive cerebral infarction, but once the slightest degree of brain stem dysfunction has occurred, the use of steroids appears to be without benefit. Patten et al[18] reported some slight benefit from the use of dexamethasone in acute stroke in a double-blind study, but if cases of cerebral hemorrhage were excluded, the results were unconvincing. Bauer and Tellez[19] found no difference in morbidity or mortality in 54 patients with acute cerebral infarcts divided into steroid-treated and placebo groups. In a recent report, Norris[20] studied 53 patients with acute cerebral infarction using a double-blind method. One group was treated with dexamethasone and the other portion with placebo, and all observations began within 24 hours of onset of the cerebral infarction. Forty-one of the total number of patients survived longer than 28 days; the patients treated with steroid did slightly worse than those in the placebo group at the end of this time. Two of five individuals who died in the placebo group died of cerebral edema; compared with three of seven patients who died in the steroid group. Because of problems with infectious complications, gastrointestinal hemorrhage, and an occasional serious worsening of diabetes mellitus in the steroid group, Norris believed that there was an increasing body of evidence against the use of such medication in the treatment of acute cerebral infarction.

B. *Hyperosmolar therapy.* In certain instances, intravenous administration of hypertonic agents may reduce the fluid content of the brain. Mannitol, in concentrations of 10% to 25%, may be administered intravenously in a dose of 1 gm/kg of body weight. When it is effective, the maximal reduction of intracranial pressure is achieved within 30 to 60 minutes. However, intracranial pressure often returns quickly to normal. At least, from the lack of reports in the literature, this substance is not widely used in the treatment of acute progressing cerebral infarction.

Meyer et al[21] reported treatment of cerebral edema due to acute cerebral infarction with glycerol. The glycerol was given intravenously in doses of 1.2 gm/kg of body weight or, in other instances, orally in doses of 1.5 gm/kg of body weight. The authors believe that glycerol "given within five days of onset of severe, progressing or sustained neurological deficit, is beneficial in patients with acute cerebral infarction." Gilsanz et al[22] compared treatment with 10% glycerol given for six days to 30 patients with acute cerebral infarction to results obtained after treating 31 similar patients with dexamethasone. One patient treated with glycerol died of hemoglobinuria and acute renal failure while six patients treated with dexamethasone died. The authors concluded that improvement was significantly greater in the glycerol group after 8 and 15 days. The results of these observations appear to require further study.

Although hypothermia, anesthesia, hyperbaric oxygenation and normobaric oxygenation might theoretically provide a favorable metabolic substrate for focal areas of brain ischemia, none of these are therapeutically practical for progressing stroke.

When convulsions, either at the time of progressing stroke or subsequently, become a problem, it is prudent to administer an anticonvulsant. The drug most commonly used is diphenylhydantoin, now called phenytoin (Dilantin®).

REFERENCES

1. JONES, HR, MILLIKAN, CH: Temporal profile (clinical course) of acute carotid system cerebral infarction. *Stroke* 7:64–71, 1976.

2. MILLIKAN, C.H.: Anticoagulant therapy in cerebrovascular disease, in MILLIKAN, CH, SIEKERT, RG, WHISNANT, JP (eds): *Cerebral Vascular Diseases. Fourth Princeton Conference*. New York, Grune & Stratton, 1965, p 183.

3. CARTER, AB: Anticoagulant treatment in progressing stroke. *Br Med J* 2:70–73, 1961.

4. BAKER, RN, BROWARD, JA, FANG, HC, ET AL: Anticoagulant therapy in cerebral infarction. *Neurology (Minneap)* 12:823–835, 1962.

5. FISHER, CM: The use of anticoagulants in cerebral thrombosis. *Neurology (Minneap)* 8:311–332, 1958.

6. FISHER, CM: Anticoagulant therapy in cerebral thrombosis and cerebral embolism. A national cooperative study, interim report. *Neurology (Minneap)* 11:119–131, 1961.

7. GILROY, J, BARNHART, MI, MEYER, JS: Treatment of acute stroke with dextran 40. *JAMA* 210:293–298, 1969.

8. FLETCHER, AP, ALKJAERSIG, N, LEWIS, M, ET AL: A pilot study of urokinase therapy in cerebral infarction. *Stroke* 7:135–142, 1976.

9. MACKEY, WA, SCOTT, LDW: Treatment of apoplexy by infiltration of the stellate ganglion with novocain. *Br Med J* 2:1–4, 1938.

10. PAULSON, OB: Discussion, in McDowell, FH, Brennan, RW (eds): *Cerebral Vascular Diseases. Eighth Princeton Conference*. New York, Grune & Stratton, 1973, pp 204–205.

11. BLAISDELL, FH: Extracranial arterial surgery in the treatment of stroke, in McDowell, FH, Brennan, RW (eds): *Cerebral Vascular Diseases. Eighth Princeton Conference*. New York, Grune & Stratton, 1973, p 13.

12. BLAISDELL, FW, CLAUSS RH, GALBRAITH, JG, ET AL: Joint study of extracranial arterial occlusion. IV. A review of surgical considerations. *JAMA* 209:1889–1895, 1969.

13. BRUETMAN, ME, FIELDS, WS, CRAWFORD, ES, ET AL: Cerebral hemorrhage in carotid artery surgery. *Arch Neurol* 9:458–467, 1963.

14. WYLIE, EJ, HEIN, MF, ADAMS, JE: Intracranial hemorrhage following surgical revascularization for treatment of acute strokes. *J Neurosurg* 21:212–215, 1964.

15. MILLIKAN, CH: Discussion, in McDowell, FH, Brennan, RW (eds): *Cerebral Vascular Diseases. Eighth Princeton Conference*. New York, Grune & Stratton, 1973, p 23.

16. DYKEN, M, WHITE, PT: Evaluation of cortisone in the treatment of cerebral infarction. *JAMA* 162:1531–1534, 1956.

17. RUBINSTEIN, MK: The influence of adrenocortical steroids on severe cerebrovascular accidents. *J Nerv Ment Dis* 141:291–299, 1965.

18. PATTEN, BM, MENDELL, J, BRUUN, B, ET AL: Double-blind study of the effects of dexamethasone on acute stroke. *Neurology (Minneap)* 22:377–383, 1972.

19. BAUER, RB, AND TELLEZ, H: Dexamethasone as treatment in cerebrovascular disease. 2. A controlled study in acute cerebral infarction. *Stroke* 4:547–555, 1973.

20. NORRIS, JW: Steroid therapy in acute cerebral infarction. *Arch Neurol* 33:69–71, 1976.

21. MEYER, JS, CHARNEY, JZ, RIVERA, VM, ET AL: Treatment with glycerol of cerebral oedema due to acute cerebral infarction. *Lancet* 2:993–997, 1971.

22. GILSANZ, V, REBOLLAR, JL, BUENCUERPO, J, ET AL: Controlled trial of glycerol versus dexamethasone in the treatment of cerebral oedema in acute cerebral infarction. *Lancet* 1:1049–1051, 1975.