Second Joint Meeting on Stroke and Cerebral Circulation

Sheraton-Four Ambassadors Hotel, Miami, Florida, February 25–26, 1977

Sponsored by
STROKE COUNCIL
American Heart Association

CEREBROVASCULAR SURGERY SECTION
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Further information about registration ($50) and hotel may be obtained from Mr. Dale Stringfellow, American Heart Association, 7320 Greenville Avenue, Dallas, Texas 75231. Registration is also available at the meeting. This continuing medical education offering meets the criteria for 11 hours of credit in Category I for the "Physician's Recognition Award of the American Medical Association."
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I-1

Experience With a Noninvasive Evaluation for Cerebral Vascular Disease — Raines JK, Schlaen H, Brewster DK, Darling RC (Massachusetts General Hospital, Boston, Massachusetts).

The purpose of this study was to determine how a newly developed noninvasive evaluation affected the management of 100 consecutive unselected cases.

Following clinical assessment the evaluation consisted of ophthalmic plexysography (OPG), carotid audiofrequency analysis (CAA) and cerebral Doppler velocity analysis.

There were 29 patients with asymptomatic bruits. Five were found to have hemodynamically significant stenoses of the internal carotid artery by our evaluation; angiography confirmed the laboratory findings and carotid endarterectomy followed in all five cases.

There were 41 patients presenting with transient ischemic attacks. Twenty had abnormal laboratory findings and angiography was performed. Nineteen patients had significant extracranial vascular disease and surgery was performed in 17 cases. The remaining 21 patients had normal laboratory studies; one patient in this group was determined by angiography to have significant internal carotid artery disease.

Nineteen patients had atypical symptoms; 11 patients were studied after completed strokes.

This evaluation has significant value in management of patients with asymptomatic bruits, atypical symptoms and transient ischemic attacks.

I-2

Clinical Results With a Color-Coded Differential Velocity Carotid Bifurcation Scanner — White DN, Curry GR (Kingston General Hospital, Kingston, Canada).

By color coding different magnitudes of Doppler frequency shift from blood flow in the carotid bifurcation in a spatial display, both occlusions and stenoses, where the blood velocity is increased, are displayed.

Since carotid stenoses are more numerous than occlusions and are amenable to surgery, which most occlusions are not, this technique greatly increases the clinical value of the scans so made.

The color scans display normal segments of the arterial bifurcation as red where the velocity of flow is normal. The sites of stenoses exceeding 50% of the arterial lumen are displayed in their correct position as yellow and blue regions corresponding to the degree of stenosis and increase in flow velocity. The scans made by this noninvasive and safe technique correlate well with conventional angiograms. They therefore serve as an excellent means of selecting patients who may be suitable for endarterectomy.

I-3

Doppler Scanning and Xerography: A Scanning Procedure — Turnipseed WD, Berkoff H, Barriga P (University Hospitals, Madison, Wisconsin).

Patients with generalized arteriosclerosis undergoing major vascular or coronary artery bypass surgery may have significant, but undetected carotid lesions. Combined use of Doppler scanning and xerography is a noninvasive method defining location and severity of lesions in cervical vessels. One hundred patients requiring major vascular surgery (72 peripheral vascular, 28 coronary revascularization) were preoperatively tested. Carotid lesions were suspected in 34 patients because of audible bruits (30) or symptoms of cerebral ischemia (four). In contrast, 41 patients had Doppler evidence of carotid stenosis. By xerography, severe vessel calcification was shown in 12 of 16 patients with extensive plaquing. Carotid arteriograms were performed on patients with symptomatic cerebral ischemia (four) and in asymptomatic individuals who had scanning evidence of severe carotid stenosis (two) or occlusion (three). The lesions identified by noninvasive screening techniques correlated precisely with arteriographic findings. As a result, seven endarterectomies were performed in five patients with asymptomatic, critical stenotic lesions which were detected by noninvasive screening prior to major abdominal or coronary vascular reconstruction. All did well postoperatively.

I-4

Real-Time Ultrasonic Viewing of Atherosclerosis in the Carotid Artery — Olinger CP (University of Cincinnati, Cincinnati, Ohio), Nigam AK, Wasserman JF, Packer BR (Kingston General Hospital, Kingston, Canada).

Carotid artery disease was detected in patients by the use of a real-time pulse-echo ultrasonic imaging system.

High resolutions were attained by the use of a large aperture transducer which was dynamically focused in depth. Real-time operation was provided by a scanning mechanism which operated at 30 frames per second. The images were displayed on a video monitor.

The carotid ultrasonic arteriograms (longitudinal and cross-sectional scans) closely correlated with the carotid angiograms (anteroposterior and lateral views) in 100 carotid arteries. The angiographic-correlated results will be presented and a videotape shown.

The results suggest the potential of this system as a safe, noninvasive method for screening, diagnosis, and follow-up of extracranial occlusive disease and for long-term evaluation of the complex dynamic phenomenon of atherosclerosis.

I-5

Computerized Tomography Patterns in Recent Cerebral Infarction — Masdeu J, Azar-Kia B, Rubino F (Hines VA Hospital, Hines, Illinois).

Twenty patients with recent cerebral infarctions were followed by sequential preinfusion and postinfusion CT scans. Within the 24 hours preceding or following the CT examinations, a 99m Tc scan was performed.

The sequential follow-up of the same lesion allowed us to evaluate the timing of edema and contrast enhancement in relation to the ictal episode.

Seventy percent of those infarctions showed a mass effect, which had disappeared in all cases by the eighth week following the ictus. In 63% of those patients enhancement occurred after the infusion of contrast. In different stages of their evolution several infarcts were visualized only after infusion of contrast. Various patterns were noted postinfusion.
Cranial Computed Tomography in the Subhuman Primate: Cerebral Infarction — Drayer BP, Dujovny M, Wolfson SK, Boehnke M, Barriomeure PJ, Cook EE (University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania)

The normal cranial computed tomographic (CT) appearance of 12 control baboons (Papio anubis) was demonstrated with pathologic correlation. Artifact-free scans with 8-mm collimation were readily obtained in the anesthetized animal. Intravenous (meglumine iothalamate) and intrathecal (oxygen, metrizamide) enhancement was quite helpful in improving anatomic definition, but revealed no CT areas of abnormal absorption.

Cerebral infarctions were produced in four baboons using a silicone rubber cylinder embolus injected into the internal carotid artery and lodging in the middle cerebral artery (MCA). CT scans were done at one, two, six and 12 weeks. An animal was killed at each of these time intervals for CT-histologic confirmation. The consistent CT scan finding was an irregular area of decreased absorption located in the distribution of the MCA. Mild contrast enhancement occurred between the CT and the gross pathology in all four animals. Therefore, CT appears to be an invaluable technique for the study of cerebral infarction in the subhuman primate, presenting precise anatomic data in the living experimental animal.

Radiolabeling of Clots in a Model of Cervical Carotid Thrombosis — Kaufman HH, Anderson JH, Woo J, Handel SF (University of Texas Medical School, Houston, Texas)

A method has been developed to radiolabel intravascular clots in a model of cervical carotid thrombosis. Using autologous fibrinogen harvested by precipitation with ammonium sulfate and radiolabeled with 14C by means of the chloramine T (Chl T) or iodine monochloride (IC1) methods, a product with 80% to 90% in vitro clottability and a satisfactory in vivo half-life (Chl T 46 hours, IC1 36 hours) has been obtained. Cervical carotid thrombi have been created in the dog by traumatizing the intima of the vessel, causing stasis with a balloon catheter, and augmenting local thrombosis by injection of thrombin. After injecting the radiolabeled fibrinogen into the animals, it was possible to localize the thrombi and follow them for three days by both scanning and counting techniques (Chl T 5/5 dogs, IC1 3/3 dogs).

We project that this method may be used in humans to detect and follow carotid thrombi and to judge clot lysis either by normal in vivo mechanisms or in coordination with the use of thrombolytic therapy. When the technique is refined, it may also be possible to use it to detect patients with carotid atheromas with ulcers and thrombus formation and thus select candidates for carotid endarterectomy.

Reduced WBC Cholesterol Ester Hydrolase (CEH) in Atherosclerosis — Yatsu F, Riddle M, Hagemenas F, Galambos T (University of Oregon Health Sciences, Portland, Oregon)

Strokes due to atherosclerosis remain of uncertain molecular pathogenesis. In six atherosclerotic carotid arteries, we demonstrated lysosomal CEH reduction (J Neuropath 35:343, 1976), supporting deDuve's hypothesis that atherosclerosis may represent a lysosomal deficiency storage disease. To determine whether this reduction is generalized, we studied WBC (leukocyte) lysosomal CEH in patients undergoing carotid endarterectomy. One million to 1.5 million isolated WBC were incubated in duplicate at pH 4.5 for one hour with labeled, acetone-dispersed cholesteryl olate. Cholesterol ester and cholesterol were extracted, isolated by TLC, and counted. Our data show eight controls, average age 61, with WBC CEH activity of 2,167 ± 273 pmoles/mg protein per hour, compared to six atherosclerotics, average age 64, of 1,065 ± 193, p < 0.005. These preliminary data showing reduction of WBC CEH in atherosclerosis warrant further studies to assess enzyme kinetics, prognostic value and response to interventional therapies.

Transient Cerebral Ischemia in Rabbits: ADP and Arachidonic-Acid-Induced Platelet Emboli and Effects of Antiplatelet Agents — Fieschi C, Volante F, Passero S (University of Siena, Siena, Italy)

Cerebral ischemia was induced in rabbits by infusing either ADP or arachidonic acid in the lingual artery. Platelet emboli are formed in the carotid artery and migrate to cerebral vessels, producing multiple temporary occlusions and ischemia (Fieschi et al: Stroke 6:617, 1975; in press, 1976). Ischemia can be observed and quantified by various areas, thus allowing study of the "in vivo" protective action of pretreatment with drugs. Thirty-three rabbits were thus protracted either with ASA at different dose schedules, and/or with dipyridamole or nicergoline (synthetic-blocking agent). Neither of these two drugs affords significant protection against platelet emboli, while ASA does prevent emboli and ischemia.

This, however, is obtained at different levels of ASA, also monitored by means of blood level determinations of the drug, for the two models. Extrapolation to human conditions of clinical prevention of embolic TIAs is attempted on the basis of dose/weight and dose/body surface ratios: there the models appear to be, within limits of any animal study, good predictors of clinical efficacy drugs.

Platelet Dysfunction as a Risk Factor in Cerebrovascular Disease — Deshmukh SV, Meyer JS (Baylor College of Medicine, Houston, Texas)

A battery of platelet function tests was performed in patients with cerebral infarction (stroke = 28), transient ischemic attacks in internal carotid circulation (TIAs = 8) and vertebrobasilar insufficiency (VBI = 17) and compared...
with age-matched and sex-matched normal controls. A significantly greater proportion of stroke patients produced a secondary wave of aggregation with 1 μM ADP (p < 0.001) and showed a higher slope of first-wave aggregation with 1 μM (p < 0.05) and 5 μM epinephrine (p < 0.001). Circulating microemboli index was low (p < 0.001) and platelet adhesiveness was significantly high (p < 0.005). TIA and VBI patients also had significantly abnormal results in all parameters.

The results of the present study support the view that platelet dysfunction may be an important risk factor in the pathogenesis of thromboembolic cerebrovascular disease, since platelets play an essential role in thrombosis and hemostasis. A clinical trial comparing the effects of platelet inhibitors, aspirin and sulfipyrazone, with a view to normalizing the platelet abnormality and possibly preventing further stroke, TIA and VBI, is presently in progress.

**Session II: Pathogenesis and Epidemiology**

**Friday (10:30 A.M. to 12:00 M.)**

II-11

The Epidemiology of Atherothrombotic Brain Infarction (ABI): The Framingham Study — Wolf PA, Dawber TR, Thomas HE, Colton T, Nickerson RJ (Boston University School of Medicine, Boston, Massachusetts)

The risk factors predisposing to stroke in general and to ABI in particular are being identified and their relative impact assessed in prospective epidemiologic studies. In the population sample at Framingham, Massachusetts, 5,184 men and women aged 30 to 62 at entry have been followed for the development of cardiovascular diseases including ABI. This presentation, utilizing data obtained as a result of 24 years of follow-up, represents the culmination of the study of stroke in this population. A sufficient number of events have occurred to permit detailed analysis of precursors of ABI. A total of 345 strokes have occurred, 175 in men and 170 in women. ABI was the most common type accounting for 60% (206 of 345) of all strokes. Unlike other manifestations of atherosclerosis, ABI occurs with equal frequency in men and women.

Hypertension is the most potent precursor of ABI and the level of risk is related to the height of the blood pressure, systolic or diastolic. Those subjects with other risk factor abnormalities — diabetes, LVH by ECG, elevated blood cholesterol, cigarette smoking and cardiac impairments — are at heightened risk of ABI. Treatment of hypertension particularly in those with other abnormalities is the key to ABI prevention.

II-12

Risk Factors and Angiographic Abnormalities in Young Patients With Acute Nonembolic Ischemic Infarction — Lee MC, Klassen AC, Heaney LM, Resch JA (University of Minnesota, Minneapolis, Minnesota)

Risk factors and angiographic abnormalities were studied in 46 patients aged 15 to 40 years with acute ischemic cerebral infarction. Patients with apparent cardiac sources of cerebral emboli, collagen vascular disease and/or renal hypertension were excluded. Risk factors studied included coronary heart disease, coagulation abnormalities, serum lipids, smoking, obesity, birth control pills, migraine and family history of stroke at an early age. One or more of these risk factors was present in 37 of 46 patients. Prior use of birth control pills had occurred in 21 and was the only risk factor present in 14. Frequencies of other risk factors were: hypertension = 11, migraine = 11, heavy smoking = 10, hyperlipidemia = 6, diabetes mellitus = 5, coronary heart disease = 3, and family history of stroke at a young age = 1. Angiographic findings in 38 patients were: internal carotid or middle cerebral artery occlusion = 8, multiple small intracerebral vessel occlusion = 7, stenosis of middle cerebral or internal carotid artery = 4, single distal small vessel occlusion = 4, multiple large and small vessel occlusions = 3 and vertebral or basilar artery stenosis = 3. Factors other than the usual risk factors for atherosclerotic ischemic cerebrovascular disease may be operative in young patients with ischemic stroke.
logical symptoms nor an aneurysm. Follow-up revealed that 40% (4/10) died, 50% (5/10) were permanently disabled, and 10% (1/10) had no residual neurological deficits. CVAs are infrequent complications of CAB and/or aneur but carry a high mortality or disability rate. Patients with neurological symptoms should be evaluated by a neurologist preoperatively with consideration given to four-vessel angiography. Better methods of thrombus control during aneurysctomy or during aneurysm manipulation during CAB should be sought.

II-15

Early Predictors of Stroke Outcome — Wood DH, Fernbach NK, Montague MC (Howard University College of Medicine, Washington, D.C.)

Previous investigations have clearly identified a number of factors predisposing to the development of acute stroke; however, it is less clear which clinical and/or physiological factors, operant during the acute phase of this illness, influence or are predictive of patient morbidity. Because this disorder exhibits a variable clinical course and outcome dependent upon a number of clinical variables and as yet unidentified pathophysiological processes, previous investigations, usually retrospective in design and/or conducted in extended care facilities, have provided only tentative conclusions. This report is an analysis of a prospective investigation conducted during the acute phase of this illness in 140 patients. The study population was evaluated daily for two weeks and then monthly for six months or until death. A preliminary computer analysis of approximately 130 variables recorded on each study patient revealed 20 variables which could be significantly correlated with patient outcome. The most significant were cerebroton, the presence of underlying medical complications on admission, the presence of a hemianopia or hemisensory deficit, and the degree of motor weakness.

II-16

Recent Cerebral Infarction in the Distribution of the Internal Carotid Artery — Bounds JV, Okazaki H, Reagan TJ, Whisnant JP (Mayo Clinic and Mayo Medical School, Rochester, Minnesota)

Thrombotic or embolic occlusions of the internal carotid artery (ICA) or its branches were found in 81 cases among 100 deaths from recent ICA distribution cerebral infarctions. Embolism was identified as a possible cause of occlusion in 63% (51/81). Only 25% (20/81) of the occlusions were definitely embolic by strict pathologic criteria. Extracranial arterial occlusion was seen in 32% (26/81), whereas the intracranial circulation was involved by thrombosis or embolism in 68% (55/81). Complicated lesions of atherosclerosis (intimal ulceration and/or hemorrhage) were infrequent, eight of 100 cases.

Of the 100 cases, transtentorial herniation was the cause of death in 32, pneumonia in 29, cardiac causes in 17, and pulmonary embolism in 12, with other causes for ten deaths. Infarcts involving the combined anterior and middle cerebral artery distribution were most commonly associated with herniation. When pneumonia was the cause of death, the deaths were distributed evenly over a 35-day period. When death was due to herniation, 60% (19/32) died within three days. There is a good correlation between patients with herniation and those with hemiplegia and altered consciousness.

II-17

Effect of Diet on Brain Pathologic Response to Blood Flow Stasis — Myers RE (NIH, Bethesda, Maryland)

Food-deprived rhesus monkeys tolerate 14 minutes of circulatory arrest and survive without neurologic or pathologic abnormalities. Circulatory arrest for from 14 to 24 minutes injures only nuclear structures of the brain stem. Magnitude and extent of injury bear little relation to duration of arrest beyond 14 minutes. Animals fed ad libitum or given glucose infusions beforehand show a dramatically different outcome. Fed animals arrested for 14 minutes have fuscitations, repetitive myoclonic jerks, decerebrate rigidity, and, finally, apnea. Brain specimens after sacrifice reveal mild edema with convolutional flattening and herniation of tonsils. Microscopic examination reveals widespread tissue injury with dissolution of nerve cells and other cellular elements. Evans blue, injected before the animals were killed, demonstrates widespread breakdown of blood-brain barrier. Studies reported elsewhere show that the principal change brought about in brain composition at termination of arrest by antecedent glucose infusion is excessive accumulation of lactic acid. This latter change appears to constitute that critical tissue change which produces blood-brain-barrier injury and brain edema.

II-18

Prevention of Retinal Cell Swelling In Vitro by Hypertonic Mannitol or Isethionate Substitution Does Not Prevent Cell Death From O2 and Glucose Deprivation — Shay J, Hein A (Massachusetts General Hospital, Boston, Massachusetts)

Does prevention of swelling during energy deprivation alter the fate of the tissue when it is subsequently resupplied with O2 and substrate? Retinas deprived of O2 and glucose 30 to 90 minutes either untreated (n = 69) or treated with 97 mM mannitol (n = 34) or with isethionate (n = 23) substituted for chloride in the medium were returned to media containing O2 and glucose for 90 minutes. Treated retinas were initially resupplied in mannitol or isethionate media, but these media were progressively diluted with control medium. Untreated retinas were resupplied in control medium. Water content was determined or retinas were fixed for microscopy. Following deprivations lasting up to 40 minutes, morphology and water content did not differ from undeprived controls (n = 45). All retinas deprived 50 minutes showed cell swelling, pyknotic nuclei, vacuolization of synaptic layers as well as increased water content. Treated retinas did not differ significantly from untreated retinas at any of the deprivation times studied.

II-19

Pathomechanisms in Ischemic Brain Edema — Klatzo I, Fujimoto T, Spatz M (NINCDS, NIH, Bethesda, Maryland)

Ischemic brain edema was studied in Mongolian gerbils
subjected to unilateral clamping of the common carotid artery. The ensuing edematous changes were assayed by measuring specific gravity of the brain tissue and the data were correlated with the behavior of the blood-brain barrier (BBB), radioautographic evaluation of the cerebral blood flow (CBF) and histopathologic changes. Our results indicated a prompt increase in water content following ischemia. The onset of necrotic changes produced a drastic further change in specific gravity. The opening of the BBB for proteins was of transitory nature and it could not be correlated with changes in CBF, nor with progression of histopathologic changes in the brain parenchyma. Ischemic brain edema can be regarded as predominantly of the cytotoxic type, starting with an intracellular accumulation of water, and later intensifying markedly due to osmotic movement of water into necrotic areas. Opening of the BBB to proteins, which occurs after some delay according to the principles of the "maturation" phenomenon, introduces in addition a vasogenic component into the ischemic pathology.

Session III: Therapy in Acute Infarction and Rehabilitation

Effect on Regional Cerebral Blood Flow in Ischemic Stroke of Vasopressor Therapy — Goldberg HI, Banka RS, Reivich M (University of Pennsylvania, Philadelphia, Pennsylvania)

Considerable controversy persists regarding the effect of blood pressure alterations in acute stroke patients. We have had the opportunity to examine the regional cerebral blood flow (rCBF) in three patients with recent ischemic strokes before and immediately after raising their blood pressure. Two of the three patients had cerebral angiograms which demonstrated severe occlusive vascular disease. The rCBF was studied with the 133 xenon inhalation technique utilizing 15 cerebral detectors. There was excellent correlation between low rCBF foci and the angiographic location of ischemic circulation. Blood pressure elevation significantly improved flow in regions with the most reduced rCBF in all patients. In two patients, blood pressure was elevated pharmacologically. In the third, antihypertensive therapy was discontinued. Vasopressor therapy was maintained only during the study period. No immediate clinical effect was observed in these two patients.

This experience suggests that in acute stroke secondary to large vessel occlusive vascular disease, rCBF in ischemic areas might be improved by vasopressor therapy. Whether increasing rCBF will be reflected in improved recovery from stroke awaits a more extensive randomized clinical study of prolonged effects of this therapy.

The Effect of Dimethyl Sulfoxide on Cerebral Infarction in the Mongolian Gerbil — McGraw CP, Lawson JW (Bowman Gray School of Medicine, Winston-Salem, North Carolina)

Dimethyl sulfoxide (DMSO) has been reported to have a beneficial effect in central nervous system trauma, possibly due to DMSO's reported anti-inflammatory, antiedemic, anticoagulate, diuretic, hypothermic, vasodilatory, respiratory stimulatory, membrane stabilization, blood-brain barrier penetration effects.

This study was performed to determine if morbidity and mortality due to experimental cerebral infarction could be decreased with DMSO.

Fifty Mongolian gerbils were utilized. Forty received unilateral common carotid ligation while ten others received sham operations. All the animals were injected with Trypan blue for gross-lesion identification. Half of the animals were administered 0.5 cc intraperitoneally of 50% DMSO solution at one hour post-ligation, then every eight hours for 72 hours in a double-blind manner.

No significant differences from saline controls were observed in number of infarctions or extent of morbidity. However, the animals who received DMSO that infarcted had a decreased incidence of staining of the infarction by the Trypan blue even though they did have an infarct and previously reported clinical signs.

Angiographic and Ultrastructural Changes in Monkey Brain Following Experimental Middle Cerebral Artery Infarction — de la Torre JC, Hill PK (University of Chicago School of Medicine, Chicago, Illinois; Mayo Clinic, Rochester, Minnesota)

The brains of 18 theses monkeys were experimentally infarcted following 17-hour occlusion of the middle cerebral artery (MCA). Treatment with dexamethasone (DX), dimethyl sulfoxide (DS) or saline (S) was begun four hours after occlusion and was continued for five days. After seven days, right and left cortical samples were taken for light and electron microscopy. Cerebral angiograms were taken before, during and following MCA infarction. Two sham animals that underwent surgery without occlusion showed no neurological or brain tissue damage. Hemispheric water content was measured in each monkey following sacrifice. Brain ultrastructural changes in the traumatized but not the contralateral hemisphere showed severe, moderate and mild changes in the groups given S, DX and DS, respectively. Subcellular neural damage included axonal compression, swelling of terminal boutons and loss of synaptic vesicles. Water content, angiograms, and gross neurological deficits reflected the treatments given and the microscopic changes observed.

It is concluded from these data that DS but not DX or S is useful in preventing the severe neurological and morphological damage seen following this cerebrovascular insult.

The Role of DMSO and Methylprednisolone in Canine Middle Cerebral Artery Microsurgical Embolectomy — Dujovny M, Barriuevo PJ, Laha RK, Solis G, Maroon J, Hellstrom RH (VA Hospital and University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania)

In our laboratory embolization of canine middle cerebral artery (MCA) by a pliable cylinder has consistently produced significant mortality and morbidity in the animals embolectomized beyond five hours postembolism. Twelve
animals (six each) embolectomized at six hours and seven hours postembolism revealed hemorrhagic infarction of brain measuring 1.412 cm³ and 1.643 cm³ respectively. In order to evaluate the protective cerebral effects of DMSO and steroids, the middle cerebral artery of dogs was embolectomized at six hours postembolism. Six animals treated with DMSO (2 gm per kilogram) did not manifest any neurological impairment or show any histological changes in the brain. Five of six animals receiving a high dosage of methylprednisolone (40 mg/kg/day) died within 48 hours postoperatively. All animals had massive neurological deficits with the average volume of infarction being 1.345 cm³. Four animals treated with a low dosage of methylprednisolone (2 mg/kg/day) showed no deficits or histological abnormality.

III-24

Serial Angiography in Cases of Acute Completed Strokes Demonstrating Resolution of Vascular Occlusions — Heilbrun MP (University of Utah College of Medicine, Salt Lake City, Utah)

Previously, we noted that in the preoperative evaluation for cerebral revascularization with angiography and flow studies, 2 of 28 lesions had resolved, eliminating the necessity for surgery. Concomitantly, to identify candidates for early revascularization procedures, we pursued a policy of analyzing acute completed stroke patients with early angiography. Initially, three patients with completed strokes, two severe and one mild, were treated with surgical modalities. All three patients did poorly. Subsequently, we treated four patients with acute severe completed strokes with anticoagulation. All four patients had middle cerebral artery occlusions, the source of the embolus being a carotid plaque in two cases. One patient died, three improved markedly, and a second angiogram during the improvement stage showed recanalization of the middle cerebral artery.

Angiography following careful clinical examination in acute stroke patients provides a rational basis for therapy. In selected cases, serial angiography after stabilization allows a more rational basis for adjustments to both medical and surgical treatment regimens.

III-25

Indications for Emergency Carotid Surgery — Goldstone J, Moore WS (VA Hospital and University of California, San Francisco, California)

Angiographic and surgical procedures are usually carried out on an elective basis for patients with cerebrovascular disease (CVD). After encountering several patients in whom the time required for this elective approach allowed a severe neurologic deficit to develop, we adopted a more aggressive plan of management. Nine patients with stroke-in-evolution and five patients with transient ischemic attacks of increasing frequency (crescendo TIAs) have undergone early angiography in the past two years. All had preocclusive (> 95%) stenosis of the appropriate proximal internal carotid artery (ICA). Fourteen other patients evaluated electively for stable CVD had similar critical arterial lesions, which we believe to be unstable. Emergency carotid thromboendarterectomy was performed on 26 patients with no deaths, no morbidity, and complete cessation of neurologic symptoms. The two patients not operated upon had severe strokes within two days. These results support the following conclusions: (1) patients with unstable arterial lesions constitute a special group who are at high risk for serious but preventable neurologic sequelae; (2) angiography should be performed immediately on patients with crescendo TIAs, stroke-in-evolution, or waxing and waning neurologic deficit of mild to moderate degree; (3) emergency carotid endarterectomy should be performed when a critical arterial lesion is identified.

III-26

Embolectomy for Acute Middle Cerebral Artery Occlusion — Piepras DG, Sundt TM Jr, Yanagihara T (Mayo Clinic, Rochester, Minnesota)

Results of emergency surgery for acute middle cerebral artery (MCA) embolic occlusion in 11 cases are reviewed. All patients had severe neurological deficits from the middle cerebral occlusion that included: altered level of consciousness, hemiplegia, forced deviation of the eyes to the side of the lesion and apparent homonymous hemianopia. The left MCA was involved in eight cases and the right MCA in three cases, the former having dense aphasia as well. Good restoration of flow was confirmed in six cases by angiography, one case by inspection at the time of reoperation for temporal lobe hemorrhage. In four cases flow could not be restored due to the propagation of a thrombus into the smaller branches of the MCA. In those patients in whom flow could be restored, there was a major improvement in neurologic function. In those patients in whom flow could not be restored there were two deaths and two patients in whom the deficit was not significantly altered. The risk of hemorrhagic infarction will be reviewed and the concept of neural tissue tolerance to ischemia considered. It is concluded that emergency surgery for acute MCA embolism is a useful procedure in properly selected cases. The criteria for surgery, including appropriate angiographic findings, will be evaluated.

III-27

Treatment of the Neurogenic Bladder in Stroke — Marks RL (Lorain Community Hospital, Lorain, Ohio)

Intermittent catheterization, as a therapy for neurogenic bladder of patients who survived cerebrovascular accidents, was studied. Thirty patients, whose ages ranged from 37 to 77 years, were treated with intermittent catheterization in the acute stages of their illnesses. Initially, a catheter was passed every six hours in order to empty the bladder. At intervals, the patient was asked to void and a post-voiding residual was measured. Catheterizations were decreased with the patient's ability to void. Cystometrograms, VPs and voiding cystometrograms were obtained in only a few patients when voiding did not occur spontaneously. This study demonstrated that such special tests were rarely necessary for success. In several cases, medication was required to stimulate detrusor action.

Following treatment, 27 of the 30 patients were able to void. Thus, intermittent catheterization appears to be an excellent treatment for the neurogenic bladder of stroke.
III-28

Rehabilitation Biofeedback for Stroke Patients — Basmajian JV (Emory University School of Medicine, Atlanta, Georgia)

A series of investigations in various rehabilitation centers, including a reported controlled study by us, has established the usefulness of muscle retraining to overcome severe chronic foot-drop in hemiplegic patients. Expanding our research series to a semi-routine clinical setting we have succeeded to the point where approximately 40% of 50 patients have been able to discard their short leg braces for gait.

Further expansion of our long-term studies in biofeedback re-education of stroke patients now includes alleviation of shoulder subluxation by biofeedback training of the scapular postural muscles combined with relaxation training. The latter approach has also contributed to the reduction of spasticity which permits better recapturing of motor functions thought to have been lost forever.

Carefully administered in a step-by-step fashion by skilled rehabilitation therapists, EMG biofeedback offers a useful tool for alleviation of both paretic and spastic symptoms, sometimes dramatically.

III-29

Academic Versus Community Hospitals: A Comparison of Diagnostic Regimens, Length of Stay, and Eventual Outcome in a Group of 483 Stroke Patients — Feigenson JS, McCarthy ML, Feigenson WD, Meese PD, Greenberg SD, McDowell FH (Burke Rehabilitation Center, White Plains, New York)

During a 27-month period 483 stroke patients were discharged from a 30-bed stroke unit at the Burke Rehabilitation Center. Detailed records outlining the etiology of the stroke, diagnostic regimens, and length of stay at the referring hospitals were obtained prior to admission using a standardized Stroke Data Transfer Form and the patients were then divided into two categories: those referred from major academic hospitals (hospitals affiliated with medical schools) and their major satellites, and those referred from community hospitals. Eventual outcome — as measured by discharge from the Burke Rehabilitation Center and ability to perform self-care activities on discharge — was retrieved at the referring hospital.

Eventual outcome — as measured by discharge from the Burke Rehabilitation Center and ability to perform self-care activities on discharge — was retrieved at the referring hospital.

Session IV: Cerebral Blood Flow and Metabolism

Friday (3:45 to 5:00 P.M.)

IV-30

Oxidative Metabolism During and Following Cortical Ischemia in Cats — Rosenthal M, Martel DL, LaManna JC (Duke University Medical Center, Durham, North Carolina)

To determine the nature of the underlying cellular vulnerability to ischemia, optical techniques were used to noninvasively monitor redox levels of NAD and cytochrome $a_a$ in cat cerebral cortex during and following arterial clamping. Incomplete ischemia produced increased levels of reduced NAD and $a_a$, which quickly returned toward baseline indicating reperfusion effects. Complete ischemia produced maximal levels of reduced NAD and $a_a$, which remained constant until clamp removal. Following complete ischemic episodes (approximately one minute in duration), reoxidation rates of NAD and $a_a$ were progressively increased indicating increased rates of O$_2$ use, while blood volume return was unchanged demonstrating that this is not a circulatory effect. These results are consistent with increased rates of respiration of uncoupled mitochondrial systems. After complete ischemia, evoked potentials were accompanied by increased and then decreased rates of NAD re-reduction. The former appear due to "substrate mobilization" possibly resulting from utilization of accumulated lactate. The latter appear due to uncoupling of oxidative phosphorylation. Thus, mitochondrial integrity, upon which the ability to form ATP is dependent, may be the most sensitive cellular component to ischemic injury.
glucose. The brains were frozen in different time intervals and processed for an autoradiographic technique. At 15 minutes and 30 minutes there is a marked decrease in 14C deoxyglucose uptake in the ischemic zone. Coincident with the decrease of glucose uptake in the center of ischemic zones, surrounding areas show a marked increase in glucose uptake. At one hour the areas shrank markedly to the immediate area surrounding the embolized microspheres. A slightly larger zone of increased glucose utilization is noted immediately surrounding the areas of decreased uptake. At four hours there was a further reduction of the size of areas not utilizing glucose, each surrounded by a zone of increased utilization. It is suggested that shrinkage of the zones of altered glucose utilization is effected by the formation of collateral circulation. It is possible that the zones of increased glucose utilization represent a manifestation of increased glycolysis secondary to the Pasteur effect.

IV-33
Ischemic and Postischemic Effects on 2-Deoxy-D-(3H)-Glucose Uptake in Cerebral Microvessels — Spatz M, Mrsulja BB, Micic D, Mrsulja BJ, Klatzo I (NINCDS, NIH, Bethesda, Maryland)

The uptake of 2-deoxy-D-(3H)-glucose (3H 2-DG) in cerebral capillaries isolated from brains of gerbils subjected to bilateral carotid artery clipping and release was investigated in order to elucidate the possible site responsible for the observed postischemic increased passage of 3H 2-DG from blood to brain.

The cerebral microvessels were separated from the nonvascular tissue by homogenization, repeated centrifugation at 1,500 × g, 1.0 to 1.5 M sucrose gradient and ultracentrifugation at 58,000 × g.

Bilateral ischemia reduced the 3H 2-DG capillary uptake up to 50% as compared to controls. Reestablishment of cerebral circulation led to recovery in 5 to 15 minutes and increase of 3H 2-DG capillary uptake which lasted for three hours. Thus, the observed changes occurring on the capillary level could be responsible for the lack or surplus of the basic brain nutrient and, therefore, have great clinical implications.

IV-34
Functional and Metabolic Responses of the Spinal Cord to Hypoxia and Hypotension — Yamada S, Sanders DC, Haugen GE, Brown DE (Loma Linda University Medical Center, Loma Linda, California)

In the earliest stage of spinal cord ischemia hypoxia and hypotension develop. In order to determine the effects of hypoxia and hypotension on cord function and metabolism the following studies were done on experimental cats: cord potential on stimulating the dorsal root; polarographic oximetry; redox of cytochrome a,a3; and electron microscopy. A progressive decrease in amplitudes of interneuron potential and oxygen availability and progressive reduction of cytochrome a,a3 occurred when PaO2 decreased from 60 to 15 mm Hg by inhalation of 100% nitrogen. The interneuron potentials suddenly disappeared along with further reduction of cytochrome a,a3 when the blood pressure dropped below 60 mm Hg at PaO2 15 to 20 mm Hg. Electron microscopy revealed enlargement of mitochondrial matrix compartments after hypoxia and hypotension, whereas there was little change in mitochondria after hypoxia alone. The authors conclude that the combination of severe hypoxia and hypotension causes depletion of ATP and consequently inadequate ion pumps of neurons. The clinical application of this status is emphasized; severe hypotension (blood pressure below 60 mm Hg) and hypoxia (PaO2 15 to 20 mm Hg) should be avoided to protect the spinal cord from irreversible damage.

IV-35
Alterations of Cyclic Adenosine Monophosphate in Cerebral Ischemia — Flamm ES, Schiffer J, Vial AT, Naftchi NE (New York University Medical Center, New York, New York)

Cyclic AMP levels were measured in brains of 25 cats after occlusion of a middle cerebral artery by a transorbital approach. The animals were anesthetized with pentobarbital. Blood gases and blood pressure were monitored. Brain samples for determination of cyclic AMP by a protein binding radioassay were obtained from the ischemic and contralateral temporal lobes before sacrifice one, three, and 24 hours after occlusion of the right middle cerebral artery. Animals were then perfused with formalin and the brains histologically examined. At one hour, no difference between the two sides was observed; a mean of 19.6 pg/mg protein was observed from the side of the occlusion and 21.5 pg/mg protein from the contralateral side. At three hours, a mean value of 11.9 pg/mg protein on the ischemic side and a level of 29.9 pg/mg protein on the contralateral side was observed. At 24 hours, the cyclic AMP level on the ischemic side remained below the nonischemic side; the values obtained were 15.5 pg/mg protein compared to 25.0 pg/mg protein. These changes in cyclic AMP as early as three hours after the onset of ischemia, when such a lesion is reversible, may indicate that an initial step in the alteration of cellular metabolism following ischemia is due to membrane perturbation and altered production of this second messenger.

IV-36
Influence of Diffuse Cerebral Ischemia Upon Mitochondrial Respiration, Brain Water and Electrolytes — Ginsberg MD, Mela L, Wrobel-Kuhl K, Giandomenico A, Reivich M (University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania)

Mongolian gerbils were subjected to profound cerebral ischemia by bilateral common carotid artery ligation under urethane anesthesia. Respiratory activity of isolated brain mitochondria was assayed in the presence of glutamate-malate. In other animals, brain water and electrolyte contents were determined.

Mitochondria from control animals and from animals with up to two hours of ischemia were well-coupled. Urethane anesthesia alone led to an initial depression and subsequent enhancement of mitochondrial State 3 respiration (substrate and ADP present). In order to depress State 3 rates below control levels, ischemia of one hour or more was required. Ischemia of even 2.5 hours reduced mean State 3 rates to only 62% of control (536 versus 860 moles
O₂/mole cytochrome a + a₃ per minute). In contrast, brain water content rose significantly following only 15 minutes of ischemia and increased by 1.3% with ischemia of two hours. There was a continuous decline in brain K⁺ content during ischemia, and a smaller rise in brain Na⁺.

Brain edema appears to begin early during ischemia, before mitochondrial respiration becomes irreversibly affected. Mitochondrial respiration itself is relatively resistant to the effects of ischemia.

IV-37
The C₁⁵O₂/H₂ ¹⁸O Static Positron Scintigram as a Representation of Blood Flow — Ackerman RH, Subramanyam R, Alpert NM, Correia JA, Roberson GH, Brownell GL, Taveras JM (Massachusetts General Hospital, Boston, Massachusetts)

Imaging dynamic functions such as cerebral blood flow and metabolism may be possible with cyclotron-produced short-lived radionuclides such as oxygen-15 (half-life 123 seconds). On inhalation of C₁⁵O₂, water in the blood is labeled with oxygen-15 and an equilibrium state eventually is achieved, at which time the incoming activity is in balance with the outgoing activity due to biological washout plus physical decay.

Following inhalation of C₁⁵O₂ to dynamic equilibrium, the tracer ¹⁸O was imaged with the positron camera at normocapnia and hypocapnia. In these subjects a 40% to 50% fall in Paco₂ resulted in a 20% to 25% drop in the countrate over the cerebrum. This change indicates that the C₁⁵O₂/H₂ ¹⁸O static positron scintigram is at least in part a representation of blood flow.

IV-38
The Role of Arterial and Venous Oxygen Tension in the Control of Cerebral Blood Flow — Traystman RJ, Pitt BR (The Johns Hopkins University, Baltimore, Maryland)

Cerebral hemodynamic responses to three different types of hypoxia (low O₂-HH, carbon monoxide-COH, cyanide-CnH) were studied in 30 anesthetized dogs. Cerebral venous blood flow (CBF) was measured at the confluence of the sagittal, straight, and lateral sinuses, with the lateral sinuses occluded. Decreasing arterial O₂ content from control (18 vol %) to 8 vol % with either HH or COH or elevating blood CNH levels to 1 μg per milliliter increased CBF to about 190% of control. Cerebral O₂ consumption (VO₂) at these levels of hypoxia was markedly different from control. Cerebral arterial and venous oxygen tensions (PAO₂ and PVO₂), however, were markedly different with each hypoxia. HH reduced PAO₂ from 108.4 to 25.9 mm Hg and PVO₂ from 30.8 to 18.5 mm Hg. COH did not alter PAO₂ (113.1 to 111.0 mm Hg), but decreased PVO₂ from 27.0 to 16.1 mm Hg. CNH did not change PAO₂ (83.4 to 87.2 mm Hg), but increased PVO₂ from 26.7 to 42.3 mm Hg. These changes in PAO₂, PVO₂, CBF and VO₂ with each hypoxia were not affected by carotid chemodenervation. The CBF response to hypoxia is independent of both carotid chemoreceptors and cerebral arterial and venous oxygen tension, and is consistent with the idea that brain tissue itself controls its own blood flow depending upon metabolic tissue requirements.

IV-39
Patterns of Change in the Cerebral Blood Flow of Patients With Completed Stroke — Chipman M, Ewing J, Gilchrist MA, Sheehe P, Keating EG (VA Hospital, Syracuse, New York)

The ¹⁸xenon inhalation technique for measuring cerebral blood flow can be a useful atraumatic tool for serially following hemodynamic changes in patients with stroke. During the past two years we have used this technique with a 16-probe apparatus to measure cerebral flow serially in 26 male patients with an average age of 58 and with focal neurological deficits due to thromboembolic occlusive disease. In each patient flow determinations expressed in terms of K₁, the gray matter decay constant of the biexponential washout curve, were made at 24, 48, and 72 hours following the stroke, then weekly for one month, and finally monthly for the remainder of the year. In all 26 patients the mean flow in both hemispheres rapidly dropped three to five days after the acute stroke. Within two to three weeks mean flows returned to normal in both hemispheres, but the clinically involved hemisphere retained a focal hemodynamic defect for the remainder of the year. These global flow deficits were independent of the location of the focal infarction or the clinical changes in the patient. Our data suggest that an acute focal cerebral infarction may result in a generalized decrease in cerebral blood flow during the first few weeks post-stroke and that more focal hemodynamic deficits appear only after the acute period has passed.

Session V: Vasospasm: Intracranial Vasculature
Saturday (8:00 to 10:00 A.M.)
V-40
Alteration of Innervation and Reactivity of Monkey Cerebral Arteries After Subarachnoid Hemorrhage — Duckles SP, Kim J, Bevan RD, Bevan JA (University of California, Los Angeles, California)

The hypothesis that changes in reactivity and innervation of cerebral arteries occur after subarachnoid hemorrhage (SAH) was examined. One internal carotid artery was exposed by a transorbital approach and punctured to induce SAH. Five to ten days later, when chronic arterial spasm as demonstrated by transfemoral angiography was most severe, animals were killed, and vessels removed for study. Catecholamine fluorescence at the medioadventitial junction of internal carotid, anterior and/or middle cerebral arteries was diminished or absent on the ipsilateral side. These same vessels were more sensitive to norepinephrine. Their ED 50 was 1.7 X 10⁻⁴ M (CI 0.4 to 7.0, n = 5) compared to 4.1 X 10⁻⁴ M (2.5 to 6.6, n = 23) for control vessels (p < 0.001). Spontaneous rhythmic contractile activity of large magnitude was observed in vitro. Further correlation of the time course of these changes with the occurrence and severity of arterial narrowing will be necessary to establish their role in the genesis and maintenance of cerebral vasospasm.

V-41
Effect of Subarachnoid Injection of Blood, Serotonin and Mock Spinal Fluid in Monkeys — Boisvert D, Weir B, Over-
ton T, Reiffenstein R, Grace M (University of Alberta, Edmonton, Alberta, Canada)

To assess the role of serotonin in the genesis of post-SAH cerebral vasospasm, a comparative study of the acute effects of subarachnoid injection of blood, serotonin and mock spinal fluid on regional cerebral blood flow, cerebral vessel caliber on angiograms, neurological state and vessel ultrastructure was carried out using cynomolgous monkeys. Subarachnoid injection of blood in ten animals caused a decrease in flow lasting less than one hour and moderate vasospasm which lasted at least three hours. In contrast, subarachnoid injection of artificial spinal fluid in ten animals had no effect. Serotonin solution at physiological concentrations (as determined by in vitro bioassay) in ten animals was also made without effect on cerebral blood flow or arterial caliber. Higher (X 10) serotonin concentrations in four animals caused a blood flow reduction similar to that seen with the subarachnoid blood injection. However, the cerebral vasospasm induced was of shorter duration than that obtained with blood. Cerebral vessel ultrastructure was normal in all groups. There were no marked differences in neurological status or survival post-injection.

V-42
Cerebral Vasospasm After Ruptured Aneurysm — A Clinicoradiologic Correlation — Fisher CM, Roberson GH, Ojemann RG (Harvard Medical School, Boston, Massachusetts)

Because of the controversy concerning the clinical significance of cerebral vasospasm after subarachnoid hemorrhage (SAH) we reviewed our experience in 48 adequately studied cases. Only cases with proved SAH and angiographically demonstrated aneurysm were included. Since detectable vasospasm does not occur in the first 48 hours we disregarded deficits predating vasospasm and took into account only new neurological events developing after day 3. The diagnosis of vasospasm was based on angiographic appearance and graded in severity from 0 to 4. In Grade 4 the lumen of the MCA and/or ACA was narrowed to an indistinct line 0.5 mm or less in diameter with delayed blood flow and retrograde filling. Twenty-six patients had delayed hemiplegia and in all there was Grade 3 or 4 vasospasm. Twenty-two did not have hemiplegia: five had Grade 1 or 2 spasm, and eight had no spasm. Of 31 with severe vasospasm 84% had delayed hemiplegia; of 17 with lesser vasospasm 0%. Of 26 with hemiplegia 100% had severe vasospasm, of 22 without hemiplegia.

V-43
Prevention of Brain Stem Stroke by Microvascular Anastomosis in the Vertebobasilar System — Khodadad G, Singh RS, Olinger CP (University of Cincinnati, Cincinnati, Ohio)

Four patients with symptoms and signs of brain stem ischemia due to occlusive disease of the vertebrobasilar system and one patient with similar cerebrovascular disease who was thought to be prone to brain stem stroke underwent a microvascular anastomosis between the occipital artery and the caudal loop of the posterior inferior cerebellar artery. There was no morbidity or mortality and neurologically all patients improved. Postoperative angiograms showed patent anastomosis in all the patients and improved circulation in three. This new operation may prove beneficial in a selected group of stroke patients who have vertebrobasilar insufficiency and cannot be treated with gross surgical techniques.

V-44
Intracranial Reconstructive Surgery Indications and Operative Results — Tew JM, Greiner AL, Berger TS (Mayfield Neurological Institute, Cincinnati, Ohio)

A series of 50 consecutive intracranial reconstructive vascular procedures performed by one surgeon during the past eight years has been reviewed. The important points regarding preoperative evaluation, operative technique and results will be discussed. The results indicate the following:

Patients with multiple carotid occlusion or unapproachable carotid stenosis may be benefited by a bypass procedure if adequate collateral circulation has failed to develop.

Patients with ipsilateral carotid occlusion or unapproachable carotid stenosis may be benefited by a bypass procedure if adequate collateral circulation has failed to develop.

Patients with multiple occluded arteries and symptoms of generalized cerebral ischemia may be improved after single or bilateral surgical procedures.

A high frequency of graft patency and a low incidence of operative complication are reported.

Long vein grafts from extracranial to intracranial carotid artery are seldom successful in occlusive vascular disease and should be reserved for certain traumatic or congenital lesions.

Surgery is contraindicated in patients with marked cerebrovascular disease.

V-45
Extracranial-Intracranial Arterial Bypass in the Treatment of “Giant” Intracranial Aneurysms — Ferguson GG, Drake CG, Peerless SJ (University Hospital, London, Ontario, Canada)

Extracranial-intracranial (EC-IC) bypass has been used as an adjunct in the treatment of three “giant” aneurysms which had proved incapable of direct surgical ablation. The purpose of the bypass was to provide collateral flow, allowing subsequent occlusion of the immediate feeding artery.

Two patients presented with dominant middle cerebral (MCA) aneurysms. Following a single superficial temporal to cortical artery anastomosis, one patient has tolerated severe stenosis of the MCA. With a double anastomosis using both the superficial temporal and occipital arteries, the second has tolerated occlusion without deficit. One patient with a carotid bifurcation aneurysm had severe ischemia on three attempts at proximal occlusion. Following bypass, occlusion has been tolerated well. In each case the aneurysms are almost completely thrombosed.

It seems that in cases such as these, EC-IC anastomosis may have a useful role in treatment.

Occlusion of the carotid artery in the neck has been treated by vein grafting from the common carotid to the supraclinoid portion of the artery. Anastomosis with the supraclinoid segment has the disadvantages of requiring temporary occlusion of the collateral circulation through the ophthalmic and posterior communicating arteries and the short length of artery available for anastomosis. In attempting to find a more suitable site for grafting, the course of the carotid within the temporal bone was reviewed in 25 cadavers. It was found that there was a greater than 1-cm segment of the artery which could be easily exposed in the floor of the middle fossa lateral to the trigeminal nerve. This portion of the artery was covered by dura only or a thin layer of cartilage in approximately half of the specimens. In the remainder there was often a thin shell of bone covering the artery and this could be drilled away. This segment of the artery is often open in carotid occlusions in the neck because of retrograde flow into branches in the temporal bone. A careful review of the angiogram in patients with carotid occlusions confirms this fact. This segment is easy to expose and offers a maximal length of 14 mm proximal to the trigeminal nerve to use for either end-to-end or end-to-side anastomosis.

Extent of Vascular Damage Following Surgical Manipulation of Surface Cerebral Arteries — Smith RW, Alksne JF (University of California, San Diego, California)

Sterile microsurgical technique was used to place a microvascular clamp on a feline surface cerebral artery for one hour. Two weeks later vascular specimens were harvested from, as well as proximal and distal to, the clamp site. These specimens were examined with electron microscopy and demonstrated severe endothelial and medial damage at the clamp site. This damage extended significantly beyond the area of clamp trauma suggesting rather widespread vascular injury to a relatively focal insult. The implications of these observations and our attempts to prevent them by chemical pretreatment of the animal will be discussed and related to the human conditions of focal vascular injury (aneurysm rupture and clipping, intracerebral vascular anastomosis) and the widespread sequelae (vasospasm) that frequently accompany such an event.

Ultramicrovascular Surgery — Fein JM (Albert Einstein College of Medicine, Bronx, New York)

Bypass grafts between extracranial and cerebral cortical arteries, approximately 1,000μ outer diameter (o.d.), may augment cerebral blood flow in the brain at risk of cerebral ischemia. Ultramicrovascular surgery has been developed to broaden the potential applications of neurovascular procedures. This has required modification in suture materials and techniques and in the use of ancillary aids to prevent suture line thrombosis. Successful arterioretomy repair has been achieved in 46% of arteries 400 to 750μ o.d. Patent end-to-side bypass grafts have been achieved in 36% of dog cortical arteries 400 to 900μ o.d. Hypertrophy of the graft has been documented in selected instances, but is important if effective augmentation of flow is to be achieved. In four ultramicrovascular grafts less than 900μ o.d., the percentage rate of hypertrophic growth was significantly greater than in five grafts more than 1,000μ o.d. Future attention will be directed at means to stimulate this postoperative change.

Intracranial Surgery in Sickle Cell Anemia — Ferguson L, Swisher C, Patel D, Chilcote R (Michael Reese Hospital and Medical Center, Chicago, Illinois)

Now that angiography can be performed in patients with sickle cell anemia associated with subarachnoid hemorrhage, it remains to be proved that surgery can be performed with equivalent efficacy. Analysis of three teen-aged sickle cell patients suggested that a modification of usual surgical techniques is in order.

Bilateral internal carotid occlusions and multiple extracranial/intracranial anastomoses were associated with multiple cerebral infarction of varying ages in one patient. In a second patient, an infundibular dilatation was seen on two consecutive four-vessel angiograms. A final patient was hemolyzed after a right brachial angiogram but following exchange transfusion had an uneventful clipping of a right posterior inferior cerebellar artery aneurysm, a postoperative angiogram and a right ventriculoperitoneal shunt.

The intimal disease common to these patients precludes hypotensive or hyperventilation during surgery. Cerebrospinal fluid drainage rather than hyperosmotic agents in increased intracranial pressure is favored. The asplenism common to these patients justified preoperative antibiotics. Exchange transfusion is necessary. The potential of intracranial surgery justifies continued neuroradiologic studies in these patients.

Hemifacial Spasm Due to Aneurysmal Compression of the Facial Nerve — Maroon J, Lunsford D, Jannetta P, Deeb ZL (University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania)

Hemifacial spasm (HFS) is a distressing movement disorder characterized by the insidious onset of involuntary twitches of the face. Despite occasional demonstrations of mass lesions in the posterior fossae associated with HFS, the majority of cases are considered idiopathic. Recent evidence suggests that vascular distortion of the facial nerve at the brain stem may cause HFS. A case of aneurysmal compression of the facial nerve will be presented. Classic HFS developed in a 54-year-old woman with a past history of hypertension and vascular headaches. Posterior fossa angiography demonstrated an aneurysm at the bifurcation of the left vertebral artery with the posterior inferior cerebellar artery. The aneurysm was clipped and its dome
was microdissected from its adherent position to the facial nerve and brain stem. Complete resolution of the HFS followed immediately.

Aneurysms, arterial malformations, and normal but aberrant blood vessels have all been implicated in the etiology of HFS. Recent surgical results of vascular decompression of the seventh cranial nerve and new pathophysiologic evidence for this etiologic mechanism in HFS will be summarized.

V-51
Increased Secretion of Antidiuretic Hormone in Patients With Intracranial Aneurysms — Nelson PB, Seif SM, Robinson AG, Wilkins RH (University of Pittsburgh, Pittsburgh, Pennsylvania)

Abnormalities in the secretion of antidiuretic hormone (ADH) are known to occur in intracranial disorders. We used a highly specific radioimmunoassay for plasma ADH (sensitive to 0.2 μU/ml plasma) to study normal individuals and neurosurgery patients. The normal plasma ADH was 0.46 μU/ml ± 0.09 SEM. Thirteen consecutive patients with intracranial aneurysms were studied serially with a total of 59 plasma samples. Twelve of 13 patients underwent surgery. Plasma ADH in patients with intracranial aneurysms was 2.80 μU/ml, significantly higher than normal (p 0.01). The aneurysm patients were divided into one group of ten patients with ruptured aneurysms and a second group of three patients without subarachnoid hemorrhage. ADH levels were significantly higher in the patients with hemorrhage, 3.11 μU/ml as compared with unruptured aneurysms, 1.32 μU/ml (p 0.05). Elevated ADH has therapeutic implication in fluid balance as the syndrome of inappropriate ADH may lead to increased cerebral edema. Hypothalamic damage may be a cause of the ADH release.

Session VI: Carotid Artery Surgery
Saturday (10:30 A.M. to 12:30 P.M.)
VI-52
Correlation of Intraoperative Electroencephalography With Neurologic Deficit Following Carotid Endarterectomy — Byer JA, Dexter JD, Henzel JA (University of Missouri School of Medicine, Columbia, Missouri)

Postoperative stroke and mortality continue to be associated with carotid endarterectomy. In an attempt to prevent these complications we monitored 42 patients with intraoperative EEG to determine which patients should be shunted during endarterectomy. The EEG was recorded after induction of anesthesia, and then during up to five minutes of test carotid cross-clamping. When EEG asymmetry between the cerebral hemispheres occurred, the clamp was immediately removed. A shunt was used in all patients who had EEG asymmetry. In the absence of EEG asymmetry, patients were not shunted. Of the 33 patients with no EEG asymmetry intraoperatively, two experienced transient deficits postoperatively. One of these patients had an abnormal EEG preoperatively. Electroencephalographic asymmetry occurred in nine patients during test carotid cross-clamping. Postoperatively, five of these shunted patients awakened neurologically intact and four patients experienced transient deficit. When the EEG was normal and no shunt was used, the patients did well; when the EEG was abnormal, and a shunt was used, there was a high incidence of transient neurologic deficit.

VI-53
Simultaneous Observations on Internal Carotid Artery and Total Cerebral Blood Flow in Man — Bloor BM, Glista GG (Loyola University Medical Center, Maywood, Illinois)

This study examines simultaneous internal carotid artery (ICA) blood flow as measured by the electromagnetic flowmeter (EMF) and total cerebral blood flow (CBF) determined by dye dilution technique in patients undergoing endarterectomy or carotid ligation for aneurysm.

In a group of 16 endarterectomy patients, the preendarterectomy ICA and total CBF were 132 ml per minute and 886 ml per minute, respectively; following endarterectomy, the respective values were 280 ml per minute and 1,092 ml per minute. The EMF/CBF ratio was 14% preoperatively and 26% postoperatively. The EMF/CBF ratio was the same whether the contralateral ICA was occluded, had a high grade stenosis, or was normal.

In 12 patients undergoing carotid artery occlusion for an intracranial aneurysm, the ICA flow was 186 ml per minute before occlusion and the simultaneous CBF was 788 ml per minute, a ratio of 24%. In eight patients in whom preocclusion and postocclusion CBFs were measured, the flow decreased significantly, 166 ml per minute (19%).

These data suggest that (a) a carotid input is only about 25% of the total, and (b) carotid occlusion is never completely compensated.

VI-54
Vascular Endoscopy — An Adjunct to Carotid Surgery — Towne JB, Bernhard VM (Milwaukee, Wisconsin)

Advances in optical instrumentation have made vascular endoscopy a potential method for intraoperative evaluation of carotid endarterectomy. A prospective protocol was designed to evaluate the efficacy of the Hopkins Optical System in 35 carotid endarterectomies. The external carotid artery was examined after completion of the endarterectomy before removal of the inlying shunt. The distal external carotid was examined after removal of the shunt when all but 1 cm of the arteriotomy was closed. Total time required for the procedure was less than five minutes in 21 cases, and between five and ten minutes in 14. Examination of the internal carotid artery following shunt removal was usually between one and two minutes and never longer than three minutes. There were no infections. The only neurologic deficit was secondary to thrombosis of the repair the night of surgery. Positive findings were noted in 71% of external carotid endarterectomies consisting of intimal flaps in 13 and intimal shreds in 25. Six percent of the internal carotid endoscopies revealed positive findings potentially capable of embolizing and causing a postoperative neurologic deficit. Carotid endoscopy is effective, rapid, and safe, a reasonable alternative to intraoperative arteriograms.
we reviewed the records of 509 carotid endarterectomies conducted to determine the operative stroke and mortality rate. These carotid endarterectomies were performed in two 600-bed community hospitals. The stroke rate for the series was 14% (32 of 228) and the mortality rate was 7% (16 of 228) for a combined stroke-mortality rate of 21.1% (48 of 228). Fifty-seven endarterectomies were performed for TIAs in the appropriate carotid artery distribution. The stroke rate was 12.3% (7 of 57); the mortality rate was 8.8% (5 of 57); the combined stroke + mortality rate was 21.1% (12 of 57). Twelve endarterectomies were performed following a severe stroke in the appropriate carotid artery distribution and the mortality rate was 41.7% (5 of 12). There was no trend toward more or less operative strokes or deaths from 1970 to 1976.

The similarity of results between the seven board-certified neurological and vascular surgeons who performed 95.2% (217 of 228) of the endarterectomies suggests that the operative stroke and mortality rates for carotid endarterectomy reported here are likely to be representative of those in other community hospitals in this country in the 1970s.

A retrospective study of 228 consecutive carotid endarterectomies was conducted to determine the operative stroke and mortality rate. These carotid endarterectomies were performed in two 600-bed community hospitals. The stroke rate for the series was 14% (32 of 228) and the mortality rate was 7% (16 of 228) for a combined stroke-mortality rate of 21.1% (48 of 228). Fifty-seven endarterectomies were performed for TIAs in the appropriate carotid artery distribution. The stroke rate was 12.3% (7 of 57); the mortality rate was 8.8% (5 of 57); the combined stroke + mortality rate was 21.1% (12 of 57). Twelve endarterectomies were performed following a severe stroke in the appropriate carotid artery distribution and the mortality rate was 41.7% (5 of 12). There was no trend toward more or less operative strokes or deaths from 1970 to 1976.

The similarity of results between the seven board-certified neurological and vascular surgeons who performed 95.2% (217 of 228) of the endarterectomies suggests that the operative stroke and mortality rates for carotid endarterectomy reported here are likely to be representative of those in other community hospitals in this country in the 1970s.

A series of 240 consecutive carotid endarterectomies has been analyzed to detect trends in morbidity and mortality rates and in patient benefit. Preoperative and postoperative oral anticoagulants conferred a higher operative morbidity but no short-term or long-term patient benefit. Stenosis or occlusion of the opposite carotid artery did not increase the morbidity or mortality of endarterectomy. Severe hypertension added slightly to the operative risk. Previous myocardial infarction did not add to the operative risk but did increase the chances of death from future myocardial infarct. Age did not affect the operative mortality.

Surgical mortality and morbidity have declined in recent years because of better patient selection, anesthetic techniques, stump pressure measurement to determine the need for bypass shunting, intraoperative heparin, prolene sutures, and other technical advances. Current operative mortality rate is 1.6% (3 of 189). There is a 1.6% risk of a new persisting neurologic deficit in the first 30 days. The late occurrence of TIAs is 1.2% per year, and of strokes is 3.3% per year following surgery. Deaths from all causes occurred at 4.9% each year following surgery.

In a TIA treatment series of 235 patients, further cerebral embolic attacks occurred in ten (1.96%) and form the basis of this report. All ten endarterectomies were done for transient ischemic attacks. Technical difficulties occurred in three patients. Heparin was given intra-arterially in three and intravenously in seven. One patient, under local anesthesia, had neurological deficit immediately after intra-arterial injection of heparin. Three patients had operative arteriograms. One stroke was very likely due to subintimal injection of contrast material. In all cases, preoperative arteriograms demonstrated either bilateral carotid stenoses (nine cases) or unilateral stenosis with contralateral occlusion (one case). From this consistency there emerged a pattern of high risk.

Technical difficulties enhance these risks. Intra-arterial injection of heparin or contrast material may cause avoidable complications. Based on this, we require the operating surgeon to have had considerable experience prior to doing these high-risk cases. We now use only systemic, intravenously injected heparin and routine operative arteriograms are no longer done.

Early Restenosis After Carotid Endarterectomy — Callow AD, Matsumoto G, Cossman D, Stein A (Tufts-New England Medical Center Hospital, Boston, Massachusetts)

Review of 361 carotid endarterectomies identified seven patients who had ten restenotic arteries (2.8%). This was discovered by repeat arteriography in the symptomatic patient, in the asymptomatic patient with a new bruit, or by check arteriography between staged bilateral endarterectomies. The time interval between operation and restenosis averaged 12.5 months. Normal postoperative arteriograms two months after surgery suggest accelerated atherosclerosis rather than hyperplastic fibrosis as the main etiologic factor. Hemodynamic changes and vessel wall-blood interactions after endarterectomy help explain this phenomenon. The lipoprotein profile, glucose tolerance test, hemogram, use of anticoagulants, use of shunts and patch grafts are also reviewed as etiologic factors. The surgical management of these patients is reviewed and included: no operation, re-endarterectomy, and re-endarterectomy with patch graft. This complication may be more common than appreciated because asymptomatic restenoses may not be discovered. If the incidence of restenosis is as high or higher than the late development of symptoms in patients with asymptomatic bruits, prophylactic carotid endarterectomy may require reassessment. Noninvasive evaluation of postoperative endarterectomies will probably reveal many more cases. Histologic sections are reviewed.

The "Stump" of the Internal Carotid Artery: A Source for Further Cerebral Embolic Ischemia — Barnett HJM, Peerless SJ, Wei M (University Hospital, London, Ontario, Canada)

In a TIA treatment series of 235 patients, further cerebral and retinal ischemic events occurred in 27 cases in the territory of an internal carotid artery known already to be occluded in the neck. The previously accepted generality...
that TIA ceases when a stenosed artery becomes occluded has a very significant number of exceptions.

The usual pathogenesis of the further ischemia in our series has been judged to be artery-to-artery emboli from disease identified by angiography in ipsilateral external (EC) and/or common carotid (CC) arteries. By radiographic criteria significant lesions were identified in both arteries (EC and CC) in 13, in one (EC or CC) in three of each, in neither in two. In six the only site radiologically identified as a potential source for the recurrent attacks was a residual stump of the internal carotid artery greater than 5 mm in length. Altogether in this series, there was a recognizable stump of the internal carotid artery in 19 of the 27.

A review of a consecutive series of 74 patients with internal carotid artery occlusion revealed that 26 have no stump, 28 have a stump of 5 mm or less and 20 have stumps longer than 6 mm. Glass-tube flow studies using Evan’s blue dye to demonstrate sites of turbulence indicate that a carotid stump would be the site of excessive turbulence.

Three patients with significant radiological stumps have been submitted to endarterectomy and “stumpectomy” because of recurrent ischemic events. In all, an ulcerative atheroma, with fresh surface thrombotic material attached, was identified. Serial angiograms had revealed progressive atheromatous ulceration in two of the cases. It is apparent that the stump of the occluded internal carotid artery cannot be regarded as an innocent remnant.

VI-60

“Spontaneous” Dissection of Cervicocerebral Arteries — Ojemann RG, Roberson GH, Fisher CM (Harvard Medical School, Boston, Massachusetts)

Nontraumatic or “spontaneous” dissection of the cervicocerebral arteries is not uncommon and we have seen 14 proved or suspected cases in the past three years. The cervical internal carotid (ICA) was involved in ten, the middle cerebral (MCA) in two, vertebral and posterior cerebral one each. Four ICA cases were confirmed surgically and one MCA case pathologically. All others were diagnosed radiologically. Six ICA and two MCA cases showed a long filamentous residual lumen, the “string sign” angiographically. There is good anatomical evidence that this sign indicates dissection. Dissection may be long or short, the latter appearing as a dissection sac, pouch or aneurysm in the wall of the upper 3 cm of the ICA. A long tapering occlusion may also indicate dissection. Dissections may heal, restoring the lumen and leaving a tell-tale pouch proximally. Short dissection sacs may become obliterated. Incessant coughing may precipitate dissection. Obscure trauma is probably a factor in other cases. Nine carotid cases had prodromal T1As or a fluctuating stroke. Horner’s syndrome, headache, a bruit and amaurosis fugax are clues. The manifestations unfold rapidly, a sort of carotid allegro.

VI-61

Penetrating Carotid Artery Injury: Protocol for Management — Lickweg WG, Greenfield LJ (Medical College of Virginia, Richmond, Virginia)

In an attempt to establish concise clinical criteria for the surgical management of patients with neurologic deficits following penetrating wounds to the carotid artery, a review of our experience was undertaken. These results were compared with similar cases from the literature reported since 1963.

There are 233 cases included in this retrospective analysis. The presence or absence of preoperative neurologic deficit was cross-matched with vascular repair or ligation of the carotid artery.

The presence of a comatose state preoperatively is the single most influential factor in determining operative management and prognosis. Patients without a neurologic defect should have restoration of vascular continuity (0% mortality, 0.6% morbidity — 1 of 155). Patients with all grades of neurologic deficit, short of coma, should have primary vascular repair. Morbidity and mortality are much less than following ligation (16%, 5 of 32 versus 50%, 3 of 6). In comatose patients, neither repair nor ligation appears to influence the poor prognosis. At the present time, ligation of the carotid artery is indicated only in the comatose patient with no evidence of prograde flow or if repair is technically impossible.
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