ABSTRACTS

Sixth Joint Meeting on Stroke and Cerebral Circulation

Century Plaza Hotel, Los Angeles, California
February 12-14, 1981

Sponsored by
STROKE COUNCIL
American Heart Association

CEREBROVASCULAR SURGERY SECTION
American Association of Neurological Surgeons

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Further information about registration ($85) and hotel may be obtained from Administrator, Postgraduate Programs, American Heart Association, 7320 Greenville Avenue, Dallas, Texas 75231. Registration is also available at the meeting.

As an organization accredited for continuing medical education the American Heart Association certifies that this continuing medical education offering meets the criteria for 14½ hours in Category I of the Physician's Recognition Award of the AMA provided it is used and completed as designed.
OPENING

Thursday, February 12, 1981
12:00 (Noon) Registration, Century Plaza Hotel
2:00 p.m. Welcome, J. Donald Easton, Chairman

SESSION I

Thursday, February 12 (2:00-4:30 p.m.)
Symposium: Cerebral Arteriovenous Malformations
Chairman: Albert Rhoton
Secretary: Robert L. Grubb, Jr.
2:00-2:40 p.m. Natural History
Henry Troupp, Helsinki, Finland
2:40-3:15 p.m. Neurological Aspects
Jay P. Mohr, Mobile, AL
3:15-3:45 p.m. Radiology
Allan Fox, London, Ont., Canada
3:45-4:05 p.m. Surgery
Henry Garretson, Louisville, KY
4:05-4:30 p.m. Panel Discussion

SESSION II

Thursday, February 12 (5:00-6:00 p.m.)
Lecture: Mechanisms of Cell Damage in Cerebral Hypoxia — Ischemia
Bo K. Siesjö, Lund, Sweden
6:30-7:30 p.m. Dutch Treat Reception

SESSION III: ARTERIOPATHIES

Friday, February 13 (8:00-10:00 a.m.)


We have investigated the possibility that a substance released from platelets during degranulation modifies PG12 synthesis by endothelial and smooth muscle cells. PG12 is a potent inhibitor of platelet aggregation and platelet adhesion to vessel walls. Regulation of PG12 synthesis by blood vessels is not well understood. We have reported that a non-dialyzable platelet-dependent factor in serum dramatically stimulates PG12 synthesis by vascular endothelial and smooth muscle cells in culture. We further report that platelet-derived growth factor (PDGF), a releasable peptide found in platelet alpha granules, stimulates PG12 synthesis by over 100 fold in the above cell types. The concentration of PDGF required to produce this effect is below that reported in human serum. Preliminary characterization of the above mentioned serum factor strongly suggests that it is PDGF. We have postulated that released PDGF acts to increase vessel wall PG12 synthesis as part of a negative feedback mechanism controlling platelet aggregation. A defect in the ability of the vessel wall to produce PG12 in response to PDGF released during platelet aggregation, as may occur in atherosclerotic vessels, may contribute to the genesis of thromboembolic events, including strokes and transient ischemic attacks.

PROSTACYCLIN — Welch MW, Mathias CJ, Jacobs D, Rubin J, Siegel BA, Neidaman P (Department of Radiology, Washington University School of Medicine, St. Louis, Missouri 63110)

We evaluated in vivo platelet aggregation in Cynomolgus and Nesmestrina monkeys. Blood was withdrawn, platelets were isolated and labeled with In-111, and red blood cells were labeled with Tc-99m. Sub-human primates, anesthetized with Sernylan and blocked with pavalon, were imaged using a gamma camera coupled with a computer for quantitative analysis. Endothelial damage was induced in the abdominal aorta with an inflated balloon catheter. The damage produced a rapid, marked increase in the platelet/RBC ratio, reflecting platelet adhesion and aggregation. This platelet accumulation remained stable for up to 2 hours. We employed prostacyclin, a potent arachidonate metabolite which blocks or reverses platelet aggregation in vitro, to reverse the stable thrombus 30 min after its formation. PG12 at 100 mg/kg/min, but not its inactive breakdown product 6-keto-PGFla (1 ug/kg/min), reversed the platelet accumulation throughout the time of its infusion. The platelets began to reaccumulate 100-140 min after the termination of the PG12 infusion. These experiments suggest that PG12 could be effective in primates even when administered after a thrombotic event.

IN VIVO MANIPULATION OF PLATELET THROMBI: PLATELET ADHESION REVERSAL USING 2 PROSTACYCLIN — Welch MW, Mathias CJ, Jacobs D, Rubin J, Siegel BA, Neidaman P (Department of Radiology, Washington University School of Medicine, St. Louis, Missouri 63110)

The combination of PG12, indomethacin, and heparin has been shown to eliminate zones of impaired microvascular reperfusion in a model of global ischemia was studied in a model of multifocal ischemia to assess the effect of the drugs on recovery of neuronal function.

Ischemia was induced in dogs by injection of 20-50 mL volumes of air via the right internal carotid artery, and the dose was regulated by the effect on the cortical sensory evoked response (CSER) to left median nerve stimulation. The air was delivered in increments just sufficient to maintain suppression of the CSER for 1 hour. Forty animals were subjected to 60 minutes of ischemic CSE recovery, then treated with one of seven drug regimens and followed for an additional hour to assess the degree of CSER recovery. The group receiving PG12, indomethacin, and heparin achieved a 57% CSER recovery relative to baseline values while untreated animals and animals receiving PG12 alone, indomethacin alone, PG12 and heparin, indomethacin and heparin, or PG12 and indomethacin, post-recoveries that clustered about 20%. The difference between these recoveries was significant at p < 0.001 by 2-tailed t test. PG12, indomethacin, and heparin may have therapeutic potential in acute occlusive stroke.

PG12, INDOMETHACIN, AND HEPARIN PROMOTE POST-ISCHEMIC NEURONAL RECOVERY IN DOGS WHEN ADMINISTERED THERAPEUTICALLY — Hallenbeck JM, Leitch DR, Dutka AJ, Greenbaum LJ Jr.
Cerebral vessels are said not to have vasa-vasorum. One questions their source of nutrition. Scanning and transmission electron microscopic studies of the adventitia of the basilar artery of the cat suggested a labyrinthine system that might provide for the diffusion of large molecules. Also, the adventitial surface appeared to have small openings that might communicate with the subarachnoid space although these might be artifacts. Horseradish peroxidase was introduced into the cerebrospinal fluid and the vessels were studied at high magnification. Horseradish peroxidase was found to easily enter the adventitia of the basilar artery and was observed in contact with smooth muscle or in some cases within the media within 1-5 minutes. The passage of horseradish peroxidase from the subarachnoid space to the depths of the arterial wall suggests that the adventitial system may be homologous to the vasa-vasorum of system arteries.

**Smooth Muscle in Human Intracerebral Arterioles:**

Hyde JB, Braekevelt CR

(Faculty of Medicine, University of Manitoba, Winnipeg, Canada)

Human intracerebral arterioles have been said to lack smooth muscle. This assertion, based on light microscopy, is an argument against the hypothesis that intracerebral vasoconstriction may increase brain damage in cerebral infarction.

We received tissue for electron microscopy from 6 patients in whom certain surgical procedures necessitated the removal of normal cerebral cortex. Within seconds after removal, tissue was fixed in freshly prepared 5% glutaraldehyde in 0.1 M Sorenson's buffer. Blocks of this tissue were prepared with standard electron microscopy techniques; thin sections from selected areas were studied in a Philips 201 electron microscope. External diameters of arterial vessels, measured on electron micrographs, ranged from 5-42 μm with a median of 14 μm; 10 of these vessels were 5-11 μm in diameter and lacked smooth muscle. In all the other vessels, smooth muscle cells were identified by the presence of dense bodies in their cytoplasm. Some of these vessels appeared to be in a state of constriction.

**Amyloid Angiopathy: Its Incidence and Complications in the Aging Brain**


Congophilic or amyloid angiopathy is recognized as an infrequent cause of massive spontaneous, nontraumatic, nonhypertensive cerebral hemorrhage. In 5 recent fatal cases in patients aged 67 to 87, the hemorrhage occurred in the frontal lobe. To assess the topographic distribution and incidence of amyloid altered cerebral intraparenchymal blood vessels, we examined 80 unselected brains from individuals 60 years of age or older. Sections from right and left frontal, parietal, temporal, occipital lobes and hippocampi were assessed in a semiquantitative manner for the presence of amyloid in parenchymal blood vessels. In the decade 60 to 69 years, 2 of 17 were positive; ages 70 to 79, 12 of 28; ages 80 to 89, 14 of 28; age 90 and over, 3 of 7. The lesions varied from focal (1+) to severe (4+) and were most likely to be positive in the occipital lobes. The focal lesions occurred in the superficial cortical layers. The changes were not found in white matter, deep gray nuclei, brain stem or cerebellum. The lesions were associated with Alzheimer's plaques, but were often found in the absence of Alzheimer changes or clinical evidence of dementia.

Intracerebral hemorrhage occurring in normotensive elderly patients in an unusual location may be due to amyloid angiopathy. The lesion likely represents an age related phenomenon rather than a specific pathologic entity.
NEOPLASTIC ANGIOENDOTHELIOSIS. Beal MF, and Fisher CM (Massachusetts General 8 Hospital, Boston, MA)

We add 2 cases of neoplastic angioendotheliosis to the previous 13. This most unusual process which represents diffuse proliferation of malignant endothelial cells features cerebral symptoms suggesting a vascular origin. A man aged 58 first had transient ischemic attacks followed by a subacute profound dementia with frontal psychomotor retardation. Remission followed steroid therapy. Abulia recurred along with a gradually progressive paraplegia from which the patient died 16 months after onset of symptoms. Pathologic examination showed tumor masses in the basal ganglia and widespread patchy cerebral infarction. The spinal cord below the mid-thoracic level was destroyed. Microscopically small mononuclear tumor cells were widespread within and largely confined to the lumens of small cerebral blood vessels which showed various degrees of occlusion and recanalization. Factor VIII antigen was not present on the surface of tumor cells. Another man aged 61 developed subacute dementia with frontal lobesigns, dysphasia and impairment of memory. CT showed multiple infarcts. Steroid treatment helped but progressive deterioration led to death in about 15 weeks. Frontal lobe biopsy revealed the same neoplastic vascular process.

Hallmark of the illness is a progressive subacute lobar dementia. Transient spells may occur. Hemiparesis is unusual. Angiography is normal.

CORRELATION BETWEEN ANGIOGRAPHIC AND HISTOLOGICAL APPEARANCE OF THE CEREBRAL VESSEL FOLLOWING SUBARACHNOID HEMORRHAGE - Smith, R.R., Clower, B. R. and Ashford, K. (Departments of Neurosurgery & Anatomy, University of Mississippi School of Medicine, Jackson, Mississippi)

In this study the cerebral vessels of 84 patients who died as a result of subarachnoid hemorrhage were reviewed and the results correlated with post-mortem angiography. Specifically, a search was made for those factors which might have produced anatomical alterations.

Structural changes were found in 32 (38%). They were time dependent but were evident as early as three days post-hemorrhage and as late as 30 days. Of the cases which showed histological changes, angiographic vasospasm was evident in only 43%. However, significant alterations were demonstrated in almost 90% of those in which luminal narrowing had been demonstrated on the angiogram. Age was not a significant factor and operative procedures seemed to have little influence on the development of arteriopathy, which was almost invariably associated with ruptured intracranial aneurysms. Vessels studied histologically within a few hours of angiography, confirmed that structural changes in the vessel wall are a prominent feature and probably contribute to the angiographic appearance. Blood in the vessel wall was a common factor in those cases showing maximum proliferative changes.

SESSION IV: CLINICAL ASPECTS Friday, February 13 (10:30 a.m.-12:00 Noon)

THE NATURAL HISTORY OF UNRUPTURED INTRACRANIAL ANEURYSMS -- Wiebers DO, Whisnant JP, O'Fallon WM (Mayo Clinic, Rochester, Minnesota)

This study defines the natural history of a selected group of 65 non-operated patients with 81 unruptured intracranial aneurysms. Cases were identified by reviewing charts of Mayo Clinic patients seen between 1955 and 1973. Follow-up information was obtained on all cases until death or for at least five years after diagnosis of intracranial aneurysm.

Eight of the 65 aneurysm patients developed intracranial hemorrhage secondary to aneurysmal rupture over a mean follow-up interval of 98.5 months. A multivariate discriminant analysis was performed to assess the relative impact of several independent variables upon aneurysmal rupture. These variables included age, sex, aneurysm size, number of aneurysms, presence of multilobed aneurysms, aneurysmal symptoms other than rupture, aneurysm location and hypertension at or before the identification of the aneurysm. The only variable of unquestionable significance was aneurysm size. Of the 64 aneurysms less than 1 cm in diameter, none ruptured, whereas eight of the 29 aneurysms 1 cm or greater in diameter eventually ruptured.
We have studied the long-term outcome in 64 conservatively treated patients, seen prior to 1962, who had a single ruptured aneurysm of the basilar (75%), Pica (17%), SCA (5%), or posterior cerebral (3%) artery, and who were followed for as long as 16 years after their original hemorrhage. During the acute periods (0-6 months) the majority (18/39) of deaths were due to the original hemorrhage. Analysis of various factors (age, sex, pre-existent hypertension, blood pressure on admission and during hospitalization, aneurysm location, neurologic state, time from hemorrhage, and arteriographic characteristics) failed to find any factor(s) which would separate the acute rebleeders from those who did not rebleed. Sixteen patients died as a result of their original hemorrhage. Coma associated with SAH had a strong association with mortality. Analysis of the long-term follow-up (range of 7-16 years) revealed a late (>6 months after original hemorrhage) rebleeding rate (3.9% per year), which is similar to that found for the anterior circulation. Discriminant function analysis has been developed to predict long-term morbidity and risk of late hemorrhage. Morbidity was correlated with age. The long-term conservative outcome of patients with a single VBA aneurysm is similar to that of patients with an anterior circulation aneurysm.

Stroke was the underlying cause in 52% (116 of 223) of the decedents. Fifteen percent (33 of 222) for brain infarction, 5% (10 of 203) for cerebral embolus, 4% (17 of 39) for subarachnoid hemorrhage and 76% (13 of 17) for intracerebral hemorrhage. For brain infarction 5 year survival was reduced by co-morbidity from 69% (46 of 67) to 41% (18 of 44) in men, but not women. Stroke was the underlying cause in 52% (116 of 223) of the decedents. Cumulative 5 year recurrence rates for brain infarction in men was 44% (29 of 66); almost double that in women. The majority were of the same type. Thus, risk of death or recurrences is substantial, greater in men than women, and greatly influenced by cardiac co-morbidity.

We conclude that carotid artery FMD is often an incidental angiographic finding. The frequency of subsequent CIE is low and caution must be exercised in advising any specific treatment for the prevention of subsequent cerebral ischemia.

Subsequent cerebral ischemic events in patients with carotid artery fibromuscular dysplasia - Corrin, LS; Sandok, BA; Houser, OW (Mayo Clinic, Rochester, Minnesota)

During the years 1962-79, 13,955 cerebral aneurysms were performed at our institution. Fibromuscular dysplasia (FMD) involving the carotid artery was identified in 82 patients (6.6%). Follow-up with reference to subsequent cerebral ischemic events (CIE) was obtained in 79 patients (96%)—age range: 18-76 yrs.; mean 57 yrs.—and form the basis for this study.

FMD was present in association with intracranial mass lesions in 29 pts. Follow-up for a mean of 50 mos. revealed three had subsequent CIE (50, 136 and 216 mos. post angiogram). FMD was present in association with intracranial aneurysm in 10 pts. Follow-up for a mean of 52 mos. revealed no subsequent CIE. FMD was present in association with other non-ischemic disorders in 27 pts. (including asymptomatic bruit and/or non-focal symptoms). Follow-up for a mean of 80 mos. revealed no subsequent CIE. FMD was found in association with focal cerebral ischemic symptoms in 13 pts. (Four had associated atherosclerosis). Follow-up in this group for a mean of 75 mos. revealed no subsequent CIE.

The colour-coded continuous wave Doppler system (Echoflow*) has been used to scan over 1000 consecutive cases on which angiograms have subsequently been performed. With normal bifurcations the Doppler scans have a specificity of 94% and negative predictive accuracy of 92%. If scans showing regions of yellow are considered within normal limits, both figures rise to 99%. With carotid occlusions the scans have a sensitivity of 97% but a positive predictive accuracy of only 78% largely due to sub-total stenoses appearing as occluded vessels. With carotid stenoses of over 50% of the arterial diameter the sensitivity of the scans is 94% declining to 85% for stenoses of 25-49% of the arterial diameter. The positive predictive accuracy for stenoses of over 50% of the arterial diameter is also 78%.

The various causes of errors in the categories above will be described.
LIMITATIONS OF CAROTID DOPPLER SCANNING AND PROPOSED SOLUTIONS—Johnston KN, Kassem, M
Demorais D(University of Toronto,Canada).

The purpose of this paper is to identify the limitations of Doppler scanning for the diagnosis of carotid disease and to propose solutions to certain problems.

A CW Doppler scanning system (Echoflow) was used to study 210 patients. By comparison to the results of 56 arteriograms, the sensitivity and specificity for detecting stenoses greater than 50% were 71% and 82% respectively. In our next 75 patients, we found that many of our initial problems could be overcome by the concomitant use of a real-time frequency analyzer. Specifically, when the Doppler waveforms were displayed we found that (1) signals which were attenuated by calcification or plaques or the velocity reduced as a result of a proximal stenosis could still be detected; (2) when the velocity of flow was increased in compensation for a contralateral carotid stenosis, the waveforms could still be of diagnostic value; (3) distinction between the internal (IC) and external (EC) carotid arteries was easier than relying on the audio signal alone; (4) when the scan showed IC occlusion morphologically, the evaluation of the IC and common carotid waveforms was helpful in verifying the scan result; (5) artifactual noise on the Doppler waveform could be recognized.

It is concluded that the simultaneous use of a real-time frequency analyzer will improve the results of CW carotid Doppler scanning.

CEREBRAL VASOSPASM: CORRELATION OF OPERATIVE FINDINGS AND ANGIOGRAPHY—Crowell RM, 17 Kistler JP, Davis KR, Ojemann RG, Fisher CM (Massachusetts General Hospital, Boston, MA)

To evaluate the relation between local subarachnoid hematoma and local cerebrovascular vasospasm, we investigated prospectively 24 patients who underwent craniotomy for aneurysm. Angiograms were studied for presence, location and severity (0-4+) of vasospasm. At surgery, we noted the presence and extent of subarachnoid clot (none 0, minimal +, about 1 mm thick ++, >1 mm thick +++).

The presence or absence of local clot was closely correlated with the presence or absence of severe angiographic spasm. The only exceptions were two cases of clot approximately 1 mm thick. In one it was located around the proximal postcommunical (A2) segment of the anterior cerebral artery with only minimal angiographic narrowing of the A2 segment on day 10. In the other case it was located around the right precommunical (A1) segment of the anterior cerebral artery with no angiographic evidence of narrowing on day 9. Although surgery was postponed until severe angiographic spasm abated in some cases arterial narrowing could be seen in the operative field and correlated well with angiographic spasm. We never observed angiographic or operative spasm without local clot.

The findings support the concept that cerebral vasospasm is caused by local subarachnoid hematoma from aneurysmal rupture.

NEUROLOGICAL MANIFESTATIONS OF MALIGNANT HYPERTENSION—Healton EB, Brust JCM, 18 Feinfeld DA, Thomson GP (Department of Neurology, Harlem Hospital Center and Columbia University College of Physicians and Surgeons, New York, New York)

Neurological abnormalities frequently occur in patients with malignant hypertension, but specific data is limited to retrospective analyses. In a prospective study, thirty-four patients with 41 admissions for malignant hypertension were examined by a neurologist before and after treatment. In 17 cases neurological examination was normal. Nineteen cases had major lateralizing signs or abnormalities of mental status which did not improve when blood pressure was lowered. The clinical course in these patients was consistent with cerebral infarction, uremic encephalopathy, dementia of uncertain cause, multiple infarction dementia, and chronic paranoid schizophrenia. In five patients, altered mental function and generalized convulsions occurred and resolved with lowering of blood pressure. These patients probably had hypertensive encephalopathy.

Neurological abnormalities occurred in 62 percent of cases (24 of 41) with malignant hypertension, and decisions about rate and degree of blood pressure lowering and the need for dialysis or other treatment depended on a specific clinical diagnosis. A generalized neurologic syndrome delineated in our patients with hypertensive encephalopathy is also consistent with experimental and neuropathological observations.

SESSION V: NEWER TECHNIQUES

Friday, February 13 (1:30–3:30 p.m.)

MEASUREMENT OF LOCAL CEREBRAL BLOOD FLOW IN MAN WITH POSITRON EMISSION TOMOGRAPHY—19 Ralchle ME, Markham J, Larson K, Grubb RL Jr, Welch MJ (Washington University School of Medicine, St. Louis, MO 63110)

Recent advances in positron emission tomograph design which allow multiple sections of the brain to be scanned simultaneously and rapidly (≤1 min) now permit the quantitative measurement of local cerebral blood flow in a manner directly analogous to the tissue autoradiographic technique (Sakurada et al, Am J Physiol 234:H59, 1978). We have adapted this technique for in vivo studies in monkeys and in man using as diffusable tracers H215O and 11C-butanol. H215O was chosen because of the ease of preparation and short physical half-life (2 min) which reduces radiation dose and permits repeat examinations in the same subject. 11C-butanol was chosen for comparison because it is freely permeable for CBF up to 180 ml·min−1·100g−1, in comparison to water (P/S = 140; Microvasc Res 20:71, 1980). In the range of flows observed in these experiments (25–55 ml·min−1·100g−1) the correlation between results obtained with the two tracers was excellent (r = 0.924). For situations in which CBF can be anticipated to be higher 11C-butanol is more suitable. This technique is now being used in the evaluation of patients for superficial temporal-middle cerebral artery bypass surgery.
Local cerebral metabolic rates for glucose (LCMRGlc) were determined in normal subjects in the resting state using F-18-2-fluoro- \(^\text{18}\)F\text{2-fluorodeoxyglucose} (FDG) and positron computed tomography (PCT). Right-handed subjects aged 21-27 were asked to relax and remain awake with their eyes patched and ears plugged. They were injected with 10 mCi of FDG and forty min later were scanned at 1 cm intervals in both the transverse and coronal directions. Clear delineation of cerebral structures was obtained. Images were converted into units of LCMRGlc (mg glc/100gm/min) using a compartmental model for deoxyglucose.

LCMRGlc was highest in the primary visual cortex (8.402.01) temporal cortex (7.942.09), lentrotic nuclei (8.161.67) and striatum (8.072.01); and lowest in white matter structures such as centrum semiovale (5.231.39) and corpus callosum (4.211.52). The global values of CMBGlc (5.910.89) are in good agreement with previous human studies using FDG-PCT (5.370.88, 5.280.76) and P-i methods (5.380.77). Comparisons of homologous regions in left and right hemispheres failed to reveal any statistically significant differences in LCMRGlc at rest. Baseline anatomical images and resting values of LCMRGlc for individual cerebral structures such as these, are a necessary prelude to the study of human cerebral metabolism in pathological states.

**METABOLIC RESPONSE OF THE BRAIN TO VISUAL AND AUDITORY STIMULATION: STUDIES IN MAN.**

Phelps ME, Mazziotta JC, Kuhl DE. UCLA, Los Angeles, California

Positron computed tomography, (F-18)2-fluoro-deoxyglucose and an extension of Sokoloff's model have been combined to provide an in vivo method that allows the study of local cerebral metabolic function in man. We have shown the method to have a precision of ± 5% (1 std. dev.) for the measurement of local (T cm\(^2\)) cerebral metabolic rate for glucose (LCMRGlc) and to provide clear delineation of cortical areas, thalamus, caudate, internal capsule etc. Visual stimulation with white light, alternating checker board pattern and complex visual scenes produced a progressive increase in LCMRGlc of the primary (PVC) and associative (AVC) visual cortex with maximal increases up to 2 over eyes closed controls. Increases in AVC were greater than PVC when scene complexity was highest. Stroke patients with homonymous hemianopsia (lesion not in visual cortex) and blind subjects showed function deficits consistant with their visual deficits. Bilateral auditory stim, with a combination of a story in English + music produced bilateral activation of auditory cortex and frontal lobe, whereas unilateral stimulation (right ear) with only the story produced left sided activation of auditory cortex and bilateral frontal lobe. This technique provides neurology with an exciting new tool for investigation of local cerebral function in normal and diseased states.
This study was designed to evaluate the clinical usefulness and accuracy of digital subtraction angiography to evaluate the common carotid artery bifurcation and intracranial vessels for arteriosclerotic disease. Examinations were performed on a specifically designed research fluoroscopic digital subtraction machine.

The carotid bifurcations were examined in 100 patients with both conventional and digital subtraction angiography. The intracranial vessels were examined with both conventional and digital subtraction angiography in 15 patients. In 70% (70 of 100) patients examined, the quality of the digital subtraction angiogram was good to excellent. There was excellent correlation of the conventional and digital subtraction angiograms in these patients. In the remaining 30% of cases, the vessels were not seen or there was a substantial chance of diagnostic error in evaluating the vessels.

Digital subtraction angiography is a safe, rapid, outpatient procedure which can very accurately evaluate the large arteries of the head and neck in at least 70% of patients.

**SESSION VI: SURGICAL ASPECTS**

Friday, February 13 (4:00-5:30 p.m.)

**CAROTID ENDARTERECTOMY IN HIGH RISK PATIENTS WITH CARDIOPULMONARY DISEASE.** Crowell, RM, Ojemann, RG, Lees, RS, deBros, F, Sundaram, P. Massachusetts General Hospital, Boston, MA

Eighty-six patients with serious cardiopulmonary disease (usually coronary artery disease) underwent 95 carotid endarterectomies between 1970 and 1980. Preoperative evaluation was done by a cardiologist, with appropriate special testing, which often included exercise stress testing. Anesthetic technique included monitoring of pre- and intra-cardiac EEG, intra-arterial blood pressure and arterial blood gases. In 7 cases pulmonary artery catheters were utilized peri-operatively. In 2 cases, cardiac pacemakers were required. In 3 cases, subsequent cardiac surgery was performed. In one case, coronary artery bypass and carotid endarterectomy were carried out under the same anesthesia. Intraoperative EEG was recorded.

Results were not significantly different from those in patients without cardiopulmonary disease. Eighty patients had neither cardiac nor neurological complications. A single death occurred from upper GI bleeding. There were 2 strokes, one mild and one moderate. Other complications included one postoperative TIA, and one wound hematoma. Only one patient had a cardiopulmonary complication, acute postoperative pulmonary edema and that patient survived.

We conclude that carotid endarterectomy can be carried out at low risk in patients with cardiopulmonary disease, with appropriate pre and intraoperative medical management.
INCIDENCE OF CAROTID ARTERIAL DISEASE IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS 28

The occurrence of stroke associated with coronary artery bypass surgery remains approximately 2-5%. This has led some centers to adopt an aggressive approach to the detection and treatment of associated carotid artery disease.

A series of 101 patients who underwent coronary artery surgery were evaluated preoperatively with the Duplex ultrasonic scanner together with spectral analysis; 24 studies were requested on the basis of clinical evaluation and 77 patients were free of symptoms or signs referable to extracranial carotid artery disease.

In the unrequested group the internal carotid artery was found to be normal in 65% (50/77); 10-49% stenosis in 29% (22/77) and 50-99% stenosis in 6% (5/77). The requested group had significantly more severe stenoses; normal 12.5% (3/24); 10-49% stenosis 33.3% (8/24); 50-99% stenosis 45.9% (11/24) and total occlusion 8.3% (2/24).

In the post-operative phase one stroke and one transient ischemic attack were noted among the unrequested group and none in the requested group; neither had a 50% or greater stenosis.

There is little evidence to support the contention that noninvasive or invasive screening of asymptomatic patients prior to coronary artery bypass surgery helps select patients who will sustain a focal neurological event.

COMPARISON OF RESULTS OF BILATERAL AND UNILATERAL CAROTID ENDARTERECTOMY FIVE YEARS AFTER SURGERY.

All patients who successfully underwent carotid endartectomy (CE) between 1970-1975 were divided into three groups and followed for five years. Group I includes 146 pts. who had unilateral CE with a patent, non-stenotic contralateral carotid artery. Group II includes 45 pts who underwent unilateral CE but in whom the contralateral internal carotid was totally occluded. Group III consists of 86 pts who underwent bilateral CE. The groups are comparable and all were maintained on antiplatelet medications postoperatively.

During the follow-up period 23 of the 277 pts. had a new hemispheric stroke; 4 others became comatose and died, presumably of stroke. Among the Group I pts., 20 had new strokes, only 8 of which involved the hemisphere ipsilateral to the CE. Five late strokes occurred in Group II, one ipsilateral to the CE. Four pts. in Group III had new strokes. The cumulative stroke rate at five years by the life-table method was 21.9% for Group I, 19.2% for Group II and 5.3% for Group III (p<.05).

The data suggest that pts. undergoing unilateral CE should have close monitoring of the contralateral vessel postoperatively, particularly if there is a history of hypertension.

VALUE OF REPEAT ANGIOGRAPHY IN PATIENTS REFERRED FOR EXTRACRANIAL-INTRACRANIAL BYPASS GRAFT - Heros, RC; Sekhar, LN University of Pittsburgh, Pittsburgh, Pa.

A substantial number of extracranial to intracranial bypass procedures are being performed around the world even though the value, complications, and indications of these procedures are still under study and discussion. This uncertainty makes it imperative to study very carefully each "candidate" for such a procedure and to consider alternative, better established forms of treatment whenever available. We have followed a policy of repeating the arteriograms in patients referred for this operation unless the available films are recent and of optimal quality.

In such cases, a number of patients initially referred for EC-IC bypass grafts have been managed with either endarterectomy or anticoagulation. The following situations will be illustrated by a representative patient: 1) "Resolved" middle cerebral occlusion 2) "Atheromatous pseudo-occlusion" of the internal carotid artery (ICA) 3) "Resolved" ICA occlusion due to spontaneous dissection 4) Completed ICA occlusion managed by endarterectomy after demonstration of patency of the petrous portion of the artery, and 5) Complete occlusion of the cervical portion of the ICA managed by anticoagulation after demonstration of a thrombus in the intracranial portion of the ICA which was presumed to be the source of embolic TIA's.

A COMBINATION OF STA-MCA BYPASS AND STAGED INTERNAL CAROTID ARTERY OCCLUSION FOR THE TREATMENT OF GIANT INTERNAL CAROTID ARTERY ANEURYSMS - Spetzler RF, Rokni RA.

In an attempt to decrease the incidence of early and late ischemic complications from carotid ligation, we treated a series of 19 patients with giant internal carotid artery aneurysms by doing a STA-MCA bypass in conjunction with a staged occlusion of the internal carotid artery. All 19 patients had an aneurysm that was considered unsuitable for direct intracranial clipping. In each case a STA-MCA bypass was performed. At the same procedure, the internal carotid artery was exposed and a Selverstone clamp was placed around it. The clamp was tightened down to the point where the flow was reduced by 50%. Three days later the clamp was closed completely. Two days later the internal carotid artery was ligated. None of the 19 patients experienced any ischemic complications during the closure of the Selverstone clamp. Over an average follow-up period of 23 months, there have been no aneurysmal rebleeds and no late ischemic complications in any of the 19 patients. This combined approach offers a reasonable way of decreasing the early and late ischemic complications associated with carotid artery ligation when it is used in the treatment of difficult internal carotid artery aneurysms.
COMPARISON OF LATE COMPLICATIONS FOR INTERNAL CAROTID VERSUS COMMON CAROTID ARTERY LIGATION - Ronki RA, Spetzler RF, Nuelsen FE

A follow-up study was done on 57 consecutive aneurysm patients who were treated with carotid ligation to establish the incidence of late complications and to compare the difference between internal carotid versus common carotid artery ligation. The acute morbidity and mortality was 32% for the overall group. 45 patients were discharged with a ligated carotid artery of whom 6 could not be located for follow up. Follow-up was obtained on 21 patients with common carotid artery ligation and on 18 patients with internal carotid artery ligation. The incidence of TIA's in the common carotid artery group was 9.5% with none of them developing a stroke in the follow-up period. The incidence of rebleeding was 9.5% in that group. The incidence of TIA's in the internal carotid artery ligation group was 16.6% and the incidence of stroke in that group was also 16.6%. The incidence of rebleeding was 5.5%. Although better than untreated aneurysm patients, neither the internal carotid nor the common carotid artery ligation was totally protective in preventing rebleeding. The group with internal carotid artery ligation also showed a significantly higher incidence of late ischemic complications.

VERTEBRAL ARTERY RECONSTRUCTION
Anthony Imparato, Thomas Riles, Geun-Eun Kim 33

Fifty eight patients had unilateral vertebral arterial reconstructions over a 16 year period. Thirty four had carotid operations as well. The first 18 had vertebral artery reconstructions in conjunction with carotid endarterectomy as mandated in the "Joint Study of Extracranial Arterial Occlusion as a Cause of Stroke". The next 40 had vertebral procedures for either brain stem symptoms, or for combined cerebral cortical and stem symptoms for specific indications after flow obstructing carotid lesions had been corrected and symptoms failed to improve. Syncopal episodes occurred as a major symptom in 16 and was controlled by either carotid and vertebral or vertebral artery operation alone except in 4 who needed correction of aortic stenosis.

Long term follow up reveals the average stroke rate for the first 14 years was 1.6% per year with only 5 strokes occurring in the follow up and 70% (N=41) of the pts sustaining no new neurologic episodes at the 14th year. Survival was 45% (N=36) at the 14th year with most deaths due to myocardial infarction.

The surgical procedure of vertebral angioplasty is indicated when bilateral vertebral arterial flow obstructing lesions are found in pts. with brain stem ischemia including drop attacks and syncopal episodes if flow obstructing carotid lesions have been corrected and symptoms persist.

THE EFFECT OF HEPARIN REVERSAL AFTER CAROTID ENDARTERECTOMY IN THE DOG: A SCANNING ELECTRON MICROSCOPE (SEM) STUDY - Chandler WF, Erclus MS, Ford JW (University of Michigan Medical Center, Ann Arbor, Michigan)

The purpose of this study is to determine if total reversal of heparin immediately after completing a carotid endarterectomy has an adverse effect on the thrombogenicity of the endarterectomized vessel wall.

After systemic heparinization, unilateral common carotid endarterectomies were performed using the operating microscope on 10 dogs. Half of the animals were given protamine sulfate to reverse the heparin. Three hours after resumption of blood flow these arteries, as well as contralateral vessels for control, were perfused with glutaraldehyde and prepared for SEM. Thrombin clotting times were performed throughout the experiments. SEM of the endarterectomized portions showed nearly total coverage of the exposed collagen of the media with flattened platelets. There were scattered leukocytes, but few erythrocytes, little fibrin, and no true thrombus. There were no differences between the animals which received heparin reversal and those which did not.

Since previous studies suggest that arterial thrombosis virtually always occurs within 3 hours of endothelial injury, we conclude that total reversal of heparin does not increase thrombogenicity of the endarterectomized vessel. This suggests that heparin may be reversed in patients to help decrease wound hematomas and infections.

SESSION VII: CLINICAL AND EXPERIMENTAL ASPECTS
Saturday, February 14 (8:30-10:00 a.m.)

BIOCHEMICAL AND HISTOCHEMICAL OBSERVATIONS ON THE FIFTH CRANIAL NERVE AND ITS RELATION TO MENINGEAL BLOOD VESSELS (95) - M Moskowitz, M Mayberg, L Chen, NIT, Cambridge, MA 02139, Harvard Medical School, Boston, MA 02115.

Histo- and biochemical expts using horseradish peroxidase and liquid chromatography were used to identify the existence of a neuronal pathway arising in the Vth nerve and terminating around the middle cerebral artery. In all 7 cats, cell bodies containing HRP were identified in V after enzyme was placed on the MCA. Neurons were found strictly ipsilaterally and were among cell bodies which project to the forehead. In other expts the chemistry of Vth nerve was examined in dog, cat, and rat. Measurable levels of both 5HT and 5-HIAA were detected in all species. Vasoactive peptides VIP and substance P are reported to be present here as well. These observations suggest that large meningeal blood vessels are surrounded by sensory neurons from the Vth ganglia and that this nerve contains at least 3 vasoactive agents.

One hypothesis concerning the origin of vascular headaches implicates circulating vasoactive substances. This postulation does not explain the sharply localized nature of hemi-crani-al vascular headaches. The existence of a unilaterally projecting pathway to large cerebral blood vessels from Vth nerve provides a mechanism for the distribution of hemi-crani-al vascular headaches in man. The presence of 5HT and 5-HIAA within V provides an alternative (or additional) site of activity for serotonin receptor blocking agents in the treatment of headaches.
LONG TERM CLINICAL OUTCOME IN PATIENTS WITH AMYAROSIS FUGAX AND IPSILATERAL INTERNAL CAROTID ARTERY OCCLUSION WITH OR WITHOUT MCA-STA ANASTOMOSIS. Lee MC, Park SH, Ausman JI, Loewenson RB (University Hospitals of Minneapolis, Minnesota and Henry Ford Hospital, Detroit, Michigan).

The long term clinical outcome in 20 patients with amaurosis fugax(AF) and ipsilateral internal carotid(ICA) occlusion was studied. Middle cerebral artery(MCA)-superficial temporal artery(STA) anastomosis was performed on 11 patients (mean age 57 years; range 44-65 years) on the side of AF and ICA occlusion (surgical group). Nine (mean age 66 years; range 54-75 years) received conservative treatment only (non-surgical group).

In the surgical group during follow-up (mean duration 37 months ± 3 (S.E.) months), two developed ischemic cerebral infarction on the ipsilateral side. There was one death from acute myocardial infarction(MI). In the non-surgical group (mean duration 44 months ± 16 (S.E.) months, two developed ischemic cerebral infarction on the ipsilateral side. There were two deaths from MI. Post-op cerebral angiograms consistently showed increased arterial filling through the anastomosis. However, the degree of ophthalmic artery filling was variable and inconsistent. No correlation was noted between recurrent AF and the degree of ophthalmic artery filling on post-op angiography. These data do not support the hypothesis that MCA-STA anastomosis prevent future ischemic cerebral infarction in patients with AF.

His Bundle Recordings in Patients with Unexplained Syncope. - Furlan AJ, Meagan VA, Castle L (Departments of Neurology and Cardiology, Cleveland Clinic, Cleveland, Ohio.).

Cardiogenic syncope may be difficult to document using standard electrocardiography (ECG) or even prolonged monitoring techniques (Holter). We review our experience with His bundle recordings in 41 patients with unexplained syncope. 26 patients (63%) had an abnormal His bundle study. The most frequent His abnormality was a prolonged HV interval. Carotid sinus hypersensitivity was also documented in several patients. Among the 32 patients who had an ECG, Holter and His study, 12 (38%) had an abnormality only on the His recording. All three studies were normal in 5 patients (16%), 12 patients (38%) had significant ECG and/or Holter abnormalities, whereas 27 patients (84%) had a conduction abnormality when all three studies were done. 34/41 patients (90%) remain free of syncope following pacemaker insertion and recurrent syncope was usually related to pacemaker failure. There was no correlation between His abnormalities and severity of coronary artery disease. His bundle recording may document a conduction disturbance when the ECG and Holter are non-diagnostic. His bundle recording should be considered in patients with unexplained recurrent syncope before pacemaker insertion is deferred.

VALUE OF SLEEP ELECTROENCEPHALOGRAPHY IN STROKE PROGNOSIS. Hachinski, V.C., Namelak, M., Norris, J.W., University of Toronto.

Sleep is highly organized physiologically. To determine whether its disruption might provide an index of cerebral function after stroke, we studied 28 cases of hemispheric infarction.

The sleep electroencephalographic patterns, eye movements and electromyogram were recorded within the first three nights of the stroke for a mean of 2.8 nights. By using discriminant analysis, the total sleep time, stages I, II, III and IV, REM sleep, waking and movement time and spindle density were correlated with outcome at three months. (Outcome: 1=functionally normal, 2=disabled but ambulant, 3=institutionalized or dead).

Actual Outcome Predicted Outcome

<table>
<thead>
<tr>
<th>Group</th>
<th>Actual</th>
<th>Predicted</th>
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<tbody>
<tr>
<td>1</td>
<td>11(79%)</td>
<td>2(14%) 1(7%)</td>
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<tr>
<td>2</td>
<td>5</td>
<td>1(20%) 3(60%) 1(20%)</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>1(11%) 2(22%) 6(67%)</td>
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Seventy-two per cent of cases were classified correctly on the basis of sleep parameters alone.

Sleep electroencephalography provides a new, objective, non-invasive measure of stroke recovery potential.

INTERNAL CAROTID OCCLUSION, HEMISPHERIC COLLATERAL PERFUSION PRESSURE AND STROKE. Lieberman, P.R., Barnes, R.W. (Medical College of Virginia and VA Hospital, Richmond, Virginia).

This study compared noninvasive estimates of hemispheric collateral circulation with the incidence of stroke in 61 patients with angiographically proven internal carotid artery (ICA) occlusion. Ophthalmic artery flow direction assessed by Doppler ultrasound during common carotid compression correlates well with hemispheric collateral perfusion pressure (HCPP) measured intraoperatively during carotid clamping. Antegrade flow indicates HCPP > 48 mmHg while absent or retrograde flow implies HCPP < 48 mmHg.

Stroke occurred in 11 of 21 (52%) patients with estimated HCPP > 48 mmHg and 24 of 40 (60%) patients with HCPP < 48 mmHg. This difference is not significant. To eliminate the contribution of external carotid collateral circulation to the HCPP, common carotid compression was performed in 36 patients. The intracranial HCPP was > 48 mmHg in 15 patients, 9 of whom suffered strokes (60%), and HCPP was < 48 mmHg in 21 patients, 12 of whom had strokes (57%).

These data suggest that stroke may occur following ICA occlusion despite good HCPP, possibly as a result of a terminal embolic event. Noninvasive evaluation of hemispheric collateral circulation thus may not accurately identify the stroke-prone individual.
THE ROLE OF EMBOLISED LIPIDS IN THE OUTCOME OF CEREBRAL ATHEROEMBOLISM (CAE)

Farr DJM, Steiner TJ and Clifford Rose F
(Charing Cross Hospital, London, England)

The consequences of CAE range from clinically manifest cerebral infarction to smaller lesions detected only at post-mortem; many emboli are harmless. The reasons behind this variable outcome were sought in the nature and behaviour of the different lipids released by plaque rupture.

In rats, pure preparations of representative lipids, separately or variously combined, or total lipid extract from human atheromatous plaques, were embolised into the internal carotid artery. In some, craniotomy was performed to visualise emboli in the cerebral surface vessels; others were allowed to survive embolisation and later sacrificed. All brains were histologically examined.

Each of the lipids was innocuous in the cerebral circulation and caused no harm. The reasons behind this variable outcome were sought in the nature and behaviour of the different lipids released by plaque rupture.

CVR decreased in normal and sympathectomized mice, 7–10 minutes after injection of 60 nmol NE in 4 cats and returned to baseline in 7–10 minutes. The injection of 60 nmol NE in 4 cats caused CBF to increase at the site within 20 seconds, followed by a peak within 1–2 minutes and return to baseline in 7–10 minutes. The injection of 60 nmol NE in 4 cats caused CBF to increase at the injection site and reach a peak within 1–2 minutes. Then, at each injected sympathomized site, flow rapidly declined. In these 4 animals, BP began to rise within 30 seconds of injection, peaked within a minute and returned to baseline in 3–4 minutes; CVR decreased in normal and sympathomized hemispheres during the first minute and then increased for 7–10 minutes in sympathomized caudate and thalamus. CVR did not increase in the control hemisphere. Levels of NE were reduced only in sympathomized hemispheres and sympathetic fibers innervating the extraparenchymal arteries and arterioles of the newborn dog are involved in this redistribution phenomenon.

We have recently reported in newborn dogs that CBF decreased in forebrain by 64% and increased by 65% in hindbrain during asphyxia. In this study we have investigated whether sympathetic fibers innervating the extraparenchymal arteries and arterioles of the newborn dog are involved in this redistribution phenomenon.

Employing 14C-iodoantipyrine, rCBF was measured in dogs 1–7 days of age during: a) normoxia, b) after 5 minutes of asphyxia, and c) after 5 minutes of asphyxia in dogs administered the 1 blocker phenoxybenzamine (PBZ, 200 mg/kg).

In addition, regional cerebral vascular resistance (rCVR) was calculated. During normoxia, rCBF was relatively homogeneous throughout the brain, and forebrain rCVR was 3.03 ± 0.22 Torr/ml·min·100 gm. During asphyxia (pO2=5 Torr and PCO2=70–110 Torr), forebrain rCVR increased significantly (P<0.001) to 5.6 ± 0.50 Torr/ml·min·100 gm in the nontreated dogs. However, in the PBZ-treated group, these increments were prevented and forebrain rCVR (2.76 ± 0.29 Torr/ml·min·100 gm) did not differ significantly from that of the normoxic dogs. Thus, the redistribution of rCBF that occurs in neonatal asphyxia appears to be largely mediated through the sympathetic nervous system.

SESSION VIII: BLOOD FLOW AND METABOLISM

Saturday, February 14 (10:30 a.m.–12:30 p.m.)

DRUG-INDUCED CEREBRAL PROTECTION ALTERED BY TEMPERATURE. Artru AA, Michenfelder JD
(Mayo Clinic, Rochester, Minnesota)

The effect on hypoxic survival time of asphyxia appears to be largely mediated through the sympathetic nervous system.
BARBITURATE PROTECTION FROM CEREBRAL INFARCTION WITHOUT SUPPRESSION OF EDEMA - Hoff JT, Nishimura M, Miranda S, Newfield P (University of California, San Francisco)

Barbiturates may protect the brain from focal infarction after acute arterial occlusion because the drug suppresses edema formation. We studied infarct size and perinfarct edema 72 hours after occlusion of the middle cerebral artery (MCA) in cats (n=40) treated with and without intravenous pentobarbital. After induction with halothane, cats were divided into four groups: I-hemorrhagic (n=8); II-MCA occlusion (n=14); III-MCA occlusion 30 min after pentobarbital, 30 mg/kg (n=11); IV-MCA occlusion 30 min after pentobarbital, 30 mg/kg plus 30 mg/kg for 24 hr after occlusion (n=9). Continuous intensive care was provided for 3 days. Infarct size, brain water, Na⁺ and K⁺ were assessed after sacrifice.

Intracranial pressure (ICP) exceeded 15 mm Hg, despite barbiturate therapy, in 9 of 17 cats treated with barbiturates. Infarct size was not reduced by a single dose of pentobarbital (Group II, 8.3 ± 1.5 % of hemisphere infarcted vs Group III, 9.0 ± 2.3 %), but was reduced (p < 0.05) by multiple doses over 24 hr (Group IV, 8.9 ± 1.1%). Brain water and Na⁺ rose while K⁺ fell after MCA occlusion in the ipsilateral hemisphere (p < 0.001). Barbiturates (Groups III, IV) had no effect on edema, despite barbiturate levels adequate to suppress infarction. Protection from infarction without suppression of edema suggests that barbiturate protection is not achieved by an "antiedema" effect.

BARBITURATE COMA: RELATION OF PROTECTION TO TIMING OF THERAPY & DURATION OF OCCLUSION - Selman WR, Spetzler RF, Roski RA

Pentobarbital coma (isoelectric EEG) was evaluated in a baboon model of acute MCA occlusion. 36 baboons were used. Each animal was observed in a primate intensive care unit for 96 hours. There were 6 groups: 6 hour occlusion with no therapy and therapy 1/2, 2, 4, 6 hours after ischemia; and permanent occlusion with no therapy and therapy after 1/2 hour.

Barbiturate anesthesia was associated with protection only in those animals that had therapy initiated 1/2 hour after the onset of neurologic deficit with reperfusion at 6 hours. A detrimental effect, and not merely a lack of protection, was noted with barbiturates used either after permanent occlusion, or with initiation more than 2 hours after temporary occlusion.

Intracranial pressure elevation was controlled by barbiturate therapy, in the early treatment of temporary middle cerebral artery occlusion. Barbiturate therapy led to malignant intracranial pressure elevation in delayed treatment or with use after permanent MCA occlusion.

These detrimental effects of barbiturate therapy found in our study emphasize the risk of indiscriminate use of barbiturate therapy in the clinical setting.

PROTECTIVE EFFECT OF FLUOSOL IN CEREBRAL ISCHEMIA - Peerless SJ, Ishikawa R, Hunter IG (The University of Western Ontario, London Ontario)

Fluosol-DA, a small particle fluorocarbon complex with a high propensity for O₂ and CO₂, was compared with Mannitol in the modification of acute focal ischemia in cats. Thirty-six animals underwent trans-orbital tourniquet ligation of the MCA and were either treated with IV Fluosol-DA (15 ml/kg), Mannitol 20% (1.2 gms/kg) or Saline (15 ml/kg). All animals were given 95% O₂ and sacrificed 1,3 and 6 hours later. Light microscopic assessment demonstrated an average percent infarction of 57% in controls, 29% in Mannitol and 27% in Fluosol-DA treated animals. Also, there was a marked decrease in severity of neuronal damage in Fluosol treated cases. It is suggested that Fluosol, because of its low viscosity, may support micro-circulation maintaining cortical collateral flow and supplying oxygen to the ischemic areas.

EFFECTS OF PHARMACOLOGICAL AGENTS ON FREE RADICAL INDUCED LIPID PEROXIDATION - MacMillan V (Dept of Medicine, University of Toronto, Toronto, Canada)

It has been proposed that the protective action of the barbiturates in cerebral hypoxia-ischemia is related to their ability to inhibit free radical reactions. In the present experiments an in vitro brain homogenate system was used to assess the ability of various drugs to block the formation of malonaldehyde from lipid peroxidation induced by ferrous sulfate. When the drugs were added prior to the induction of lipid peroxidation significant suppressant activity was observed with thiopental (1 mM), chlorpromazine (0.3 mM), and dexamethasone (1 mM); whereas barbitone (10 mM), pentobarbital (5 mM), methohexital (1 mM), gamma-hydroxybutyrate (10 mM), imidazole-acetic acid (10 mM), ketamine (5 mM) and diazepam (1 mM) were ineffective. Studies in which the drugs were added 15 min after the induction of lipid peroxidation revealed that promethazine (1 mM) had a marked ability to totally block further lipid peroxidation, whereas thiopental (1 mM) was ineffective. These results suggest that thiopental acts to inhibit the initiation of the free radical reaction whereas promethazine acts to block the autocatalytic reactions occurring within the membrane lipids.
CEREBRAL HEMODYNAMIC EFFECTS OF NITROGLYCERIN (NTG) IN NORMOXIC AND HYPOXEMIC DOGS - 48
Traystman RJ, Rogers MC (Johns Hopkins Medical Institutions, Baltimore, Maryland)

The effects of NTG (14) on cerebral blood flow (CBF) and cerebrospinal fluid pressure (Pcsf) were studied in anesthetized, paralyzed, ventilated dogs under normoxic and hypoxic conditions. CBF was measured with the venous outflow technique. Cerebral perfusion pressure (CPP) was calculated as the difference between mean arterial pressure and Pcsf. In animals with normal Pcsf (10-15 mm Hg), NTG (5, 25, 50 ug/kg) increased CBF by 90, 139 and 164%, and decreased CPP by 18, 32, and 36%. CBF remained unchanged from control values. Following elevation of Pcsf to 30-40 mm Hg, NTG increased CBF by 49, 57, and 56%, and decreased CPP by 30, 39, and 47%. CBF decreased by 9, 14, and 24% with each dose of NTG. When animals were ventilated with a low O2 gas mixture (Pao2 = 30 mm Hg), CBF increased from 20 ±2 to 42 ±3 ml/min and Pcsf increased from 12 ±3 to 36 ±3 mm Hg. During hypoxemia, NTG increased CBF by 40, 46, and 58% while CPP decreased by 35, 53, and 60%. CBF decreased by 20, 33, and 38% with each dose of NTG. We conclude that NTG may have deleterious effects on CBF by reducing CPP below the autoregulatory range. The mechanism for the elevation of CBF with NTG is probably related to a change in cerebral venous capacitance leading to an increase in cerebral blood volume.

EFFECTS OF HEMORRHAGE AND PHARMACOLOGIC HYPTENSION ON CEREBRAL BLOOD FLOW AND OXYGEN UTILIZATION - Grubb RL Jr, Raichle ME (Department of Neurology and Neurological Surgery; Division of Radiation Sciences, Washington University School of Medicine, St. Louis, MO 63110)

Cerebral blood flow (CBF) and cerebral oxygen utilization (CMRO2) were measured in baboons during hypotension produced by acute hemorrhage, trimethaphen and sodium nitroprusside. CBF and CMRO2 were measured by of oxygen-15 isotopes injected in the internal carotid artery. Acute hemorrhage, trimethaphen, and sodium nitroprusside lowered blood pressure (BP) to 52%, 55% and 47% respectively of control. There were corresponding falls in CBF to 76% (p<0.01), 81% (p<0.05) and 75% (p<0.01) of control. When BP was decreased 11% with hemorrhage, autoregulation was preserved and CMRO2 increased 13% (p<0.01). When CBF autoregulation was lost with acute hemorrhage, CMRO2 declined 22% (p<0.05). When CBF autoregulation was lost with pharmacologic hypotension CMRO2 was preserved with trimethaphen and actually rose with nitroprusside (15%; p<0.05). These data indicate that hypotension produced by trimethaphen and sodium nitroprusside is better tolerated than with acute hemorrhage. The reason for the increase in CMRO2 with nitroprusside hypotension and hemorrhage (autoregulation preserved) is unexplained.

CEREBRAL BLOOD FLOW AND GLUCOSE METABOLISM COUPLE WITH DOUBLE RADIONUCLIDE AUTORADIOGRAPHY - Jones SC, Lear J, Reivich M, (Cerebrovascular Research Center, Univ. of Penna., Phila., PA)

Double label autoradiography using I-123 iodoantipyrine and C-14 2-deoxyglucose can be used for the simultaneous determination of local cerebral blood flow (LCBF) and glucose metabolism (LCMRglu).

The purpose of this study is to investigate the LCBF-LCMRglu couple in normal awake rats. Two autoradiographs are produced, the first primarily from I-123 disintegrations, the second primarily from C-14. To obtain LCBF and LCMRglu values, the two exposures are subtracted. Data analysis involves sampling the same area in each exposure repetitively with a densitometer (spot size 230μm). In a series of rats, LCBF (ml/min-g) and LCMRglu (μmole/min-g) were determined. The LCBF-LCMRglu couple was investigated in nine structures. The linear regression equation is LCBF=1.5 LCMRglu-7.9 (p<0.01). This is the first direct evidence in the same animal that LCBF and LCMRglu are coupled in the normal state.
CEREBROVASCULAR AND CARDIAC RESPONSES TO INTRAVASCULAR VOLUME EXPANSION FOLLOWING FOCAL CEREBRAL ISCHEMIA

Wood, JH, Snyder, LL, Simeone, FA, Golden, MA, Fink, EA (Pennsylvania Hospital, Philadelphia)

Splenectomized dogs having mean regional (85Kr washout) cortical blood flow (rCoBF) of 89±6 (SEM) ml/100g/min underwent cerebral artery occlusion causing 51±6% reduction (p<0.001) in rCoBF without change in (thermodilution) cardiac output (CO) of 1.7±0.1 L/min and producing 10±5% hemispheric infarction (HI). Initial infusions of agents given 4 hour after arterial clipping in dose equal to 20% of total blood volume (51Cr RBC label) were followed 1 hour later by second such infusion.

Two autologous whole blood infusions caused 36±10% and 60±1% elevations in CO (p<0.001), failed to raise rCoBF and was associated with 7±6% HI. Two low molecular weight dextran infusions evoked 77±14% and 114±10% (p<0.001) increases in CO, raised rCoBF by 35±7% and 42±7% (p<0.001) and was associated with 4±7% HI. Two autologous plasma infusions induced 51±7% and 96±7% (p<0.001) elevations in CO, increased rCoBF by 25±7% and 52±7% (p<0.001) and was associated with 1±7% HI.

Hypervolemic therapy is currently being advocated for treatment of focal cerebral ischemia. Our data imply that intravascular volume expansion consistently raises CO but requires hemodilution to improve cerebral perfusion to ischemic regions.

DIXYRAZINE DECREASES PROTEIN LEAKAGE IN RAT BRAIN IN ACUTE HYPERTENSION - Johansson BB, Auer LM, Linder LE (University of Göteborg, Sweden)

Drugs can reduce hypertension-induced protein leakage in the brain by decreasing vascular tone or by changing the endothelial cell membrane probably by inhibiting pinocytosis. Phenothiazines can reduce pinocytosis in other cells. We have studied if dixyrazine protects the blood–brain barrier (BBB) during acute hypertension and if it changes pial arterial diameter.

Pial arteries were inspected through a closed cranial window and the diameters continuously measured with a videoangiometer before and after i.v. dixyrazine (5 mg/kg) in anesthetized rats. Hypertension was induced in conscious rats with chronic catheters in the aorta and a jugular vein by i.v. adrenaline or bicuculline. Evans blue and 1251 labelled serum albumin were used as tracers. The brains were perfused in situ 3 min after the pressure increase.

Dixyrazine induced a slight, transitory decrease in blood pressure. No change in arterial diameter was observed except for a transient autoregulatory dilatation. Protein leakage was markedly reduced in dixyrazine treated rats compared to controls with comparable increase in blood pressure (P < 0.001). It is concluded that dixyrazine decreases protein leakage probably by an effect on the endothelial cell membrane.
Sixth joint meeting on stroke and cerebral circulation. Los Angeles, California, February 12-14, 1981. Abstracts.

doi: 10.1161/01.STR.12.1.116

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