Cerebral Aneurysms

**AB-13966-98**

**Differential Distribution and Expressions of Collagens in the Cerebral Aneurysmal Wall**—Minnata C (Dept of Neurosurgery, Kumamoto University School of Medicine, 1-1-1-Honjou, Kumamoto 860, Japan), Kitooka M, Nagahiro S, Iyama KI, Hori H, Yoshioka H, Ushio Y—*Acta Neuropathol.* 1997;94:197-206.

To investigate the role of collagens in the formation and rupture of cerebral aneurysms, we examined the distribution and synthesis of vascular collagens in the wall of normal human cerebral main trunks and of cerebral aneurysms using immunohistochemistry and in situ hybridization techniques. Fifteen cerebral aneurysmal walls were resected at operation: control cerebral main trunks were obtained from seven autopsy cases. Semiserial sections from the specimens were subjected to immunofluorescence and immunohistochemical staining with antibodies to collagen types I, III, IV, V, VI, desmin and α-smooth muscle actin. In addition, type III collagen mRNA was examined by in situ hybridization. Immunohistochemical study showed that all collagen types were grossly preserved in the aneurysmal wall, although the distribution patterns were different for each collagen. The distribution of major fibbrillar collagen types I and III was more diffuse and homogeneous in the luminal layer of the aneurysmal wall than the media of the control artery, although the intensity of immunohistochemical staining was weaker in the abluminal layer of the aneurysmal wall than the adventitia of the control artery. Collagen types IV and V were distributed more sparsely in the luminal layer of the aneurysmal wall than the media of the control artery. Collagen type VI was noted in the luminal as well as the abluminal layer of the aneurysmal wall, whereas it was located exclusively in the adventitia of the control artery. In situ hybridization showed that the signal for collagen type III mRNA on fibroblastic and smooth muscle cells was higher in the aneurysmal walls than the control arteries, suggesting up-regulation of type III collagen transcription in the cerebral aneurysmal wall. The study of the distribution and synthetic regulation of various types of collagen in the aneurysmal wall may be essential for understanding the formation of the aneurysmal wall and its protection against enlargement or rupture.

**AB-13967-98**


**Purpose:** To evaluate the safety and efficacy of endovascular treatment of ophthalmic segment aneurysms with Guglielmi detachable coils (GDCs), as well as the primary indications for such treatment. **Methods:** We conducted a prospective study of 26 patients with 28 aneurysms of the ophthalmic segment in whom treatment with GDCs was attempted. Anatomic results were measured by statistical analysis of variance for such factors as age, sex, presence of subarachnoid hemorrhage, anatomic type (ophthalmic or superior hypophyseal), size of aneurysmal sac, and width of aneurysmal neck. Clinical evaluation and control angiography were performed at 6 and 18 months. **Results:** Overall, complete occlusion was obtained in 14 aneurysms (50%) and small residual necks were left in 11 aneurysms (39%). Three treatment attempts failed (11%). Complete1 occlusion was obtained in 76% of small-necked aneurysms as opposed to 9% of aneurysms with a large neck. The best predictor of anatomic result was the size of the aneurysmal neck. Complete occlusion was obtained in 85% of superior hypophyseal aneurysms of the parachoid variant. One permanent complication was related to treatment. **Conclusion:** Endovascular treatment with GDCs appears to be a safe and efficient alternative approach for ophthalmic segment aneurysms, especially for parachoid variants of superior hypophyseal aneurysms, which tend to have a small neck.

**AB-13968-98**

**Cigarette Smoking—Induced Increase in the Risk of Symptomatic Vasospasm After Aneurysmal Subarachnoid Hemorrhage**—Lasner TM (Division of Neurosurgery, Hospital of the University of Pennsylvania, Fifth Floor, Silverstein, 3400 Spruce St, Philadelphia, PA 19104), Weil RJ, Rama HA, King JT, Zager EL, Raps DC, Flamm ES—*J Neurosurg.* 1997;87:381-384.

Vasospasm following aneurysmal subarachnoid hemorrhage (SAH) is correlated with the thickness of blood within the basal cisterns on the initial computerized tomography (CT) scan. To identify additional risk factors for symptomatic vasospasm, the authors performed a prospective analysis of 75 consecutively admitted patients who were treated for aneurysmal SAH. Five patients who died before treatment or were comatose postoperatively were excluded from the study. Of the remaining 70 patients, demographic (age, gender, and race) and clinical (hypertension, diabetes, coronary artery disease, smoking, alcohol use, illicit drug use, sentinel headache, Fisher grade, Hunt and Hess grade, World Federation of Neurological Surgeons grade, and ruptured aneurysm location) parameters were evaluated using multivariate logistic regression to determine factors independently associated with cerebral vasospasm. All patients were treated with hypervolemic therapy and administration of nimodipine as prophylaxis for vasospasm. Cerebral vasospasm was suspected in cases that exhibited (by elevation of transcranial Doppler velocities) neurological deterioration 3 to 14 days after SAH with no other explanation and was confirmed either by clinical improvement in response to induced hypertension or by cerebral angiography. The mean age of the patients was 50 years. Sixty-three percent of the patients were women, 74% were white, 64% were cigarette smokers, and 46% were hypertensive. Ten percent of the patients suffered from alcohol abuse, 19% from sentinel bleed, and 49% had a Fisher Grade 3 SAH. Twenty-nine percent of the patients developed symptomatic vasospasm. Multivariate analysis demonstrated that cigarette smoking (p=0.033; odds ratio 4.7, 95% confidence interval [CI] 2.4–8.9) and Fisher Grade 3, that is, thick subarachnoid clot (p=0.008; odds ratio 5.1, 95% CI 2–13.1), were independent predictors of symptomatic vasospasm. The authors make the novel observation that cigarette smoking increases the risk of symptomatic vasospasm after aneurysmal SAH, independent of Fisher grade.

**Clinical**

**AB-13969-98**


**Background:** Carotid artery disease and hypertension are associated, and carotid endarterectomy is often followed by acute changes in blood pressure. As the carotid sinus is responsible for short-term blood pressure control, occlusive carotid disease may contribute to the mechanism of preoperative hypertension. **Methods:** Ten patients undergoing carotid endarterectomy and eight having a peripheral bypass procedure were studied 2 weeks before and 2 weeks after operation, using home ambulatory blood pressure measurement.
Results: A significant fall in both mean systolic (~14.4 mm Hg) and mean diastolic (~12.7 mm Hg) pressure was observed after carotid endarterectomy (P<0.006), whereas no change was seen in controls.

Conclusion: These results suggest that there is an increase in carotid sinus activity in patients following carotid endarterectomy and supports the hypothesis that carotid sinus dysfunction contributes to hypertension in patients with carotid artery disease.

AB-13970-98

Previous studies have reported left ventricular (LV) thrombus in 20% to 56% of patients after anterior wall acute myocardial infarction (AMI). The Healing and Early Afterload Reducing Therapy (HEART) study was a prospective study comparing effects of early (24 hours) or delayed (14 days) initiation of ramipril, an angiotensin-converting enzyme inhibitor, on LV function after anterior wall AMI. This ancillary study assessed prevalence of LV thrombus. Two-dimensional echocardiography was performed on days 1, 14, and 90 after myocardial infarction. The cohort consisted of 309 patients. Q-wave anterior wall AMI occurred in 78%; 87% received reperfusion therapy. The prevalence of LV thrombus was 2 of 309 (0.6%) at day 1, 11 of 295 (3.7%) at day 14, and 7 of 283 (2.5%) at day 90. One patient had thrombus at 2 examinations. The day 1 echocardiogram was not correlated with thrombus development. LV size increased more in patients with thrombus than in those without thrombus. Patients with thrombus had more wall motion abnormality after day 1 than patients without thrombus (p=0.03). Thus, the current prevalence of LV thrombus in anterior wall AMI is lower than previously reported, possibly due to changes in AMI management. Preservation of LV function is likely to be an important mechanism. Most thrombi are seen by 2 weeks after AMI. Resolution documented by echocardiography is frequent. © 1997 by Excerpta Medica, Inc.

AB-13971-98

The best anticoagulation level in patients with mechanical heart valve prostheses is still being debated. D-dimer, which detects the presence of cross-linked fibrin degradation products, has been demonstrated to be a useful marker of coagulation activation. This study was designed to verify whether heart valve prostheses in anticoagulated patients are associated with abnormalities in D-dimer plasma levels, and if so, whether such levels are related to the anticoagulation level and/or whether they could be predictive of acute vascular or hemorrhagic events. In 132 patients with single and 10 with double mechanical valve replacement, international normalized ratio (INR) and D-dimer plasma levels were determined. The INR levels of the previous 8 months were reviewed to assess the time that each patient spent in the therapeutic range. The D-dimer plasma levels were compared with those obtained from 102 matched control subjects. The patients were then followed up for 2 years to record acute vascular and hemorrhagic events. For the entire group, D-dimer plasma levels in patients were the same as those in the control group. Patients with double valve replacement had higher D-dimer plasma levels than either monovalveular implant patients or control subjects. Patients who had spent <75% of the time within the assigned anticoagulation range had higher values for D-dimer plasma levels (median, 270 vs 198 ng/mL, P=0.02). The major determinants of D-dimer plasma levels were age (R²=0.7, P=0.009) and the percentage of time spent below the predetermined INR level (R²=0.49, P=0.001). During follow-up, 19 acute vascular and 16 hemorrhagic events occurred. High D-dimer tertile was the only parameter predicting the occurrence of thromboembolic events. In patients with mechanical heart valve prostheses, the D-dimer plasma level depended on the thoroughness of anticoagulation. Patients in the upper tertile of D-dimer values have an ~5-fold risk of vascular thromboembolic events. D-dimer determination can therefore be useful in detecting patients who are at a higher risk of severe vascular events.

AB-13972-98

Background: Oropharyngeal dysphagia occurs in up to a third of patients presenting with a unilateral hemispheric stroke, yet its neurophysiological basis remains unknown. To explore the relation between cortical motor function of swallowing and oropharyngeal dysphagia, myolohyoid, pharyngeal, and thenar electromyographic responses to stimulation of affected and unaffected hemispheres were recorded in dysphagic and non-dysphagic patients.

Methods: The 20 patients studied had unilateral hemispheric stroke confirmed by computed tomography. Eight of them had associated swallowing difficulties. Electromyographic responses were recorded after suprathreshold transcranial magneto-electric stimulation of affected and unaffected hemispheres with a figure-of-eight coil.

Findings: Stimulation of the unaffected hemisphere evoked smaller pharyngeal responses in dysphagic patients than in non-dysphagic patients (mean 64 μV, median 48, interquartile range 44–86 vs 118 μV, 81, 73–150) (p<0.02). With stimulation of the affected hemisphere, the pharyngeal responses were smaller than for the unaffected hemisphere but similar between the two patient groups (26 μV, 0, 0–48 vs 54 μV, 0, 0–80). Dysphagic and non-dysphagic patients showed similar myohyoid and thenar responses to stimulation of the unaffected hemisphere as well as to stimulation of the affected hemisphere—unaffected myohyoid (269 μV, 239, 89–372 vs 239 μV, 163, 133–307), thenar (572 μV, 463, 175–638 vs 638 μV, 485, 381–764); affected myohyoid (60 μV, 41, 0–129 vs 96 μV, 0, 0–195); thenar (259 μV, 258, 0–538 vs 451 μV, 206, 8–717).

Interpretation: The findings indicate that dysphagia after unilateral hemispheric stroke is related to the magnitude of pharyngeal motor representation in the unaffected hemisphere.

AB-13973-98

To clarify the perioperative stroke risk in patients with carotid stenosis or occlusion having coronary artery bypass graft (CABG) surgery, we retrospectively reviewed the records of 1,022 patients who had CABG during a 2-year period (1992, 1993). Of these, 224 had preoperative carotid duplex studies, usually for bruit or remote symptoms. We analyzed clinical and neuroradiographic findings for all patients who had strokes to determine the subset of patients who would benefit from CABG surgery. In this ancillary study, we assessed prevalence of LV thrombus. Two-dimensional echocardiography was performed on days 1, 14, and 90 after myocardial infarction. The cohort consisted of 309 patients. Q-wave anterior wall AMI occurred in 78%; 87% received reperfusion therapy. The prevalence of LV thrombus was 2 of 309 (0.6%) at day 1, 11 of 295 (3.7%) at day 14, and 7 of 283 (2.5%) at day 90. One patient had thrombus at 2 examinations. The day 1 echocardiogram was not correlated with thrombus development. LV size increased more in patients with thrombus than in those without thrombus. Patients with thrombus had more wall motion abnormality after day 1 than patients without thrombus (p=0.03). Thus, the current prevalence of LV thrombus in anterior wall AMI is lower than previously reported, possibly due to changes in AMI management. Preservation of LV function is likely to be an important mechanism. Most thrombi are seen by 2 weeks after AMI. Resolution documented by echocardiography is frequent. © 1997 by Excerpta Medica, Inc.
Epidemiology

AB-13974-98

Background: Researchers have suggested that the deletional allele of the ACE (angiotensin-converting enzyme) gene insertion-deletion polymorphism is a potent risk factor for myocardial infarction. This association could not be confirmed in the Copenhagen City Heart Study, in which 10,150 persons were studied. The ACE gene polymorphism has also recently been suggested as a potent risk factor for ischemic cerebrovascular disease.

Objective: To investigate the association between ACE gene polymorphism and ischemic cerebrovascular disease.

Design: Two case-referent studies and a cross-sectional study.

Setting: University hospital in Copenhagen, Denmark.

Participants: Case-referent study 1: 35 women and 38 men who developed ischemic cerebrovascular disease before 50 years of age compared with 1454 women and 1737 men from a general population sample. Case-referent study 2: 82 women and 137 men with ischemic cerebrovascular disease and carotid stenosis greater than 40% compared with 4273 women and 3091 men from the general population sample. Cross-sectional study of the general population sample: 67 women and 93 men with ischemic cerebrovascular disease compared with 4077 women and 3156 men without such disease.

Measurements: Genotype; age; body mass index; smoking habits; levels of lipids, lipoproteins, apolipoproteins, and fibrinogen; and diagnosis of hypertension, diabetes mellitus, and ischemic cerebrovascular disease.

Results: Odds ratios for ischemic cerebrovascular disease by ACE genotype classes were not significantly different from 1.0 in women or men in any of the three studies, separately or combined. In a logistic regression analysis that controlled for age and conventional cardiovascular risk factors, odds ratios in either sex still did not significantly differ from 1.0 in any study, separately or combined.

Conclusion: In two case-referent studies, a cross-sectional study, and the three studies combined, no statistically significant difference was found in the development of ischemic cerebrovascular disease between genotype classes of the ACE gene polymorphism in women or men.

AB-13975-98

The purpose of this study was to determine the effect of serum lipids, lipoprotein fractions, and apolipoprotein (apo) A-1, B, and E on mortality from vascular and nonvascular causes in an unselected elderly population. The random sample of 347 community-living individuals aged 65 years or older was obtained in 1982. Serum total cholesterol, LDL cholesterol (LDL-C), HDL cholesterol (HDL-C), triglyceride, and apo A-1, B, and E were determined at baseline. After the 11-year follow-up, 199 of the participants had died, and 148 were still alive. Mortality data from vascular and nonvascular causes by the end of 1993 were obtained from official registers. In the univariate analysis, a low total cholesterol level was associated with death due to both vascular and nonvascular causes (P value for trend, .021 and .0027, respectively). After the adjustment for other risk factors, the inverse association between total cholesterol and vascular mortality disappeared, but low total cholesterol was still a significant predictor of death due to nonvascular causes. Adjusted relative risks (RRs) of death due to nonvascular causes for those with elevated total cholesterol (5.1 to 6.5, 6.6 to 8.0, and ≥8.0 mmol/L) compared with the reference group (≤5.0 mmol/L) were 0.5 (95% confidence interval [CI], 0.2 to 1.2), 0.6 (0.2 to 1.0), and 0.2 (0 to 0.8), respectively. Neither concentrations of HDL-C, LDL-C, triglyceride, nor apo B were associated with vascular or nonvascular mortality. On the other hand, low concentration of apo A-1 predicted vascular death. The RR for the lowest tertile was 1.6 (1.1 to 2.5) compared with the highest tertile. Furthermore, the occurrence of the apo E 4 allele was associated with increased risk of vascular mortality (RR, 1.5; 95% CI, 1.0 to 2.2), but the risk was not related to the levels of lipids, lipoproteins, or other apolipoproteins at baseline. Nonvascular mortality also tended to be predicted by the presence of the 4 allele (RR, 1.5; 95% CI, 0.9 to 2.5). In an unselected elderly population, the allelic variation of apo E, ie, the presence of the 4 allele, and a low concentration of apo A-1 were more accurate indicators of vascular mortality than total cholesterol or lipoprotein fractions. The risk associated with the apo E polymorphism is unrelated to dyslipidemia.

Experimental Pathology

AB-13976-98
Fibrin Glue Containing Fibroblast Growth Factor Type 1 and Heparin Decreases Platelet Deposition—Zarge JJ, Husak V, Huang P, Greuter HP (Dept of Surgery, Loyola University Medical Center, 2160 S First Ave, Maywood, IL 60153)—Am J Surg. 1997;174:188-192.

Background: The early success rates of endarterectomy and angioplasty are influenced by the thrombogenicity of the deendothelialized surface. We previously reported decreased platelet deposition after 30 and 120 minutes and after 28 days on expanded polytetrafluoroethylene (ePTFE) grafts coated with fibrin glue (FG) containing fibroblast growth factor type 1 (FGF-1) and heparin in canine aortoiliac bypass grafts compared with control uncoated grafts. The FG/FGF-1/heparin coating has been shown to enhance spontaneous endothelialization at 28 days in canine ePTFE bypass grafts. The current study evaluates the thrombogenicity of this FG/FGF-1/heparin suspension applied to a balloon deendothelialization model of endarterectomy in canine carotid arteries.

Methods: Nine dogs underwent bilateral, deendothelialization balloon injury to 6-cm segments of their carotid arteries. Fibrin glue (fibrinogen 32.1 mg/mL, thrombin 0.32 U/mL) containing FGF-1 (11 ng/mL) and heparin (250 μg/mL) was applied to the luminal surface of one carotid artery in each dog. Both femoral arteries were circumferentially dissected but not balloon injured; one femoral artery was clamped for the same period as the carotid arteries. In the 6 adult dogs, 10 minutes prior to the restitution of flow in both carotid arteries and one femoral artery, 4 to 8×106 111In-labelled autologous platelets were injected intravenously. Four-cm segments of both carotid and femoral arteries were excised after 15 or 120 minutes of circulation (n=3/time/artery, 24 arteries). In the 3 chronic dogs, the radio-labelled platelets were injected 30 days after carotid injury. The carotid and femoral vessels were then excised after 120 minutes of perfusion. Radioactive platelet deposition was quantitated by gamma counting.

Results: After 2 hours, the injured carotid arteries demonstrated significantly more platelet deposition than either uninjured femoral artery controls (P<0.001). There was also a significant 45.2% decrease (P=0.008) in platelet deposition on the balloon injured carotid arteries treated with FG/FGF-1/heparin when compared with balloon injured carotid arteries alone. At 30 days there was an insignificant trend toward decreased thrombogenicity in the FG/FGF-1/heparin treated injured carotids.

Conclusion: Surface coating with FG/FGF-1/heparin significantly decreases platelet deposition on balloon injured canine carotid arteries after 2 hours of perfusion and may be clinically applicable in endarterectomy and angioplasty procedures. The long-term induction of reendothelialization of arterial surfaces by this technique is under investigation. © 1997 by Excerpta Medica, Inc.

AB-13977-98
Relation of Plaque Lipid Composition and Morphology to the Stability of Human Aortic Plaques—Felton CV (Wynn Dept of Metabolic Medicine, 21 Wellington Rd, St John’s Wood, London NW8 9SQ, United Kingdom), Crook D, Oliver MF—Arterioscler Thromb Vasc Biol. 1997;17:1337-1345.
The propensity of atherosclerotic plaques to disrupt may be influenced by their lipid content and the distribution of these lipids within the plaque. To investigate this, we analyzed the morphological and lipid profiles of 668 human aortic plaques from 30 males who had died of ischemic heart disease. Plaques were classified as disrupted or as intact types A or B, the latter distinction being based on the absence or presence, respectively, of disrupted plaques within the same aorta. Disrupted plaques have a greater content of lipid ($P < 0.001$) and macrophages ($P < 0.001$) as well as a thinner cap ($P < 0.001$) than intact plaques. Lipid concentrations are positively associated with macrophage accumulation in all plaque types and are negatively associated with minimum cap thickness at the edge of disrupted plaques ($P < 0.05$). Free cholesterol concentration is inversely associated with minimum cap thickness at the center of type B plaques only ($P < 0.05$).

At the center of intact type A and B and disrupted plaques, the free-to-esterified cholesterol ratios were 0.9 (range, 0.0 to 2.7), 0.8 (0.0 to 3.9), and 1.6 (0.2 to 4.0), respectively. Esterified cholesterol concentrations were higher at the center of type B plaques, and those of free cholesterol were higher at the center of disrupted plaques. At the edge of disrupted plaques, the free-to-esterified cholesterol ratio was 0.5 (0.0 to 2.7) because of the accumulation of esterified cholesterol. Concentrations of all fatty acids were increased at the edge of disrupted plaques compared with the center, but as a proportion of total fatty acids, omega6-polyunsaturated fatty acids (PUFAs) were lower (44% versus 46%, $P < 0.01$), possibly reflecting oxidation of PUFAs. These data demonstrate differences in lipid composition and intraplaque lipid distribution between intact and disrupted plaques. At the edge of advanced plaques, increased esterified lipid concentrations, inversely associated with cap thickness, may reflect macrophage activity and a predisposition to rupture.

**AB-13978-98**

**Angiotsentin-Converting Enzyme Gene and Atherosclerosis—**


Common variants of the angiotensin-converting enzyme (ACE) gene (ACE in humans, ACE in mice) associated with changes in circulating ACE activities have been suggested to confer differential risks for atherosclerosis. Using a mouse model of atherosclerosis induced by heterozygosity for apolipoprotein E gene disruption and an atherogenic diet, we have studied the impact on atherosclerosis of a mutation that changes the level of function of Ace. We find that this genetically determined change does not influence the size or complexity of atherosclerotic lesions. Ace genotype was not a significant determinant of lesion size in female (+/+) = 12.9 ± 2.15 and −/− = 11.7 ± 1.6 $\mu m^2 \times 10^3$ or male (+/+) = 0.95 ± 0.25 and −/− = 1.83 ± 0.99 $\mu m^2 \times 10^3$ mice; however, lesions were significantly larger ($P < 0.001$) in female than male mice. Ace genotype also did not affect lesion complexity; however, lesions in females showed significantly increased frequency of cholesterol clefts, acellular cores, fibrous caps, and calcifications compared with those in males. The hypothesis that genetic variation in the level of ACE gene expression affects the development of atherosclerosis is not supported by these findings.

**Imaging / Cerebral Blood Flow**

**AB-13979-98**

**Ischemic Lesion Volumes in Acute Stroke by Diffusion-Weighted Magnetic Resonance Imaging Correlate With Clinical Outcome—**


Diffusion-weighted magnetic resonance imaging detects ischemic injury within minutes after onset, and has been used to demonstrate drug efficacy in animal models of stroke. In 50 patients diagnosed with acute ischemic stroke (<24-hour duration) within the middle cerebral artery territory, lesion volume was measured by diffusion-weighted imaging. Thirty-four patients also had volumes measured by T2-weighted imaging chronically (median time, 7.5 weeks; mean, 15.9 weeks). Clinical severity was measured by the National Institutes of Health Stroke Scale Score and the Barthel index. Acute lesion volumes correlated with the acute stroke scale score ($r = 0.56$), the chronic stroke scale score ($r = 0.63$), and chronic lesion volumes ($r = 0.84$). Chronic volumes correlated with the chronic stroke scale score ($r = 0.86$) and the Barthel index ($r = -0.60$). When only cortically based lesions were considered, the correlations relating acute lesion volume measured by diffusion-weighted imaging ($r = 0.61$) and chronic lesion volume measured by T2-weighted imaging ($r = 0.90$) to the chronic stroke scale score were higher. These results provide evidence that lesion volumes determined by diffusion-weighted imaging acutely may be predictive of clinical severity and outcome, and may support a role for diffusion-weighted imaging in the assessment of acute stroke therapies in clinical trials.

**AB-13980-98**


Previous studies have demonstrated that some intravascular radiographic contrast media (CM) used in angiography, especially non-ionic monomers, may cause platelet activation. This study was designed to elucidate which properties of the CM were responsible for this activity. Platelet activation engendered by CM was studied using flow cytometry to detect platelet degranulation (as CD62 expression) and fibrinogen binding. In order to elucidate the relevant characteristics of the CM responsible, contrast agents of differing structures, properties, formulations and osmolalities were studied; ionic and non-ionic, monomeric and dimeric. Gadolinium chelate MR enhancing agents and saline solutions of differing osmolalities were also investigated. Ionic dimeric sodium meglumine ioxaglate, non-ionic dimeric ioxilan and non-ionic dimeric iotrolan did not produce increased degranulation compared with saline controls. However, all agents produced a mild increase in bound fibrinogen. Experiments using saline solutions demonstrated that these effects are not attributable to the high osmolality of some CM. The broad comparison facilitated by this study shows that previous generalizations regarding platelet activation by CM, based on an ionic–non-ionic division, are not valid. We presume that some chemical structural property of the compounds is responsible and it is of note that the chemically distinct gadolinium chelates, gadolinium DTPA and gadolinium DTPA-BMA, also caused platelet activation to a similar degree. CD62 expression correlated with fibrinogen binding suggesting that at least one common pathway of platelet activation is involved.

**AB-13981-98**

**Initial Experience With Helical CT and 3D Reconstruction in Therapeutic Planning of Cerebral AVMs: Comparison With 3D Time-of-Flight MRA and Digital Subtraction Angiography—**


**Purpose:** We report our initial experience with helical CT and CT angiography (CTA) in evaluating cerebral arteriovenous malformations (AVMs) in comparison with time-of-flight MR angiography (MRA) and digital subtraction angiography (DSA).

**Method:** Twelve AVMs were studied with CTA, non-gadolinium-enhanced MRA, and DSA. Reconstructed images were obtained in three display methods (maximum intensity projection, shaded surface black and white, shaded surface color). Shaded surface color display was obtained by assigning different colors to vessels and “presumed” nids. The number of feeding arteries and draining veins associated with each AVM was independently counted in each modality. The relative ease of depicting the nids and vessels was also determined in each display method. AVM nids dimensions were measured on CTA and MRA source images and interobserver differences were compared.
Abstracts of Literature

265

RESULTS: CTA-reconstructed images depicted more veins but fewer arteries than MRA. Shaded surface color displays best delineated vessels and nidus. Nidus dimension measurement was possible on CTA in all AVMs but impossible on MRA in four AVMs due to interference by methemoglobin (three AVMs) and phase artifact (one AVM). The interobserver difference in nidus dimension as measured on CTA was significantly smaller than that on MRA.

CONCLUSION: Reconstructed CTA images and CTA source images seem to be valuable adjuncts or alternatives to MRA.

AB-13982-98

The authors assessed the reliability of magnetic resonance (MR) imaging contrast enhancement for the detection and follow-up evaluation of dissecting aneurysms of the vertebrobasilar circulation. Twenty consecutively admitted patients who underwent both gadolinium-enhanced MR imaging and conventional angiography were reviewed. Enhancement of the dissecting aneurysm was seen in all but one of the 20 patients, including 10 (71%) of 14 patients examined in the chronic phases, when the T₁-hyperintensity signal that corresponded to the intramural hematoma was unrecognizable. The enhanced area corresponded to the “pearl sign” or aneurysm dilatation noted on the comparable angiogram. On follow-up, MR studies enhancement had spontaneously disappeared in four patients at a time when comparable vertebral angiograms revealed disappearance of the aneurysm dilatation. The enhancement persisted in five of nine patients examined more than 24 weeks after symptom onset: in all five patients the aneurysm dilatation remained on comparable angiograms. Dynamic MR studies showed rapid and remarkable enhancements with their peaks during the immediate dynamic phase after injection of the contrast material. The authors conclude that gadolinium-enhanced MR imaging is useful for the detection and follow-up evaluation of dissecting aneurysms of the vertebrobasilar circulation.

AB-13983-98

Purpose: To evaluate the degeneration of the ipsilateral substantia nigra after striatal infarction by using magnetic resonance (MR) imaging.

Materials and Methods: Twenty-five adult patients with embolic cerebral infarction of the middle cerebral artery distribution underwent MR imaging 0–4, 5–9, 12–15, and 27–29 days after the stroke. Sixteen of them also underwent follow-up MR imaging 2–12 months after the stroke.

Results: Ten patients had an infarct in the striatum with or without a cortical infarct (striatal infarction group); the other 15 patients had an infarct in the cerebral cortex of the middle cerebral artery distribution without a striatal infarct (cortical infarction group). In all 10 patients with striatal infarction, a hyperintense spot appeared in the ipsilateral substantia nigra on T₂-weighted fast spin-echo images 7–12 days after the onset. This area became less intense and smaller 3 months later. In the cortical infarction group, no hyperintense spot in the ipsilateral substantia nigra was observed at any time.

Conclusion: Degeneration of the substantia nigra ipsilateral to the striatal infarction was clearly demonstrated at MR imaging. This finding should not be mistaken for further cerebral infarction.

Neurosonology

AB-13984-98

We studied 110 carotid arteries of 55 patients with unilateral or bilateral carotid stenosis diagnosed with selective angiography, by using Transcranial Doppler to detect high intensity transient signals (HITS) in the middle cerebral arteries (MCAs). HITS identified as embolic signals were prevalent (P<0.05) in the MCAs on the same side as severe (70–99%) stenosis (22 of 51=43.1%) compared to moderate (30–69%) stenosis (5 of 37=13.5%). No HITS were observed in the MCA on the same side as normal control carotid arteries (n=17) [occluded arteries (n=5) were not considered]. HITS were more prevalent (P<0.05) in the MCAs on the same side as ulcerated plaques (14 of 23=60.9%) compared to non-ulcerated plaques (13 of 65=20%), and all moderate stenoses producing HITS presented ulceration of the plaque. Ulcerated plaque groups showed a higher mean number of HITS than non-ulcerated plaque groups and no significant difference was noted between moderate and severe stenosis, between superficial or deep ulcerations and between ulcerations with flap or without flap. Therefore, severe carotid stenosis and moderate stenosis with plaque ulceration result in angiographic findings most frequently associated with HITS. Further studies are necessary to evaluate the clinical significance of this finding.

AB-13985-98

BACKGROUND AND PURPOSE: Color duplex ultrasound has been advocated as an alternative to arteriography before carotid endarterectomy. However, one limitation of color duplex ultrasound is that it sometimes fails to differentiate high-grade stenosis from total carotid occlusion. This study was done to determine (1) the accuracy of carotid duplex ultrasound in diagnosing total carotid occlusion, and (2) when angiography is necessary.

PATIENT POPULATION AND METHODS: Carotid duplex ultrasound and angiography results were compared for 520 carotid arteries, and 103 of these had a duplex diagnosis of total carotid occlusion or suspected almost total-to-total occlusion. The diagnosis of total carotid occlusion was primarily based on the absence of flow in the internal carotid artery as visualized on B-mode imaging for at least 1 inch beyond the bifurcation (optimal study). If the internal carotid artery was not optimally seen beyond the bifurcation, but secondary criteria were present, such as dampening of the common carotid signal and internalization of the external carotid artery, a diagnosis of suspected subtotal to total occlusion was made (limited study).

RESULTS: In the optimal studies, 91 arteries had total carotid occlusions and of these, 87 were confirmed by angiography. The accuracy of carotid duplex ultrasound in diagnosing total carotid occlusion was 97% with a positive predictive value of 96%, negative predictive value of 98%, sensitivity of 91%, and specificity of 99%. Twelve arteries were diagnosed as suspected subtotal to total occlusion (limited studies), and of these, three were occluded on angiography, eight had stenoses ranging from 90% to 99%, and one had 80% stenosis.

CONCLUSIONS: A carotid duplex ultrasound study is an acceptable alternative to arteriography before carotid endarterectomy. However, one limitation of color duplex ultrasound is that it sometimes fails to differentiate high-grade stenosis from total carotid occlusion. This study was done to determine (1) the accuracy of carotid duplex ultrasound in diagnosing total carotid occlusion, and (2) when angiography is necessary.

Pharmacology / Therapeutics

AB-13986-97
Relationship Between Clot Location and Outcome After Basilar Artery Thrombolysis—Cross DT (Dept of Radiology, Washington University, 510 S Kingshighway Blvd, St Louis, MO 63110), Moran CJ, Akins PT, Angtuaco EE, Drinter MN—An J Neuroradiol. 1997;18:1221-1228.
Purpose: To identify factors that predict survival and good neurologic outcome in patients undergoing basilar artery thrombolysis. Methods: Over a 42-month period, 20 of 22 consecutive patients with angiographic proof of basilar artery thrombosis were treated with local intraarterial urokinase. Brain CT scans, neurologic examinations, symptom duration, clot location, and degree of recanalization were analyzed retrospectively. Results: Overall survival was 35% at 3 months. Survival in patients with only distal basilar clot was 71%, while survival in patients with proximal or midbasilar clot was only 15%. At 3 months, 29% of patients with distal basilar clot and 15% of patients with proximal or midbasilar clot had good neurologic outcomes (modified Rankin score of 0 to 2 and Barthel index of 95 to 100). Complete recanalization was achieved in 50% of patients; 60% of those survived and 30% had good neurologic outcomes. Of patients with less than complete recanalization, only 10% survived. Neither duration of symptoms before treatment (range, 1 to 79 hours), age (range, 12 to 83 years), nor neurologic status at the initiation of treatment (Glasgow Coma Scale score range, 3 to 15) predicted outcome. Pretreatment CT findings (positive or negative for related ischemic changes) did not predict outcome or hemorrhagic transformation. Conclusion: The single best predictor of survival after basilar thrombosis and intraarterial thrombolysis was distal clot location. Complete recanalization favored survival. Radiologically evident related infarctions, advanced age, delayed diagnosis, and poor pretreatment neurologic status did not predict poor survival and therefore should not be considered absolute contraindications for intraarterial thrombolysis in patients with basilar artery thrombosis.

AB-13987-98

Elevated plasma homocysteine concentration is an independent risk factor for vascular disease in humans. In addition to nutritional and genetic factors, an interruption of the coordinate regulatory function of S-adenosylmethionine has been proposed to be involved in the occurrence of hyperhomocysteinemia. The effect of oral S-adenosylmethionine on homocysteine metabolism in humans is unknown. We investigated the effect of oral S-adenosylmethionine (400 mg) on plasma levels of 5-methyltetrahydrofolate, which is the active form of folate in the remethylation of homocysteine to methionine, S-adenosylhomocysteine, the demethylated product of S-adenosylmethionine, homocysteine and methionine over 24 hr in 14 healthy subjects. After oral administration, S-adenosylmethionine increased from 38.0±13.4 to 361.8±66.4 nmol/liter (mean±SE, P<0.001) and returned to baseline values with a half-life of 1.7±0.3 hr. Both S-adenosylhomocysteine and 5-methyl-tetrahydrofolate showed a significant transient increase (from 29.9±3.7 to 51.7±7.1 nmol/liter, and from 25.1±2.5 to 36.2±3.5 nmol/liter, respectively, P<0.001), although homocysteine and methionine did not change over the time of measurement. These changes were not found in subjects without previous S-adenosylmethionine administration. The observed metabolic changes suggest that S-adenosylmethionine, at least in concentrations obtained in this study, does not inhibit 5,10-methylenetetrahydrofolate reductase, the 5-methyltetrahydrofolate forming enzyme. Rather they indicate a positive effect on 5-methyltetrahydrofolate, a key cofactor in homocysteine metabolism, which should be considered in homocysteine lowering strategies for the prevention of vascular disease.

AB-13988-98

Citicoline (CDP-choline) is a key intermediary in the biosynthesis of phosphatidylcholine, an important component of the neural cell membrane. It has been shown to produce beneficial effects in both animal models and non-US clinical stroke trials. This study comprised a randomized (3 doses of citicoline to 1 placebo), vehicle-controlled, double-blind trial at 21 US centers. Treatment was to be started within 24 hours of stroke onset and was continued orally for 6 weeks. Final outcome assessments were at 12 weeks. Two hundred fifty-nine patients were enrolled, with approximately 65 in each of the four groups. Mean time from stroke onset to treatment was 14.5 hours, and there were no significant differences in baseline characteristics between the four groups except for patient weight. A significant difference between the groups, favoring citicoline treatment, was seen in terms of functional outcome as measured by the Barthel Index and Rankin scale, neurologic evaluation as measured by the National Institutes of Health (NIH) stroke scale, and cognitive function as measured by the Mini Mental Status Examination. When the baseline NIH stroke scale was used as a covariate, both the 500-mg citicoline group and the 2,000-mg citicoline group had a significant improvement in terms of the percent of patients who had a favorable outcome on the Barthel Index at 90 days. There were no drug-related serious adverse events or deaths in this study. This study suggests that oral citicoline can be used safely with minimal side effects in acute stroke treatment. Citicoline appears to improve functional outcome and reduce neurologic deficit with 500 mg of citicoline appearing to be the optimal dose.

AB-13989-98

In a double-blind, randomized, cross-over study the effects of single subcutaneous doses of 120 anti-Xa units/kg body wt. of three different molecular weight heparin (LMWH) preparations were investigated in 15 healthy subjects by determination of thrombin-antithrombin III complex (TAT), prothrombin fragment 1.2 (fl.2), and β-thromboglobulin (β-TG) in shed blood and in venous blood. Certoparin, dalteparin, and enoxaparin significantly inhibited coagulation activation marker formation in shed blood. The substantial inhibition of TAT and fl.2 formation was slightly more pronounced in response to certoparin. β-TG was decreased following certoparin and enoxaparin, but not following dalteparin. However, no difference between groups was detectable. A small but consistent decrease of fl.2 formation in venous blood was noted for all LMWHs and dalteparin and enoxaparin, but not certoparin, inhibited TAT formation. Only a minor impact of the three LMWH preparations was noted on β-TG plasma concentrations.

Our data indicate that the studied LMWH preparations have a major impact on blood clotting in the activated state and inhibit in vivo the hemostatic system to a comparable extent.

Surgery

AB-13990-98

BACKGROUND: The optimal material for carotid patch angioplasty after endarterectomy remains uncertain. This study compares the early outcome and recurrent stenosis rates between saphenous vein (SV) and expanded polytetrafluoroethylene (ePTFE) carotid patch angioplasty.

METHODS: The results of 421 consecutive carotid endarterectomies performed over a 72-month period were reviewed. Postoperative complications and restenosis rates, defined as ≥50% narrowing measured by color flow duplex, were compared.

RESULTS: Patch angioplasty was performed with SV in 287 and with ePTFE in 110 cases. Patients who had undergone primary closure (n=20) or whose form of closure was unknown (n=4) were excluded. The mean
age of patients and length of follow-up was similar between groups. Women were more likely to be patched with ePTFE than were men (36% versus 23%, \( P=0.02 \)). One death occurred in each group (0.3% SV, 0.9% ePTFE, \( P=0.69 \)). Cervical hematomas requiring operative evacuation occurred in five SV closures and in three ePTFE closures (1.7% versus 2.7%, \( P=0.35 \)). The 60-month restenosis rates by life table analysis were 2.6%±2.1% for SV and 10.7%±7.9% for ePTFE (\( P=0.17 \)).

**CONCLUSIONS:** The incidence of postoperative complications is similar with SV or ePTFE patch angioplasty; however, vein harvest site complications are avoided with the use of ePTFE. Recurrent stenosis at 5 years occurs infrequently with either SV or ePTFE. © 1997 by Excerpta Medica Inc.

**AB-13991-98**


**BACKGROUND:** Retrospective analysis was performed to assess the effect of gender, age, hypertension, diabetes, and smoking upon residual disease, recurrent disease, and progression of disease following carotid endarterectomy (CE). The effect of patch versus primary closure was also studied.

**METHODS:** Postoperative duplex studies were performed following 323 CEs at months 1, 6, 12, and 24. Residual disease was defined as luminal stenosis >59% at 1 month. Progression of disease was defined as stenosis at any month that was greater than stenosis at month 1. Recurrent disease was nonresidual stenosis >79%.

**RESULTS:** Correlation was found between age at operation, <65 years and cigarette smoking; both also correlated with progression of disease on serial studies, as well as recurrent stenosis <79%. Primary closure of the arteriotomy correlated with residual disease.

**CONCLUSION:** Primary closure of the arteriotomy following CE increases the likelihood of residual disease. Smokers and those aged <65 years are predisposed to progression of postoperative disease, and to development of recurrent stenosis. © 1997 by Excerpta Medica, Inc.

**Items of Interest**

**Contrast-Enhanced MR Angiography: Methods, Limitations and Possibilities**—Kouwenhoven M (Philips Medical Systems, MR Clinical Science, Veenpluis 4-6, PO Box 10000, NL-5680 DA Best, Netherlands)—*Acta Radiologica*. 1997;38:57-67.

**Familial Cerebral Aneurysms**—Leblanc R (3801 University St, Montreal, Quebec, Canada H3A 2B4)—*Can J Neurol Sci.* 1997;24:191-199.

**Cerebral Hemodynamics and Metabolism During Infant Cardiac Surgery: Mechanisms of Injury and Strategies for Protection**—du Plessis AJ (Dept of Neurology, Fegan 1110, Children’s Hospital, 300 Longwood Ave, Boston, MA 02115)—*J Child Neurol.* 1997;12:285-300.


**Problems in the Diagnosis of Intracranial Venous Infarction**—Bakac G, Wardlaw JM (Depts of Clinical Neurosciences, University of Edinburgh, Western General Hospital, Crewe Road, Edinburgh EH4 2XU, UK)—*Neuroradiology*. 1997;39:566-570.

**Low-Molecular-Weight Heparins**—Weitz JI (Hamilton Civic Hospitals Research Centre, 711 Concession St, Hamilton, ON L8V 1C3, Canada)—*N Engl J Med*. 1997;337:688-698.

**Warfarin and Heparin-Induced Skin Necrosis and the Purple Toe Syndrome: Infrequent Complications of Anticoagulant Treatment**—Sallah S (Center for Thrombosis and Hemostasis and the Division of Hematology/Oncology, University of North Carolina at Chapel Hill, Campus Box 7035, Chapel Hill, NC 27599-7035), Thomas DP, Roberts HR.—*Thromb Haemost.* 1997;78:783-790.
Abstracts of Literature
Askiel Bruno
Linda S. Williams

Stroke. 1998;29:261-267
doi: 10.1161/01.STR.29.1.261
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1998 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/29/1/261

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

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

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