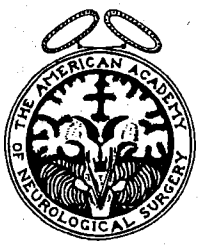
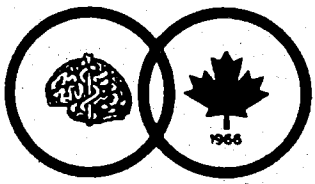
Barker

# JOINT MEETING
# OF
# THE AMERICAN ACADEMY OF NEUROLOGICAL SURGERY
# AND
# THE CANADIAN NEUROSURGICAL SOCIETY




# 59th Annual Meeting

*The* RIMROCK
RESORT HOTEL

BANFF, ALBERTA
CANADA

**September 10 - 13, 1997**

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# OF
# THE AMERICAN ACADEMY OF NEUROLOGICAL SURGERY
# AND
# THE CANADIAN NEUROSURGICAL SOCIETY

# 59th Annual Meeting

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**September 10 - 13, 1997**

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Julian T. Hoff

## PRESIDENT ELECT

Edward Connolly

## VICE PRESIDENT

George Ojemann

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Roberto C. Heros

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Charles H. and Carol Tator

# JOINT MEETING

# THE AMERICAN ACADEMY OF NEUROLOGICAL SURGERY

# and

# THE CANADIAN NEUROSURGICAL SOCIETY

## Schedule of Activities

**Tuesday, September 9th**

| | |
|---|---|
| 3:00 PM | ABNS Primary Exam Committee - Boardroom IV |
| 7:00 PM | ABNS Dinner - Dining Room |

**Wednesday, September 10th**

| | |
|---|---|
| 8:00 AM - 3:00 PM | ABNS Primary Exam Committee - Boardroom IV |
| 4:00 PM - 8:00 PM | Registration - Wildrose Ballroom Prefunction area |
| 5:00 PM - 6:30 PM | American Academy Executive Committee Meeting - Bluebell Room |
| 6:30 PM - 9:30 PM | Welcoming Reception - Salon A & B |

**Thursday, September 11th**

| | |
|---|---|
| 7:00 AM - 2:00 PM | Speaker Ready Room/ Editing Room - Boardroom II |
| 7:30 AM - 1:00 PM | Registration - Wildrose Ballroom Prefunction area |
| 7:00 AM - 1:00 PM | Breakfast Meeting - Members of the American Academy of Neurological Surgery - Yarrow Room |
| 7:00 AM - 8:00 AM | Breakfast meeting - Members of the Canadian Neurosurgical Society and Guests - Salon A |
| 8:00 AM - 8:30 AM | Initial Scientific Session - Lecture by Peter Allen, M.D. *"Geological History of the Canadian Rockies"* Open to all members, spouses and guests - Salon B & C |
| 8:30 AM - 1:00 PM | Scientific Session I - Salon B & C |
| 10:00 AM - 10:30 AM | **Coffee Break** - Wildrose Ballroom Prefunction area |
| 12:00 PM | ABNS Advisory Council Luncheon - Bluebell Room |
| 12:00 - 1:50 PM | Golf - Banff Springs Hotel* (hors d'oeuvres and beverages included) |
| 1:30 PM | Tennis* - Banff Springs Hotel* |
| 7:00 PM | BBQ Extravaganza - Do Nut Tent - Banff (transportation provided) |

*Sign up at Registration Desk - Road West

**Friday, September 12th**

| | |
|---|---|
| 7:00 AM - 2:00 PM | Speaker Ready Room/Editing Room - Boardroom II |
| 7:30 AM - 1:00 PM | Registration - Wildrose Ballroom Prefunction area |
| 7:00 AM - 8:00 AM | Closed breakfast meeting - (Business Meeting) Members of the American Academy of Neurological Surgery - Yarrow Room |
| 7:00 AM - 8:00 AM | Canadian Neurosurgery Society Executive Breakfast - Boardroom 1 |
| 7:00 AM - 8:00 AM | Breakfast meeting - Members and Guests of the Canadian Neurosurgical Society - Salon A |
| 8:00 AM - 1:00 PM | Scientific Session II - Salon B & C |
| 10:00 AM | Group photograph |
| 10:15 AM - 10:30 AM | Coffee Break - Wildrose Ballroom Prefunction area |
| 12:24 PM - 1:00 PM | Presidential Address: Julian T. Hoff |
| 1:30 PM | Banff Local Tour* |
| 2:00 PM - 3:30 PM | Meeting of the Editorial Board of the *Journal of Neurosurgery* Board Room |
| 7:00 PM - 8:00 PM | Cocktails - Wildrose Ballroom Prefunction area |
| 8:00 PM - 12:00 | Dinner - Banquet/Dance* Wildrose Ballroom |

*Sign up at Registration Desk - Road West

**Saturday, September 13th**

| | |
|---|---|
| 6:00 AM - 2:00 PM | Speaker Ready Room/Editing Room - Boardroom II |
| 7:30 AM - 11:00 AM | Registration - Wildrose Ballroom Prefunction area |
| 7:00 AM | Combined breakfast for all members of both Societies - Salon A |
| 8:00 AM - 1:00 PM | Scientific Session III - Salon B & C |
| 10:00 AM - 10:30 AM | Coffee Break - Wildrose Ballroom Prefunction area |
| 1:00 PM | Adjourn |
| 1:30 PM | Cycling the Rockies* |
| 1:30 PM | Lake Louise Tour* |
| 2:00 PM | Lake Minnewanka Tour* |

Saturday evening - free

**Sunday, September 14th**

| | |
|---|---|
| 8:00 AM | Columbia Icefields* |
| 8:00 AM | Mountain Lakes Tour* |
| 8:30 AM | Fly fishing expedition* |
| 9:00 AM | Whitewater Rafting* |

*Sign up at Registration Desk - Road West

# SCHEDULE OF ACTIVITIES FOR SPOUSES

**Wives of American Academy members, Canadian Society members and guests are welcome to all events.**

**Wednesday, September 10th**

| | |
|---|---|
| 6:30 PM - 8:00 PM | Welcome Reception<br>Wildrose Ballroom - Salon A & B |

**Thursday, September 11th**

| | |
|---|---|
| 7:00 AM | Breakfast - Hospitality Suite - Hawthorne Room |
| 8:00 AM | Lecture - Peter Allen, M.D.<br>*"Geological History of the Canadian Rockies"* - Salon B & C |
| 7:00 AM - 1:00 PM | Hospitality Suite open - Hawthorne Room |
| 8:30 AM | Book Review - *Crossing to Safety* by Wallace Stegner - Reviewed by Ellen Dunsker<br>Hospitality Suite - Hawthorne Room |
| 12:00 - 1:50 PM | Golf* - Banff Springs Hotel - light hors d'oeuvres included |
| 1:30 PM | Tennis* - Banff Springs Hotel |
| 7:00 PM | BBQ Extravaganza - Do Nut Tent - Banff<br>Transportation provided |

**Friday, September 12th**

| | |
|---|---|
| 7:00 AM - 10:00 AM | Breakfast – Hospitality Suite - Hawthorne Room |
| 7:00 AM - 1:00 PM | Hospitality Suite open - Hawthorne Room<br>Strolling and shopping in Banff<br>Meet in Hospitality Suite - Hawthorne Room |

*Sign up at Registration Desk - Road West

| | |
|---|---|
| 1:30 PM | Banff Local Tour* |
| 7:00 PM | Cocktails - Wildrose Ballroom Prefunction area |
| 8:00 PM - midnight | Dinner - Banquet/Dance** Wildrose Ballroom, Salon A & B |

* Sign up at registration Desk - Road West
** Edelweiss Theme - Black and White (Black Tie optional)

**Saturday, September 13th**

| | |
|---|---|
| 7:00 AM - 10:00 AM | Breakfast – Hospitality Suite - Hawthorne Room |
| 7:00 AM - 1:00 PM | Hospitality Suite open - Hawthorne Room |
| 9:00 AM - 10:00 AM | "Share Your Talents" - Hospitality Suite - Hawthorne Room |
| 1:00 PM | Meeting Adjourns |
| 1:30 PM | Cycling the Rockies Tour* |
| 1:30 PM | Lake Louise Tour* |
| 2:00 PM | Lake Minnewanka Tour* |

**Sunday, September 14th**

| | |
|---|---|
| 8:00 AM | Columbia Icefields Tour* |
| 8:00 A.M. | Mountain Lakes Tour* |
| 8:00 A.M. | Fly fishing, Walk and Wade Tour* |
| 9:00 AM | Whitewater Rafting* |

* Meet at Registration Desk - Road West

NOTES

# SCIENTIFIC PROGRAM

## AMERICAN ACADEMY OF NEUROLOGICAL SURGERY

September 10th - 14th, 1997

**Thursday, September 11**

8:00 - 8:35 *Geological History of the Canadian Rockies*
Peter Allen

8:35 - 8:40 Break

**SCIENTIFIC SESSION I**
Moderator: **Ralph G. Dacey, Jr.**

8:40 - 8:58 *Eposure of Low-lying Basilar Apex Aneurysms via the Trans Sylvian or Anterior Temporal Approaches*
Duke S. Samson, Michael B. Horowitz, Thomas A. Kopitnik, Jr., H. Hunt Batjer, Coimbra

8:58 - 9:16 *Selection of Cerebral Aneurysms for Treatment with GDC Coils: Preliminary Experience*
Gerard Debrun, James I. Ausman, Victor Aletich, Fady T. Charbel, Harish Shownkeen, Mukesh Misra, Pierre Kehrli

9:16 - 9:34 *A Comparison Between Endovascular and Surgical Management of Basilar Apex Aneurysms*
John M. Tew, Jr., Gary A. Zimmerman, David P. Gruber, Thomas A. Tomsick, Harry R. van Loveren, C. Ralph Buncher

9:34 - 9:52 *A Regional Performance of Carotid Endarterectomy*
J.M. Findlay, J. Wong, T. Lubkey, M. Suarex-Almazor

9:52 - 10:10 *Adenosine Triphosphate as a Possible Cause of Vasospasm in Monkeys*
R. Loch Macdonald, Bryce Weir, John Zhang, Linda Marton, Michael Sajdak, Lydia Johns

10:10 - 10:28 *Carotid Stent: An Alternative to Surgery in High Risk Patients*
LN Hopkins, LR Guterman, AK Wakhloo

10:28 - 10:58 **Coffee Break**

10:58 - 11:16 *Treatment of Grade V AVM's*
Roberto C. Heros, Harold J. Pikus

11:16 - 11:34 *Vascular Reconstructions are Facilitated by Non-Penetrating Arcuate-Legged Clips*
Wolff M. Kirsch, Yong Hua Zhu, Stanley Rouhe

11:34 - 11:52 *Risk of Rebleeding After First Hemorrhage from Cavernous Malformations: Natural History and Response to Proton Beam Radiosurgery*
Fred G. Barker, II, Sepideh Amin-Hanjani, William E. Butler, Sue Lyons, Christopher S. Ogilby, Robert G. Ojemann, Paul H. Chapman

11:52 - 12:10 *Posterior C1-C2 Transarticular Screw Fixation for Alantoaxial Anthrodesis*
Volker K. H. Sonntag, Curtis A. Dickman

12:10 - 12:28 *The Future of Medical Education*
Charles B. Wilson

12:28 - 12:46 **Academy Award Presentations - Academy Award Paper**
*The Hydroxyurea-induced Loss of Double-Minute Chromosomes Containing Amplified Epidermal Growth Factor Receptor Genes Reduces the Tumorigenicity and Growth of Human Glioblastoma Multiforme*
Gregory W. Canute, Sharon Longo, John Longo, Michele Shetler, Thomas Cole, Jeffrey Winfield, Peter Hahn

12:46 - 12:56 **Academy Award Honorable Mention**
*Cajal-Retzius Cells and the Role of Spontaneous Correlated Layer Electrical Activity in the Laminar Organization of the Developing Neocortex*
Theodore H. Schwartz, Vikram Kumar, Daniel Rabinowitz, Rafael Yuste

**Friday, September 12**

**SCIENTIFIC SESSION II**
Moderator: **William F. Chandler**

8:00 - 8:18 *DNA Damage and Repair via Methyl guanine-Methyltransferase (MGMT) Activity in Adult Gliomas: Correlation with Patient and Tumor Characteristics*
Mitchel S. Berger, John Silber

8:18 - 8:36 *Unresectable Meningiomas of the Skull Base: Management Strategies*
Fred Gentili, Patrick Gullane

8:36 - 8:54 *MRI and PET Guidance in Surgery of Epilepsy and Intrinsic Brain Tumors*
Andre Olivier, Martin Cyr, David Reutens, Denise Klein, Brenda Milner, Terry Peters

8:54 - 9:12 *Intraoperative Magnetic Resonance Imaging for Guidance of Transsphenoidal Pituitary Adenoma Resection*
Warren R. Selman, ML Hlavin, J Duerk, BS Clampitt, A Cesar, JS Lewin

9:12 - 9:30 *The Trigemino-vagal Reflex in Transsphenoidal Surgery*
Felipe C. Albuquerque, Vladimir Zelman, Martin H. Weiss

9:30 - 9:48 *Transsphenoidal Surgery - Lessons Learned from 2900 Cases*
Edward R. Laws

9:48 - 10:06 *Radical Surgery and 90 Gy proton/Photon Irradiation for Glioblastoma Multiforme*
Griff Harsh, Markus Fitzek, James Rabinov, Michael Lev, Francisco Pardo, Ilana Braun, Fred Hochbewrg, Dianne Finkelstein, Rees Cosgrove, Paul Okunieff, Allan Thornton

10:06 - 10:36 **Coffee Break**

10:36 - 10:54 *HSV-TK Gene Therapy for Glioblastoma: Suicide Gene Approach or a Novel Form of Immunotherapy*
Ronald E. Warnick, Mitchel S. Berger, M. Prados, John C. Van Gilder, S.G. Marcus, P.J. Stambrook, John M. Tew

10:54 - 11:12 *Experience with Vagus Nerve Stimulation for Medically Refractory Epilepsy: Rationale Technique and Outcome*
Michael L.J. Apuzzo, Christopher M. Degiorgio, Christi N. Heck, Michael Llevy, M.D., Ph.D.

11:12 - 11:30 *p16-induced Regulation of Astrocytoma Tumorigenicity*
Peter B. Dirks, James T. Rutka

11:30 - 11:48 *The Role of Ras Activation in Human Astrocytomas and Neurofibromas*
Abhijit Guha, Mathias Feldkamp, Nelson Lau

11:48 - 12:06 *Neurons in Human Temporal Cortex Active with Verbal Associative Learning*
George A. Ojemann, Julie A. Schoenfield

12:06 - 12:24 *Academic Surgeons Should Manage Hospital Resources - The Willy Sutton Principle*
Alan Hudson, Paul Walker

12:24 - 1:00 **Presidential Address: Julian T. Hoff**
Introduced By: George Ojemann

**Saturday, September 13**

**SCIENTIFIC SESSION III**
Moderator: **Joseph F. Hahn**

8:00 - 8:18 *Operative Electrophysiologic Studies in 70 Presumed Thoracic Outlet Cases*
David G. Kline, L. Happel, R. Voorhies, R. Tiel

8:18 - 8:36 *Mixed Vascular Malformations of the Brain: From Phenotypic Riddles to Questions of Genotype*
Issam A. Awad

8:36 - 8:54 *Long Term Outcome in Patients with Lumbar Stenosis and Associated Spondylolisthesis Treated with both Lumbar Decompression and Fusion.*
Paul B. Nelson

8:54 - 9:12 *Decompression of Post-Injury Spinal Stenosis: An Animal Model*
Christopher B. Shields, G.H. Raque, Y.P. Zhang, D.J. Morassutti, S.D. Glassman, J.R. Dimar

9:12 - 9:30 *Angiographic Anatomy of the Vein of Labbé*
Mitesh V. Shah

9:30 - 9:48 *Attenuation of Post Traumatic Head Injury in Transgenic Mice Expressing an Inhibitor of the ICE Neuronal Cell Death Gene*
Robert M. Friedlander, Klaus Fink, William E. Butler

9:48 - 10:06 *The Pathophysiology and Regulation of the Glutamatergic System in Traumatic Brain Injury*
Robert J. Dempsey, Rao Vemuganti, Mustafa K. Kaskaya, Rao Adibhatla, Aclan Dogan

10:06 - 10:36 **Coffee Break**

**SCIENTIFIC SESSION IV**
Moderator: **T.S. Park**

10:36 - 10:54 *Fusiform Dilation of the Internal Carotid Artery Following Parasellar Tumor Surgery in Children*
Stephen J. Haines

10:54 - 11:12 *Preliminary Outcome of Trans-parahippocampal Limbic Resection for Treatment of Mesial Temporal Lobe Epilepsy*
T.S. Park, M.D., Blaise F.D. Bourgeois

11:12 - 11:30 *Laminoplasty vs. Laminectomy in Children Requiring Selective Dorsal Rhizotomy*
Gary A. Dix, Mark G. Hamilton, S. Terry Myles

11:30 - 11:48 *Frameless Stereotactic Selective Microsurgical Amygdalohippocampectomy for Medically Intractable Partial Complex Seizures*
Kim J. Burchiel, Joshua Dowling, Facques Favre, Martin Salinsky

11:48 - 12:06 *Developmental Pathways and Medulloblastoma*
Corey Raffel, Russell H. Zurawel, Robert Jenkins, C. David James

12:06 - 12:24 *A New Endoscopic Tool for Stereotactic Systems*
F. Duffner, D. Freudenstein, B. Will, E.H. Grote

12:24 - 12:42 *Posterior Fossa Re-exploration for Recurrent Trigeminal Neuralgia and Hemifacial Spasm: Surgical Findings and Therapeutic Implications*
Sohaib A. Kureshi, Robert H. Wilkins

12:42 - 1:00 *Endoscopic Third Ventriculostomy: A New Look at an Old Technique*
Alan R. Cohen

1:00 Adjourn

Thursday, September 11
8:40 - 8:58 AM

**Eposure of Low-lying Basilar Apex Aneurysms via the Trans Sylvian or Anterior Temporal Approaches**

Duke S. Samson, Michael B. Horowitz,
Thomas A. Kopitnik, Jr., H. Hunt Batjer, Coimbra

Exposure of low-lying basilar apex aneursyms via the trans-sylvian or anterior temporal approaches has proven problematic, especially when the lesion in question is situated well below the level of the posterior clinoid processes. Recently a trans-cavernous extension of the routine trans-sylvian approach has been used in fifteen such cases with promising results. Proximal control of the basilar artery was obtained and employed in each patient for effective temporary occlusion. All lesions were definitively clipped as proven by post-operative angiography, and morbidity related to the exposure has been limited to one instance of incomplete sixth nerve palsy. In most patients, the entire basilar trunk from the origins of the anterior inferior cerebellar arteries to the level of the superior cerebellar arteries can be visualized through this limited incision in the posterior cavernous sinus.

Thursday, September 11
8:58 - 9:16 AM

**Selection of Cerebral Aneurysms for Treatment with GDC Coils: Preliminary Experience**

Gerard Debrun, James I. Ausman, Victor Aletich, Fady T. Charbel, Harish Shownkeen, Mukesh Misra, Pierre Kehrli

**Introduction:** Patient selection in aneurysm treatment with GDC coils is crucial to the success of the technique. This paper describes our approach in the treatment of intracranial aneurysm with GDC and summarizes our results over the last two years.

**Methods:** 91 consecutive cases of intracranial aneurysms treated with GDC, both ruptured and unruptured, were reviewed. Two groups emerged. The first consists of aneurysms incompletely treated or associated with high morbidity and includes aneurysms with wide necks. The second, consists of aneurysms which were completely cured with essentially no morbidity, and includes aneurysms with small neck to diameter ratios (< 1 to 2) and are spherical in shape.

**Results:** Overall morbidity and mortality: Group one (24 patients), 2/1, Group two (67 patients), 2/1. At 18 months follow-up the complete obliteration rate is 65% (16) for Group one, and > 95% (64) for group two. There has been no instance of recanalization to date in aneurysms that were completely obliterated with dense coil packing at time of treatment. Using aneurysm geometry and neck size as major factors in selection of patients for coils versus microsurgery, our total experience in 222 consecutive aneurysms will be summarized emphasizing the indications for neurosurgery or coiling.

**Conclusion:** The geometry of the aneurysm, and neck size to aneurysm diameter was the most important selection criteria in considering treatment with GDC coils and in selected cases is preferable to microsurgery. Aneurysm location, Hunt Hess and Fischer grades was relatively less important in determining the success of the technique.

Thursday, September 11
9:16-9:34 AM

**A Comparison between Endovascular and Surgical Management of Basilar Apex Aneurysms**

John M. Tew, Jr., MD, Gary A. Zimmerman, MD,
David P. Gruber, MD, Thomas A. Tomsick, MD,
Harry R. van Loveren, MD, C. Ralph Buncher, ScD
Departments of Neurosurgery, Radiology, and Environmental Health,
University of Cincinnati College of Medicine,
231 Bethesda Avenue, PO Box 670515, Cincinnati, Ohio 45267-0515

**Purpose:** Endovascular techniques have been proposed as treatment of choice for some basilar apex aneurysms. To evaluate this controversial issue, we compared the microsurgical and endovascular (i.e., Guglielmi detachable coils [GDC]) treatment of basilar apex aneurysms.

**Materials and Methods:** Forty-one patients were treated (1993 - 1996) for saccular basilar apex aneurysms with angiographically definable necks that were judged suitable for either coiling or surgery. Patients were treated by a team of vascular neurosurgeons and interventional neuroradiologists who have worked together for more than 10 years. Twenty patients (mean age 50) underwent surgical treatment; 15 (75%) were treated acutely after subarachnoid hemorrhage (SAH). Twenty-one patients (mean age 52) underwent endovascular treatment with GDC; 11 (52%) were treated acutely after SAH. Of the 26 patients who were treated acutely after SAH, 23 presented with Hunt and Hess grades I - III and three were grade IV. Fifteen patients were treated electively (unruptured or ruptured more than 14 days post-SAH). There were no significant differences in aneurysmal dimensions and configurations between patients who underwent surgical and endovascular treatment.

**Results:** Of the patients treated after acute SAH, 66% of the surgical group and 90% of the endovascular group had a good outcome (Glascow Outcome Score of 1-2) ($p<0.005$); there was one (6.6%) mortality in the surgical group and there were no mortalities in the endovascular group. Of the patients treated electively, 80% of the surgical group and 100% of the endovascular group had good outcomes; there was one (20%) death in the surgical group and there were no deaths in the endovascular group ($p<0.005$). Surgical patients remained in the hospital twice as long and accrued hospital charges that were twice those of the endovascular group ($p<0.001$). No patient sustained subsequent aneurysmal hemorrhage.

**Conclusions:** Endovascular treatment of basilar apex aneurysms is a safe and efficacious approach that reduces morbidity and improves cost effectiveness. Patients who present with a saccular basilar apex aneurysm with a definable neck should be evaluated for coiling. Surgery should be reserved for patients who fail coiling, or for whom coiling is not an appropriate option. Long-term follow-up is needed to determine the outcome of partially and completely coiled aneurysms.

Thursday, September 11
9:34-9:52 AM

## A Regional Performance of Carotid Endarterectomy

J.M. Findlay, J. Wong, T. Lubkey, M. Suarex-Almazor

**Background and Purpose:** We are examining the appropriateness of CEAs performed in our city and determining the incidence of postoperative stroke and death. We wish to determine if the combination of a surgical audit and distribution of guidelines for CEA use would improve the local performance of this procedure.

**Methods:** In the first part of the study we retrospectively reviewed 291 consecutive CEAs performed in our region over 18 months. The indications for CEA were considered appropriate for symptomatic carotid stenoses 70%, uncertain for <70% symptomatic or 60% asymptomatic stenoses, or inappropriate for <60% asymptomatic stenoses and for patients with preoperative neurological or medical instability. These results were then announced to all surgeons performing CEA in the region both at meetings and in a mail-out, along with CEA guidelines and notification that CEAs were undergoing continued review (part 2 of the study).

**Results:** In part one of this study 41% of patients (118/291) were asymptomatic. Surgical indications were appropriate in 33% of cases (92/281), uncertain in 49% (138/281) and inappropriate in 18% (51/281). Stroke or death occurred within 30 days postoperatively in 5.2% (9/174) of symptomatic patients and 5.1% (6/117) of asymptomatic patients. At the present time we have prospective data on 60 CEAs performed during the second part of this study.

**Conclusion:** In the first part of this study, almost 1 in 5 patients underwent CEA inappropriately and half had uncertain indications. A high complication rate negated any overall surgical benefit in the large group of asymptomatic patients. Data collected from the second part of the study (to be announced) will indicate if this audit has had an effect on the local use and performance of CEA.

Thursday, September 11
9:52 - 10:10 AM

**Adenosine Triphosphate as a Possible Cause of Vasospasm in Monkeys**

R Loch Macdonald MD, PhD, Bryce Weir MD, John Zhang MD, Linda Marton PhD, Michael Sajdak, Lydia Johns

Adenosine triphosphate (ATP) is a vasoactive compound that is found in high levels inside erythrocytes and that could contribute to vasospasm after subarachnoid hemorrhage (SAH) when it is released by hemolysis. This study tested whether ATP could cause vasospasm after placement in the subarachnoid space of monkeys. Thirty-two monkeys were randomized to 4 groups to undergo cerebral angiography at baseline (day 0) and then 7 days (day 7) after subarachnoid placement of: 1. agarose (n = 8), 2. ATP (n = 8), 3. autologous erythrocyte hemolysate (n = 8), or 4. purified human hemoglobin $A_0$ (n = 8). Vasospasm was assessed by comparison of day 0 and day 7 angiograms between and within groups, and by pathological examination in a subset of perfusion-fixed monkeys. Levels of adenine nucleotides were measured in subarachnoid clots by high pressure liquid chromatography (HPLC). There was significant vasospasm of the right middle cerebral artery in groups given ATP (-28% ± 7% reduction, paired t-test, $p < 0.05$), hemolysate (-23% ± 7%, $p < 0.05$) or purified hemoglobin (-15% ± 2%, $p < 0.005$). There were no significant differences between groups in diameters of cerebral arteries on day 7 (ANOVA). Pathology showed mild inflammation in the subarachnoid spaces of animals exposed to hemolysate or hemoglobin but not ATP or agarose. Levels of adenine nucleotides in subarachnoid compounds were highest on day 7 in animals exposed to hemoglobin or hemolysate. These results suggest that ATP can contribute to vasospasm after SAH. Further investigations will have to determine if levels of ATP adjacent to vasospastic cerebral arteries after subarachnoid hemorrhage are sufficient to contribute to vasospasm.

Thursday, September 11
10:10-10:28 AM

**Carotid Stent: An Alternative to Surgery in High Risk Patients**

LN Hopkins MD, LR Guterman PhD MD,
AK Wakhloo MD PhD
Department of Neurosurgery SUNY at Buffalo 14209-1194

The North American Symptomatic Carotid Endarterectomy Trial and the Asymptomatic Carotid Endarterectomy Trial have demonstrated that symptomatic as well as asymptomatic carotid artery stenosis 70% or greater is best treated by carotid endarterectomy if the operative morbidity and mortality is less than 6%. There is a sizable sub-group of patients who because of medical co-morbidities, recurrent stenoses or anatomical considerations are considered high risk for carotid endarterectomy. These patients were largely excluded from the NASCET and ACAS studies. Fro these patients the risk of carotid endarterectomy is greater than 6% and for this reason the procedure is not scientifically validated. In this sub-group of high-risk patients, angioplasty and stent is a reasonable, minimally invasive alternative to open surgery. In patients with acceptable surgical risk, we perform carotid endarterectomy. We have performed angioplasty and/or stent in 90 high-risk patients. To date we have not experienced ipsilateral hemispheric stroke in any patient undergoing carotid angioplasty and stent. However, we have lost two patients to myocardial infarction in the perioperative period. A third patient suffered a middle cerebral artery embolus at the time of stent deployment which was successfully treated with superselective intra-arterial thrombolysis. Three additional patients suffered transient cerebral ischemia; all recovered fully with no evidence of ischemia on MRI scans. All stented patients were treated with commercially available Palmaz (J&J) or Wallstents (Schneider). Our current protocol includes perioperative treatment with aspirin and Ticlid and intraoperative heparin. Procedures are performed under local anesthesia and the patients are routinely discharged within 24 hours. Good results depend on attention to detail and an understanding of the cerebral vascular system.

Thursday, September 11
10:58 - 11:16 AM

**Treatment of Grade V AVMs**

Roberto C. Heros, M.D., Harold J. Pikus, M.D.

A personal series of 51 patients that underwent complete surgical resection of a grade V (Spetzler and Martin) AVM was reviewed. In addition, the literature concerning the natural history of AVMs treated conservatively and the results of alternative treatments such as radiosurgery alone, radiosurgery preceded by embolization and embolization alone were reviewed.

Our results indicate that during the immediate postoperative period, only 29% of the patients were well and 41% had a major neurologic deficit (one of these died). In 1988, we reported a formal late (minimum of 6 months) follow-up result from the earliest group of patients and although many had improved with time, there were still only 62% with good results and 19% of the patients remained in poor condition.

The literature indicates that the risk of hemorrhage in these patients is no higher and may be lower than the risk for patients with smaller AVMs. Most patients treated with radiosurgery alone for grade V AVMs have been treated with heavy particles with reported obliteration rates of 22 to just under 50% and a complication rate close to 10%; these results are no better than the natural history of the disease. It has been impossible to extract from the literature the results of radiosurgery preceded by embolization, but it does appear that embolization in this setting carries a risk of about 10% and that recanalization after embolization is common; long-term data is not available. Although many patients have been treated with palliative embolization alone, there is no good long-term data to evaluate the results of this therapy.

My conclusion is that most patients with grade V AVMs should receive no treatment, be reassured of the "low" risk of hemorrhage and be advised to live a normal life. In patients with progressive neurologic deficit or multiple hemorrhages, treatment by embolization, embolization plus radiosurgery or embolization plus surgical excision should be considered.

Thursday, September 11
11:16 - 11:34 AM

**Vascular Reconstructions are Facilitated by Non-Penetrating Arcuate-Legged Clips**

WM Kirsch, M.D., YH Zhu, M.D.

**Introduction:** Non-penetrating, arcuate-legged clips have been used successfully for treating vascular surgical disorders. The device is approved by the FDA (VCS Ò clips, United States Surgical Corporation).

**Conditions Treated and Results:** Over 5,000 Vascular cases have been performed world-wide with VCSÒ clips (carotid endarterectomies, femoral popliteal bypasses, and vascular accesses). Complications are 7 per 10,000 applications (compared to vascular stents 80 per 10,000). Neurovascular applications include cervical, cavernous, intracranial carotid reconstructions, bypass operations for large inoperable intracranial aneurysms, and control of sinus bleeding. One case of Takayasu's arteritis (reconstruction of aorta, carotids) and basilar aneurysm intraoperative rupture have been successfully treated. Clips originally designed for a small vessel arterial and venous vascular anastomosis are being used clinically for anastomosing vessels with O.D.s of 1.8 - 3.0mm (coronary bypass, free tissue transfer, and superficial temporal to middle cerebral cortical artery anastomoses). An automated device is capable of doing an end-to-side vascular anastomosis on 2mm O.D. vessels with the "one-shot" application of 12 VCSÒ clips (video demonstration). This device facilitates microvascular reconstructions.

**Conclusions:** Post-operative follow-ups extending over two years and prospective randomized controlled clinical trials indicate that the clip is biologically and technically superior to needle and suture. For example, a patient who underwent bilateral carotid endarterectomies (left-sided conventional suturing, right-sided clipping) twelve months postoperative demonstrated progressive intimal hyperplasia at the sutured anastomotic line and none at the clipped. These events have been documented by "fly through" imaging. Clips provide an interrupted, non-penetrated, compliant vascular anastomotic line reducing the incidence of anastomotic intimal hyperplasia.

Thursday, September 11
11:34-11:52 AM

**Risk of rebleeding after first hemorrhage from cavernous malformations: natural history and response to proton beam radiosurgery**

Fred G. Barker II, Sepideh Amin-Hanjani, William E. Butler, Sue Lyons, Christopher S. Ogilvy, Robert G. Ojemann, Paul H. Chapman
Neurosurgical Service, Massachusetts General Hospital, Boston, MA

**Introduction.** Reported hemorrhage rates from cavernous malformations (CMs) vary widely, complicating patient counseling and treatment efficacy assessment. In addition, while temporal variation in rebleeding risk has been posited to explain hemorrhage "clustering", this risk variation over time has not been demonstrated. We reviewed pretreatment rebleeding rates after a first hemorrhage in patients selected for surgery or radiosurgery to clarify the natural history of CMs presenting with overt hemorrhage.

**Methods.** Retrospective review of 142 CM pts treated with surgery or proton beam radiosurgery during an 18 yr period. Multistate survival methods allowed analysis of multiple events per person and rebleeding rates that varied with time.

**Results.** 64 patients suffered a 2nd hemorrhage before treatment and 15 had 3 or more hemorrhages. 538 patient-yrs elapsed between first hemorrhages and treatment. Hemorrhage-free survival after 1st hemorrhage was 86% after 1 yr, 67% after 2 yr, 52% after 3 yr, 43% after 5 yr, and 28% after 10 yr. The monthly rehemorrhage risk fell below 2% after 2 yr and < 1% after 3 yr. Risk was relatively constant for 2.5 yr after first hemorrhage, then dropped sharply to a low rate. Rehemorrhage rates were higher in younger patients ($p < 0.01$) and after >1 prior hemorrhage ($p < 0.01$). This spontaneous decrease in risk of rehemorrhage will bias analyses toward a spurious decrease in hemorrhage risk 2 years post-radiosurgery if patients are treated soon after hemorrhage. A multivariate, multistate model showed no reduction in rebleeding risk < 2 yr after proton beam treatment, but > 2 yr post-treatment rebleeding risk fell 70% ($p < 0.02$), even after adjustment for natural history.

**Conclusions.** Rehemorrhage risk from CMs is initially high and decreases after 2 yr. Proton beam radiosurgery reduced the rebleeding risk even after adjustment for natural history.

Thursday, September 11
11:52 AM - 12:10 PM

**Posterior C1-C2 Transarticular Screw Fixation for Atlantoaxial Arthrodesis**

Volker K. H. Sonntag, Curtis A. Dickman

**Introduction**: Transarticular screw fixation has gained popularity as a method for rigidly fixating C1-C2 for arthrodesis.

**Methods**: Clinical and radiographic outcomes were assessed in 121 patients (57 males, 64 females) treated for atlantoaxial instability with posterior C1-C2 transarticular screws in conjunction with an autologous wired posterior C1-C2 bone strut. Atlantoaxial instability was caused by rheumatoid arthritis ($n$=48), C1 and/or C2 fractures ($n$=45), traumatic transverse atlantal ligament disruption ($n$=11), os odontoideum ($n$=9), tumors ($n$=6), or infection ($n$=2). All patients had preoperative clinical and radiographic findings consistent with C1-C2 instability; 23 had prior nonunions of C1-C2 wiring procedures. Bilateral C1-C2 transarticular screws were placed in 105 patients; 16 patients had only one transarticular screw placed. All screws were placed under lateral fluoroscopic guidance.

**Results**: Postoperative plain radiographs and CT showed that 221 (98%) of the 226 screws were positioned satisfactorily; five (2%) were malpositioned. No patient had clinical sequelae. Of the 5 malpositioned screws, one was repositioned and three were removed. A single vertebral artery occlusion remained asymptomatic after treatment with aspirin and screw removal. There were no neurological complications.

Perioperatively, one patient died from aspiration pneumonia and one from a hypertensive left hemispheric stroke. The mean long-term follow-up was 22 months in 114 of the 119 surviving patients: 112 (98%) patients achieved fusion. The two nonunions (1.9%), associated with delayed screw fractures and recurrent C1-C2 hypermobility, required reoperation for occipitocervical fixation.

**Conclusions**: C1-C2 transarticular screw fixation rigidly fixates unstable motion segments, increasing fusion rates.

Thursday, September 11
12:10 - 12:28 PM

**The Future of Medical Education**

Charles B. Wilson

One year ago Richard Atkinson, President of the University of California, appointed a commission, the University of California Commission on the Future of Medical Education, with the charge of advising the University on the future of medical education in the light of the State's health care needs. The report was to create a view of the future direction of medical education as well as the appropriate size and specialty composition of the physician workforce. This involved an understanding of epidemiology, demographics and the non-physician healthcare workforce in California.

The report, submitted to the President in June, included a description of the State's present and future needs and the proposed response of the University of California's five academic medical centers. Recommendations were made in regard to the number of medical students educated in the UC system as well as the number and composition of graduate medical education programs within the system. Finally, specific recommendations were made concerning implementation of the report.

Thursday, September 11
12:28 - 12:46 PM

**Academy Award Presentations - Academy Award Paper**

**The Hydroxyurea-induced Loss of Double-Minute Chromosomes Containing Amplified Epidermal Growth Factor Receptor Genes Reduces the Tumorigenicity and Growth of Human Glioblastoma Multiforme**

Gregory W. Canute MD, Sharon L. Longo BA, John A. Longo BA[2], Michele M. Shetler BA, Thomas E. Coyle MD[3], Jeffrey A. Winfield MDPhD[4], and Peter J. Hahn PhD[2]
Departments of Neurosurgery, Radiation Oncology[2] and Medicine[3], State University of New York Health Science Center, Syracuse, New York, 13210 and 1000 E. Genesee St., Syracuse, NY 13210[4]

**OBJECTIVE:** We investigated whether the hydroxyurea-induced loss of double-minute chromosomes (dmin) containing amplified epidermal growth factor receptor (EGFR) genes would lead to a loss of tumorigenicity of a glioblastoma multiforme (GBM) cell line.

**METHODS:** GBM cells were treated in vitro with 0 (HU0) or 100μmol/L (HU100) hydroxyurea and then injected into the flanks of nude mice. Survival and tumor volumes were evaluated. Pulsed-field gel electrophoresis (PFGE), Southern blot hybridization and slot blot analysis were used to determine EGFR amplification levels. Flow cytometry and immunofluorescent staining were used for cell cycle analysis and EGFR protein expression.

**RESULTS:** Prior to injection, HU100 cells lost 95% of their amplified EGFR genes and developed into tumors 6 weeks after injection versus 3 weeks for HU0 cells. Mice with HU100 tumors had a median survival of 62 days versus 43 days for control mice with HU0 tumors. PFGE analysis showed that HU100 tumors had reamplified the EGFR gene as dmin of the same size as those originally present before hydroxyurea treatment. When HU100 cells were cultured in the absence of hydroxyurea, the EGFR gene also reamplified. HU100 cells grew at less than half the rate of untreated HU0 control cells in culture and showed a decreased number of cells entering the cell cycle. Immunofluorescent staining of HU150(150μmol/L) cells showed decreased EGFR protein expression.

**CONCLUSION:** The EGFR gene is important for tumorigenicity in mice and growth in culture. Hydroxyurea induces the loss of dmin amplified EGFR genes against a selection gradient and significantly delays the onset of tumors. These results support the potential use of low dose hydroxyurea for the treatment of human GBM.

Thursday, September 11
12:46 - 12:56 AM

**Academy Award Honorable Mention**

**Cajal-Retzius Cells and the Role of Spontaneous Correlated Layer Electrical Activity in the Laminar Organization of the Developing Neocortex**

Theodore H. Schwartz, Vikram Kumar, Daniel Rabinowitz, Rafael Yuste

**Introduction:** Abnormalities of neuronal migration are a major cause of focal epilepsy. Cajal-Retzius (CR) cells appear transiently in layer I of embryonic and early post-natal neocortex and, although little is known about their pharmacology and electrophysiology, they have been shown to play a role in orchestrating neuronal migration through release of diffusible growth factors. While correlated spontaneous activity is particularly important in the development of other neural systems, it is not knows if such activity is present in layer I and if CR cells are involved.

**Methods:** We imaged spontaneous and evoked calcium dynamics simultaneously in 50-200 layer 1 cells loaded with fura-2 or calcium green-1 in isolated, perfused hemispheres (n=16) and in tangenital slices (n=56) from PND1-8 rate somatosensory neocortex. Cell types were identified with DIC and fluorescent microscopy. Time-lapse and video-rate movies were taken using NIH Image controlling at SIT camera. Calcium transients were measured as deltaF/F. We performed similar experiments on the *reeler* mouse, whose cortex is inverged as a result of abnormal CR cells.

**Results:** Spontaneous activity was characterized by both rapid and slow calcium influxes into all cell types, with CR cells exhibiting less activity ($p<0.001$), and longer duration events ($p<0.01$) than other cells. This activity was more rapid in the younger animals and decreased with age ($p<0.001$). CR cells were activated by glutamate, NMDA, AMPA, NE, carbachol and muscimol. Bipolar stimulation with tungsten electrodes (n=27) particularly activated CR cells and was reversibly blocked by TTX, nickel, and propranolol. Under control conditions, there were significant ($p<0.05$) correlations in the calcium transients between the non-CR cells of layer I in 15/19 experiments. Significant correlations were eliminated by the addition of TTX (n=3), propranolol (n=3), atropine (n=3) and bicuculline (n=3), but not strychnine (n=3), octanol (n=3) or APV/CNQX indicating that they were mediated synaptically, not by gap junctions, and that the CR cells were not involved. In the *reeler* mouse, significant correlations were preserved (n=3).

**Conclusions:** Our results indicate that CR cells exhibit spontaneous and electrically-induced calcium transients and possess NMDA, NE, AMPA, glycine and GABA receptors, all of which are excitatory. We also show that layer I exhibits spontaneous correlated activity during development involving predominantly non-CR cells. This circuit is mediated by GABA, acetylcholine and norepinephrine but not glutamate or glycine and is not effected by the *reeler* mutation.

Friday, September 12
8:00 - 8:18 AM

**DNA Damage and Repair via Methylguanine-Methyltransferase (MGMT) Activity in Adult Gliomas: Correlation with Patient and Tumor Characteristics**

Mitchel S. Berger, M.D., John Silber, Ph.D.

In this work, we present our experience with a key DNA repair pathway that mediates nitrosourea drug resistance in brain tumors, namely, MGMT (methylguanine-methyltransferase). MGMT was assayed in gliomas and adjacent histologically normal brain in patients to determine if correlations exist between MGMT and patient/tumor characteristics, and, examine the contribution of MGMT to brain tumor response to alkylating agents and radiation.

MGMT activity was detectable in 75% (114/151) of specimens ranging from .30 to 89 fmol/$10^6$ cells. Mean activity varied with histology, i.e., 2.1 to 8.2 fmol/$10^6$ cells, for mixed gliomas to glioblastoma, respectively. The incidence of specimens lacking MGMT activity ranged from 9% for oligodendrogliomas to 42% for mixed gliomas. Neither the mean activity or lack of activity differed by sex. MGMT activity showed a statistically significant inverse correlation with age and degree of aneuploidy, but not S-phase fraction of cells. Comparison of tumor and adjacent normal brain from 85 patients revealed a 5-fold higher mean MGMT content in tumor vs. adjacent normal tissue. While only 25% of tumor specimens lacked MGMT activity, 62% of adjacent normal brain was considered to be MGMT deficient. Newly diagnosed gliomas (n=97) and tumors recurring after radiation (n=54) did not differ in mean MGMT content or in MGMT negative status. Yet, mean MGMT activity of tumors recurring after radiation and nitrosourea based therapy (n=21) was much higher. In addition, the incidence of MGMT negative status in tumors treated with radiation and nitrosoureas was 6-fold less than in untreated tumors and 4-fold less in tumors treated with radiation only.

These results imply that nitrosoureas induce expression of MGMT and/or select for MGMT expression in gliomas. In contrast, treatment with radiation and nitrosoureas had no effect on MGMT activity in histologically normal brain adjacent to tumor. Time to tumor progression in patients treated with nitrosoureas did not differ between tumors with MGMT activity and those without MGMT expression. This indicates that MGMT is not a major determinant of in-vivo drug resistance to nitrosourea based therapies.

Friday, September 12
8:18 - 8:36 AM

**Unresectable Meningiomas of the Skull Base: Management Strategies**

Fred Gentili, Patrick Gullane

Despite the use of modern skull base approaches and microsurgical techniques certain meningiomas arising from the skull base cannot be totally resected. The management of these unresectable meningiomas with their increased patient morbidity and mortality remains a serious clinical problem for skull base surgeons. We report on a series of 30 patients with unresectable meningiomas treated between 1982 and 1996. The majority of lesions involved extensive areas of the skull base, cavernous sinus, and petroclival region. A rare subset(9)extensively transgressed the skull base invading the paranasal sinuses and infratemporal and pterygopalatine fossae. The age and sex distribution of the patients was similar to lesions considered resectable. Although major morbidity at 16% was high in the unresectable group there was no operative mortality. Histology revealed no frankly malignant lesions. Management strategies have included 1) observation alone 2)hormonal manipulation (antiprogesterone agents, somotastatin) 3)radiotherapy (gamma knife, proton beam, conventional radiotherapy) 4) chemotherapy (hydroxy urea) 5) re-operation and a combination of the above. The average follow-up has been 8 years (1-13 years). All patients are alive with residual disease. Functional status based on Karnofsky rating revealed 85% to be fully functional. 90% of patients have stable disease with no evidence of progression. In summary, a multi-modality approach including repeat surgery, hormonal manipulation, chemotherapy and radiation can result in prolonged functional survival in this group of patients.

Friday, September 21
8:36-8:54 AM

**MRI & PET Guidance in Surgery of Epilepsy and Intrinsic Brain Tumours**

A. Olivier, M.Cyr, D. Reutens, D. Klein, B.Milner & T. Peters
Montreal Neurological Hospital-Institute
McGill University

Over a period of five years we have carried out more than 500 procedures using the Allegro Viewing Wand System in the surgical treatment of epilepsy and intrinsic brain tumours.

In epilepsy, the frameless stereotactic MRI guidance has been applied to a variety of procedures such as transcortical selective amygdalohippocampectomy, callosotomy, resection of cortical dysplasia and implantation of intracranial depth and surface electrodes.

The main impact of this image guided surgery has been a reconsideration of the concept of cerebral localization. The crisp and accurate reconstruction of gyri and sulci has provided a quick and easy mean of identifying the topography of the central area and specifically of the central sulcus. For most cases of extratemporal surgery we have now used routinely PET activation studies for identification of sensori-motor zones of the hand, foot and tongue. For procedures on the dominant hemisphere we have relied more and more on speech activation studies which revealed with constancy speech activation centres to passive listening, word repetition and synonym generation.

The experience gained in the field of epilepsy has been readily applied to the resection of intrinsic brain tumours and other lesions located in the vicinity of speech centres and other high functional areas.

Examples will be provided to illustrate the rapid evolution of functional image guidance in neurosurgery.

Friday, September 12
8:54 - 9:12 AM

**Intraoperative Magnetic Resonance Imaging for Guidance of Transsphenoidal Pituitary Adenoma Resection**

Selman WR, Hlavin ML, Duerk J, Clampitt BS, Cesar A, Lewin JS

Introduction: We sought to determine imaging parameters, develop localizer tools, and assess the feasibility of intraoperative transsphenoidal surgical guidance with MRI.

**Materials and Methods:** A surgical suite was developed in the MR Department, with antimicrobial precautions including surveillance monitoring, disinfection, ventilation, and scrub zone set up. Standard surgical instruments were tested to determine the distance from the magnet at which torque was noted. Procedures were performed on a 0.2T imager (Siemens Open) with the MR table fully extended, placing the head 6 feet from the magnet isocenter. An operating microscope was placed by the head. Localizer probes were constructed on 5 mm. diameter plastic tubing filled with diluted Gd-DTPA and gas sterilized

Three patients underwent transsphenoidal tumor resection with the entire procedure performed in the MRI imaging suite. Intraoperative sequences included 3D T1W FLASH, T1W SE and T2W TSE.

**Results:** Instrument torque was not measurable in operating position. The patients were imaged 3 to 6 times during surgery. T1 images could clearly document optic apparatus decompression for macroadenomas, and was useful for localizing a recurrent 6 mm. adenoma. The localizer probe yielded a clearly visible moveable linear market on T1 and T2 images, and allowed different surgical landmarks to be readily correlated with their location on the intra-operative MR images. T2 images were necessary to differentiate fluid accumulating within the surgical bed from residual tumor.

**Conclusions:** Intraoperative MRI can be safely performed with a minimum of modifications in surgical instrumentation and technique and may be useful for interactive imaging in transsphenoidal resection of sellar tumors.

Friday, September 12
9:12-9:30 AM

**The Trigemino-vagal Reflex in Transsphenoidal Surgery**

Felipe C. Albuquerque, MD; Vladimir Zelman, MD, PhD; and Martin H. Weiss, MD

**Introduction**: Bradycardia resulting from manipulation, traction or damage to the branches of the trigeminal nerve is a well-known complication of facial surgery. Examples include bradycardia following manipulation of the bones of the orbit and its contents, following percutaneous compression of the trigeminal ganglion for the relief of trigeminal neuralgia, and during elevation or reduction of complex maxillary and mandibular fractures.

**Methods**: As manipulation of the trigeminal nerve is a common occurrence in the extraction of tumors from the cavernous sinus during transsphenoidal surgery, we investigated retrospectively the occurrence of this complication.

**Results**: We report 10 cases, from a series of 1900 transsphenoidal craniotomies, in which sinus bradycardia ensued during cavernous dissection for the excision of pituitary tumors of varying histology and size. In one case, asystole rapidly followed the onset of bradycardia. In all cases, no evidence of prior cardiac disease existed or persisted post-operatively. Normal heart rate was easily restored after the administration of atropine in nine patients and glycopyrrolate in one.

**Discussion**: Compression of either the ophthalmic or maxillary divisions of the trigeminal nerve during cavernous sinus dissection is the likely afferent arm of this reflex in all cases. Internuncial fibers connecting the main sensory nucleus of the trigeminal nerve to the motor nucleus of the vagus nerve are well-established as the efferent path of this reflex in head and neck surgery.

**Conclusion**: This series represents the first report of this potentially life-threatening reflex in transsphenoidal surgery and underscores the need for fastidious, intraoperative monitoring of electrocardiographic changes. The rapid administration of anti-cholinergic agents abolishes this reflex and should be the first therapeutic maneuver in all such cases.

Friday, September 12
9:30 - 9:48 AM

**Transsphenoidal Surgery -**
**Lessons Learned from 2900 Cases**

Edward R. Laws, Jr., MD

The author has been fortunate in having the support and opportunity to deal with a large number of patients treated by transsphenoidal surgery for sellar and parasellar lesions.

The design of a comprehensive Neuroendocrine Service is described, along with factors important in success. Surgical emergencies are described, along with other indications and limitations of the transsphenoidal approach.

The details of the technique of transsphenoidal surgery are described, and the modifications that have occurred over a 25 year time period. Optimization of management is emphasized, with the twin goals of safety and efficacy.

Complications of surgery and postoperative management are discussed, including CSF rhinorrhea and its treatment, intraoperative vascular injuries, diabetes insipidus, SIADH and hyponatremia.

Details of the management of difficult patients (Cushing's disease, acromegaly) are discussed, along with indications and techniques of reoperation, and indications for adjunctive therapy, including stereotactic radiosurgery.

Long term results and recurrence rates are described for the different categories of pituitary tumor.

Friday, September 12
9:48 - 10:06 AM

**Radical Surgery and 90 Gy Proton/Photon Irradiation for Glioblastoma Multiforme**

Griff Harsh, Markus Fitzek, James Rabinov, Michael Lev, Francisco Pardo, Ilana Braun, Fred Hochberg, Dianne Finkelstein, Rees Cosgrove, Paul Okunieff, Allan Thornton

**Introduction:** Historically, resection and irradiation (50-60 Gy) of glioblastomas yields a mean survival duration of 9 months and a two-year survival rate of 11%. Brachytherapy (50 Gy) or radiosurgery (15 Gy) boosts extend median survival to 18-27 months and the two-year rate to 40% in highly selected patients. No dose effect has been established; the effect on local control is controversial. This study assessed the effect of radical resection and fractionated high-dose radiation on local control and survival in patients with grade 4 astrocytoma.

**Methods:** Twenty-three patients with newly diagnosed grade 4 astrocytoma were enrolled prospectively on an institutional protocol specifying craniotomy for radical tumor resection followed by combined proton/photon therapy to 90 CGE (1.8 CGE b.i.d.). Eligiblity required: (1) age 18-70, (2) Karnofsky $\geq$ 70, and (3) unilateral tumor $<$ 5 cm in postoperative diameter. Outcome variables included time to radiographic change (increased T1-gad), isodose, histology at which radiographic change occurred, and survival.

**Results:** Mean enhancing tumor volume was 39 cc preoperatively (median 33 cc) and 5 cc postoperatively (median 0.5 cc). Median survival time from first surgery was 20 months; actuarial survival at 1, 2, and 3 years was 78%, 26%, and 9%, respectively. All 23 patients demonstrated enlarging enhancing masses, first appearing at a mean of seven months after starting radiation. Tissue was obtained from 14. Ten had only necrotic material; four had both tumor and necrosis. Necrosis persisted,either alone (4) or with tumor (3) in seven patients operated upon for a third time. In summary, seven of 14 patients assayed pathologically following radiation had no tumor. These showed a trend towards prolonged survival. Radiographic failure occurred locally in 21 and was distant in two.

**Conclusion:** The survival of this group of patients is comparable to that of patients treated with brachytherapy or radiosurgery. Local failure persists. Radiation toxicity warrants dose modification and prophylaxis.

Friday, September 12
10:36 - 10:54 AM

**HSV-TK Gene Therapy for Glioblastoma: Suicide Gene Approach or a Novel Form of Immunotherapy**

Warnick RE, Berger MS, Prados MD, Van Gilder JC, Marcus SG, Stambrook PJ, Tew JM

The most common gene therapy strategy for glioblastoma involves the selective introduction of the Herpes simplex thymidine kinase (HSV-Tk) gene into tumor cells, thus rendering them sensitive to the antiviral drug ganciclovir (GVC). A Phase II study of HSV-Tk/GCV gene therapy was recently completed in a group of 30 patients with recurrent glioblastoma. We will present the results of this study with emphasis on the five long-term survivors (17-32 months) and the low incidence of serious adverse events. Transient neurological symptoms occurred in ten patients within days to weeks after injection of the murine vector producer cells (VPC) and in three patients during ganciclovir administration. MR scans in these patients showed a transient increase in contrast enhancement around the resection cavity. Histological analysis after reoperation in two patients demonstrated an intense inflammatory infiltrate )T-lymphocytes).

Experimental studies from our laboratory and others support the important role of the immune system in the tumoricidal effect of this form of gene therapy. HSV-Tk/GCV gene therapy is: (1) more effective in immunocompetent animals and impaired by immunosuppressive drugs (e.g., dexamethasone), (2) induces both cellular (T cell and macrophage) and cytokine (IL-1 and IL-6) responses in experimental tumors, and (3) can produce tumor immunity in animals. Based on this evidence, we propose that HSV-Tk/GCV gene therapy in glioblastoma produces an initial immune response to the thymidine kinase transgene and/or the murine VPCs. Subsequent administration of GCV results in tumor cell death through the suicide gene mechanism which releases tumor antigens and elicits an even greater tumoricidal immune response. This supports the role of HSV-Tk/GVC as a novel immunotherapy approach in brain tumor patients.

Friday, September 12
10:54 - 11:12 AM

**Experience with Vagus Nerve Stimulation for Medically Refractory Epilepsy: Rationale Technique and Outcome**

Michael L.J. Apuzzo, Christopher M. Degiorgio,
Christi N. Heck, Michael Llevy, M.D., Ph.D.

**Background:** Preclinical studies in animal models indicate that chronic vagus nerve stimulation inhibits epileptic spiking and shortens seizures in both maximal electroshock and pentylenetetrazol models of epilepsy. Safety studies indicate no evidence of nerve injury after chronic stimulation when duty cycles are less than 50%. Prior clinical studies of VNS support its efficacy and safety in refractory epilepsy. We report the USC experience as part of a largest and most rigorously controlled trial of VNS to date, the E05 study.

**Methods:** 21 subjects with medically refractory epilepsy and at least 6 partial onset seizures with alteration of consciousness per month were enrolled in a Multicenter double-blind study of high versus low vagus nerve stimulation. After a three month baseline, subjects were implanted with a NCP pulse generator and helical platinum bipolar lead attached to the left cervical vagus nerve trunk. Subjects were then randomized to HIGH stimulation (up to 3.5 ma, 30 seconds on, 5 minutes off, 30 hertz) or LOW stimulation (up to 3.5 ma, 30 seconds on, 180 minutes off, frequency 1-2 hertz). The principal investigator and study assistant were blinded to the randomization status throughout the study. Programming was performed by an unblinded investigator and programmer who did not reveal the randomization status to the PI. Seizure frequency, adverse events, blood chemistries, pulmonary function and holter recordings were monitored at monthly intervals for three months during the blinded treatment phase.

**Results:** Of the 21 subjects enrolled, 18 subjects completed the three month baseline and were randomized. One subject was excluded from analysis due to inadequate seizure calendars. Seven subjects were randomized to high stimulation, and ten to low stimulation. None of the 10 randomized to low intensity VNS had a >50% reduction in seizures, and the mean reduction for the low group was .05%. Four of the seven randomized to high stimulation had a greater than 50% reduction in seizures, and two had a greater than 75% reduction, of who one remained seizure free. The mean reduction in the high group was 74%. No significant changes were noted in pulmonary functions, cardiac rhythm, blood pressure or pulse. The most common adverse effects were hoarseness during stimulation, throat discomfort, and cough.

**Conclusion:** Vagus nerve stimulation is a safe and effective treatment for intractable epilepsy.

Friday, September 12
11:12 - 11:30 AM

**p16-induced Regulation of Astrocytoma Tumorigenicity**

Peter B. Dirks, MD, PhD, and
James T. Rutka, MD, PhD, FRCSC, FACS
Division of Neurosurgery, #1504, The Hospital for Sick Children, The University of Toronto, Toronto, Ontario CANADA

Transformation of glial cells into malignant astrocytomas involves significant dysregulation of the cell cycle control machinery. Several groups have now shown that the proteins in the p16-cyclin D1/cdk4-pRB pathway are mutated in a high percentage of malignant astrocytomas. One frequent aberration in this pathway observed in primary astrocytomas is loss of expression of the cyclin dependent kinase inhibitor, $p16^{Inka4a}$. We demonstrate here that reconstitution of the $p16^{Ink4a}$-deficient malignant astrocytoma, U343, with $p16^{Ink4a}$ under the control of the tetracycline repressor system results in profound changes in cellular morphology and cell cycle gene expression. Induction of $p16^{Ink4a}$potently blocked proliferation of these cells and resulted in a shift of the pRB-family proteins, pRB, p107 and p130 to their active, hypophosphorylated forms. E2F-1 was also repressed to undetectable levels while E2F-4 levels remained constant. The loss of E2F-1 was associated with formation of E2F-site binding complexes containing pRB and E2F-4, determined independently in electrophorectic mobility shift assays and by co-immunoprecipitation. Morphologically, a "cell cycle arrest" phenotype was observed. When $p16^{Ink4a}$ was induced in the presence of retinoic acid (RA), U343 cells demonstrated a novel phenotype characterized by a complete rearrangement of intermediate filaments, specifically, GFAP and vimentin. The resultant arrangement of the U343 cytoskeleton was phenotypically indistinguishable from that of normal astrocytes. These date demonstrate that the proliferative block imposed by $p16^{Ink4a}$ on these malignant astrocytomas results in important changes in the expression and activity of cell cycle regulatory factors. Furthermore, when a potent proliferative block is provided in the presence of RA, a well-characterized differentiation factor, these malignant astrocytomas can be induced to resemble primary astrocytes. The striking effects we have observed suggests that a combination of agents which cause cells cycle arrest and differentiation may be a novel strategy by which malignant astrocytomas can be treated.

Friday, September 12
11:30-11:48 AM

**The Role of Ras Activation in Human Astrocytomas and Neurofibromas**

Abhijit Guha, Mathias Feldkamp, Nelson Lau

One of the best understood and most important intracellular signaling pathway, utilized by a variety of activated growth factor receptors to transmit extracellular cues from the cell surface to the nucleus, involves activation of ras. Oncogenic mutations resulting in activated ras contributes to the pathogenesis of about 30% of all human cancers, but are not present in primary human nervous system tumors, including malignant astrocytomas and neurofibromas.

Growth factors/receptors have been implicated in the pathogenesis of human malignant astrocytomas by autocrine and/or paracrine stimulation. Epidermal Growth Factor (EGFR) and Platelet Derived Growth Factor (PDGF-R) receptors are highly mitogenic to astrocytoma cells, while Vascular Endothelial Growth Factor (VEGF) stimulates tumor angiogenesis. A significant proportion of GBM's also express a truncated EGFR, which is constitutively activated. Our work demonstrates that these receptors send their mitogenic signals to the nucleus via activation of the ras pathway. Inhibition of the ras pathway by transfecting the Ha-ras-Asn17 dominant negative mutant or by farnesyl transferase inhibitors inhibits astrocytoma tumorgenic growth in-vitro and blocks secretion of VEGF by the astrocytoma cells. These results forms the basis for our current work utilizing ras inhibitors in animal models as potential biological therapy of human malignant astrocytomas.

Loss of neurofibromin which inactivates ras is postulated to lead to functional up-regulation of the ras pathway in Neurofibromatosis-1(NF-1). Although increased levels of activated ras have been measured in neurogenic sarcoma cell lines derived from NF-1 patients, the status of ras activity in actual tumor specimens was unknown due to lack of a tissue based assay. We have developed an enzymatic assay, that demonstrates NF-1 neurofibromas and neurogenic sarcomas compared to non-NF-1 Schwannomas, to have levels of activated ras that are 6 and 15 times elevated respectively. Increased ras activity was associated with increased tumor vascularity in the NF-1 neurogenic sarcomas, perhaps related to increased VEGF secretion as currently being examined. The role of ras inhibitors as potential biological therapy in this second nervous system tumor where the ras pathway is also functionally activated without direct oncogenic mutations, is under current study.

Friday, September 12
11:48-12:06 AM

**Neurons in Human Temporal Cortex Active with Verbal Associative Learning**

Ojemann, George A., Schoenfield, Julie A.

As a part of our investigation of changes in human neuronal activity with cognition during awake craniotomies for epilepsy, activity in middle temporal gyrus was recorded during a verbal word pair-association learning measure in 9 patients (3 right). Activity during the learning measure was compared to that reading the same world aloud, and recent memory for those words. In recordings from 21 neurons, a population of 8 neurons (in 6 patients including 3 right), was identified that during initial encoding in the learning measure had significantly greater activity for associations learned rapidly compared to those learned slowly or not at all by an individual patient. This population was separated from other neurons by the combination of inhibition during word reading (when no learning is required) and excitation during recent memory for words. Human associative learning depends in part on activity of this specific population of "association" neurons, identified here for the first time.

Friday, September 12
12:06-12:24 PM

**Academic Surgeons Should Manage Hospital Resouces – The Willy Sutton Principle**

Alan Hudson, Paul Walker

Optimal organization of surgery in major teaching hospitals is a debatable matter. This paper describes a decentralized structure instituted in 1991, following the 1986 merger of Toronto Western and General Hospitals. This structure was extended following the 1997 merger of The Toronto Hospital (created by the 1986 merger) with Ontario Cancer Institute/ Princess Margaret Hospital. Vice President, Surgical Directorate (Surgeon-in-Chief, TTH) is given a budget in excess of $100 million and has the authority, responsibility, and accountability vested in that position. His Directorate includes all who use the operating room, their wards, ambulatory services, and line nursing responsibility. Vice President, Surgical Directorate is responsible for finance, quality, and workload measurements of surgery, ophthalmology, otolaryngology, anaesthesia, obstetrics/gynaecology, and dentistry. The neuroscience priority program reports to that same individual. The internal relationship of the business units, all led by physicians, will be described.

In the last five years we have increased the number of surgical cases done each year, despite major reduction in funding. We have had a significant increase in market share of weighted cases. There have been 45 new appointments within the Surgical Directorate, of which 25 had post-clinical training leading to Masters/Doctorate levels in research.

The major advantage of this administrative structure is that individuals primarily responsible for cost generation are responsible for budget. Decision making is decentralized to individuals with the greatest information. The organization strongly rewards quality patient care, efficient use of Hospital resources, and supports the academic aspirations of the University, the Hospital, and individual staff.

Saturday, September 13
8:00-8:18 PM

**Operative Electrophysiologic Studies in 70 Presumed Thoracic Outlet Cases ***

D. G. Kline, M.D., L. Happel, PhD.,
R. Voorhies, M.D., R. Tiel M.D.

Thoracic outlet syndrome (TOS) remains one of the most controversial diagnoses in all of medicine. Underdiagnosed by some and overdiagnosed by others, it lacks clearcut criteria and even an anatomic etiology except for the occasional case. Diagnosis, when entertained, is usually by exclusion. The myriad of operations tried over the years for its surgical treatment speaks to an inadequate knowledge of its origin.

In a series of 112 presumed TOS cases felt to merit surgery, we carried out sequential intraoperative NAP studies on 70. Studied were spinal nerves and trunks comparing C5 and C6 to upper trunk with C7 to middle trunk and C8 and T1 to lower trunk traces. Included in this group of patients were 11 who had Gilliat-Sumner hands, where there was hand intrinsics loss involving hypothenar and thenar muscles, as well as that of interossei and lumbricales. Plexus was approached anteriorly by a supraclavicular exposure and any unusual relationship between spinal nerves, trunks, divisions and soft tissues and/or bone was noted. NAP conductive and amplitude abnormalities were greatest for T1 to LT and then C8 to LT and less so for C7 to MT When there were anatomical findings, they consisted of a thickened middle scalene with or without a fibrous edge impinging on C8 and/or T1 to LT junction with or without an elongated C7 transverse process. Less frequently, an extra scalene, usually scalenus intimis or Sibson's fascia entrapped C8, T1 to LT.

Electrically, the abnormality for most of our TOS cases was found to be close to the spine and involved spinal nerve to truncal levels rather than trunk to division or more lateral subclavicular or 1st rib abnormalities. Thus, the site for TOS appears to be at a spinal nerve or spinal nerve to trunk and not a divisional or division to cord level. Dissections for presumed TOS should extend close to the spinal column and not be laterally oriented, if they are to be effective.

* From Dept. Of Neurosurgery LSUMC, Charity, University and Ochsner Hospitals, N.O., LA, 70112

Saturday, September 13
8:18 - 8:36 AM

**Mixed Vascular Malformations of the Brain: From Phenotypic Riddles to Questions of Genotype**

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New Haven, Connecticut

Improved radiologic imaging and careful pathologic examination of surgical specimens have allowed the increasing recognition of mixed vascular malformations of the brain. A continuum of mixed lesion types have been identified. We review a series of forty-eight consecutive cases harboring a vascular malformation with pathologic and/or radiologic features of more than one lesion type (capillary, venous, arteriovenous, cavernous, dural). Distinct categories or mixed lesions appeared to behave in a stereotype fashion, with symptomatic presentation typically attributable to one component of the mixed lesion. Cavernous or arteriovenous components of mixed lesions were associated with clinical symptomatology in every case, and appeared to behave in a similar fashion to lesions with pure cavernous or arteriovenous phenotype respectively. Other unique features of mixed lesions included rare lesion multiplicity and familiality among mixed cavernous/venous malformations in comparison to cavernous malformations without associated venous anomaly. There were frequent de novo genesis of cavernous malformations in the setting of pre-existing venous anomalies, suggesting causation rather than simple association of these two lesion types. These clinical and phenotypic observations are interpreted within the framework of novel hypotheses related to newly recognized human genotypes predisposing to familial cavernous malformations (CCM) and arteriovenous malformations (HHT), and the newly mapped gene for familial extracerebral venous malformations. A comprehensive classification of vascular malformations of the brain is proposed, consistent with the molecular basis predisposing to each lesion type, while categorizing clinically relevant pathologic-radiologic entities including mixed lesions.

Saturday, September 13
8:36 - 8:54 AM

**Long Term Outcome in Patients with Lumbar Stenosis and Associated Spondylolisthesis Treated with both Lumbar Decompression and Fusion**

Paul B. Nelson

A retrospective study was done to determine the long term outcome of patients with lumbar stenosis and associated spondylolithesis treated with both lumbar decompression and fusion. Seventy six consecutive patients (54) females and (22) males that underwent lumbar decompression and fusion for spinal stenosis and associated degenerative spondylolithesis from 1986-1991 were studied. Long term follow-up (mean 5.1 years) was available in 43 patients (56%).

Thirty one patients (72%) had an excellent result. Six patients (14%) had a fair result, and six patients (14%) had a poor result. Four of the six poor result patients required additional surgery. Three of these patients had a second decompression and fusion at the original level of surgery. One patient required decompression and fusion at the level above the previous lumbar fusion.

The surgical treatment of patients with lumbar stenosis and associated degenerative spondylolithesis is controversial. There continues to be debate as to whether or not the patient should undergo decompression alone or decompression and fusion. The overall results in the present series was in general better than the long term results of patients with spinal stenosis treated with decompression alone. A randomized, perspective, controlled study may be needed in the future.

Saturday, September 13
8:54-9:12 AM

**Decompression of Post-Injury Spinal Stenosis: An Animal Model**

Christopher B. Shields, G.H. Raque, Y.P. Zhang, D.J. Morassutti, S.D. Glassman and J.R. Dimar.
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There has been no agreement on the timing of surgery following spinal cord injury associated with a persistent anatomical spinal cord compression. To address this issue we have developed an experimental rat model using mild spinal cord injury and various degrees of spinal canal stenosis.

T10 laminectomies were performed on forty adult Sprague-Dawley rats and a mild spinal cord injury was made (125g-cm) using the NYU impactor. Three sizes of wedge shaped spacers were inserted to produce 20%, 35%, and 50% spinal stenosis. The spacers were attached to a fine tungsten wire, passed through the skin to allow their removal.

Control animals had a laminectomy without spinal cord injury and insertion of the spacers. The experimental group had a laminectomy, spinal cord injury, and insertion of the spacers. The spacers were removed 6 hours following insertion. Locomotor functions of the hindlimbs were measured using the BBB locomotor scale. BBB locomotor tests were performed preoperatively, at 24 hours postoperatively, and weekly for 6 weeks following the procedure.

Using this rat model, the threshold of spinal stenosis that results in irreversible deficits in hindlimb locomotor function lies between 35 and 50% in uninjured animals. However, with superimposed mild spinal cord injury, the threshold of spinal stenosis that causes irreversible changes in locomotor function is less than 20%. Having established this model, we are now assessing the timing of decompression following spinal cord injury and its relation to locomotor function.

Saturday, September 12
9:12 - 9:30 AM

**Angiographic Anatomy of the Vein of Labbé**

Mitesh V. Shah, MD, J. Kevin Kaufman, MD,
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**Objective:** To evaluate the angiographic anatomy of the vein of Labbé and associated venous structures in order to provide a better understanding for planning surgical approaches to the petrous region.

**Materials ansd Methods:** Thirty nine normal angiograms from 6/94 to 9/96 were selected for review. Twenty eight were suitable for final analysis. The AP and lateral venous phase views were independently examined for the following: 1) presence of a well formed vein of Labbé; 2) entry point into transverse sinus; 3) dominance of transverse sinus; 4) relationship of the size of Labbé to size of transverse sinus and 5) reciprocal relationship of the vein of Labbé, Trolard, and superficial middle cerebral vein.

**Results:** Fifty six bilateral studies (N= 28) revealed 46% (N=26) presence and a 54% (N= 30) absence of a well formed vein of Labbé. Of the 26 patients with well formed vein, 50% (N=13) had entry points proximal (closer to the torcula) and 50% (N=13) had entry points at the transverse sigmoid junction (near superior petrosal sinus). In thirty patients, multiple cortical veins drained the inferior lateral temporal region. Of these 43% (N=13) entered proximal, 40% (N=12) entered near transverse sigmoid junction, and in 7% (N=5) it was indeterminate. The unilateral dominance of the transverse sinus was also graded: R>>L in 18%, R>L in 39%, R=L in 21%, R<L in 18%, R<<L in 4%. The size of the transverse sinus did not correlate with the presence of a dominant vein of Labbé. The reciprocal relationship of associated veins was noted to be dominant as follows: Superficial middle cerebral = 34%, vein of Labbe' = 30%, vein of Trolard = 16%, and indeterminate = 20%.

**Conclusions:** The vein of Labbé enters the transverse sinus with near equal frequency close to the transverse sigmoid junction as more proximally (near torcula). It appears as a well formed single vein (46%) or as multiple cortical veins (54%). The size of the transverse sinus does not predict presence of a dominant vein of Labbé.

Saturday, September 13
9:30-9:48 AM

**Attenuation of post traumatic head injury in transgenic mice expressing an inhibitor of the ICE neuronal cell death gene**

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Dr. Nicholas T. Zervas)

**Introduction:** Considerable evidence suggests an important role for apoptotic cell death following head trauma. We have previously demonstrated that the cell death gene Interleukin-1° converting enzyme (ICE) plays a pivotal role in mediating apoptosis in focal cerebral ischemia models. In addition, peptide inhibitors of ICE attenuate cerebral ischemia mediated injury. The purpose of the present study was to determine if the ICE cell death cascade might also play a role in mediating apoptosis following head trauma.

**Methods:** We subjected transgenic mice that express a dominant-negative inhibitor of ICE activity in neurons (NSE-M17Z mice) to a standard weight-drop head trauma model (20 gm weight dropped 15 cm). Cerebral injury was evaluated by TTC staining 24 hours after the injury.

**Results:** In wild-type mice, ICE activity in lysates of contused brain was elevated when compared to lysates from non-traumatized brain. Cerebral injury volume was significantly smaller in the transgenic mice expressing a mutant ICE (n=6) compared to wild type littermates (n=6) (23.3 vs.39.5 % corrected volume of ipsilateral hemisphere, $p = 0.05$ [Mann Whitney U test]).

**Discussion and Conclusions:** ICE is activated following brain trauma. In this head trauma model, inhibition of ICE attenuates posttraumatic cerebral injury. Inhibition of apoptosis by the use of peptide ICE inhibitors may warrant testing in the treatment of head trauma.

Saturday, September 13
9:48 - 10:06

**The pathophysiology and regulation of the glutamatergic system in traumatic brain injury**

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Excess activation of NMDA receptors is felt to participate in the secondary neuronal damage after traumatic brain injury. Increased extracellular glutamate is active in this process and may result from either an increased release or a decreased reuptake. Normally, glutamate will be cleared from the synaptic cleft by high-affinity transporters. We studied the protein expression of the two glial glutamate transporters (GLT-1 and GLAST) in the brains of rats as a function of time (6, 24 and 168h) after controlled cortical impact. GLT-1 and GLAST proteins were examined in the ipsilateral and contralateral cortex by immunoblotting using subtype-specific antibodies. Both GLT-1 and GLAST protein levels were significantly down-regulated at 6h (by ~30 to 40%) and 24h (by ~ 50 to 60%) after the injury in the ipsilateral cortex compared to contralateral cortex or sham-operated controls. There was a complete recovery in both GLT-1 and GLAST proteins by 168h.

Down-regulation of glutamate transporters leads to increased synaptic glutamate which stimulates NMDA receptors and thereby nitric oxide production. We confirmed this by studying the protein expression of neuronal nitric oxide synthase (nNOS) after traumatic brain injury. The levels of nNOS immunoreactive protein were significantly up-regulated in the ipsilateral cortex at 6h (~3 fold) and 24h (~2 fold) after the injury compared to the contralateral cortex or sham-operated controls. nNOS immunoreactive protein levels recovered completely by 168 h after the injury. This study showing altered expression of glutamate transporters and nNOS in traumatic brain injury suggests that they are important in neurochemical regulation after brain trauma.

Saturday, September 13
10:36 - 10:54 AM

**Fusiform Dilation of the Internal Carotid Artery Following Parasellar Tumor Surgery in Children**

Stephen J. Haines

**Background:** Aneurysmal dilation of the internal carotid artery (ICA) has occasionally been reported following surgery for parasellar tumors. This phenomenon appears to be restricted to children. Because of the limited information available, the natural history and appropriate treatment are controversial. Our experience with this phenomenon is reported in order to expand the available information base.

**Methods:** Three cases encountered in the author's practice are presented. A survey of the AANS/CNS Pediatric Section and the Neurosurgical Society of America was then carried out to identify others with a significant experience with this problem.

**Results:** From a total of approximately 250 questionnaires distributed, 24 replies were received from surgeons still practicing. In addition to the 11 patients reported by Sutton, et. al., 7 surgeons, including the author, reported a single case, for a total of 18 identified cases. Fourteen followed surgery for craniopharyngioma, 15 involved the right ICA, 5 had received post-operative irradiation. Only 5 were symptomatic and all of these were treated surgically. Two asymptomatic patients was also treated. Of the 7 surgically treated patients, one remains in a persistent vegetative state and one is moderately disabled.

**Discussion:** Although some surgeons have not identified this phenomenon in relatively large series of parasellar operations in children, it has been documented by a number of surgeons from a variety of practice settings. It appears to have a direct association with unilateral surgery. Seventy-two percent of the patients in this survey were and remained asymptomatic. Direct surgical treatment is difficult and significant morbidity has been seen in the small number of children so treated. Except in unusual circumstances, dilation of the internal carotid artery following parasellar surgery in children should be treated with watchful waiting.

Saturday, September 13
10:54-11:12 AM

**Preliminary Outcome of Trans-parahippocampal Limbic Resection for Treatment of Mesial Temporal Lobe Epilepsy**

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Among accepted surgical options for treatment of medically refractory mesial temporal lobe epilepsy is amygdalo-hippocampectomy (AH). AH can be performed via the sylvian fissure, the superior temporal sulcus, the middle temporal gyrus and the fusiform gyrus. Although trans-sylvian AH is well known to neurosurgeons, the procedure can extensively damage the temporal stem.

We have previously reported a surgical technique for AH via the parahippocampal gyrus that allows to preserve the fusiform gyrus and the rest of the temporal lobe. The main advantages of the trans-parahippocampal AH are: 1) It can be performed without language mapping, because it spares the language cortex in the fusiform gyrus and the lateral temporal lobe; 2) The temporal stem is spared; 3) It is technically easier and hence safer than trans-sylvian AH.

We have thus far performed the operation on 15 patients (age 10-25 years). In a short term follow-up (2 months-3 years), 80% are seizure free and 20% had significant reductions of seizures. We will present the preliminary outcome of the trans-parahippocampal AH for surgical treatment of mesial temporal lobe epilepsy.

Saturday, September 13
11:12-11:30 AM

**Laminoplasty vs. Laminectomy in Children requiring Selective Dorsal Rhizotomy**

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Selective dorsal rhizotomy (SDR) is currently the treatment of choice for managing spasticity in children with cerebral palsy (CP). Whilst CP is associated with an increased incidence of spinal degeneration, numerous reports attest to the frequent occurrence of spinal deformity associated with multiple level laminectomy. Laminoplasty is currently considered to be a superior surgical technique for children undergoing SDR, having a lower incidence of both post surgical spinal deformity and post operative pain.

We conducted a retrospective review of 37 children at our institution, upon whom SDR was performed for severe spasticity secondary to CP between April 1989 and September 1993. Twenty five patients were available for long term follow up and of these, nine had multi-level laminectomies performed (Group A), whilst fourteen had multi-level laminoplasty (Group B). Seven of the nine operations performed in the Group A cohort were carried out on quadriplegic patients, whilst in Group B, six patients were quadriplegic and eight diplegic. Six of the patients undergoing laminectomy have progressed to post operative spinal deformities, including scoliosis and hyperlordosis, and four have subsequently required thoraco-lumbar instrumentation. None of the 14 patients with laminoplasties has developed a post operative spinal deformity.

Our findings support the theory that multi-level laminoplasty for SDR in children carries with it a lower incidence of post operative spinal deformity when compared to laminectomy. In addition, children with quadriplegia may have a higher incidence of spinal instability requiring instrumentation following multi-level laminectomy.

Saturday, September 13
11:30 - 11:48 AM

**Frameless Stereotactic Selective Microsurgical Amygdalohippocampectomy for Medically Intractable Partial Complex Seizures**

Kim J. Burchiel[1], Joshua Dowling[1], Jacques Favre[1], Martin Salinsky[2]
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**Introduction:** Resective surgical procedures for seizures of temporal lobe origin have become progressively more limited and discrete. Selective microsurgical amygdalohippocampectomy is now technically feasible, particularly given advances in frameless stereotactic neurosurgery. The question remains as to whether the outcome from these highly selective operations will match that from more traditional anterior temporal lobectomy.

**Materials and Methods:** Forty-six patients underwent resective surgery for medically-intractable partial complex seizures at Oregon HealthSciences University between 7/6/90 and 2/2/97. Mean patient age at the time of surgery was 32 (range 4-55) 45.7% were female, 32.6% of the resections were on the left, and mean follow-up was 14.5 months (range 1-63). Pathological diagnoses included 25 cases of mesial temporal sclerosis (MTS-hippocampal atrophy on preoperative imaging and consistent pathology), 10 tumors, 5 vascular lesions, 2 hamartomas, and 4 other (2 encephalitis, 1 post-traumatic, 1 no pathological abnormality). On 16 of these patients, a frameless stereotactic image-guided selective amygdalohippocampectomy was performed. Twenty-seven patients underwent anterior temporal lobectomy and amygdalohippocampectomy. Three patients underwent lesionectomy only. Outcome was evaluated using the Engle outcome scale.

**Results:** Overall, 69.6% of the patients had a class 1 outcome, 15.2% class 2, 6.5% class 3 and 8.7% class 4. Patients with MTS did better with 80% class 1, 16% class 2, 0% class 3 and 4% class 4. Those patients with MTS who underwent image guided selective amygdalohippocampectomy (12 patients) had outcomes of 83.3% class 1, 8.3% class 2., 0% class 3, and 8.3% class 4. The MTS patients with anterior temporal lobectomy and amygdalohippocampectomy (13 patients) had outcomes of 76.9% class 1, 23.1% class 2, 0% class 3 and 4.

**Conclusion:** (1) Medically-intractable partial complex seizures associated with MTS are highly amenable to surgery, (2) Frameless stereotactic image-guided selective amygdalohippocampectomy appears to yield results similar to those with more extensive resective surgery.

Saturday, September 13
11:48-12:06 PM

**Development Pathways and Medulloblastoma**

Corey Raffel, Russell H. Zurawel, Robert Jenkins, C. David James

Medulloblastomas are associated with two inherited cancer syndromes, Gorlin's syndrome (GS) and Turcot's syndrome. GS is characterized by multiple basal cell carcinomas, skeletal abnormalities, and medulloblastoma. The gene altered in GS is *PTC*, a component of the sonic hedgehog (shh) pathway. This complex pathway plays a major role in the development of the CNS. Turcot's syndrome patients develop colon polyps, colon carcinomas, and brain tumors. Patients with Turcot's who develop medulloblastomas have germ line mutations in the *APC* gene. APC is involved in the regulation of the transcription factor, ß-catenin. Interestingly, no mutations in APC have been identified in sporadic medulloblastomas. We hypothesize that medulloblastomas contain mutations in shh pathway or APC pathway genes, We have examined 24 sporadic medulloblastomas for LOH on 9q22.3, the location of the Saturday, September *PTC* locus. Five of the tumors (20.8%) demonstrated LOH in this region. In three of these, a mutation in the remaining *PTC* allele was identified using SSCP and direct sequencing analysis. Two of the mutations consisted of duplication insertions; the third consisted of a single base deletion. We have examined the same group of tumors for ß-catenin mutations by direct sequencing of exon 3 which encodes an important functional domain. One of the 24 tumors has an activating mutation in this region of ß-catenin. Interestingly, 2nt-1 is upregulated by shh and 2nt-1 increases ß-catenin activity. While the two inherited syndromes that include medulloblastoma effect different genes and pathways, the ultimate effect may be increased cell turn-over induced by ß-catenin.

Saturday, September 13
12:06 - 12:24 PM

**A New Endoscopic Tool for Stereotactic Systems**

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**Objective:** The CRW-apparatus (Cosman-Roberts-Wells) is used in our department for stereotactic biopsies and LINAC based stereotactic Radiosurgery. In addition to stereotactic methods we established endoscopic procedures. It became necessary to adapt the endoscopes to our system .

**Method:** Nine available endoscopes were tested in human cadavers. Because of deficiencies like wrong size, insufficient optical quality or disadvantageous regarding centre of gravity after connecting the video-camera, we decided to develop our own instrument.

**Results:**A new endoscope was designed in cooperation with the Sch÷lly-Company. The special optical bundle has 20000 pixel and is cauterized. The image quality is very close to the Hopkins optic. Because of the length of the endoscope (2.30m) the camera can be positioned to the none-sterile area in the operation theatre. The optic and the light bundle are leaving the operation field within one cable. The outer diameter of the endoscope is 4.0 mm. The diameter of the guiding-cannula measures at the tip 4.5mm and at the bottom 6.35mm (according to the Radionics Guide-Block). A millimeter-screw is integrated at the bottom of the guiding-cannula. In addition a multifunctional instrument with 2mm in diameter was created. It fits to the working-channel of the endoscope. Furthermore a multifunctional catheter was developed. It has a diameter with 2 mm and fits through the working channel of the endoscope. Additionally several coagulation probes for different needs were manufactured.

**Conclusions:** We hearby present a new endoscopic tool. It has been designed and manufactured for the CRW-apparatus and for neurosurgical procedures. Previous instruments were tested and found insufficient for our needs.

Saturday, September 13
12:24 - 12:42 PM

## Posterior Fossa Re-exploration for Recurrent Trigeminal Neuralgia and Hemifacial Spasm: Surgical Findings and Therapeutic Implications

Sohaib A. Kureshi, Robert H. Wilkins

**OBJECTIVE:** To evaluate the surgical findings and subsequent therapeutic implications in posterior fossa re-explorations for recurrent trigeminal neuralgia and hemifacial spasm after failed microvascular decompression (MVD).

**METHODS:** Between December, 1975, and October, 1996, the senior author performed 446 posterior fossa explorations through a retromastoid craniectomy; 331 for trigeminal neuralgia or a related facial pain syndrome, and 115 for hemifacial spasm. There were 31 re-explorations for failure or recurrence following MVD, 23 for trigeminal neuralgia and 8 for hemifacial spasm. Operative reports and records concerning the clinical course were analyzed retrospectively for evidence of vascular compression in both primary and secondary operations, other pertinent intraoperative findings, intraoperative therapeutic interventions, and postoperative outcome and complications.

**RESULTS:** New vascular compression from an arterial source was found in only 3 patients during posterior fossa re-exploration; 1 with trigeminal neuralgia and 2 with hemifacial spasm. New vascular compression from a venous source was seen in 1 patient with hemifacial spasm. A scarred Teflon implant or Ivalon sponge with apparent mass effect upon the respective nerve root was identified in 7 re-explorations. One bony source of compression was seen. A previously placed Ivalon sponge or Teflon implant was found in good position in 100% (23 of 23) of patients with trigeminal neuralgia, and 100% (8 of 8) of patients with hemifacial spasm. No new compressive elements or other sources of root irritation were appreciated in 61% of re-explorations. Partial sensory trigeminal rhizotomy was performed in 83% of re-explorations for recurrent or failed MVD for trigeminal neuralgia. Of 8 patients undergoing re-exploration for hemifacial spasm, 5 (62.5%) suffered severe sequelae. These included profound hearing loss or facial weakness. Of those with recurrent trigeminal neuralgia, 1 suffered profound hearing loss and 3 sustained minor hearing impairment.

**CONCLUSIONS:** Recurrent vascular compression was seldom identified during posterior fossa re-exploration for failed MVD in patients with recurrent trigeminal neuralgia or hemifacial spasm. The previously placed Ivalon sponge or Teflon implant was consistently found to be in good position. Partial sensory trigeminal rhizotomy is an often effective alternative in cases of recurrent trigeminal neuralgia when neurovascular compression is not identified. However, due to the high incidence of complications associated with re-explorations, the authors recommend other ablative or medical treatments for recurrent trigeminal neuralgia or hemifacial spasm after failed MVD.

Saturday, September 13
12:42 - 1:00

**Endoscopic Third Ventriculostomy: A New Look at an Old Technique**

Alan R. Cohen, M.D.

Although ventricular shunting has revolutionized the management of hydrocephalus, shunts are fraught with complications related to malfunction and infection. Third ventriculostomy to bypass aqueductal obstruction has been proposed as an alternative treatment for some forms of hydrocephalus. First performed by Dandy in 1922, it eventually fell out of favor because of primitive instrumentation and high morbidity and mortality rates. Recent advances in endoscopic technology have prompted a resurgence of interest in third ventriculostomy, although the indications for this procedure, as well as the optimal surgical technique, have not been established.

In an attempt to establish better selection criteria, the author retrospecitvely reviewed a series of 38 patients with non-communicating hydrocephalus who underwent endoscopic third ventriculostomy during the past 7 years. The procedure was carried out using a rigid endoscope introduced through a coronal burr hole. The third ventricular floor was punctured using a blunt probe, and the fenestration in the floor was enlarged using a balloon catheter.

Ventriculostomies were deemed successful in 27 of 38 patients (71%) with a median follow-up of 3.5 years. Of the 11 failures, 7 occurred early (within 1 month of surgery) and 4 occurred late (after 1 year). More than half of the failures were related to problems of patient selection rather than fenestration closure. Complications included 1 case of diabetes insipidus and 2 cases of weight gain. No patient developed a new neurologic deficit. There we no hemorrhages.

In appropriately selected patients, endoscopic third ventriculostomy can control hydrocephalus without the need for ventricular shunting. The surgical technique reported here resulted in a low morbidity. The optimal candidate for third ventriculostomy has late onset "acquired" adeductal stenosis with no history of prior hemorrhage or infection.

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