



Chairman's welcome to Pittsburgh Neurosurgery News

by L. Dade Lunsford M.D., FACS
Lars Leksell Professor and Chairman

During its 30-year history the Department of Neurological Surgery at the University of Pittsburgh has sought to provide state of the art and innovative leadership in the diagnosis and treatment of brain, spinal, and peripheral nerve disorders. This first issue of our quarterly departmental newsletter is designed to introduce our department to you. During subsequent publications, we plan to highlight each of our 'Centers of Excellence.' These quarterly reports will provide topical discussions of current techniques and outcomes of neurological surgery.

Our department is one of the largest in the United States, having 24 neurological surgeons and more than 15 doctoral researchers. Our training program attracts some of the best and brightest students leaving medical schools. Our faculty provides service at multiple UPMC hospitals, with more than 4000 surgical procedures annually. We also cover Children's Hospital, the Oakland VA Medical Center, Latrobe and Westmoreland and provide consultative services to many other UPMC institutions.

But an academic practice is more than just excellent patient care. Our faculty are deeply dedicated to pushing the frontier of neurosurgery into the future: by making it more minimally invasive, by incorporating advances in molecular and cell biology, by enhancing outcomes, and by building even greater patient satisfaction. Our faculty believes that both basic science and clinical research, funded by prestigious national sources, will help guide our future. We are proud of the



▲
Dr. Lunsford
Chairman,
Department of
Neurosurgery

▶
Neurosurgeons
using microvascular
decompression
technique for
treatment of
trigeminal neuralgia,
(see story, page 6).



commitment to education shown by our recruitment of talented residents and fellows, by our role in the education of medical students from both the university and elsewhere, and by our participation in local, regional, national, and international courses and symposia.

I hope that you find this, as well as subsequent communications, helpful and informative. Feel free to contact us with any suggestions about improving our newsletter or our service to you and your community. ■

Department launches newly enhanced website

The Department of Neurological Surgery at the University of Pittsburgh introduced a new website this past April providing physicians, patients and researchers a quick source for departmental information.

The site, located at www.neurosurgery.pitt.edu, provides a wealth of information on our faculty, our 'Centers of Excellence' and our many specialized areas of interest. Treatments, background information and links to other useful neurosurgical-related sites are easily accessible. You'll also find detailed information on our research activities and on our training programs.

Users will find contact information – phone numbers, addresses, e-mail addresses, etc. – for the department, our 'centers' and each of our faculty members. Maps and directions to our facility are also available.

To help the user quickly find a subject, we've included a search engine. Specify a topic and our search engine will return a list of all our web pages dealing with that topic.

Plans are in the works to complement our web presentation with video and audio, thus providing a better forum for neurosurgical issues. One such video is already in place: an introduction to our Gamma Knife capabilities, detailing many aspects of our involvement with this leading-edge technology.

If you have any questions or comments regarding our website, please direct them to our web manager at webmanager@neuronet.pitt.edu. ■

Patient Referrals:
(412) 647-3685

Modern management of brain metastases

by Douglas Kondziolka, M.D., M.Sc., FRCS(C), FACS
and L. Dade Lunsford, M.D., FACS



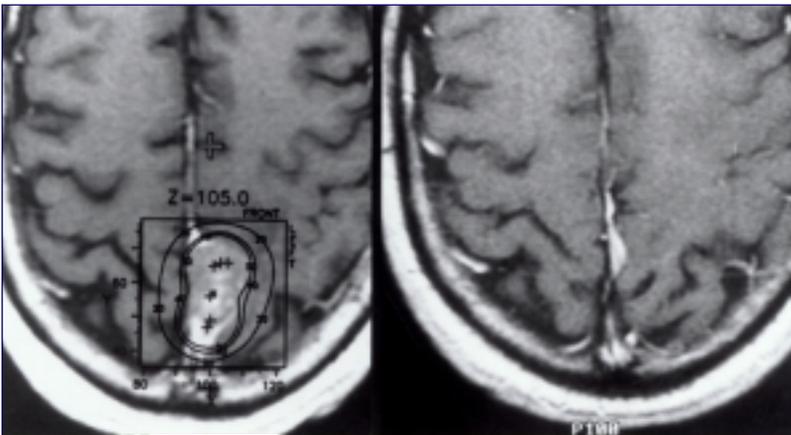
▲
Dr. Kondziolka
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Brain metastases commonly challenge patients with cancer. Patients with brain metastases usually are managed by medical and radiation oncologists. Neurosurgeons often become involved in the management of patients with brain metastases only when a large tumor has been found or when other treatments have failed. It is likely that surgical resection is usually withheld because physicians seek to avoid a major surgical procedure in patients with active systemic cancer. Powerful and precise single-session irradiation of the tumor (Gamma Knife radiosurgery) has been found to be an effective treatment for patients with smaller brain metastases and survival benefits that equal surgical resection. Radiosurgery is attractive due to its minimally invasive nature, its ability to provide effective palliation with low risk, and its cost effectiveness.

In an attempt to obtain better results than those found after whole brain radiation therapy alone, surgical resection has long been used in selected patients. Randomized trials by Patchell et.al. and Vecht et.al. showed superior tumor control rates and improved patient survival following surgical resection plus radiation therapy compared to radiation therapy alone. A third trial did not confirm the efficacy of surgery plus radiation therapy; likely related to a higher proportion of patients with active systemic disease. Unfortunately, many deep brain locations limit the possibility of surgical resection. Surgical resection remains the most effective way of treating a patient with a large brain metastasis that has caused a rapid and marked neurologic decline. Resection usually is followed by whole brain radiotherapy to treat any residual microscopic disease.



▲
(left) Radiosurgical plan for a brain metastasis from lung carcinoma that had caused leg weakness. **(right)** Six weeks later the tumor had regressed in size. The weakness resolved.

The powerful radiobiologic effect of stereotactic radiosurgery initially was used to replace the therapeutic benefit provided by surgical resection. Using single-session, stereotactic irradiation of the defined tumor, radiosurgery was performed to arrest tumor growth and reduce parenchymal brain edema. The growth potential of metastatic brain tumors after radiosurgery was shown to be significantly diminished. The initial results of phase I and II studies at centers using the Gamma Knife confirmed the benefits of treatment on survival, clinical symptoms, and tumor control defined on imaging. A phase 3 trial of radiosurgery for multiple metastases has also been completed at the University of Pittsburgh and showed a significant improvement in tumor control after radiosurgery plus radiotherapy versus radiotherapy alone.

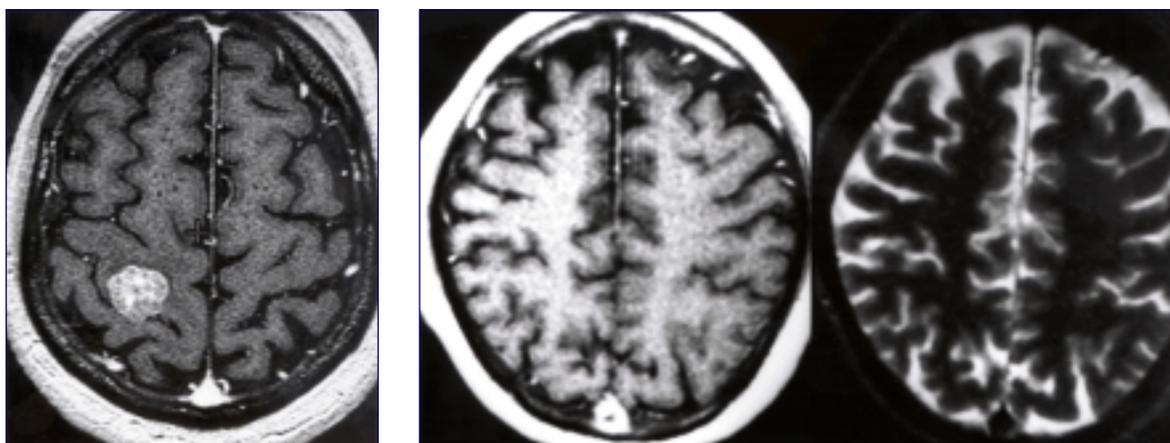
Gamma Knife Radiosurgery at the Univ. of Pittsburgh

We have performed radiosurgery in over 650 patients with metastatic brain tumors. Mean patient age was 57 years (range, 3-86). A neurologic deficit was present in 323 patients (54%), and a prior history of seizures was identified in 49 patients (8%). Whole brain external beam radiation therapy (WBRT) was delivered to 351 patients (58%). Three years ago, use of WBRT was 70%, indicating that WBRT is used much less frequently now for patients with solitary tumors than in years past.

Brain Metastases from Lung Cancer

An analysis of patients with brain metastasis from non small-cell lung cancer (n=77) was performed. The overall median survival for the entire series was ten months after radiosurgery and median survival from diagnosis of brain metastasis was 15 months. Median survival of patients with neurological deficits was eight months compared to 17 months for patients without neurological deficits. The effect of extracranial metastasis and/or systemic disease on survival was evaluated. The median survival of patients with active systemic disease was two months compared to 12 months in patients with stable disease at the time of radiosurgery.

Sixteen of 77 patients first had surgical resection of tumor followed by radiosurgery. Most of these patients had a large tumor before surgical removal. We defined a "favorable group" of 14 patients who had no neurological deficit, no active systemic disease, and tumor diameters < 2cm. These patients had a median survival of 26 months. In contrast, median survival was only eight months (p=.003, log-rank test) in an "unfavorable" group of 63 patients who had at least one adverse outcome predictor (either neurological deficit, active systemic disease, or larger tumor diameter). There were no early deaths from brain disease or from



▲ (left) Metastatic lung cancer to the motor cortex in a man with a seizure. One year later (middle and right), images showed no tumor remaining. The patient remained well.

radiosurgery. Over 60% of patients achieved excellent palliation; 27% eventually had delayed neurological deterioration. Twenty seven of 52 patients with preradiosurgical neurological deficits had either improvement (22/27) or remained clinically stable (5/27).

Local control on imaging (defined as the absence of tumor growth) was achieved in 77 (85%) of 91 tumors and 88% of patients. Postradiosurgical complications included the onset of peritumoral edema in 12 patients. Symptomatic edema responded to short treatment times (2-4 weeks) with corticosteroids.

Brain Metastases from Renal Cancer

Patients with renal cell carcinoma fared similarly to patients with lung cancer demonstrating an overall median survival of 11 months after radiosurgery and 14 months from diagnosis of brain metastasis. The one-year survival after radiosurgery was 43% and the two-year survival 22%. Eighteen patients (72%) died from progression of systemic disease. Only three patients (12%) died as a result of progressive metastatic disease within the central nervous system. [Local control was achieved in 35 tumors (90%) in 23 patients (88%)]. Local tumor progression was observed in four tumors (10%). Of this group, two required a second radiosurgery and one received WBRT.

Brain Metastases from Melanoma

Melanoma patients fared poorer than other brain metastasis patients, again to problems in management of extracranial disease. Overall median survival for the entire series was seven months after radiosurgery and 10 months from the diagnosis of brain metastasis (20). Thirty-five patients (58%) died from non-neurologic progression of systemic disease.

Local control was achieved in 65 evaluable tumors (90%) in 39 patients (85%). Local tumor

progression was observed in seven tumors (10%) in seven patients (15%). Of this group, two required surgery, one received WBRT and one received chemotherapy. No patient developed delayed radiation injury within the follow-up period.

Brain Metastases from Breast Cancer

In a recent analysis of 30 patients with breast cancer metastases (total of 58 tumors), we found a median survival of 13 months from radiosurgery and 18 months from diagnosis. The tumor control rate on imaging was 93%. Patients with a single tumor fared better than those with multiple metastases. Interestingly, the presence of active systemic disease did not predict a worse outcome for this group in contrast to other tumor types.

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Hydrocephalus cases number almost 70,000 each year in U.S.

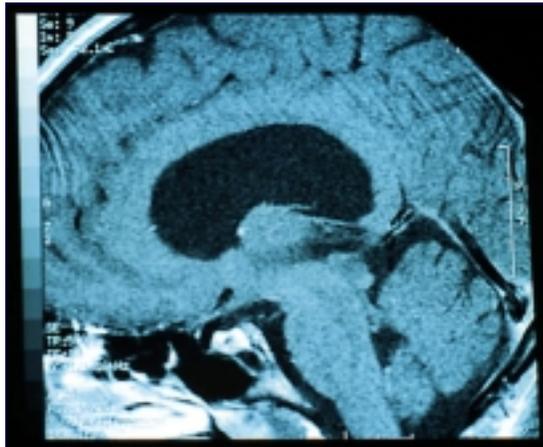
by Ian Pollack, M.D.



▲ **Dr. Pollack**
Co-Director, UPCI
Brain Tumor Center

Hydrocephalus is one of the most common neurosurgical problems in both children and adults, accounting for approximately 70,000 hospital admissions each year in the United States. Hydrocephalus can result from blockage in the normal cerebrospinal fluid (CSF) conductance pathways through the ventricular system and the fourth ventricular exit foramina (so-called non-communicating hydrocephalus) or from impaired CSF absorption (communicating hydrocephalus). In non-communicating hydrocephalus, the ventricular system proximal to the blockage is significantly enlarged on computerized tomography (CT) or magnetic resonance imaging (MRI), whereas the distal CSF pathways are either normal in size or small (*Figure 1*). This form of hydrocephalus can result from congenital obstructing lesions, such as aqueductal stenosis, Dandy-Walker malformation, and arachnoid cyst, as well as acquired lesions, such as an intracranial tumor. In contrast, communicating hydrocephalus manifests with diffuse enlargement of the ventricular system and subarachnoid spaces (*Figure 2*), and can result from processes that limit CSF absorption at the arachnoid granulations, such as hemorrhage and meningitis. However, many cases are idiopathic.

▶ (*Figure 1*) MRI appearance of obstructive hydrocephalus from aqueductal stenosis, illustrating enlargement of the lateral ventricles, with a normal-sized fourth ventricle.



Infants with hydrocephalus typically present with progressive macrocephaly, often in conjunction with developmental delay, sutural splitting, scalp vein distension, and bulging of the anterior fontanel. Vomiting, irritability, lethargy, opisthotonus, and “sun-setting” of the eyes can occur in severe cases. Older children and adults characteristically present with headache, often in association with nausea, vomiting, and lethargy. Diplopia (from sixth nerve paresis), ataxia, incontinence, and visual deterioration can also occur.

The optimal treatment of hydrocephalus depends on the underlying cause. In those individuals with an acquired obstructive lesion, such as a tumor, removal of the lesion often leads to resolution of the hydrocephalus. In patients with an unresectable obstructing lesion, such as aqueductal stenosis, the hydrocephalus can often be effectively treated endoscopically, by creating a ventriculocisternostomy, a small opening in the floor of the third ventricle that diverts the CSF directly into the subarachnoid spaces to bypass a site of CSF flow obstruction. These approaches are not applicable for individuals with communicating hydrocephalus, and insertion of a CSF shunt (*Figure 3*) remains the treatment of choice.

Shunt Insertion

Refinements in the development of flow-regulated shunting devices have led to substantial improvements in the prognosis of individuals who require shunt insertion for hydrocephalus management. Contemporary valve designs can be broadly classified as differential pressure, siphon-control, and flow-regulated. Differential pressure valves allow CSF flow when the pressure difference across the valve exceeds a chosen level and permit hydrostatic siphoning of CSF in the upright position. Siphon-control valves incorporate a mechanism that increases the resistance to CSF flow in the upright position, which maintains intracranial pressure in a fairly consistent range regardless of position. Flow-regulated valves are siphoning valves that incorporate a mechanism to achieve increasing resistance to CSF flow with increasing pressure differentials, which keeps the overall flow rate in a limited range over normal CSF pressures.

Each of these valve systems has certain theoretical advantages, but all are subject to problems related to either overdrainage (e.g., extra-axial fluid collections, slit ventricle syndrome, and repetitive proximal obstructions) or underdrainage (e.g., persistent ventriculomegaly). Although siphon-control and flow-regulated valves were developed in the hope of minimizing these complications, neither design entirely eliminates these problems. Recognition of these challenges led to the development of programmable shunt valves, which permit noninvasive adjustments in drainage characteristics. This type of design, while potentially advantageous in certain clinical situations, adds to the complexity of the valve. Although a randomized, controlled, multi-institutional study (recently reported by our group), failed to demonstrate any overwhelming differences in comparison to conventional valves. Nevertheless, the ability to

combine these valves with a siphon-control mechanism allows the surgeon to further “fine tune” the control of CSF drainage.

Shunt Failure

During the first several months after shunt insertion, the most frequent causes of shunt malfunction are infection and catheter malposition. Infection occurs in approximately 5% of newly placed shunts, although percentages vary widely between centers and are influenced by the general health of the patient in whom the shunt is placed. Shunt infections generally require removal of the shunt, followed by a period of external CSF drainage and intravenous antibiotics, prior to shunt replacement. In rare instances, shunt infections can occur several years after the initial shunt has been placed, usually resulting from indolent bacteria, such as *Propionibacterium acnes*. Acute shunt infections commonly manifest with fever, headaches, meningismus, lethargy, irritability, and systemic signs of infection; in contrast, more chronic infections may present with gradually worsening headache and abdominal pain or with abdominal pain alone (as a result of a CSF pseudocyst, which can be detected by abdominal ultrasound or CT).

In addition to infection, shunts can malfunction acutely as a result of catheter malposition, proximal or distal catheter occlusion, and inappropriate valve selection. Although malposition can be avoided by adherence to good surgical technique, even a well-positioned catheter can become occluded over time. The use of distal slit valves, rather than a more conventional valve design, has also been associated with a higher incidence of obstruction, and such valves are now used less commonly in most centers in North America. Problems with valve selection can lead to underdrainage with inadequate reduction of ventriculomegaly or overdrainage with the development of collapsed ventricles and repetitive proximal obstructions. The recent shunt design trial, which compared differential pressure, siphon control, and flow-regulated valves, found no major differences in outcome between these valves in a broad population of patients undergoing shunt insertion, a result similar to our recently published comparison of programmable and non-programmable shunt systems. Although this observation implies that most patients with hydrocephalus can be successfully treated using any one of a number of valve types (and, conversely, that no existing system entirely avoids complications), there are clearly

situations in which the properties of a particular valve design may present theoretical advantages for patient management.

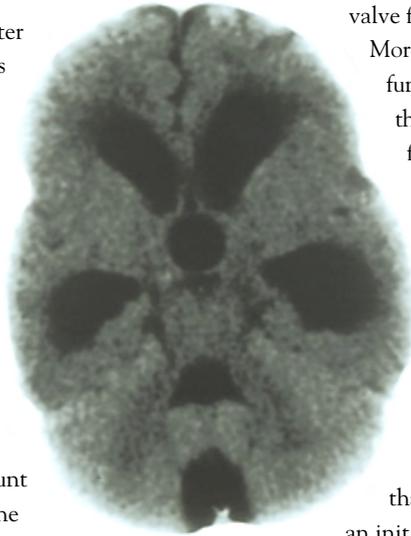
Nonetheless, the goal of finding the “ideal” shunt valve for a given individual remains elusive.

Moreover, even though a given shunt may function well for an extended interval, the system remains at risk for malfunction from proximal and distal obstruction or tube fracture. Accordingly, in individuals with symptoms suggestive of shunt malfunction, the initial work-up includes a “shunt series” to radiographically confirm integrity of the shunt system and a CT scan to assess ventricular size. Long-term studies have demonstrated a consistent rate of shunt malfunction that appears to extend indefinitely after an initial shunt insertion, with a median

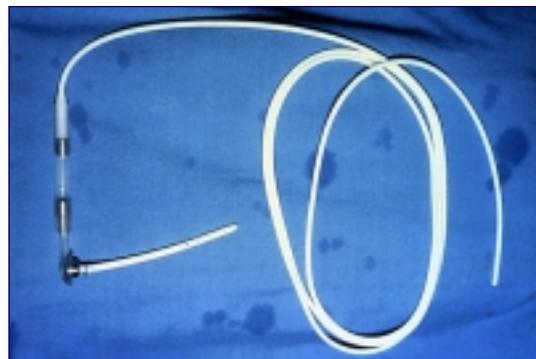
shunt survival ranging from 3 years to 8 years in different studies. Thus, the statement that a child or adult with a longstanding, non-manipulated shunt has “probably become shunt-independent” is not only inaccurate, but potentially dangerous, because this gives the patient and family a false sense of security, and may lead to their ignoring subsequent symptoms of shunt malfunction, with disastrous consequences.

The latter warning is particularly relevant in that approximately 0.1% of children with longstanding shunts will die each year from shunt malfunction. Having gone for many years without requiring a shunt revision, many such individuals and their families assume the shunt will work forever or is no longer needed, despite warnings to the contrary, and ignore the tell-tale symptoms of headache, nausea, vomiting, lethargy. Accordingly, periodic follow-up of shunted patients by the neurosurgeon and primary care provider is advisable to provide an annual or biennial review of

(see *Hydrocephalus* on page 7)



◀ (Figure 2) CT appearance of communicating hydrocephalus, demonstrating enlargement of the lateral, third, and fourth ventricles, with associated enlargement of the subarachnoid spaces.



▲ (Figure 3) Appearance of a CSF shunt.

Multidisciplinary team establishes Univ. of Pittsburgh as world leader in cranial nerve disorder treatment

by Amin Kassam, M.D. and Michael B. Horowitz, M.D.

Supported by a multi-faceted team of neurosurgeons, therapists, neurologists, neurophysiologists and researchers, the University of Pittsburgh has positioned itself as the world leader in the treatment of cranial nerve disorders.

These disorders, which include trigeminal neuralgia, atypical trigeminal neuralgia, hemifacial spasm, glossopharyngeal neuralgia, disabling positional vertigo and tinnitus, and spasmodic torticollis, can prove devastating but very treatable.

Since 1998 the Center for Cranial Nerve Disorders has been led by Dr. Amin Kassam, a former assistant to Dr. Peter Jannetta. Dr. Kassam has been director of the center since 1999 when he was joined by Dr. Horowitz who trained under Dr. Jannetta for six years. Dr. Horowitz now functions as the center's associate director. Together they perform approximately 200 surgical procedures per year for cranial nerve disorders and evaluate another 500-600 patients who do not require surgical intervention. Dr. Howard Yonas serves as a consultant to the center.

The one common thread linking all of the above mentioned disorders together is the presence of a small artery or vein resting on the cranial nerve and injuring it or disturbing its function. Surgical treatment amounts to decompressing the nerve by lifting the offending blood vessel from its surface and placing padding over the nerve and beneath the vessel so that it no longer pulsates directly on the nerve tissue (Figures 1,2). The more commonly encountered disorders are discussed below so that patients and physicians alike can become familiar with these rare and troubling conditions.

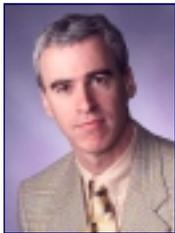
Trigeminal Neuralgia (TGN) is described as a sudden, short duration (seconds to minutes), severe, sharp, lancinating or electric shock-like pain occurring in the face. The discomfort can occur in any part of the face and in 5% of cases it is bilateral. Pain can be triggered by laughing, chewing, teeth brushing, talking, wind on the face, or touching the face. An MRI scan, with and without, contrast is essential to rule out the presence of a tumor, arteriovenous malformation, or multiple sclerosis all of which can cause trigeminal neuralgia in a small number of patients. Medical therapy with drugs such as Tegretol, Neurontin, and Dilantin represent the first line of therapy, however, if these fail microvascular decompression (MVD) is recommended. Following MVD for TGN immediate complete relief is achieved in 82% of patients with

an additional 16% obtaining partial relief. One year following surgery 75% of patients continue to have complete pain relief while an additional 8% have partial relief. Major complications occur in fewer than 5% of cases. Aside from MVD (of which over 100 cases for TGN have been performed in the last 12 months at UPMC by Drs. Kassam and Horowitz), TGN can be treated less invasively in some cases using high dose radiation (Gamma Knife radiosurgery) and percutaneous glycerol injection around the nerve (glycerol rhizotomy). L. Dade Lunsford, chairman of the University of Pittsburgh's Department of Neurosurgery, was instrumental in bringing these technologies from Sweden to the United States 20 years ago and remains a world authority on such therapies.

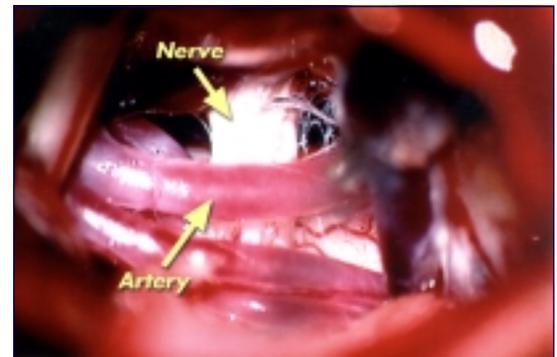
Hemifacial spasm (HFS) is an involuntary twitching of one side of the face. It usually starts around the eye and slowly progresses to involve the lower face. Twitching can be observed during sleep and is rarely painful. Unfortunately there is no medical treatment for HFS. Botulinum toxin injections are ineffective in



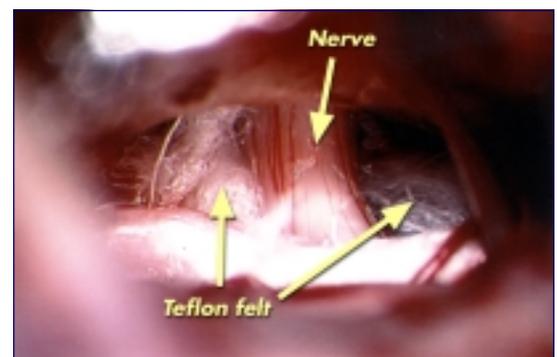
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▲
(Figure 1) Before MVD, artery is compressing trigeminal nerve.



▲
(Figure 2) After MVD, artery is no longer compressing trigeminal nerve.

producing long term control of the spasm and result in varying degrees of facial weakness. It has recently been learned that such injections may negatively impact on subsequent definitive surgery. Drs. Kassam and Horowitz currently perform approximately 75 MVDs for HFS each year. With the advent of the endoscope they have been able to relieve spasm in 100% of patients over the last 12 months with a less than 2% complication rate.

Glossopharyngeal neuralgia (GN) is described as sharp, jabbing, electric shock-like pain located deep in the throat on one side. It is generally located near the tonsil although pain may extend deep into the ear. It is usually triggered by swallowing or chewing. There is usually no abnormality noted on the physical examination although such pain can be caused by throat cancers. A small blood vessel compressing the ninth and tenth cranial nerves as they exit the brainstem is felt to be the underlying pathology when cancer is ruled out. Medications such as Dilantin, Tegretol, Neurontin, and Baclofen can be used to treat GN. When they are not effective MVD can be successful in over 85% of cases.

Geniculate neuralgia may be related to vascular compression of a small nerve known as the nervus intermedius which travels between the seventh and eighth cranial nerves. This severe deep ear pain described as an "ice pick in the ear" can be alleviated in some cases by cutting the nervus intermedius fascicles if medical therapy with Tegretol or Sansert fails to provide relief.

Occipital Neuralgia is defined as paroxysmal jabbing in the distribution of the greater or lesser occipital nerves accompanied by diminished sensation over half the scalp at the back of the head. This syndrome is best managed with medical and physical therapy, however, when such therapies fail, sectioning of the nerves as they exit the spinal cord can provide relief in 66% of patients. All patients undergo CTguided nerve blocks with lidocaine prior to performing the surgical procedure to help predict which individuals will benefit.

New clinical trial for epilepsy begins at Univ. of Pittsburgh

An NIH-sponsored study to evaluate the role of Gamma Knife radiosurgery for patients with medically intractable temporal lobe epilepsy has begun at five universities including the University of Pittsburgh. For more information, contact Dr. Douglas Kondziolka or Dr. David Adelson at (412) 647-3685. ■

Management of cranial nerve disorders at the University of Pittsburgh's Center for Cranial Nerve Disorders is multidisciplinary with patient evaluations carried out by two neurosurgeons who trained and practiced for many years at UPMC under Dr. Peter Jannetta prior to his leaving the institution. Patients are also seen by specially trained Ear, Nose and Throat surgeons, neurologists and neurophysiologists all of whom have studied the syndromes for years and perfected a team approach to the management of these varied disease processes. The availability of medical therapy, microvascular decompression, endoscopic surgery, Gamma Knife radiosurgery, glycerol rhizotomy, and radiofrequency rhizotomy allows the center to continue on as the world leader in vascular compression syndromes.

For more information on the Center for Cranial Nerve Disorders at the University of Pittsburgh or to find out how to arrange a consultation with one of our physicians, please visit us on the internet at www.neurosurgery.pitt.edu/cranialnerve. ■

Hydrocephalus

(from page 5)

the symptoms and signs of concern and to remind the patient and family that the manifestations of a shunt malfunction can be even more devastating than those that occurred before the initial shunt insertion. Fortunately, with timely intervention, most shunt malfunctions are easily detected and treated without adverse sequelae.

Summary

The management of hydrocephalus remains a challenging clinical endeavor, in large part because shunts have a high frequency of eventual malfunction. Accordingly, ongoing vigilance is required for the development of symptoms and signs of shunt failure. Optimal management is provided by a skilled generalist working in conjunction with a neurosurgeon to help identify and expeditiously evaluate patients with symptoms and signs suggestive of shunt malfunction. Although the "perfect" shunt system remains to be developed, existing systems are sufficiently effective that the majority of shunted individuals are able to enjoy a good quality of life. Rather than adding to underlying functional limitations, the shunt allows the opportunity to optimize the individual's developmental prognosis. Although most shunts require revision at some point, with prompt diagnosis and intervention, this can usually be accomplished with minimal morbidity and mortality. ■



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