Progressive Neuroscience

A publication for physicians produced by the Institute for Neurosciences at Winthrop-University Hospital

• Boosting Safety & Efficiency of Spine Surgery
• Management of Pituitary Adenomas
• Understanding Anoxic Injury to the Nervous System
To Our Colleagues:

With the continuous advances in neuroscience, our knowledge of the function — and malfunction — of the intricate nervous system is expanding more rapidly than ever imagined. That knowledge — coupled with sophisticated technology, innovative techniques, advanced pharmacology and breakthrough treatments — clearly enhances our ability to meet the challenges of caring for individuals with neurological diseases and disorders — conditions that often have a profound, life-long impact on patients and families.

Most of all, however, the power to heal is fueled by people — highly trained practitioners with understanding and compassion. At Winthrop's Institute for Neurosciences, the comprehensive interdisciplinary team includes neurologists, neurosurgeons, neurointensivists, neuroradiologists and neuro-oncologists, as well as support-service professionals specially trained to handle the complexities of diseases of the nervous system. Their skills, expertise, experience and collaboration are reflected in each issue of this publication.

The current issue of Progressive Neuroscience focuses on:

- Advanced technologies used to boost the safety and efficiency of spine surgery
- The multimodal treatment of neuropathic facial pain
- The management of secretory pituitary adenomas
- Escalating MS therapy
- Research on peripheral nerve anoxia
- Deep vein thrombosis and pulmonary embolism in stroke patients

As always, our objective is to publish clinically relevant articles. But, our goal is to provide the patients you refer to us with excellent outcomes while continuing to strengthen the robust collaborative relationships we’ve forged through the years.

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Winthrop-University Hospital’s Institute for Neurosciences specializes in the latest and most effective neurological procedures for:

- Acoustic Neuroma
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- Brain & Spinal Traumas
- Brain Tumors
- Carotid Stenosis
- Cerebral Aneurysms
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The nervous system is very susceptible to injury stemming from anoxia — lack of oxygen. In fact, the brain, which is metabolically active, can be permanently injured after as few as three minutes of anoxia at body temperature of 37°C. Understanding and preventing injury from lack of oxygen is critical to many areas of clinical neuroscience. It is particularly important to mitigating the damage produced by occlusion of a blood vessel that supplies either the brain or the peripheral nervous system.

Currently, there is no “magic bullet” that prevents anoxic injury to the nervous system. However, we do know that lowered body temperature reduces metabolic activity and increases the nervous system’s ability to tolerate anoxia. This strategy is extremely effective during surgery on the aorta, which can interrupt blood flow to the brain. At very low temperatures (15°C to 28°C), the brain and spinal cord can tolerate anoxia for 20 minutes or longer without difficulty. Such low temperatures are utilized only during surgical procedures that involve placing the patient on cardiopulmonary bypass because the heart develops arrhythmias below about 30°C. However, even slight reductions in temperature — from 37°C to 34°C — can help and are often used to improve neurologic outcomes in patients that have sustained anoxic injury due to cardiac arrest.

Although many other interventions and pharmacological treatments have been shown to reduce some phenomena that occur with anoxic nervous system injury — such as the production of free radicals, inflammatory cascades, apoptosis, excitatory neurotoxicity and osmotic swelling — they have not successfully entered routine clinical practice.

In order to rationally develop new therapies to prevent anoxic injury, it is important to understand the sequence of cellular events that occur during anoxia and reperfusion. One essential requirement for such studies is a good model system. The isolated peripheral nerve is a very useful model system for several reasons. First, its status can be probed using the same type of nerve conduction studies utilized in humans to diagnose peripheral nerve injuries, so it is possible to connect changes in the test to clinical symptoms that might be expected. Second, is its anatomical simplicity: The isolated peripheral nerve contains mainly axons and myelin, but no neurons. Additionally, the peripheral nerve has a low metabolism rate, so that diffusion of oxygen from a solution is sufficient to satisfy its metabolic needs. This allows us to study the nerve’s function apart from any effects relating to the flow of blood through vessels.
The basics of the apparatus we are using to study anoxia in the peripheral nerve are shown in Figure 1. Under computer control, the nerve can be perfused by either an oxygen-containing solution or an anoxic nitrogen-containing solution. The apparatus also allows for computer control of temperature, medication infusions and recording of the nerve action potential (NAP). Figure 2 shows an example of the NAP that can be recorded, and illustrates the numerical data abstracted from each trace. Figure 3 illustrates the NAP changes over time during five cycles of anoxia and re-oxygenation, and Figure 4 reflects the changes in the amplitude of the NAP during a typical experiment. The NAP amplitude drops slowly over a period of roughly 20-50 minutes before disappearing, recovering rapidly when the nerve is again exposed to oxygen. This process takes much longer in the peripheral nerve than in the brain because the metabolic activity of peripheral nerve is significantly slower than that of the brain.

Gradually, over time, the NAP amplitude drops slowly even during oxygenation due to injury accumulated from the periods of anoxia. It is interesting to note that response to the lack of oxygen is different in each period of anoxia. In particular, the time required for the NAP to disappear after the onset of anoxia is prolonged after each successive period. This suggests that with each period of anoxia, there are changes in the nerve’s biochemical pathways that allow it to better resist the impact of oxygen deprivation. These changes can improve the tolerance of peripheral nerve to anoxia. Figure 5 shows the effect of temperature on the amplitude of the NAP at the beginning (cycle 1) and the end (cycle 2) of a 12-hour experiment. The nerve withstands the effects of anoxia best at the end of an experiment at 17°C. The amplitude of the NAP is lower at higher and lower temperatures by the end of an experiment. Thus, hypothermia does protect the nerve in this model system. It also significantly delays the rate at which the effects of anoxia become evident in the peripheral nerve.

With a good model system, many other studies can begin to try to understand the effects discussed above.

For more information call the Institute for Neurosciences at 1-866-NEURO-RX or visit www.winthrop.org.

REFERENCES
**MS Treatment — It’s Time to Adopt a “Zero Tolerance” Policy for Disease Activity**

Multiple sclerosis (MS) patients with relapsing remitting disease should have rapid escalation of treatment to more aggressive therapy to prevent ANY disease activity. This entails employing treatments, often with more risk, to prevent disability and achieve total freedom from disease activity.

I, idealistically, suggest a “Zero Tolerance” policy, striving to eliminate:

1. New clinical attacks (as well as asymptomatic findings on neurologic examination)
2. New MRI findings (no new lesions, gadolinium enhancement or enlargement of existing lesions)
3. Worsening of disability status

It is well known that all MS therapies are “partially effective” treatment agents. All do a good job suppressing MRI activity and a fair job of suppressing relapses; they are much less effective in preventing disease progression.

There is controversy about whether the “platform medications” (Avonex®, Betaseron®, Copaxone®, Rebif®) provide clinically meaningful suppression of disability progression. Clinical trials conducted under ideal conditions have shown modest efficacy. However, a 2012 “real world” Canadian study found no disability benefit from interferon treatment. The study has many methodological limitations, but highlights the modest efficacy of the platform agents to curtail disability.

MS is both an inflammatory and degenerative disease. All the existing disease-modifying medications diminish inflammation, but they have no proven neuro-protective effect that could limit degeneration.

Acute MS attacks are caused by the entry of immune cells from the blood stream into the central nervous system, where they then attack myelin. Progressive MS is caused by axon death without inflammation.

**Inflammatory (Relapsing Remitting)**

MS is marked by:

- Clinical relapses
- New MRI lesions
- Steroid responsiveness
- Low Expanded Disability Status Scale (EDSS) score (0-6), with the ability to ambulate
- Partial response to existing disease modifying medications

**Degenerative (Progressive) MS is marked by:**

- Slow deterioration without relapses
- MRI: No new lesions, no gadolinium enhancement
- Lack of steroid responsiveness
- Significant disability, grossly impaired or unable to ambulate, typical EDSS of 6 or greater
- No response to existing disease modifying medications

The inflammatory and degenerative processes occur simultaneously. Inflammation predominates early in the course of MS (Relapsing Remitting Disease) and degeneration in the later stages (Secondary Progressive MS).

The EDSS is the standard rating scale for MS status. The scale is not linear and emphasizes walking.

<table>
<thead>
<tr>
<th>EDSS (0-10)</th>
<th>Clinical Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal examination</td>
</tr>
<tr>
<td>1-3</td>
<td>Abnormal exam with no limitations in function</td>
</tr>
<tr>
<td>4</td>
<td>Walks 500 meters</td>
</tr>
<tr>
<td>5</td>
<td>Walks 200 meters</td>
</tr>
<tr>
<td>6</td>
<td>Cane</td>
</tr>
<tr>
<td>7</td>
<td>Wheelchair</td>
</tr>
<tr>
<td>9</td>
<td>Bed bound</td>
</tr>
</tbody>
</table>

Once an EDSS of 4 is reached, the rate of clinical deterioration is a constant. There is a limited window of opportunity to change the course of MS during the early inflammatory course.
MS is a chronic disease often spanning 30 or more years. Data on almost 10,000 European patients found 14.5% of patients at 30 years had an EDSS of 3 or less; that is, they had no functional limitations.2 The overwhelming majority of patients, 85.5%, had limitations in function. Most patients over the course of their illness suffer some degree of limitations. Escaping unscathed is the exception, not the rule.

Benign MS, a frequently used but rarely defined term, should in my opinion, be used only for patients who have no functional limitations after 30 years.

These patients have biologically mild MS (the top 14.5% in the above study). This group is much more readily identified years later retrospectively, not prospectively early in the course of the disease. I feel that once the patient has accrued significant functional limitations much of the opportunity to treat has been lost. Early intervention is the key to achieving the ideal of “Zero Tolerance.”

FDA-approved medications for the treatment of relapsing forms of MS are listed in the above table. The percentage reductions in relapse rate, MRI lesions and disability progression are relative risks compared to placebo. I have omitted Novantrone®, an FDA approved chemotherapy agent, which is rarely used because of its risk for malignancy and hepatic and cardiac damage.

Will complete freedom from all disease activity prevent disability progression? The compensation for widespread demyelination and axonal injury may make deterioration inevitable even if inflammation is completely halted.

My approach to medication management is to attempt to achieve complete freedom from disease activity: This means no new clinical attacks, no new MRI activity and stability of the EDSS.

Newly diagnosed patients should be monitored frequently with rapid escalation to a more effective therapy, if there is any clinical or MRI indication of disease activity. MRI is far more sensitive to disease activity and should be performed yearly or even more frequently in newly diagnosed patients to ensure there is no clinically silent disease activity. It is estimated that there are 10 asymptomatic MRI lesions for every clinical event.

I propose we employ the existing treatments vigorously to stop inflammation early in the course of MS. Implementing a “Zero Tolerance” policy with the existing therapeutic armamentarium will not prevent — but, hopefully, significantly slow — disability and improve the lives of people with MS. There is a desperate need to develop therapies that repair neurons and prevent neuronal degeneration.

Admittedly, “Zero Tolerance” isn’t enough, but it is the best option we have available today.

For more information call the Institute for Neurosciences at 1-866/NEURO-RX or visit www.winthrop.org.

**REFERENCES**


**Table:**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mode</th>
<th>Relapse rate reduction</th>
<th>MRI lesions</th>
<th>Disability reduction</th>
<th>Efficacy</th>
<th>Risk</th>
<th>Potential serious adverse reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tysabri® (Natalizumab)</td>
<td>IV</td>
<td>68%</td>
<td>83-92%</td>
<td>42-54%</td>
<td>High</td>
<td>High</td>
<td>PML, Progressive Multifocal Leukoencephalopathy</td>
</tr>
<tr>
<td>Gilenya® (Fingolimod)</td>
<td>Oral</td>
<td>48-54%</td>
<td>70-82%</td>
<td>30%</td>
<td>Moderate</td>
<td>High</td>
<td>Cardiac arrhythmias</td>
</tr>
<tr>
<td>Fumarate (BG-12)</td>
<td>Oral</td>
<td>44-53%</td>
<td>71-90%</td>
<td>38%</td>
<td>Moderate</td>
<td>Low</td>
<td>None</td>
</tr>
<tr>
<td>Teriflunomide® (Aubagio)</td>
<td>Oral</td>
<td>31-36%</td>
<td>57-80%</td>
<td>24-30%</td>
<td>Low</td>
<td>Moderate</td>
<td>Hepatic</td>
</tr>
<tr>
<td>“Platform Medications” (Avonex® Betaseron® Copaxone® Rebif®)</td>
<td>Injection</td>
<td>30% (approx.)</td>
<td>60-80%</td>
<td>Only Avonex shown to reduce disability (38%), Controversial</td>
<td>Low</td>
<td>Low</td>
<td>None</td>
</tr>
</tbody>
</table>

Escalation to more efficacious and often riskier therapy must be made early before permanent axonal loss and irreversible disability occurs. MS is like a 26-mile marathon. We must judge the clinical course (mild, moderate or aggressive MS) at the five-mile mark or earlier and take appropriate action before a clear winner and loser are declared. This is not an easy task. Our treatments for MS are only beneficial if applied early in the inflammatory stage (Relapsing Remitting Disease) before the degenerative aspect occurs. At present, there is no treatment for the degenerative aspect of MS.
Risk Factors for Deep Venous Thrombosis & Pulmonary Embolism in Patients with Stroke & Intracranial Hemorrhage

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Department of Neuroscience, Winthrop-University Hospital

*Presented at the 2013 AAN Conference, San Diego, CA, by Feliks Koyman, MD

### Objective

Understand the factors that influence the risk of deep venous thrombosis and pulmonary embolism (DVT/PE) in a large group of patients hospitalized for stroke, intracerebral hemorrhage and subarachnoid hemorrhage.

### Background

DVT and PE are serious complications in patients admitted to the hospital with stroke and intracerebral hemorrhage as they occur in up to 3%-8% of patients, and if left untreated, 26% of these patients can have a subsequent fatal embolic event. Despite the frequency and seriousness of these complications, there is much controversy about diagnosis and treatment. A deeper understanding of the factors that influence the risk of deep venous thrombosis and pulmonary embolism (DVT/PE) in a large group of patients hospitalized for stroke, intracerebral hemorrhage and subarachnoid hemorrhage may help guide therapy.

### Methodology

Data on a total of 2613 patients admitted to a large general hospital with stroke, transient ischemic attack (TIA) or intracranial hemorrhage from 1/2008 to 3/2012 were analyzed retrospectively. The data set included 28 variables, including length of stay, initial NIH stroke scale; and whether the patient had heart failure, had altered mental status, among others. Univariate analyses of effects of each variable on DVT/PE were carried out following by linear discriminant analysis. Subsequently a multidimensional cross-tabulation table with the variables identified as significant in the multivariable analysis was computed.

### Results

A total of 33 patients (1.3%) had a diagnosis of DVT/PE. Of the 33 patients, 25 had only DVT, 3 had only PE and 5 had both. In the univariable analysis, the risk of DVT/PE was highest in patients with subarachnoid hemorrhage and intracerebral hemorrhage and smallest in patients with TIA. Patients with longer length of stay and higher admission NIH stroke scale, higher weight, not ambulatory by day two, as well as patients with altered level of consciousness and heart failure were at increased risk of developing DVT/PE. In the multivariable analysis only patients with altered level of consciousness and heart failure were statistically significant risk factors. Patients with both heart failure and altered level of consciousness had a seven-fold increase in risk for DVT/PE. Whether the patient received prophylaxis with heparin or enoxaparin had no statistically significant effect in any group of patients.

### Conclusions

The risk of DVT/PE in patients with stroke and intracranial hemorrhage can be influenced by different factors, many of which are interdependent. Thus, the multivariate analyses are critical in order to sort through all the factors to determine which would be independent risk factors. Heart failure and altered level of consciousness were important risk factors in our study. Our study is limited by its retrospective design, as well as the small number of patients with DVT/PE. In addition, there are many differences in the treatment of patients with stroke, TIA and intracerebral hemorrhage that are not codified, as well as differences in treatment protocols among different institutions. Additional studies to confirm our findings would be important.

### References


### Table 1. Risk of DVT/PE for the different diagnoses

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No DVT/PE</th>
<th>DVT/PE</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subarachnoid Hemorrhage</td>
<td>183</td>
<td>6</td>
<td>2.69</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>1376</td>
<td>16</td>
<td>1.33</td>
</tr>
<tr>
<td>Transient Ischemic Attack</td>
<td>697</td>
<td>3</td>
<td>0.35</td>
</tr>
<tr>
<td>Intracranial Hemorrhage</td>
<td>264</td>
<td>8</td>
<td>2.5</td>
</tr>
</tbody>
</table>

### Table 2. Factors Contributing to DVT/PE in the aggregated group of all patients

<table>
<thead>
<tr>
<th>Factor</th>
<th>No DVT</th>
<th>DVT</th>
<th>Statistic</th>
<th>Relative Risk</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of Stay (days)</td>
<td>8.6</td>
<td>2.2</td>
<td>t=4.95</td>
<td>0.0001</td>
<td>1.0 (-0.001)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>71.3</td>
<td>70.7</td>
<td>t=1.7</td>
<td>NS</td>
<td>1.0</td>
</tr>
<tr>
<td>Race</td>
<td>-</td>
<td>-</td>
<td>c=7.4</td>
<td>NS</td>
<td>-</td>
</tr>
<tr>
<td>Gender (male/female)</td>
<td>56%</td>
<td>52%</td>
<td>c=0.25</td>
<td>NS</td>
<td>1.08 females</td>
</tr>
<tr>
<td>Height (inches)</td>
<td>65.9</td>
<td>66.6</td>
<td>t=4.64</td>
<td>NS</td>
<td>0.78-1.5 female</td>
</tr>
<tr>
<td>Weight (pounds)</td>
<td>167</td>
<td>182</td>
<td>t=1.85</td>
<td>p=0.06</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>27.6</td>
<td>29.8</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alib/Flutter</td>
<td>0.1</td>
<td>0.2</td>
<td>c=0.28</td>
<td>NS</td>
<td>1.25</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>0.06</td>
<td>0.1</td>
<td>c=2.22</td>
<td>p=0.04</td>
<td>2.95</td>
</tr>
<tr>
<td>Prior TIA</td>
<td>0.13</td>
<td>0.1</td>
<td>c=0.45</td>
<td>NS</td>
<td>2.2</td>
</tr>
<tr>
<td>CAD/MI</td>
<td>0.23</td>
<td>0.24</td>
<td>c=0.02</td>
<td>NS</td>
<td>0.95</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.26</td>
<td>0.24</td>
<td>c=0.02</td>
<td>NS</td>
<td>0.95</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.69</td>
<td>0.73</td>
<td>c=0.19</td>
<td>NS</td>
<td>1.2</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>0.02</td>
<td>0.0</td>
<td>c=0.70</td>
<td>NS</td>
<td>0.987</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.09</td>
<td>0.06</td>
<td>c=0.37</td>
<td>NS</td>
<td>0.64</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.09</td>
<td>0.06</td>
<td>c=0.37</td>
<td>NS</td>
<td>0.64</td>
</tr>
<tr>
<td>Carotid Stenosis</td>
<td>0.02</td>
<td>0.00</td>
<td>c=0.75</td>
<td>NS</td>
<td>0.987</td>
</tr>
<tr>
<td>Initial NIH Stroke Scale</td>
<td>0.15</td>
<td>0.21</td>
<td>c=1.0</td>
<td>NS</td>
<td>1.7</td>
</tr>
<tr>
<td>Prophylactic Heart Valve</td>
<td>0.025</td>
<td>0.03</td>
<td>c=0.04</td>
<td>NS</td>
<td>1.2</td>
</tr>
<tr>
<td>Initial NIH Stroke Scale</td>
<td>5.8</td>
<td>11.4</td>
<td>t=2.84</td>
<td>p=0.04</td>
<td>0.027</td>
</tr>
<tr>
<td>Discharge NIH Stroke Scale</td>
<td>2.15</td>
<td>9.2</td>
<td>t=3.28</td>
<td>p=0.02</td>
<td>0.027</td>
</tr>
<tr>
<td>Weakness</td>
<td>0.42</td>
<td>0.27</td>
<td>c=0.31</td>
<td>p=0.08</td>
<td>0.5</td>
</tr>
<tr>
<td>Altered LOC</td>
<td>0.14</td>
<td>0.30</td>
<td>c=1.73</td>
<td>p=0.07</td>
<td>2.7</td>
</tr>
<tr>
<td>Aphasia</td>
<td>0.27</td>
<td>0.24</td>
<td>c=0.12</td>
<td>NS</td>
<td>0.87</td>
</tr>
<tr>
<td>Ambulatory by Day 2</td>
<td>0.254</td>
<td>0.1</td>
<td>c=0.46</td>
<td>p=0.03</td>
<td>0.29</td>
</tr>
<tr>
<td>Heparin or LMWH</td>
<td>0.44</td>
<td>0.36</td>
<td>c=0.74</td>
<td>NS</td>
<td>0.73</td>
</tr>
<tr>
<td>Compression Devices</td>
<td>0.37</td>
<td>0.32</td>
<td>c=0.05</td>
<td>NS</td>
<td>0.73</td>
</tr>
<tr>
<td>Warfarin</td>
<td>0.026</td>
<td>0.03</td>
<td>c=0.02</td>
<td>NS</td>
<td>1.2</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>0.33</td>
<td>0.36</td>
<td>c=0.02</td>
<td>NS</td>
<td>1.0</td>
</tr>
</tbody>
</table>

### Table 3. Cross-tabulation showing the relationship of DVT/PE as a function of both failure and altered mental level of consciousness

<table>
<thead>
<tr>
<th>Factor</th>
<th>No DVT/PE</th>
<th>DVT/PE</th>
<th>% Patients with DVT/PE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF=0,Altered=0</td>
<td>1995</td>
<td>20</td>
<td>1.0</td>
</tr>
<tr>
<td>HF=0,Altered=1</td>
<td>318</td>
<td>8</td>
<td>2.5</td>
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Advanced Technologies Boost Safety & Efficiency of Spine Surgery
Focus is on Sparing Soft Tissue & Reducing Blood Loss

By William J. Sonstein, MD
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While numerous factors affect the outcome of spine surgery, obtaining a positive resolution often entails going back to basics. Patient selection is undeniably critical to a good outcome, but the surgeon’s ability to control bleeding and prevent spinal fluid leak also has a profound impact on the course of the surgery — in many instances, even more so than the type of interbody device or other instrumentation used in the procedure.

Over the past 20 years, many innovations have improved spine neurosurgery. Advances have primarily focused on the development of better implants that utilize various materials, such as titanium and PEEK (polyether ether ketone — an advanced organic polymer thermoplast used in medical implants), as well as the creation of retractors that permit less invasive access to the spine.

However, these advances are mechanical variations dedicated principally to restoring spine function. Very few tools have been created to make the surgery safer and more efficient.

Following are descriptions of two relatively new technologies used at Winthrop-University Hospital to improve the safety and efficiency of spine surgery.

Ultrasonic Bone Emulsification

The sophisticated ultrasonic bone emulsification technology (the Sonopet® ultrasonic aspirator-Stryker) being used by the Hospital’s spine surgeons effectively addresses fine dissection of bone traditionally performed with rotating drills. Utilizing ultra-light hand pieces with metal tips that vibrate longitudinally and torsionally, the device emulsifies bone during decompresive spine surgery or laminectomy, while simultaneously aspirating and irrigating the surgical field.

The tips are smooth, acting as gentle retractors of the eloquent structures as the bone is removed around them. As tissue is excised through the rapid longitudinal motion, cavitation occurs, affecting hydrous tissue, such as tumor or fat, while anhydrous tissue, such as vessels and tendons, remains unaffected.

Especially effective for tough-to-resect lesions where normal soft tissue tips are inadequate, this technology allows the surgeon to dissect bone with minimal pressure. It eliminates the danger of the kicking or grabbing sometimes experienced with high-speed cutting burs, and reduces the possibility of harming soft tissue at times associated with use of a kerrison or similar instruments. The technique is particularly useful in patients with “floppy” or significantly adhered dura that presents a challenge during laminectomy.

A “smart” console sets and controls the multiple frequencies of the hand pieces, enabling tissue selectivity for in situ evacuation in eloquent areas. The surgeon can literally “sculpt” the bone around the nerves, effectively relieving the pressure without fear of spinal fluid leak.

Hemostatic Sealing of Soft Tissue

Another new advancement (the Aquamanitys® System and Transcollation® Technology-Medtronic) used during spine surgery integrates radiofrequency (RF) energy and saline for hemostatic sealing of soft tissue and bone at the surgical site. Vessels up to 1 mm may be occluded, reducing bleeding.

The technique is useful with a variety of spine surgery procedures, including posterior lumbar interbody fusion (PLIF), transforaminal lumbar interbody fusion (TLIF), minimally invasive TLIF, scoliosis surgery, posterior cervical discectomy and fusion and laminotomy, discectomy and decompression.

In addition to reducing blood loss, clinical value includes the possibility of reducing the need for other blood management products during or after the procedure, maintenance of patient hemoglobin levels, decreased need for postoperative drains, improved visibility in the surgical field and reduced surgical time.

While the use of innovative techniques and technology is part of our mission to provide world-class care, these two technological advances underscore our focus on improving patient safety during spine surgery.

For more information call the Institute for Neurosciences at 1-866NEURO-RX or visit www.winthrop.org.

REFERENCES
The pea-sized pituitary gland — nestled in the sella turcica of the sphenoid bone at the base of the brain and covered by a dural fold — is as powerful as it is small. It controls most of the body’s endocrine functions via the secretion of several hormones that regulate homeostasis.

Secretory pituitary adenomas, though generally benign, cause excessive production of one or more of these hormones, creating hormonal imbalances that can significantly impair bodily functions and result in death, if untreated. Classified by anatomy, histology and functional criteria, with signs and symptoms reflecting the endocrinopathies produced by the hypersecretion, the lesions can also compress the optic nerve and increase intracranial pressure.

Given the complexity, location and size of the gland, successful management of secretory pituitary tumors depends upon the confluence of a wide range of factors — not the least of which is the physicians’ expertise and experience.

“These tumors can be treated medically, surgically and/or with radiotherapy,” explained Michael Brisman, MD, Winthrop-University Hospital’s Chief of Neurosurgery — an expert in transsphenoidal surgery and stereotactic radiosurgery.

The major types of secretory pituitary tumors treated at Winthrop include:

- Prolactinoma, the most common secretory pituitary adenoma, accounts for an estimated 40% of pituitary gland tumors.\(^1\) Formation occurs due to neoplastic transformation of ante-
rior pituitary lactotrophs — prolactin-secreting cells — that results in excess synthesis and hypersecretion of prolactin (PRL). In addition to menstrual cycle changes in women, symptoms include headaches, vision problems due to compression of the optic chiasm, mood swings and changes in behavior or weight.

“Prolactinomas are typically managed medically,” explained Dr. Brisman. Bromocriptine or cabergoline are usually the treatment of choice. They are dopamine agonists that decrease the synthesis and secretion of prolactin, as well as the rate of tumor cell division and the growth of individual cells. If drug treatment is unsuccessful, surgery or stereotactic radiosurgery can be considered. Surgery is also indicated in cases of acute tumor bleeding or swelling (pituitary apoplexy).

• **Acromegaly** results from hypersecretion of growth hormone (GH). Approximately 90% of acromegaly cases are caused by a pituitary adenoma. The syndrome is associated with hypertension, diabetes and cardiovascular disease, as well as premature death, if unchecked. Typically, acromegaly develops slowly between ages 30 and 50, with symptoms including a deepening of the voice, enlargement of the extremities and facial bones, and hirsutism.

“The most effective way to treat acromegaly is with surgery,” said Dr. Brisman. “If the entire tumor cannot be excised, stereotactic radiosurgery is indicated. Should hormone levels remain high, medications — such as cabergoline, may be used if surgery and stereotactic radiosurgery are unsuccessful at controlling cortisol levels.

“While patients with acromegaly and Cushing’s disease are usually treated with surgery first, in some instances, we use all three options,” Dr. Brisman said. “The treatment of choice generally depends upon the type and size of the tumor, and whether or not it has invaded, or is pressing on, surrounding structures. Early diagnosis can usually result in an excellent prognosis.”

**Transsphenoidal Surgery**

The surgical approach used to remove pituitary adenomas has evolved from traditional craniotomy to the advanced, far less invasive transsphenoidal approach, using a microscope for anterior transseptal dissection or an endoscopic endonasal technique.

“We have had a great deal of experience with transsphenoidal surgery,” Dr. Brisman stated. “The technique entails carefully threading microsurgical or endoscopic instruments through the nose into the sphenoid sinus up to the floor of the sella. It usually results in minimal swelling and reduced postoperative discomfort, and is considered a safe and effective way to remove even very large tumors.”

“Very large tumors — especially those invading cavernous sinus laterally — may be somewhat more challenging and more likely to require multimodality treatment,” he added, “but our success rate for treating all secretory pituitary adenomas is excellent.”

For more information call the Institute for Neurosciences at 1-866NEURO-RX or visit www.winthrop.org.

**REFERENCES**


**Neuropathic Facial Pain: Failure to Relieve Pain in the Past Does Not Mean Failure to Relieve Pain in the Future**

What is neuropathic pain? It is not associated with any detectable injury to the body. Rather, it is comparable to a short circuit in a nerve.

Neuropathic facial pain (NFP) arises out of injury to the trigeminal nerve (TN) — the sensory nerve of the face. Most often, the cause is a loop of an artery or vein close to the brainstem that comes in contact with the nerve and short circuits it. The result can be episodic lightening bolts of pain (TN1) or constant electrical burning sensations (TN2).

To treat NFP, one must reduce the amount of electricity that gets to the site of the short circuit. This can be achieved with medication or a variety of surgical procedures that injure the nerve, modulate nerve function with stimulation or move the blood vessel away from the nerve.

Most facial pain sufferers get temporary relief from anticonvulsant drugs, such as carbamazepine or gabapentin, which reduce electrical activity in the central and peripheral nervous systems. Over time, the pain can require higher doses of medication — sometimes to toxic levels.

If patients cannot tolerate medication, or the pain is refractory, sophisticated surgical intervention is indicated. At Winthrop-University Hospital’s Institute for Neurosciences — a tertiary care center for patients with the most complex facial pain — all advanced pain treatment options are available, including microvascular decompression, percutaneous balloon compression, radiofrequency rhizotomy, glycerol rhizotomy, CyberKnife® radiosurgery, peripheral trigeminal stimulation and motor cortex stimulation.

**Neuropathic facial pain arises out of injury to the trigeminal nerve — the sensory nerve of the face.**

**Microvascular Decompression (MVD)**

**Case Report**

A 69-year-old-man developed stabbing face pain 20 years ago. Twelve years ago, he underwent MVD that lessened the pain for eight months. Four years later, gamma knife radiosurgery helped briefly. His pain progressed to the point where it was refractory, despite near-toxic doses of anticonvulsant medication.

When he was referred to Winthrop, magnetic resonance imaging (MRI) showed residual compression of the trigeminal nerve by a vascular loop that had previously been

*Continued on pg. 12*
decompressed near the brainstem. Another MVD was performed, and a loop of a large vein adhering to the trigeminal nerve in the mid-portion of the nerve was coagulated and sectioned, completely decompressing the nerve. The patient awakened pain free. His medication was tapered, and he has remained free of facial pain for the past two years.

The treatment of facial pain after unsuccessful — or briefly successful — MVD is complex and requires a multimodal effort. The most common reasons for failure to achieve lasting pain relief after MVD are an unrecognized secondary source of vascular compression or insufficient decompression of the nerve. Recent innovations in MRI allow us to learn whether there is postoperative residual vascular compression. If pain persists postoperatively, a repeat MRI with specialized imaging parameters should be conducted. If residual, or recurrent, compression is seen, then a repeat MVD should be considered.

Large series suggest that there may be an 80% success rate when MVD is performed by a neurosurgeon with expertise in the re-operative surgery of neuropathic facial pain.¹

Other Therapies

Techniques practiced at Winthrop that are designed to injure the more peripheral insulation of the trigeminal nerve in order to reduce the input to the short circuit and thereby interrupt the pain by damaging the nerve fibers include the following:

Percutaneous Balloon Compression is a simple and effective treatment, especially for stabbing eye pain. Under anesthesia, a cannula is directed to the foramen ovale at the skull base, and a balloon catheter is positioned at the entrance to Meckel’s cave. The balloon is inflated for one minute and injures the myelin insulation of trigeminal sensory fibers. This mild nerve injury blocks the trigger to the short circuit that is causing the electric shock-like pain. Myelin is capable of regeneration, and pain recurs in 25% of patients in three-to-five years.²

The procedure can be repeated. Radiofrequency Rhizotomy and Glycerol Rhizotomy are also percutaneous means of injuring the trigeminal nerve. Radiofrequency current is used to injure the nerve by selectively heating fibers. Glycerol selectively injures myelin insulation chemically.

Cyberknife® Radiosurgery paints a homogenous 6 mm portion of the trigeminal nerve with radiation that also injures nerve insulation. The goal of each procedure is to injure the nerve sufficiently to stop lightening-bolt pain, but not to cause dense, bothersome numbness. Ablative procedures are indicated for TN1, but not for TN2.

Peripheral Nerve Stimulation (PNS)

PNS, a neuromodulation technique, is a recent advance used especially for TN2. The peripheral branches of the trigeminal nerve are reached by percutaneous placement of electrodes in the region of the pain. Low-level electrical current inhibits pain perception, creating a barrier that stops pain signals from traveling between the peripheral nerves and the brain. The procedure occurs in two phases: First, trial stimulation is conducted as an outpatient procedure. If successful, the electrodes are connected to a pacemaker-like device implanted under the skin of the chest. Nerve function is modulated to relieve the bother-some burning caused by nerve injury. Many parameters of stimulation can be modified to optimize pain relief after implantation.

Motor Cortex Stimulation (MCS)

MCS is indicated for burning facial pain that may result from trigeminal nerve injury, stroke or brain injury. The technique is thought to be effective because stimulation of the contralateral motor cortex inhibits electrical hyperactivity in the sensory thalamus that occurs after injury to sensory input. Studies suggest that 50% of patients with one-sided burning facial pain, or pain associated with facial numbness, will most likely experience 50%-75% relief of pain.³ The electrodes are positioned over the motor cortical dura using computer imaging and cortical mapping under general anesthesia.

Surgical outcome for facial pain also depends on the quality of postoperative pain management. At Winthrop, an anesthesiology pain medicine specialist is integrated into the postoperative care of every patient.

Winthrop’s program is guided by the strong belief that failure to relieve pain in the past does not mean failure to relieve pain in the future. Because of this approach, the Hospital truly is a world-class resource for patients suffering from the most debilitating, complex facial pain.

For more information call the Institute for Neurosciences at 1-866NEURO-RX or visit www.winthrop.org.

REFERENCES
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Dr. Michael Brisman specializes in stereotactic surgery and radiosurgery for brain tumors and trigeminal neuralgia. He is Board Certified by the American Board of Neurological Surgeons and is a Fellow of the American College of Surgeons. His postgraduate training includes a neurosurgical residency and surgical internship at the Mount Sinai Medical Center in New York, where he was Chief Resident. He received his medical degree from Columbia University’s College of Physicians and Surgeons. Dr. Brisman has published numerous articles in professional journals. He is past President of the Nassau County Medical Society and serves on the Board of Directors of the New York State Neurosurgical Society.

Malcolm H. Gottesman, MD
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Dr. Malcolm Gottesman specializes in the treatment of multiple sclerosis (MS), and is the founder of Winthrop’s Comprehensive MS Care Center. The Center conducts original clinical research and participates in state-of-the-art clinical trials. Dr. Gottesman was also instrumental in establishing the Hospital’s Stroke Program and Neuroscience Intensive Care Unit. He is Board Certified in Psychiatry and Neurology. His postgraduate training includes a residency in neurology at Long Island Jewish Medical Center, where he was Chief Resident. He also completed an internship and residency in psychiatry at Boston University Medical Center. Dr. Gottesman received his medical degree in an accelerated BS-MD program jointly sponsored by Rensselaer Polytechnic Institute and Albany Medical College. He has published numerous articles in professional journals and presents at national and international conferences. Dr. Gottesman received an MS Leadership award from the Long Island MS Society.

Jeffrey A. Brown, MD
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Dr. Jeffrey Brown — a pioneer in the development and use of motor cortex stimulation (MCS) — is nationally recognized for his expertise in complex and chronic pain syndromes, especially facial pain. He is a past member of the Board of Directors of the American Association of Neurological Surgeons and chair of the Joint Section on Pain of the American Association of Neurological Surgeons and Congress of Neurological Surgeons. Currently, he is co-chair of the Medical Advisory Board of the TNA-Facial Pain Society, an international support group for patients in pain. He has published more than 50 peer-reviewed research articles on pain, spine and vascular, brain tumor and functional neurosurgery in addition to 20 book chapters, and has delivered more than 200 invited lectures at local, regional, national and international venues.

Feliks Koyfman, MD
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Dr. Feliks Koyfman, a vascular neurologist and Director of Winthrop’s Neurovascular Laboratory, has a special interest in stroke prevention and the use of imaging modalities in acute stroke treatment and workup. His postgraduate training includes Fellowships in Advanced Vascular Neurology and Imaging, as well as Vascular Neurology at Boston University Medical Center, where he also completed a residency in neurology. He earned his medical degree from the Stony Brook University School of Medicine. Dr. Koyfman has co-authored many abstracts and articles, including “Pelvic Magnetic Resonance Venography for Detection of Deep Vein Thrombosis in Young Patients with Cryptogenetic Stroke and Patent Foramen Ovale” published in Stroke. He also presents frequently at professional meetings.

William J. Sonstein, MD
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Dr. William Sonstein, a Board-Certified Diplomate of the American Board of Neurosurgery, has a special interest in complex spine surgery. He is one of Long Island’s most experienced practitioners of Posterior Lumbar Interbody Fusion (PLIF). Whenever possible, he uses minimally invasive procedures, such as kyphoplasty and X-Stop®, to treat spinal compression fractures and spinal stenosis. His postgraduate training includes a Fellowship in Spine Surgery at Tampa General Hospital, as well as a neurosurgical residency at New York’s Montefiore Medical Center, where he was Chief Resident. He earned his medical degree from Temple University School of Medicine. Dr. Sonstein has participated extensively in neurosurgery research and clinical trials, and has authored and co-authored journal articles, scientific abstracts and book chapters.
Winthrop-University Hospital’s Institute for Neurosciences

Winthrop-University Hospital is a 591-bed teaching hospital located on Long Island in Mineola, NY. A major regional healthcare resource, the Hospital has been a leading healthcare provider for more than a century, dedicated to the integrity, dignity and well-being of every individual. Winthrop offers a full complement of advanced inpatient and outpatient services with a deep commitment to medical education and research.

Physicians and surgeons in Winthrop’s Institute for Neurosciences are pioneering the use of technologically advanced approaches for the diagnosis and treatment of diseases of the brain and spine, including computerized imaging systems, state-of-the-art surgical interventions and the latest generation of medication therapies.

The Institute’s interdisciplinary team includes neurologists; neurosurgeons; neurointensivists; pediatric neurologists and neurosurgeons; neuroradiologists; vascular surgeons; orthopaedic spine surgeons; neuro-oncologists; neuro-pathologists; neurophysiologists; and specially trained nurse practitioners, physician assistants and nurses. Specialized physical and occupational therapy, social work and other supportive services are also key components of the Institute. The Institute’s experts are up to date on the latest developments in neuroscience and help pave the way for new discoveries through participation in clinical research trials, which enable them to provide patients with access to tomorrow’s most promising therapies.

Programs & Services Offered by the Institute for Neurosciences

Neuroscience Intensive Care Unit
The 14-bed acute care NeuroICU is reserved for patients with serious, complex neurological issues. The focus is on providing continuous monitoring and instantaneous results of critical values, allowing the expert staff, experienced in using advanced technology and providing neurocritical care, to employ aggressive interventions that treat neurological deterioration.

Neurology
Comprehensive Level 4 Epilepsy Center
Movement Disorders Program
Multiple Sclerosis Care Center
Neurodiagnostic Laboratory
Neurovascular Laboratory

Neurosurgery
Aneurysm Coiling & Clipping
Disc Replacement
Brain Aneurysm Program
Brain Tumor Program
Brain & Skull Base Surgery
Carotid Stenting & Endarterectomy
Cerebrovascular & Endovascular Surgery
Chiari Decompression Surgery
Complex & Minimally Invasive Spinal Surgeries
Complex Cranial Surgery
Computer-Assisted Resection of Brain Tumors
CyberKnife® Radiosurgery
Endoscopic Pituitary Surgery
Epilepsy Surgery Program
Facial Pain/Trigeminal Neuropathy Program
Image-Guided Spine Surgery
Kyphoplasty

Neuroradiology
Aneurysm Treatment
CT Perfusion Scanning
Interventional Neuroradiology
Neuroangiography

Pediatric Neurology & Neurosurgery
Attention Disorders & Learning Disabilities Treatment
Craniostenosis Surgery
Brain Tumor Treatment
Evaluation & Treatment of Children with Headaches
Evaluation & Treatment of Neurological Disorders Myelomeningocele Surgery

For more information, call the Institute for Neurosciences at 1-866-NEURO-RX.