EDITORIAL

197 Why Would a Spinal Tumor Cause Increased Intracranial Pressure?

Harold L. Rekate

ORIGINAL CONTRIBUTIONS

199 Papilledema as the Presenting Manifestation of Spinal Schwannoma

Fiona Costello, Randy H. Kardon, Michael Wall, Patricia Kirby, Timothy Ryken, and Andrew G. Lee

204 Isolated Acquired Unilateral Horizontal Gaze Paresis from a Putative Lesion of the Abducens Nucleus

Neil R. Miller, Valérie Biousse, Thomas Hwang, Saurabh Patel, Nancy J. Newman, and David S. Zee

208 Orbital Tuberculosis with Abscess

Deepak Aggarwal, Ashish Suri, and Ashok K. Mahapatra

211 Spontaneous Resolution of Aneurysmal Third Nerve Palsy

Rod Foroozan, Thomas L. Slamovits, Susan M. Ksiazek, and Rochelle Zak
THE HOYT LECTURE

Oculomotor Ophthalmoplegic Migraine: Is It Really Migraine?

Thomas J. Carlow

The Golden Age of Neuro-Ophthalmology at the Bascom Palmer Eye Institute

Joel S. Glaser

THE LEGACY

The Legend of Lawton

Jonathan D. Trobe

IN OTHER JOURNALS

Dan Boghen and Martin ten Hove

CALENDAR

Jonathan D. Trobe

Noble J. David, MD, Reminiscences

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Why Would a Spinal Tumor Cause Increased Intracranial Pressure?

Harold L. Rekate, MD

Abnormalities of intracranial pressure dynamics have been reported to occur in the context of a variety of spinal cord tumors. In this issue of the *Journal of Neuro-Ophthalmology*, Costello et al. describe a woman with visual symptoms caused by papilledema. A magnetic resonance imaging scan of the brain was normal, and lumbar puncture showed an opening pressure of 290 mm water and a protein content of 114 mg/dl but an otherwise normal cerebrospinal fluid (CSF) formula. Spine imaging later disclosed a low sacral tumor. The papilledema resolved after the resection of the tumor.

Extramedullary and intramedullary spinal cord tumors apparently cause both hydrocephalus (increased intracranial pressure with ventriculomegaly) and the pseudotumor cerebri syndrome (increased intracranial pressure without ventriculomegaly). The causes of the CSF absorptive problems in the context of these tumors have been adequately explained in a majority of the cases. Malignant tumors, including glioblastomas in adults and neuroblastomas in children, usually cause hydrocephalus resulting from widespread meningeal spread. Whereas CSF cytology is often noncontributory in these cases, the diagnosis can usually be made either by neuroimaging or by meningeal biopsy if needed. In some cases, however, the only abnormalities involve mild increases in the CSF protein levels, as seen in the patient described here. Why do these patients have increased intracranial pressure? At present, there are no compelling answers to this question.

It is very unlikely that the tumor itself has any direct blocking effect on the absorption of the CSF. Although there are several proposed alternative sites for CSF absorption, most of the CSF is absorbed at the interface between the cortical subarachnoid space and the dural venous sinuses. Other causes of compression of the thecal sac, such as fracture or epidural tumor, have not been reported in association with either hydrocephalus or pseudotumor cerebri.

In some cases, the CSF protein levels are sufficiently high to lead to sludging at the level of the arachnoid villi, but not all reports of hydrocephalus or the pseudotumor cerebri syndrome in patients with spinal cord tumors are associated with high levels of protein. Most cases show only modest increases. The most likely explanation for elevated intracranial pressure in those cases may relate to the release of a tumor-generated chemical into the CSF that leads to failure of CSF absorption. Removal of the tumor will then lead to the normalization of intracranial pressure. Several potential chemical markers have been suggested. One is fibrinogen, which is converted to fibrin in the CSF. If fibrin creates a blockage at the level of the basal cisterns, it would cause hydrocephalus. If it creates a blockage at the level of the arachnoid villi, it could lead to the pseudotumor cerebri syndrome (1). Another interesting candidate is the inflammatory cytokine TGFβ. Found in a variety of primarily vascular structures such as the choroid plexus, TGFβ is present in high concentrations in...
platelets and has been shown to result in the proliferation of leptomeningeal cells and the creation of scarring both at the base of the brain and in the area of the arachnoid villi (2). The final explanation for increased intracranial pressure in the presence of spinal cord tumors will have to await further delineation of the chemical composition of the CSF in these patients.

REFERENCES


Papilledema as the Presenting Manifestation of Spinal Schwannoma

Fiona Costello, MD, Randy H. Kardon, MD, PhD, Michael Wall, MD, Patricia Kirby, MD, Timothy Ryken, MD, and Andrew G. Lee, MD

A 63-year-old woman with headache, blurred vision, bilateral optic disc edema, and normal cranial magnetic resonance imaging scan underwent lumbar puncture that revealed an elevated opening pressure (290 mm water), a protein level of 114 mg/dl, and mild pleocytosis. Spinal magnetic resonance imaging later demonstrated a sacral tumor, which proved to be a schwannoma with sarcoid-like features. After surgical removal of the tumor, the patient’s manifestations resolved. This case emphasizes that low spinal cord tumors can cause elevated intracranial pressure without causing markedly elevated cerebrospinal fluid protein or cells, or any myelopathic manifestations, perhaps by obstructing sacral cerebrospinal drainage. Comprehensive spine imaging should be a part of the evaluation of a patient with papilledema who has normal brain imaging but abnormal spinal fluid constituents.

(Spinal tumors are an uncommon cause of increased intracranial pressure (1-8). Papilledema may be the sole clinical manifestation (1,2,6). We present a case of a sacral schwannoma that caused papilledema without symptoms of spinal dysfunction, and discuss the reported tumor types and locations, as well as possible mechanisms for increased intracranial pressure.

CASE REPORT
A 63-year-old woman came for treatment because of a 3-month history of intermittent blurred vision and occasional headaches. She did not describe experiencing pulsatile tinnitus or double vision. Her medical history included diabetes, hypothyroidism, controlled hypertension, hyperlipidemia, and remote seizures. Her regular medications were Lipitor, Glucophage, Synthroid, and multivitamins; She did not describe using lithium, tetracycline, vitamin A, or corticosteroids. Her weight had been stable in the previous year.

The patient’s height was 5’ 1”, and her weight was 200 pounds. The results of a general neurologic examination were completely normal. The ophthalmology evaluation revealed a best-corrected visual acuity of 20/25 OD and 20/20 OS. Slit lamp biomicroscopy showed nuclear cataract. The pupils, intraocular pressures, and ocular motility were normal. Ophthalmoscopy showed bilateral optic disc edema with surrounding peripapillary hemorrhages (Fig. 1). Goldmann perimetry showed enlargement of the blind spots in both eyes (Fig. 2).

Magnetic resonance imaging (MRI) scans of the head were normal except for dilation of both optic nerve sheaths and flattening of the posterior globes in both orbits; these findings were consistent with raised intracranial pressure. The sella turcica was normal. A lumbar puncture revealed an opening pressure of 290 mm water. Analysis of the cerebrospinal fluid demonstrated an elevated protein of 114 mg/dl (normal <46 mg/dl) and 20 leukocytes mm$^3$ (normal <5 leukocytes), 98% of which were monocytes. The CSF formula was otherwise normal, as were urinalysis and baseline serologic studies. Magnetic resonance imaging was performed along the entire spinal axis in search of a source of...
meningeal inflammation. It revealed an ovoid, soft tissue mass within the thecal sac at the S1–S2 disc space (Fig. 3A), measuring 1.7 cm craniocaudally, 1 cm anteroposteriorly, and 1 cm transversely. The lesion enhanced intensely and homogeneously (Fig. 3B). Subtle enhancement was also noted along both the anterior and posterior aspects of the distal spinal cord near the conus medullaris. No other enhancing lesions were found within the spinal cord. An incidental hemangioma was demonstrated within the T11 vertebral body, but the marrow signal was otherwise normal throughout the spine. On the basis of the appearance of the lesion, the diagnosis of drop metastases or filum terminale ependymoma was considered.

**FIG. 2.** Goldmann perimetry, showing enlarged blind spots.

**FIG. 3.** (A) Sagittal T2-weighted magnetic resonance imaging scan of lumbosacral spine shows T11 vertebral body hemangioma (open arrow) and soft tissue mass within the thecal sac at S1–S2 (closed arrow). (B) Sagittal enhanced T1-weighted magnetic resonance imaging scan of lumbosacral spine showing T11 vertebral body hemangioma (open arrow) and enhancement of the thecal mass at S1–S2 (closed arrow).
The patient underwent L5 and S1 laminectomies, intradural tumor exploration, excision, and microscopic exploration. Histopathology showed myxoid lobules of spindle and oval cells, without atypia, arranged in fascicles and whorls, with no increased mitotic activity (Fig. 4A). Immunohistochemistry showed positive staining with S100, but keratin and epithelial membrane antigen stains were negative. Myxoid areas of the tumor stained with mucicarmine and alcian blue. Numerous large multinucleated giant cells were seen in multiple noncaseating granulomas throughout the tumor (Fig. 4B). No organisms were seen, and stains for acid-fast bacilli and fungi were negative. The pathologic diagnosis was schwannoma with sarcoid-like reaction.

Within a month of surgery, the patient had resolution of her visual symptoms and optic disc edema. In light of the sarcoid-like reaction in the tumor, several investigations were performed to exclude systemic sarcoidosis, including a chest radiograph, total body gallium scan, and serum angiotensin-converting enzyme level (23 U/L), and all results were negative.

**DISCUSSION**

Spinal tumors are an uncommon but well-documented cause of papilledema (Table 1). This case is distinct because of the presentation with papilledema as the only clinical abnormality, and the unusual histopathologic appearance of the tumor. To our knowledge, this presentation was reported in only four cases in the English literature before 1992 (1,2,6). In most cases, spinal cord tumors have manifested localizing clinical signs, including back pain, weakness, and sensory loss, to suggest pathologic changes in the spine (1–3,5–7). In their review of cases reported until 1992, Matzkin et al. (1) noted that spinal tumors often present with lumbar pain (65 to 70% cases), yet those associated with papilledema are more likely to present with headache, nausea, vomiting, and vision loss. Oikawa et al. (2) reported a case, similar to ours, of progressive vision loss and papilledema in a patient with multiple spinal neuromas, in whom there were no spinal symptoms. In that review (2), 6 of 34 patients had a visual disturbance as their presenting manifestation of spinal cord tumor. Of these 6, neurologic examination disclosed that 4 had signs or symptoms of spinal dysfunction, one received a diagnosis with a spinal tumor 3 months later with pain in the right leg and back, and 1 patient had no spinal symptoms or signs.

In our case, the tumor was a sacral schwannoma, a tumor noted in only 11% of the 53 cases reported by Matzkin et al. (1). To our knowledge, there have been no reports of spinal schwannoma with associated granulomatous reaction. Ependymoma has been the predominant spinal tumor associated with papilledema (40 to 50% of cases) (1–8). Other less common tumors have included schwannoma (11%), meningioma (7%), neurofibroma (7%), and glioma (7%) (1). The finding of a sarcoid-like reaction within tumors but without clinical or radiologic evidence of systemic sarcoidosis has been previously reported (9), most often in the lymphatics draining a primary tumor and in the parenchyma adjacent to primary and secondary metastatic lesions (9). Sarcoid reaction in the parenchyma of embryonic lesions is extremely rare but has been reported in a 9-month-old child with neuroblastoma (9). The cause of the sarcoid reaction was not clear in that case (9); it may have been caused by tumor-related antigens shed by the tumor, or released by cell death.

The sacral location of the spinal tumor in our case, and the associated CSF analysis findings, were consistent with other reports of papilledema-associated spinal cord tumors. Most have been located in lower spinal levels, usually in the thoracolumbar or lumbosacral regions (1–6).

Several mechanisms have been proposed to explain how such spinal tumors may increase intracranial pressure.

**FIG. 4.** (A) Photomicrograph of tumor, showing palisading nuclei consistent with schwannoma (closed arrow) and a multinucleated giant cell (open arrow). (B) Higher magnification of multinucleated giant cell (open arrow).
TABLE 1. *Previously reported spinal tumors manifesting with papilledema*

<table>
<thead>
<tr>
<th>Author (reference)</th>
<th>Cases</th>
<th>Tumor diagnosis</th>
<th>Tumor location</th>
<th>CSF opening pressure &gt;150 mm water*</th>
<th>Range of CSF protein (mg/dl)f</th>
<th>Percent without spinal manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glasaeur (4)</td>
<td>20</td>
<td>Ependymoma—11</td>
<td>Lumbar—9</td>
<td>10/11</td>
<td>50–10,500 in 15</td>
<td>Not reported</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Astrocytoma—1</td>
<td>Thoracic—7*</td>
<td>(Not reported in 9)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Oligodendroglioma—1</td>
<td>Thoracolumbar—5</td>
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<td>Spongioblastoma—1</td>
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<td></td>
<td>Medulloblastoma—1</td>
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<td></td>
<td></td>
<td>Neurofibroma—3</td>
<td>(1 patient had 2 tumors)</td>
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<td></td>
<td></td>
<td>Meningioma—1</td>
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<td></td>
<td>Luetic granuloma—1</td>
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<td>Raynor (5)</td>
<td>37</td>
<td>Ependymoma—15</td>
<td>Cervical—6</td>
<td>Not reported</td>
<td>&gt;60 in 19; ≤60 in 4</td>
<td>Not reported</td>
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<td>Oligodendroglioma—1</td>
<td>Thoracic—7</td>
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<td></td>
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<td>Undetermined—5</td>
<td>Thoracolumbar—25</td>
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<td></td>
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<td>Neurinoma—2</td>
<td>(1 patient had 2 tumors)</td>
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<td>Medulloblastoma—1</td>
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<td>Astrocytoma—1</td>
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<td></td>
<td>Sarcoma—1</td>
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<td>Vascular lesion—1</td>
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<td>Granuloma—1</td>
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<tr>
<td>Farmilo et al. (6)</td>
<td>32</td>
<td>Ependymoma—17</td>
<td>Thoracic or lumbosacral</td>
<td>14/15</td>
<td>38–10,500;†&gt;120 in 22; ≤60 in 3</td>
<td>4/14 with adequate reporting</td>
</tr>
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<td></td>
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<td>Ependymoblastoma—3</td>
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<td>Granuloma—1</td>
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<td>Oligodendroglioma—1</td>
<td>Medulloblastoma—1</td>
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<td></td>
<td></td>
<td>Spongioblastoma—1</td>
<td>Neurofibroma—2</td>
<td>Neurinoma—2 Neurolemmoma—1 Meningioma—1 Vascular lesion—1</td>
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<td></td>
</tr>
<tr>
<td>Matzkin et al. (1)</td>
<td>54</td>
<td>40% ependymoma‡</td>
<td>Predominantly lower thoracic or lumbar region</td>
<td>Not reported</td>
<td>38–10,500;&gt;100 in 66%†</td>
<td>7%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11% schwannoma</td>
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<td></td>
<td></td>
<td>7% meningioma</td>
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<td></td>
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<td>7% neurofibroma</td>
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<td></td>
<td></td>
<td>7% glioma</td>
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</table>

* Denominator represents total cases in which measurement was reported.
† The range of CSF protein in the Farmilo and Matkin series is the same because the authors reviewed the same cases.
‡ Numbers of cases of different tumor types not available.
In cervical cord lesions, raised intracranial pressure has been ascribed to rostral extension and CSF flow obstruction at the level of the medullary exit foramina (1). This mechanism is not plausible in cases of papilledema resulting from lower spinal lesions, which represent the majority of cases. Elevated CSF protein and protein degradation products have been proposed to cause CSF flow obstruction. In the reviews to date, more than 60% of the spinal tumors associated with papilledema have been associated with elevated CSF protein levels. In the review by Matzkin et al. (1), the range of CSF protein was 38 mg/dl to 10,500 mg/dl, and greater than 100 mg/dl in 66% of 54 cases (our patient’s CSF protein was 114 mg/dl). It has been postulated that elevated protein may raise intracranial pressure by decreasing CSF absorption at the arachnoid villi (1–8).

Among the spinal tumors that cause papilledema without elevated CSF protein, the mechanism may be compromise of the lumbosacral elastic reservoir. The lower spinal location of the tumors may represent a source of mechanical obstruction to CSF flow at the level of the lumbar cul-de-sac. The lumbar portion of the spinal sac has been described as an “elastic reservoir” for CSF flow (1,7,8). Hence, changes in CSF volume and flow dynamics have been attributed to a reduced “decompressive” capacity in this distensible region of the spinal canal (1,7,8). The size of the tumor has not been a contributing factor, given that even small tumors have caused raised intracranial pressure when located within the venous plexus or intrathecal space (1). Other proposed mechanisms of raised intracranial pressure have included dissemination of tumor cells, production of mucinous material, secondary hemorrhage, and venous stasis with impaired CSF flow (1–4,7,8).

In summary, the finding of papilledema with normal cranial imaging and raised CSF protein may herald a spinal tumor, and appropriate spinal imaging is necessary to secure the diagnosis.

REFERENCES
Isolated Acquired Unilateral Horizontal Gaze Paresis from a Putative Lesion of the Abducens Nucleus

Neil R. Miller, MD, Valérie Biousse, MD, Thomas Hwang, MD, Saurabh Patel, MD, Nancy J. Newman, MD, and David S. Zee, MD

In three patients, acute horizontal gaze pareses developed that could not be overcome with the oculocephalic maneuver, indicating a putative lesion of the ipsilateral abducens nerve nucleus. None of the patients had a facial nerve paresis or evidence of a trigeminal sensory neuropathy. Although most lesions that affect the abducens nerve nucleus also damage the ipsilateral fasciculus of the facial nerve, small lesions in this region can produce an isolated horizontal gaze paresis.

Small lesions affecting the abducens nucleus cause ipsilateral gaze palsy for both voluntary and reflex-induced movements. The gaze palsy is typically associated with ipsilateral peripheral facial palsy caused by damage to the adjacent facial nerve fascicle that loops around the abducens nucleus (1-3). We report two patients in whom acute horizontal gaze pareses developed, unassociated with ipsilateral facial weakness or evidence of any other cranial neuropathy.

CASE REPORTS

Case 1

A 57-year-old woman with a history of acute intermittent porphyria, taking no medications was visually well until May 2001, when she experienced a tight sensation behind both eyes and noted that she could see clearly only when she turned her head to the left. Shortly thereafter, a friend told her that she seemed to be having difficulty moving her eyes. She was then evaluated at the Wilmer Eye Institute of the Johns Hopkins Hospital.

On initial examination, the patient's visual acuity was 20/20 OU, with normal color vision by pseudoisochromatic plates and normal visual fields by automated perimetry. The pupils were isocoric and normally reactive to light and near stimulation. There was no ptosis and no proptosis. The patient had a left face turn, and her eyes were deviated to the right. She could not voluntarily move them out of rightward gaze, nor was there any improvement in movement with the oculocephalic maneuver. Her vertical gaze was intact. Optokinetic stimulation produced normal saccades when the drum was rotated to the patient's left, but there were no saccades with rotation of the drum to the patient's right. There was no evidence of facial weakness on either side, and facial sensation was normal bilaterally.

A lesion of the left abducens nucleus was suspected, and the patient underwent thin-section magnetic resonance imaging (MRI), including diffusion-weighted images, showing no lesions. She then underwent a lumbar puncture that showed no abnormalities, and several serologic studies whose results were negative, including a complete blood count and differential, an erythrocyte sedimentation rate, an assay for angiotensin-converting enzyme, a serologic test for syphilis, Lyme titers, and assays for antinuclear, anti-GQ1b, antiphospholipid, and fluorescent treponemal antibodies.

One week after the onset of symptoms, the patient underwent quantitative assessment of ocular motility. At this time, she still had a face turn to the left, but it was not as marked as in the initial evaluation. She was now able to move her eyes to the left but still not to midline (Fig. 1). Saccades to the right were normal with respect to both amplitude and velocity, but saccades to the left were hypometric and showed reduced velocities; convergence was intact (Fig. 2). The findings were thought to be most consistent with a lesion of the left abducens nucleus.

The patient was monitored at regular intervals. One month after the onset of symptoms, she could move her eyes to the midline, and 2 months after the onset of symptoms, her ocular motility had returned to normal.

Case 2

A 57-year-old man was referred to the Neuro-Ophthalmology Unit at Emory University for evaluation of...
diplopia after embolization of a basilar tip aneurysm. His medical history was remarkable for systemic hypertension and diabetes mellitus type 2. Eighteen days earlier, he had experienced a sudden, severe headache associated with a stiff neck and had been found to have evidence of a subarachnoid hemorrhage. A cerebral angiogram had revealed a basilar tip aneurysm, and the patient had undergone aneurysm embolization using detachable platinum coils. Immediately afterwards, the patient experienced diplopia and intermittent dizziness associated with a sensation of falling to the left.

The patient’s visual acuity and visual fields were normal. The pupils were isocoric and normally reactive to light and near stimulation. The patient had full vertical eye movements and full left gaze in both eyes. He had complete absence of right gaze for both saccades and pursuit (Fig. 3). Ocular motility did not improve with the oculocephalic maneuver. In primary position distance viewing, he had a 25-prism diopter left hypertropia and a 10-prism diopter esotropia. He also had upbeat nystagmus with a counterclockwise torsional component. The results of the remainder of

![Image](Fig. 1. Case 1: right gaze is normal (left), but on attempted left gaze, the eyes do not move beyond midline (right).)

![Image](Fig. 2. Case 1: quantitative eye movement recordings. A: Right gaze. Saccades have a normal amplitude and velocity (arrowhead). REPOS, OD position; REVEL, OD velocity; LEPOS, OS position; LEVOS, OS velocity. Position is measured in degrees from center; velocity is measured in degrees/second; time is measured in milliseconds. B: Left gaze. Saccades have reduced amplitude and decreased velocity (arrowhead). REPOS, OD position; REVEL, OD velocity; LEPOS, OS position; LEVOS, OS velocity. C: Convergence. Both eyes adduct normally, including the OD, which did not adduct (move to the left) on attempted versions. RE, OD position; LE, OS position.)
his cranial nerve examination were unremarkable. He had normal facial strength and no evidence of a trigeminal sensory or motor neuropathy. Ophthalmoscopic examination revealed bilateral optic disc swelling but no evidence of intracranial hemorrhage. Thin-section MRI revealed no lesions. Within 1 month, his disc swelling had resolved and his ocular motility had begun to improve.

Case 3
A 4-year-old African-American girl was referred to the Neuro-Ophthalmology Unit at Emory University for evaluation of abnormal eye movements. Her medical history was unremarkable. She had been the product of a full-term pregnancy and normal vaginal delivery, and her development had been normal. Her mother had had a cerebral infarction at 32 years of age. Two days before she visited our unit, the child’s parents noticed that she was looking to the right with her face turned to the left. They also noted that she had become sleepy and abnormally quiet.

The patient’s visual acuity and confrontation visual fields were normal. Her pupils were isocoric and normally reactive to light and near stimulation. The patient had full vertical eye movements and full right gaze in both eyes. She had complete absence of left gaze for both saccades and pursuit. Ocular motility did not improve with the oculocephalic maneuver. In primary position for distance viewing, she was orthophoric. The results of the remainder of her cranial nerve examination were unremarkable. She had normal facial strength. The results of ophthalmoscopic examination were normal. The results of general and neurologic examinations were otherwise unremarkable. Thin-section MRI revealed a small lesion in the pons in the region of the left abducens nerve nucleus (Fig. 4). The patient’s gaze improved spontaneously over the next few days, and no further evaluation was done. One month later, her ocular motility was normal.

DISCUSSION

Complete absence of unidirectional horizontal gaze for saccades, pursuit, and vestibulo-ocular reflexes localizes a lesion to the ipsilateral abducens nerve nucleus (1). Most cases of damage to this structure are associated with ipsilateral facial nerve paresis caused by damage to the facial nerve fascicle as it loops around the abducens nerve nucleus (2–5). We believe our cases to be the first examples of abducens nuclear lesions causing a horizontal gaze paresis without an associated facial nerve paresis.
MRIs were normal in two of our patients (Patients 1 and 2), we believe it most likely that all of the causative lesions were ischemic. The first patient probably experienced a small hypoxic lesion, possibly related to her porphyria. Indeed, several authors have reported patients with acute intermittent porphyria who experienced transient (6) or permanent (7) blindness from ischemia thought to be vasospastic. The second patient probably had a small infarction from occlusion of a circumpontine perforating vessel during embolization. In the third patient, the MRI did show a small lesion, presumably ischemic, in the region of the abducens nerve nucleus ipsilateral to the gaze paresis.

Many lesions of the brainstem that affect ocular motor structures cause neurologic deficits in addition to those affecting the ocular motor pathways, but small focal brainstem lesions can cause both complete and partial isolated oculomotor nerve pareses, trochlear nerve pareses, and abducens nerve pareses (8–17). Our three cases provide evidence that small lesions can damage the abducens nerve nucleus without causing either trigeminal or facial neuropathies.

REFERENCES
Orbital Tuberculosis with Abscess

Deepak Aggarwal, MD, Ashish Suri, MD, and Ashok K. Mahapatra, MD

The authors present a case of progressive unilateral proptosis caused by tuberculous osteoperiostitis of the orbital walls and sphenoid bone with extraconal orbital and extradural intracranial cold abscess formation. The patient responded well to surgical evacuation and antituberculous medical therapy.


Orbital tuberculosis is a rare entity that may involve the soft tissues as well as the bones forming the orbit (1–3). Differentiating it from a neoplastic process may be difficult, and the true diagnosis may reveal itself only on the operating table. Our case exemplifies the pitfalls associated with dependence on radiology for diagnosis.

CASE REPORT

A 7-year-old girl was brought for treatment of progressive painless proptosis in the OS for 3 years. She experienced diplopia on looking to the left side. On examination, she was afebrile and well-nourished, and had a visual acuity of 20/20 bilaterally. A mass was palpable in the superolateral aspect of the left orbit, causing slight proptosis, and a nonpulsatile and compressible mass of the supraorbital region extended to the left lower eyelid. The overlying skin was healthy, and there were no signs of inflammation. Restriction of abduction was present in the left eye. The fundus was bilaterally normal, and the results of the general and neurologic examination were otherwise normal.

Laboratory investigations revealed a hemoglobin of 11 gm/dl and an erythrocyte sedimentation rate of 40. A chest radiograph was normal. Contrast-enhanced computed tomography of the head and orbits revealed a soft tissue lesion in the superolateral part of the left orbit with extension into the temporal fossa extradurally. Erosion and destruction of the roof and lateral orbital wall, as well as the greater and lesser wings of sphenoid bone, were also seen (Fig. 1). Contrast-enhanced magnetic resonance imaging of the orbits showed a homogenously enhancing extracranial mass lesion with an enhancing dural tail along the left sphenoid bone and extraconal left orbit displacing the eyeball inferomedially (Fig. 2). After imaging, a differential diagnosis of a benign neoplasm (meningioma or a primary osseous tumor) involving the lateral sphenoid wing and orbit was made.

The patient was taken for surgery. When the left frontotemporal skin flap was reflected from the supraorbital margin, thick straw-colored fluid flowed out. A burr hole was made, and the fluid was evacuated from the extradural sphenoidal and basitemporal region. The lateral wall of the orbit and the sphenoid were found to be eroded by the disease process. The dura was thickened and covered with granulation tissue. The granulation tissue was scraped, and the diseased bone was nibbled. After evacuation of pus, the orbital and eyelid swelling resolved almost immediately. The pus contained lymphocytes and acid-fast bacilli, and when cultured grew *Mycobacterium tuberculosis*. Cultures for aerobic, anaerobic, and fungal microorganisms were sterile. Frozen-section and definitive histopathologic examination of the involved bone showed granulomatous inflammation consistent with tuberculosis. The patient was given antituberculous therapy and is currently asymptomatic after 6 months of follow-up.

DISCUSSION

Tuberculosis of the orbit is extremely rare, even in places where tuberculosis is endemic. An extensive literature search revealed that fewer than 35 cases of orbital tuberculosis have been reported to date (1–22). Of these, the majority (4–20) were tuberculomas, and only two involved "cold abscess" formation within the orbit (21). A cold abscess, as the name suggests, is a purulent collection lacking signs of acute inflammation, such as brawny induration, edema, or tenderness (21,23). Characterized by liquefaction of the central caseous necrosis, cold abscesses are usually tuberculous, although rare instances of association with brucellosis, nocardiosis, actinomycosis, or trichophyton infection have been reported (23–27).

The disease may involve the soft tissues, lacrimal gland, periosteu, or bones of the orbital wall (3). Sphenoidal extension is rarer still; only two cases have been reported (1,2). There is no description of intracranial extension from orbital tuberculosis. Our patient had tubercular...
osteoperiostitis of the orbital roof as well as the lateral wall of the orbit, with involvement of the greater and lesser wings of the sphenoid bone associated with cold abscess in the extradural region. Orbital tuberculosis is more commonly seen in children (2), girls being more susceptible than boys (2), and is usually unilateral (22). For unknown reasons, the left orbit has been found to have a higher propensity of involvement than the right orbit (2).

The primary tuberculous focus is commonly pulmonary, but extrapulmonary sites, such as cervical lymphadenopathy or abdominal disease, may be present (2). The disease reaches the intraorbital space either by contiguity from the paranasal sinuses or through the bloodstream (11). Involvement of the lateral wall of the orbit implies a hematogenous source (11). There has usually been evidence of disseminated tuberculosis in previously reported cases (7,9). Although our patient was not investigated extensively for primary tuberculosis of the abdomen, she did not have evidence of pulmonary tuberculosis or lymphadenopathy. We could not ascertain the origin of the tuberculoma in the present case.

FIG. 1. (A) Contrast-enhanced computed tomographic scan of the head, showing an enhancing lesion in the superolateral part of the left orbit with extension into the temporal fossa extradurally. (B) Computed tomographic scan of bone windows, showing erosion and destruction of the roof and lateral orbital wall, as well as the greater and lesser wings of sphenoid bone.

FIG. 2. Enhanced magnetic resonance imaging scans of the brain in axial (A), sagittal (B), and coronal (C) projections, showing a homogenously enhancing extradural orbitocranial mass (black arrow) with an enhancing dural tail (white arrow) along the left sphenoid bone.
The recommended treatment of orbital tuberculoma is wide surgical removal of all diseased tissue, combined with antituberculous chemotherapy for 18 months (2,4). Some authors have used antituberculous therapy alone as the primary therapy, with excellent results (1,10-12,16). However, in the presence of a cold abscess, surgical evacuation of the pus (by simple aspiration and drainage or wide surgical removal) should be combined with antituberculous medical therapy.

REFERENCES
Spontaneous Resolution of Aneurysmal Third Nerve Palsy

Rod Foroozan, MD, Thomas L. Slamovits, MD, Susan M. Kstazek, MD, and Rochelle Zak, MD

Palsy of the third cranial nerve developed in a 33-year-old woman in her third trimester of pregnancy as a result of compression by a posterior communicating artery aneurysm. Prepartum complications forced postponement of surgical treatment. The palsy spontaneously resolved over 3 weeks after delivery by cesarean section. Repeat angiography suggested that the aneurysmal sac had shrunk. Spontaneous complete resolution of a third nerve palsy does not exclude an aneurysmal cause.


Palsy of the third cranial nerve occurs in 30% to 40% of patients with internal carotid-posterior communicating artery (ICA-PCoA) aneurysms (1). Studies on the prognosis of third cranial nerve palsy in patients with aneurysms of the ICA-PCoA have reported spontaneous recovery as a rare occurrence, without an easily identifiable mechanism for resolution (2,3).

Pregnancy-induced hypertension has been identified as a risk factor for intracranial aneurysm development and rupture (4). Pregnancy is a state with an apparent stimulatory effect upon aneurysm growth (5), and hormonal, hemodynamic, and metabolic factors have been implicated in documented cases of rapid aneurysmal growth (6,7). We report spontaneous resolution of a third nerve palsy resulting from an ICA-PCoA aneurysm.

CASE REPORT

A 33-year-old nulliparous woman experienced painless diplopia and partial left-sided ptosis at 32 weeks gestation. She did not describe neck stiffness, nausea, or vomiting. The results of previous evaluations by her obstetrician were reportedly unremarkable and revealed normal blood pressures.

At the time of neuro-ophtalmic presentation, her blood pressure was 140/100 mm Hg, and there was 2+ pedal edema bilaterally. Examination revealed a best-corrected visual acuity of 20/25 OD and 20/30 OS. The right pupil measured 4 mm in dim illumination and reacted briskly to light; the left pupil measured 6.5 mm and reacted sluggishly to light. There was no relative afferent pupillary defect. In the OD, ductions were full. In the OS, there was a mild supraduction, adduction, and infraduction deficit. The left upper eyelid was ptotic, with palpebral fissures measuring 10 mm on the right and 6.5 mm on the left. The results of slit lamp examination and applanation tonometry were normal bilaterally. There was no evidence of papilledema or retinal hemorrhages, and visual fields to confrontation were normal bilaterally.

Magnetic resonance imaging (MRI) was normal; magnetic resonance angiography (MRA) showed an area of high signal intensity posterior to the carotid artery, below the level of the left PCoA, consistent with an aneurysm of the PCoA. A cerebral angiogram revealed an aneurysm 10 mm in diameter, arising from the left supraclinoid carotid artery just below the origin of the PCoA and oriented inferiorly and posteriorly to it (Fig. 1). Admission laboratory studies included an elevated partial thromboplastin time (PTT): 65 seconds (normal 26-36 seconds) and serum glutamic-oxaloacetic transaminase (SGOT): 65 U/L (normal 5-40 U/L). A lumbar puncture revealed no evidence of xanthochromia. Although a simultaneous craniotomy and delivery were planned, the patient's medical condition rapidly deteriorated, with signs of pre-eclampsia, fetal distress, hemolytic anemia, elevated liver enzymes, and thrombocytopenia (HELP syndrome). An emergent cesarean section was performed. Craniotomy was further precluded by a complicated postpartum course, including postpartum cardiomyopathy and gram-negative sepsis, which were reversed by medical treatment.

Three days after admission, the patient was noted to have progression of her third nerve palsy to complete left-sided ptosis and a complete left adduction deficit. However, over the next 3 weeks, the third nerve palsy...
gradually improved, and 4 weeks after initial presentation, her deficit was limited to a mildly hyporeactive left pupil 4.5 mm in diameter in dim illumination, compared with a briskly reactive right pupil measuring 4.0 mm. Extraocular movements were normal, without evidence of aberrant regeneration.

Evaluation for recurrent thrombocytopenia revealed positive antinuclear antibodies and the lupus-anticoagulant, consistent with a diagnosis of systemic lupus erythematosus. Six weeks after admission, the patient was discharged receiving oral corticosteroid treatment. A repeat cerebral angiogram, performed 2 months after hospital discharge, revealed that the aneurysm diameter had shrunk from 10 mm to 4.5 mm (Fig. 2). Two weeks later, elective craniotomy and clipping of the aneurysm were performed without complication. On postoperative follow-up examinations, extraocular movements were full, without evidence of aberrant regeneration, and there was no evidence of anisocoria.

**DISCUSSION**

Our patient’s aneurysm spontaneously shrank from 10 mm to 4.5 mm in diameter after cesarean delivery, and the third nerve palsy completely resolved. In their review of 161 unruptured intracranial aneurysms, Wiebers et al. (8) noted that with two exceptions, all symptomatic aneurysms were 10 mm in diameter or greater. Although a true measure of aneurysm size cannot be determined solely by angiography (9), this finding suggests that a reduction in the size of the aneurysm sac, and hence a relief of compression on the third nerve, was responsible for the spontaneous clinical resolution. However, we cannot exclude the possibility that the aneurysm sac, while initially patent, became partially thrombosed after the first angiogram, and that this accounted for an apparent reduction in intraluminal diameter.

Spontaneous resolution of third cranial palsy resulting from intracranial aneurysm formation has been reported (3,10). In a review of isolated third cranial nerve palsy caused by intracranial aneurysms, Jefferson (11) noted that partial recovery occurs in several cases and speculated that “the cause of recovery is partly shrinkage by thrombosis sufficient to free the nerve...” Giombini et al. (3) reported five patients with third cranial nerve palsy caused by ICA-PCoA aneurysms who recovered within 3 months after the onset of the motility deficit and before surgery, although the mechanisms for recovery could not be identified. Greenspan and Reeves (10) reported a case of transient oculomotor nerve paresis that resolved before cerebral

**FIG. 1.** Cerebral angiogram of left internal carotid artery injection, lateral view, obtained shortly after onset of left third cranial nerve palsy, showing a left posterior communicating artery aneurysm (arrow) oriented posteriorly and inferiorly to the left supraclinoid carotid artery.

**FIG. 2.** Cerebral angiogram obtained 2 months after onset of third cranial nerve palsy and before surgical intervention, showing an attenuated left posterior communicating artery aneurysm (arrow) in the same position as seen in Figure 1.
angiography documented the presence of a PCoA aneurysm. They postulated that a temporary conduction block or a shift in aneurysm position may have been responsible for the transient third nerve palsy, although sequential angiograms were not available for comparison. Similarly, our patient's deficit may have resolved because of a shift in aneurysm position, relieving compression on the third nerve.

Although initial evaluation of the cerebrospinal fluid revealed no evidence of xanthochromia, a reduction in aneurysm size may have subsequently occurred by leakage of small amounts of blood. Wiebers et al. (8) have postulated that bleeding into the cerebrospinal fluid may be responsible for a reduction in the diameter of some intracranial aneurysms, suggesting that a newly formed clot may seal the point of rupture. In addition, Hamer (2) has suggested that bleeding of some intracranial aneurysms may occur without producing the typical symptoms of subarachnoid hemorrhage.

The occurrence of our patient's deficit in the third trimester of pregnancy and in the setting of pre-eclampsia offers another explanation for aneurysmal growth followed by diminution before craniotomy. Pregnancy has been identified as a state that has stimulatory effects on aneurysmal growth, with the majority of aneurysms occurring during the third trimester (12). Hemodynamic changes during pregnancy include an increase in cardiac output, total blood volume, and stroke volume, with an associated decrease in arterial blood pressure (13). Histologic studies of arterial walls have shown alterations in elastic fibers, smooth muscle cells, and intimal thickening during pregnancy (14-16). In their review of the risk factors for the development and rupture of intracranial aneurysms, de la Monte et al. (4) noted that many of the predisposing factors led to a reduction in prostaglandin levels. They suggested that a reduction in prostaglandins, which is believed to occur in pre-eclampsia (17,18), may be responsible for an increase in local cerebral blood flow, which could cause stretching of the arterial walls. Other investigators have stressed the importance of nitric oxide (NO) in maintaining vascular tone during pregnancy, and patients with pre-eclampsia are thought to have abnormalities in NO metabolism (13).

Several cases support the belief that alteration of the aneurysmal sac may occur during pregnancy. Pool (6) reported the case of a 21-year-old woman who, in her third trimester of pregnancy, experienced a subarachnoid hemorrhage and, by angiography 5 weeks later, had documented growth of the aneurysm sac. Weir and Drake (7) reported a 34-year-old woman in the 20th week of pregnancy who underwent surgical clipping of an aneurysm of the superior cerebellar artery. Postoperatively, the aneurysm neck underwent rapid growth over the ensuing 4 months, documented by angiography. Ortiz et al. (19) reported enlargement of a cavernous carotid aneurysm during pregnancy, which produced an ipsilateral Horner's syndrome and abduction deficit that partially resolved in the postpartum period. A reduction in the size of the aneurysmal sac was noted with MRI; repeat angiography was not performed in the postpartum period.

The third cranial palsy in our patient could have been caused by lupus erythematosus, and the aneurysm could have been merely an incidental finding. Corticosteroid treatment could have been responsible for its resolution. The elevation in the PTT noted on admission, while thought to be an early marker of the ensuing HELLP syndrome, may have been caused by the lupus anticoagulant. Rosenstein et al. (20) reported a 29-year-old woman who had an isolated, pupil-sparing third nerve palsy as an initial manifestation of lupus erythematosus. The third nerve palsy resolved after 4 weeks, during which time the patient received corticosteroids. They noted that the deficit spared the pupil and hence was most likely vasculopathic. Our patient's pupil was not spared, and the presence of an ipsilateral aneurysm in close proximity to the course of the third cranial nerve suggests that the neuropathy was caused by aneurysmal compression rather than by lupus-related vasculopathy. Furthermore, resolution of our patient's third nerve palsy was nearly complete before the introduction of corticosteroid therapy, which began 3 weeks after initial presentation.

REFERENCES

Oculomotor Ophthalmoplegic Migraine: Is It Really Migraine?

Thomas J. Carlow, MD

Oculomotor ophthalmoplegic migraine is a rare episodic childhood condition in which a unilateral oculomotor palsy is preceded by headache. I describe six new cases that had magnetic resonance imaging signal abnormalities during the acute phase, consisting of a thickened and enhancing ipsilateral oculomotor nerve at its exit from the midbrain. During the quiescent phase, when the headache had resolved, the signal abnormalities were still present but less dramatic. Seventeen similar cases have been previously reported. The pathophysiology may be a trigeminovascular migraine epiphenomenon that is dependent on the unique oculomotor nerve anatomy and porous blood–nerve barrier at the emergence of the oculomotor nerve from the brainstem and the sequelae of demyelination. Early high-dose corticosteroid treatment is recommended to rapidly resolve an acute episode and to potentially prevent permanent abnormal oculomotor nerve signs.

Definitions

Notta contributed the first clinical description of ophthalmoplegic migraine in 1854 (2,3). In 1884, Möbius termed it “periodic oculomotor paralysis” (4). In 1890, Charcot coined the term “ophthalmoplegic migraine” (5). Möbius required that a structural process involve the oculomotor nerve, whereas Charcot did not. The concept of ophthalmoplegic migraine has been controversial since the original Möbius and Charcot debate (3).

In a three-volume text in 1969, Walsh and Hoyt stated, “At the root of the problem has been a lack of strict criteria for the clinical diagnosis of ophthalmoplegic migraine and insufficient knowledge of the pathophysiologic events that occur during a migraine attack” (6). I intend to document that children with the clinical criteria for oculomotor ophthalmoplegic migraine also have specific magnetic resonance imaging (MRI) findings, to propose a hypothesis to explain the pathophysiology, and to suggest treatment.

The generally accepted clinical criteria for oculomotor ophthalmoplegic migraine are: 1) childhood onset; 2) headache preceding and ipsilateral to the third nerve paresis; 3) a commonly dilated pupil; 4) ophthalmoplegia that may be permanent and rarely accompanied by aberrant oculomotor regeneration; 5) a minimum of two episodes; and 6) no evidence for a structural lesion (7,8). The incidence of the condition, as so defined, is estimated to be 0.7 in 1,000,000 (9).

My Series

Over the past 7 years, I have examined six children who fulfilled these clinical criteria. The exception was that all children had abnormal MRI scans at the oculomotor midbrain exit, suggesting a focal pathologic process. In my series, five of six patients were girls. The age of onset varied from 16 months to 9 years, with a mean of 3.7 years. Headache preceded the onset of a third nerve paralysis by up to 11 days. The pupil was dilated in 5. Each child had at least two and as many as 12 events. Permanent oculomotor paresis or paralysis was present in four of the six children after multiple episodes, and two developed aberrant regeneration. Four of the six children had headaches unassociated with oculomotor paresis. A family history of migraine was present in five.

MRI brain signal abnormalities were present in all cases. In the scans obtained during the acute phase, when the children had headache and ophthalmoplegia, non-contrast T1-weighted images documented thickened ipsilateral oculomotor nerves at the midbrain exit that were isointense with brain (Fig. 1A). Contrast T1-weighted MRI scans showed enhancement of the ipsilateral oculomotor nerves at the midbrain exit (Figs. 1B and 2). A trapezoid
Fig. 1. Axial T₁ MRI before (A) and after contrast (B) through the midbrain at the exit of the oculomotor nerve in a child with right oculomotor ophthalmoplegic migraine. Precontrast study (A) shows thickened right oculomotor nerve (arrow) that enhances intensely after contrast (B, arrow).

configuration was typically seen, with the widest area adjacent to the midbrain.

MRI scans were also acquired during the quiescent phase when the children no longer had headache or ophthalmoplegia, between one and eight months (average = 3.5 months) after an acute episode. All noncontrast T₁-weighted MRI scans continued to show thickened ipsilateral third cranial nerves at the brainstem exit (Fig. 3). The contrast scans demonstrated persistent oculomotor nerve enhancement that was less intense than during the acute phase (Figs. 4 and 5).

Cases with Abnormal MRI Scans
In addition to my six cases, 17 patients have previously been reported to have MRI abnormalities for a total of 23 cases (10–19). All have exhibited ipsilateral third nerve MRI abnormalities at the midbrain exit. Combining my cases and previously reported cases, there have been 17 girls and six boys, with an age of onset ranging from 7 months to 19 years (average = 6 years).

A partial clinical history is available in 17 of the 23 children who have had abnormal MRI scans (10–14,16–19) (Table 1). Headache occurred simultaneously or preceded the onset of the oculomotor paresis by 11 days in 15 cases (average = 3.3 days). Six children have had a persistent partial or complete third nerve paresis. In three of the six permanent palsy cases, the ophthalmoplegia developed after the first episode; in the remaining three cases, it developed after multiple episodes. Two children from my series eventually demonstrated oculomotor nerve aberrant

Fig. 2. Sagittal T₁ postcontrast MRI through the oculomotor nerve brainstem exit in a child during an acute phase of ophthalmoplegic migraine. The clinically involved oculomotor nerve shows marked contrast enhancement at its midbrain exit (arrow).

Fig. 3. Coronal T₁ precontrast MRI through the brainstem exit of the oculomotor nerves in a child that had developed right oculomotor ophthalmoplegic migraine nearly three months earlier. No clinical abnormalities were evident at the time of this scan. The right oculomotor nerve (large arrow) is thickened and is several times larger than the normal left third nerve (small arrow).
Fig. 4. Axial T1 contrast-enhanced MRI through the brain stem exit of the oculomotor nerves in a child with right oculomotor ophthalmoplegic migraine. (A) Acute phase. The right oculomotor nerve enhances intensely (arrow). (B) Quiescent phase. Six weeks after the acute episode, the right oculomotor nerve enhances less dramatically (arrow).

regeneration, which was not reported in the other 15 cases. The time to resolve the oculomotor paresis, when it did clear, ranged from four days to twelve weeks (average = 4.1 weeks). The pupil was dilated in 15 of 16 cases. There was a family history of migraine in 10 of 15; headaches occurred without ophthalmoplegia in 13 of the 15 cases that documented these findings.

Twenty-two of the 23 reported cases (including my own) with MRI abnormalities have had abnormal T1-weighted MRI scans during the acute phase. Twenty received contrast and all showed enhancement of the oculomotor nerve at the midbrain exit. Two children had only noncontrast MRI scans, and both showed a thickened third nerve at the brainstem exit.

Twenty children had abnormal MRI scans during the quiescent period, from 5 weeks to 8 months (average = 2.6 months) after the acute phase. Of the 17 who had contrast MRI scans, all demonstrated reduced residual oculomotor nerve enhancement at the midbrain exit. Three children had only noncontrast MRI scans, which showed a thickened oculomotor nerve at the brainstem exit.

In my opinion, the diagnostic criteria for oculomotor ophthalmoplegic migraine should include an MRI contrast-enhanced thickened third nerve at the oculomotor midbrain exit during the acute phase with less enhancement during a quiescent phase. If these MRI findings are not present, other diagnostic etiologies must be excluded (20).

Nine children, including two from my series, have had recurrent oculomotor paresis without headache. They had all been initially diagnosed as having an “ophthalmoplegic migraine variant” (12,16,21–23). The average age of onset was 20 months. Seven of the 9 children later developed headache episodes followed by an oculomotor paresis, at an average age of 5 years. Five of these seven children had contrast MRI scans, all demonstrating

Fig. 5. Axial T1 contrast-enhanced MRI through the oculomotor nerve brainstem exit in a child with right oculomotor ophthalmoplegic migraine. (A) Acute phase. The right oculomotor nerve enhances intensely at the brainstem exit (arrow). (B) Quiescent phase. Four months after an acute episode, the right oculomotor nerve enhances less dramatically (arrow).
TABLE 1. Clinical information in reported cases of ophthalmoplegic migraine and abnormal MRI scans

<table>
<thead>
<tr>
<th>Case #</th>
<th>Study</th>
<th>Sex</th>
<th>Age at onset</th>
<th>Headache to 3rd d</th>
<th>Time to resolve</th>
<th>Persistent 3rd</th>
<th>Aberrant 3rd regeneration</th>
<th>Pupil dilated</th>
<th>Headache without 3rd</th>
<th>Family History migraine</th>
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<tbody>
<tr>
<td>1</td>
<td>Stommel et al. (10)</td>
<td>M</td>
<td>18 y</td>
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<td>NR</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>2</td>
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<td>F</td>
<td>19 y</td>
<td>4</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>3</td>
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<td>F</td>
<td>18 mo</td>
<td>3-4</td>
<td>4.5-6 wks</td>
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<td>Yes</td>
<td>Yes</td>
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<tr>
<td>4</td>
<td>Ostergaard et al. (12)</td>
<td>F</td>
<td>7 mo</td>
<td>1</td>
<td>4 wks</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>?</td>
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<tr>
<td>5</td>
<td>Aers et al. (13)</td>
<td>F</td>
<td>14 y</td>
<td>1</td>
<td>1 wk</td>
<td>No</td>
<td>NR</td>
<td>Yes</td>
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<tr>
<td>6</td>
<td>Wong and Carlow (14)</td>
<td>M</td>
<td>6 y</td>
<td>4</td>
<td>12 d</td>
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<td>7-12</td>
<td>Mark et al. (15)</td>
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<td>20 mo</td>
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<td>F</td>
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<td>F</td>
<td>3 y</td>
<td>5</td>
<td>4</td>
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<td>NR</td>
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<td>9 mo</td>
<td>3-4</td>
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<td>2 y</td>
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<td>3 mo</td>
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<td>18</td>
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<td>M</td>
<td>3 y</td>
<td>2</td>
<td>4 wks</td>
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<td>18 mo</td>
<td>2-3</td>
<td>4 wks</td>
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<td>9 y</td>
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<td>5 y</td>
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<td>2 wks</td>
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<td>2 wks</td>
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<td>No</td>
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<td>Yes</td>
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</tr>
</tbody>
</table>

* When the third nerve paresis did resolve.
† No Clinical History Available.
‡ Includes one case from (20).
NR, Not Reported.

Oculomotor nerve enhancement at the brainstem exit. (They are included among the 23 abnormal MRI cases previously discussed.)

**Treatment**

Multiple drug regimens have been used to treat or prevent ophthalmoplegic migraine with variable to poor results. Corticosteroids have been prescribed for 12 reported children (10-12, 14, 17, 21, 22, 24, 25), only six of whom have had MRI scans. The response to treatment was not documented or considered of no benefit in six; however, the dose or length of treatment was not noted. A beneficial response was reported in six, including one child from my series (12, 14, 22, 24). Prompt resolution of the headache and ophthalmoplegia appeared related to the early institution of corticosteroids (prednisone or methylprednisone) and to the amount prescribed. The minimum effective dose was equivalent to 2 mg of prednisone/kg/d given over several weeks with a slow taper. In the six patients who improved with corticosteroids, the resolution time was typically measured in days. Among those not treated, resolution occurred in weeks to months.

Six of the 12 corticosteroid-treated children had MRI scans; all displayed a thickened third nerve at the midbrain exit. Three of the six children with abnormal MRI scans had a beneficial response to corticosteroids when prescribed at the onset of the ophthalmoplegia and headache. In the three cases with abnormal MRI scans that did not respond to...
treatment, corticosteroids were given for only a few days or after the headache had resolved.

Pathogenesis

Why do these children have a thickened oculomotor nerve at the brainstem exit that enhances after contrast on MRI during the acute phase and becomes less intense after contrast during the quiescent phase? Possible pathogenetic mechanisms include compression (7), ischemia (26), a vascular anomaly (27), a Tolosa-Hunt variant (9,11,22), or demyelination (19).

I propose a hypothesis for the pathophysiology of oculomotor ophthalmoplegic migraine based on the trigeminovascular theory of migraine, the unique oculomotor nerve anatomy at the brainstem exit, the blood–nerve barrier, and the pathology of demyelination.

Current theory suggests that there is a trigeminovascular basis for migraine (28). At the onset of a migraine, the ophthalmic division of the trigeminal nerve is triggered to release neuropeptides at intracranial sites innervated by the ophthalmic branch of the trigeminal nerve (28). A sterile inflammatory vascular response is induced. The greatest intracranial trigeminal receptor density is located in the arteries that comprise the circle of Willis and the proximal adjacent arteries emanating from the circle (29).

The oculomotor nerve is the only cranial nerve adjacent to the circle of Willis at its exit from the brainstem. The vascular supply to the oculomotor nerve is derived from the posterior aspect of the circle of Willis and adjacent vessels, which are abundantly innervated, by the ophthalmic division of the fifth nerve (30). That the oculomotor nerve is frequently penetrated by the circumflex mesencephalic artery or a perforating vessel of the posterior cerebral artery may also be significant (31).

The blood–nerve barrier is dependent on tight closure of capillary endothelial vessels. Neuropeptides do not normally cross the blood–brain barrier or the blood–nerve barrier junctions. The blood–nerve barrier junction is, however, relatively porous at nerve root junctions (32).

Schwann cells begin to myelinate the oculomotor nerve approximately 0.6 mm from the brainstem exit (33). Demyelination causes Schwann cell proliferation and onion bulb formation. With repeated episodes of demyelination and remyelination, there is nerve hypertrophy and axonal loss (34). These pathologic findings have been reported in diabetic third nerve pareses (35–37).

I propose that the oculomotor nerve enlargement in oculomotor ophthalmoplegic migraine is initiated by a migraine stimulus of the trigeminovascular system. Neuropeptides are secreted at the level of the circle of Willis and adjacent vessels that cross a relatively open blood–nerve barrier junction at the oculomotor nerve exit. A sterile inflammation is induced that further opens the blood–nerve barrier. Demyelination results in Schwann cell proliferation and edema in the oculomotor nerve as it emerges from the brainstem. A contrast-enhanced third nerve at the midbrain exit is then visible on MRI. With repeated demyelination and remyelination, the oculomotor nerve enlarges focally. Less contrast enhancement is seen during the quiescent period when the blood–nerve barrier returns to a relatively normal state and the edema resolves. Subsequent third nerve compression from nerve hypertrophy and scar formation after repeated episodes of demyelination and remyelination could result in permanent oculomotor paralysis or aberrant regeneration. Postcontrast MRI demyelinating nerve root enhancement has been reported in the Guillain-Barré syndrome (38) and chronic inflammatory demyelinating polyneuropathy (CIDP) (39,40). Proximal spinal nerve root demyelination with hypertrophy (41) and gadolinium enhancement is seen in CIDP. Contrast enhancement of the spinal nerve root resolves during remission (40). Corticosteroids may decrease matrix metalloproteinasises at the oculomotor–midbrain junction and tighten the relatively porous blood–nerve barrier (42,43). Prompt resolution of a third nerve paresis would be the ultimate result.

In conclusion, I would formally like to thank Dr. Hoyt for the tremendous influence he has had on my life and career, for being an incredible role model, for making NANOS possible, and for his life’s work in neuro-ophthalmology.

REFERENCES


The Golden Age of Neuro-Ophthalmology at the Bascom Palmer Eye Institute

Joel S. Glaser, MD

In February 2002, the Bascom Palmer Eye Institute (BPEI) of the University of Miami celebrated its 40th anniversary. This milestone provides an opportunity to review the role of its neuro-ophthalmology service, replete with a cast of remarkable and memorable clinicians and dedicated teachers. A single institution, a single department of ophthalmology, at one time sustained a stable of six "card-carrying" neuro-ophthalmologists. It is a story of natural selection, small-world coincidences, and fortuitous inbreeding.

This writer has fortunately been involved with the BPEI since 1962, precisely this 40-year interval, and has had the distinct privilege of close associations with the principals as student, colleague, and friend. The circular nature of these recurrent connections will be apparent; indeed, they constitute the leading theme. The reader will, I trust, forgive any personal intrusions in the interest of authenticity, and excuse unwitting omissions.

The neuro-ophthalmology program at the BPEI has been the successful outcome of one of the consuming interests of Edward Norton, MD, who assumed the initial chairmanship of the ophthalmology department in 1958. Already an avid student of neurology while at Cornell Medical College, and indeed himself a survivor of self-diagnosed bulbar polio in the 1948 epidemic, Norton completed a 15-month residency in neurology under the direction of Harold Wolfe, MD, at New York Hospital–Cornell Medical Center and at the Bronx Veteran’s Administration Hospital. There, Norton also enjoyed a close collaboration with the Cushing-trained neurosurgeon Bronson Ray, MD. In an era before the advent of computed tomography or magnetic resonance imaging, it is said that Ray frequently planned surgical procedures based principally on Norton’s clinical assessments.

Under the subsequent tutelage of David Cogan, MD, at Harvard University and Frank Walsh, MD, at Johns Hopkins University, Norton was enthusiastically primed for a lifetime’s fascination with neuro-ophthalmology. Walsh, Cogan, and Norton sustained a deep lifelong mutual admiration (1). Norton told me early during my own residency training that he was also especially influenced by a book of Alfred Kestenbaum, MD, a refugee from Vienna at the time of the 1938 Nazi anschluss: Clinical Methods of Neuro-Ophthalmologic Examination (1946).

Serendipitously while in Boston, Norton learned to effectively use the indirect ophthalmoscope that Charles Schepens, MD, had brought from Belgium. Thus, the origins of Norton’s exceptional second (2) career as a retinal detachment surgeon. Among his earliest surgical successes was Harry Belafonte.

Housing the clinical facilities, faculty offices, library, and research laboratories of the department of ophthalmology, the BPEI opened formally in 1962. The original full-time faculty in 1958 consisted only of Norton and Victor Curtin, MD, Norton’s lifelong friend, colleague, and confidante. Interestingly, the next faculty member recruited was medical student Ed Norton’s drawing of midbrain, 1945.
a neuro-ophthalmologist, J. Lawton Smith, MD, from Duke (see accompanying interview). Donald Gass, MD, and John Flynn, MD, came next, to make up the “Founding Five Forefathers.”

Smith was the product of Duke Medical School, an Emory-Grady Hospital internship, and the Wilmer ophthalmology residency at Johns Hopkins, but he marched to his own inimitable percussion section. Smith must be considered the principal popularizer of neuro-ophthalmology in the second half of the 20th century. No one who has heard his down-in-the-country style, spiked with clinical “pearls and gems,” can soon forget the encounter. To the various rhythms of nystagmus patterns, Lawton provided synchronous tongue-clucking soundtracks. His re-enactment of an expanding pituitary adenoma was described by Dr. Noble David, a medical school classmate, colleague at Duke, and lifelong interpreter, as follows: “Anyone who has seen Dr. Smith in conference at half crouch in his far-from-silent pantomime of the inflamed intrasellar growth, arms and legs aggressively flailing out at imaginary regional anatomy, will not easily forget the lesson” (2). It was Smith’s extraordinary talent and forte to clarify clinical conditions by vigorous and dramatic body language and unique distillation of medical terms (see “The Language of Lawton” in the accompanying interview of Smith in this issue). For these reasons, he was an incomparably popular lecturer and teacher.

Robert Daroff, MD, (Cleveland, OH) (left), William Hoyt, MD, (San Francisco, CA) and Noble David, MD (Miami, FL) at ease, 1976.

An important lifelong association was sealed between Smith and William F. Hoyt, MD, while both were at the Wilmer Institute in 1957. Hoyt recalls Smith as “a phenomenon and a fascinating, entertaining, redheaded southern-ner. Unbelievable...Lawton was the fastest typist. No secretary could keep up with him. Lawton used to carry a typewriter around with him on ward consultations” (3). Their fond friendship blossomed: “If I wasn’t going to get famous doing what I was doing, Lawton was going to make me famous because he constantly kept referring to me as ‘Toughy Hoyt’” (2). Hoyt’s loyal support helped establish the University of Miami Neuro-Ophthalmology Symposia. Moreover, Hoyt has also been instrumental in the careers of three other BPEI faculty members: Robert Daroff, MD, Todd Troost, MD, and Joel Glaser, MD (that would be me).

 Accompanying Smith south to the University of Miami in 1962 was Noble (“Nobbie”) David, MD, a Duke neurologist first excited by Walsh’s textbook and later drawn naturally into the circle of the active neuro-ophthalmology mafia (see accompanying interview of Dr. David in this issue). Specializing in pituitary apoplexy and progressive supranuclear palsy (he enjoyed pronouncing “Olszewski”), David was the Shakespeare- and limerick-reciting intellectual foil and complement to Smith’s southern-fried jargon. It was David who brought to the BPEI the nascent Duke experience with fluorescein angiography of the fundus, which blossomed under master ophthalmic photographer Johnny Justice. The development of angiographic techniques provided the substrate for the remarkable career of Donald Gass, MD.

Stunned by the rumor that Hoyt had, in 1965, accepted a neurologist as a postgraduate fellow, and aware that no less a figure than Walsh had cautioned that “neurologists cannot be trained in neuro-ophthalmology,” Smith, irresistibly challenged, took a gamble and told Hoyt that “my neurologist is gonna be better than yours.” The constellations were in the

J. Lawton Smith, MD (Miami, FL) in action with a patient at Saturday Neuro-Ophthalmology Conference.

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right alignment. Within hours, Smith signed up his neurologist-fellow, Norman Schatz, MD!

It was clear, however, that Smith and Schatz were not cut precisely from the same cloth, their shared enthusiasm for neuro-ophthalmology notwithstanding. By his actions and words, Smith had been called to represent the forces of Good, leaving Schatz no choice but to align himself with "the forces of Evil." (This is, of course, an in-joke not to be taken too seriously.) Schatz, proud of his historic Philadelphia medical upbringing, and claiming direct descent from Polish royalty-of-a-sort, resolutely refused to be called "Dockey" (see "The Language of Lawton" in accompanying interview of Smith). And I, a restrained second-year resident at the BPEI in 1965, watched in wonder as Schatz regularly passed himself off as "Dr. Smith," entertaining and startling patients by employing an optokinetic tape studded with photos of semiattired Playmates. (Here was a man whose examination techniques were worth watching, and I still do). Schatz later returned to Philadelphia to direct the neuro-ophthalmology service at Wills Eye Hospital and to train a generation of admiring residents, fellows, and nurses.

Another of Smith's earliest (1966-67) and brightest postgraduate fellows was John "Tex" McCrary, MD, who stayed on as a BPEI faculty member in 1967-69 before returning westward to Baylor to spread the word as an outstanding teacher.

My own involvement at the BPEI began in 1962, when an extramural senior medical student elective was arranged. The dean at Duke was Barnes Woodhall, MD, a renowned neurosurgeon, who was well acquainted with Smith's salad days at Duke and was entirely supportive of my plans for a fall vacation with "Red Smith" in Miami. It was, for me, the opportunity of a lifetime. Smith, who had just arrived at the BPEI, was often joined for lunch by Norton—"The Chief"—and David. I tagged along, often stunned at the breadth of luncheon topics. As a familiar presence I was not only tolerated by my heroes but expected
to participate in clinical presentations at the Saturday morning neuro-ophthalmology conference, organized in the mold of the famous Walsh Saturday conference at Hopkins. These 10:30 to noon meetings were clearly the educational highlight of the week, attended enthusiastically by the housestaffs of ophthalmology, neurology, and neurosurgery.

Before my arrival to study with Smith in Miami, I had interviewed for internship at the University of California, San Francisco, and had rather casually dropped by to investigate the ophthalmology program there. Absolutely by chance, while I was speaking to his secretary, Michael Hogan, MD, the chairperson of ophthalmology, walked by. Informed of my interest in ophthalmology, and that I was to do a student elective with Smith in Miami, Hogan suggested that I "go around and see Bill Hoyt," of whom I had never heard! After a short and unexpectedly warm conversation, Hoyt offered to have me spend a 4-month Fight-for-Sight student fellowship under his supervision. So, after 3 months of rigorous basic training with Smith, off I went to San Francisco in January 1963: the first student ever to do an elective with Hoyt, and surely the first to train for 7 months in neuro-ophthalmology before even beginning an internship!

I returned to San Francisco after finishing my ophthalmology residency in 1969 for a postgraduate neuro-ophthalmology fellowship under Hoyt. Together with Todd Troost, MD, and James Corbett, MD, we provided mutual support and encouragement while learning with a not-yet-mellow Hoyt. It was, of course, a marvelous year, during which the neuro-ophthalmology unit was visited by Alan Bird, MD (just finishing his fellowship with Smith in Miami and about to head back to London’s famous Moorfield’s Eye Hospital and The National Hospital for Nervous Diseases), Ronald Burde, MD (just beginning his faculty position as neuro-ophthalmologist at Washington University in St. Louis), and Tadashi Fujino, MD (on his way back to Tokyo after 2 years at the BPEI).

Also along for a 3-month elective during that time was a young medical student from Nebraska, who was so enthusiastic that on his second day he accepted the responsibility of presenting a patient to "The Master" on ward rounds. The freshman presentation did not go especially well. Afterward, Hoyt pulled me aside to say, "See if you can teach that guy how to present a patient!" Indeed, "that guy" learned—well enough to later co-edit the 5th edition of the incomparable Walsh & Hoyt textbook (Clinical Neuro-Ophthalmology). He was, of course, Neil Miller, MD.

Wait, the plot thickens. Corbett joined Schatz at Wills, Troost joined Daroff in Miami, and Glaser, before returning to the BPEI, wrangled 4 months at The National
1972 BPEI neuro-ophthalmology fellows Thomas Carlow, MD (Albuquerque, New Mexico) (left), James Sharpe, MD (Toronto, Ontario) (center), and John Susac, MD (Lakeland, Florida) (right) with their mentors, Smith and Glaser.

Hospital for Nervous Diseases, working with Alan Bird, Michael Sanders, MD (a 1968 Hoyt fellowship graduate, along with Daroff), Ralph Ross Russell, MD, Ian McDonald, MD, and a keen Moorfields Eye Hospital registrar named Ivor Levy, MD (later to become a BPEI neuro-ophthalmology fellow in 1973).

Thus, in 1970, gathered on the faculty at the University of Miami were Smith, David, Glaser, and the world-class Ocular Motor Laboratory consisting of Daroff, Troost, Louis Dell’Osso, PhD, and Larry Abel, PhD. Norton also continued an active interest in neuro-ophthalmology. Also on the Miami scene was the

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<th>TABLE 1. Bascom Palmer Eye Institute neuro-ophthalmology fellows</th>
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<td>Nabih Al-Sheikh, 2002</td>
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<td>Debra Barrett, 1991</td>
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<td>Norma Barton-Boschetti, 1980</td>
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<td>Walter Gilbert, 1968</td>
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<td>Kong Yong Goh, 1995</td>
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<td>Yochanan Goldhammer, 1974</td>
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<td>Todd Goodglick, 1993</td>
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<td>Brian James, 1971</td>
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<td>Raananah Katz, 1981</td>
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<td>Lanny Kline, 1978</td>
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<td>Bruce Kohrman, 1989</td>
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<td>Pierre Laffamme, 1974</td>
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<td>Byron Lam, 1991</td>
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<td>Robert Lessier, 1972</td>
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<td>Ivor Levy, 1972</td>
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<td>James Lewis, 1990</td>
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1993 BPEI neuro-ophthalmology fellows Grant Liu, MD (Philadelphia, Pennsylvania), Todd Goodglick, MD (Chevy Chase, Maryland), and Mitchell Strominger, MD (Boston, Massachusetts). Seated are mentors Schatz and Glaser.
extraordinary series of almost-annual neuro-ophthalmology symposia that regularly featured such guest speakers as Frank Walsh, MD, David Cogan, MD, Richard Lindenberg, MD, Hoyt, Hans Newton, MD (neuroradiologist at the University of California, San Francisco), Ronald Burde, MD, Robert Hollenhorst, MD, Swithin Meadows, MD, A. Earl Walker, MD, Blaine Nashold, MD, Maurice Victor, MD, Henry van Dyk, MD, Dwight Parkinson, MD, Simmons Lessell, MD, Michael Sanders, MD, Stanley Thomp­son, MD, Alan Bird, MD, Lars Friesen, MD, Elizabeth Gould, MD, Ian MacDonald, MD, Albert Rhoton, MD, and many others.

The lectures from the programs of the Miami symposia series provided the principal substrate for the series of ten neuro-ophthalmology books, published from 1963 to 1979 under the shared editorship of Smith and Glaser.

The bibliography of other publications of the BPEI neuro-ophthalmology faculty in texts and refereed journals is substantial, including major contributions to the Duane-edited Clinical Ophthalmology volumes. But one other contribution is especially noteworthy. While others formed committees and argued the pros and cons of a dedicated neuro-ophthalmology journal, Smith just forged ahead. With the cooperation of the Masson Publishing Company, the Journal of Clinical Neuro-Ophthalmology was born in 1978, dedicated to "the treating doctor," with "no abbreviations," and with the bonus of a "new pearls checklist" if the reader is "just too tired and too busy to read anything" (4). Of course, gentle reader, you hold in your hands at this moment the fruits of that forward-looking decision: the present Journal of Neuro-Ophthalmology, the Chief Editor of which, Jonathan Trobe, MD, was a BPEI neuro-ophthalmology fellow in 1976.

In 1980, Daroff, Troost, and Dell’ Osso left Miami with the Ocular Motor Laboratory for Case Western Reserve University in Cleveland, where Daroff became chairperson of the neurology department. Schatz replenished the BPEI neuro-ophthalmology faculty in 1982, when he began a bigamous existence: 6 months in Philadelphia, 6 months at the BPEI. At Norton’s invitation, Schatz became a full-time faculty member in 1986, joining Smith, Glaser, and David.

After an exceptional career, Smith retired from practice in 1994. Ronald Tusa, MD, reconstituted the eye movement facility from 1989 to 1997. Matthew Kay, MD, joined the faculty from 1993 to 1994. BPEI neuro-ophthalmology fellowship graduate Michael Siatkowski, MD, was a faculty member from 1994 to 1997 (now at the University of Oklahoma), and BPEI neuro-ophthalmology fellowship graduate Byron Lam, MD, came in 1996. Presently, Lam, Schatz, and Glaser hold the fort. The bona fide mark of a successful clinical service surely must also include its impact on post-graduate education. The members of the BPEI neuro-ophthalmology faculty have had the responsibility and privilege of playing a part in the training of almost 90 bright young physicians, most of whom have assumed academic positions (see Table). BPEI-trained neuro-ophthalmology fellows now play important roles at training institutions in North Carolina, Virginia, Texas, Florida, Boston, New York, Philadelphia, Cleveland, Chicago, Detroit, and Ann Arbor in the United States; in Edmonton, Toronto, Kingston, and Montreal in Canada; and in London, Tokyo, Switzerland, Israel, and Mexico. They include department chairpersons, deans, editors of journals, and founders of the North American Neuro-Ophthalmology Society (NANOS). At the end of the day, these men and women who carry on the tradition of excellence in patient service, clinical research, and enthusiastic teaching are the most important contribution of BPEI to worldwide neuro-ophthalmology.

It is unlikely that a single institution will ever again mount the sustained interest sufficient to match the multitude of neuro-ophthalmic clinicians once gathered under the BPEI roof. How much less likely still to encounter the variety and depth of its cast of characters. This is history worth recalling, one still paying rich dividends. How we yearn to be able to repeat it!

REFERENCES
For most of the second half of the 20th century, the best-known ophthalmologist in the world was J. Lawton Smith, MD. In his heyday, his medical argot and antics transfixed audiences. Even when the other “top dogs” of ophthalmology were gathered in the same room, no one took their eyes off the “simple country doctor” with the South Carolina twang. Soon everyone was describing patients in “Lawtonesque” (see “The Language of Lawton,” below). Mixing medicine with evangelism, he converted scores of medical students to ophthalmology, if not to Christianity. After completing his three-hour examination of patients, he would kneel down and pray for their health and their souls. On an old Smith-Corona typewriter, he was to hammer out definitive descriptions of ischemic optic neuropathy, internuclear ophthalmoplegia, skew deviation, opsoconus, optokinetic nystagmus, light-near dissociated pupils, and isolated homonymous hemianopia. In addition to his journal articles and books, he produced nearly 100 audiotapes organized around interesting neuro-opthalmic patients, which are still quoted as gospel. Retired from his post at the Bascom Palmer Eye Institute for nearly a decade now, the Elmer Gantry of ophthalmology still exudes an uncommon energy at the age of 73.

Born into a medical family in South Carolina, Smith attended college at Emory University and medical school at Duke University. He completed his ophthalmology residency at the Wilmer Institute, Johns Hopkins University, and his neuro-opthalmology fellowship with David Cogan, MD, at Harvard. He signed on to the Duke faculty in ophthalmology in 1960 but was drawn away in 1962 by Edward Norton, MD, who was recasting the ophthalmology department at the University of Miami. On the basis of his reputation for being outrageous but breathtakingly innovative, Smith became Norton’s second faculty hire at the Bascom Palmer Eye Institute (after Victor Curtin, MD). Shortly after his arrival, he was joined by several other neuro-opthalmologists. They made up the finest roster ever assembled in the field (see accompanying article in this issue by Joel S. Glaser, MD, and an interview with Noble J. David, MD).

This “high-powered interview” took place at Dr. Smith’s home in South Miami on February 25, 2002.

JDT: What got you started in medicine?

JLS: Well, I enjoyed chemistry in high school, but I decided if I studied chemistry, I’d have to live in some place like New Jersey or Delaware. I wanted to work with people, and my Daddy was a board-certified internist, so I thought about studying medicine. My Daddy kept trying to talk me out of it. When I asked him later why he did that, he said, “I knew if you really wanted to do it, you’d do it anyway.” I applied to two schools: Duke and Emory.

JDT: Why do you think Duke accepted you?

JLS: I happened to be interviewed by old Dr. Hetherington, the histology professor, who was keeping track of who smoked cigarettes, pipes, cigars, and what not. I was probably the first bird he’d seen who was smoking a big old cigar.

JDT: What do you recall of the medical school days at Duke?

JLS: They were some of the happiest days of my life. Only three things I did not like: psychiatry, the well-baby clinic, and orthopedics. I liked medicine, I liked surgery, I liked OB-GYN. I delivered about 75 babies, but I got tired of getting up at two in the morning, so I decided to go into internal medicine.

JDT: How did you get sidetracked into ophthalmology?

JLS: At Duke I used to go to the Tuesday night lectures in ophthalmology by Dr. Banks Anderson, Sr. One night he talked for two hours about diseases of the sclera. That really impressed me. I couldn’t imagine someone talking for two hours about the sclera! So I began to read about ophthalmology. Then I had my big dilemma. I didn’t know whether I should go into ophthalmology or neurology.

After a year of medical internship at Emory, I was still agonizing over what to do. So I volunteered for two years in the Air Force. After that, I still wasn’t sure, but I remember my Daddy saying, “If you’re having such a hard time making a decision, do either one and you’ll be happy.” I decided I’d take a year of ophthalmology and find out whether I liked it or not. I applied to the Wilmer Eye Institute and the Massachusetts Eye and Ear Infirmary.

JDT: How did you decide on those programs?

JLS: Very simple. I asked just about every ophthalmologist I met or knew, “What are the best residencies?” In short order, I found out the secret. Where they trained was always
number one. So I crossed that one off the list. The rest were always the same ones, and Wilmer and Mass Eye and Ear were among them. I got accepted to Wilmer right away. I didn’t hear from Mass Eye and Ear, so I accepted Dr. Alan Woods’ invitation at Wilmer. Three months later, I got a telegram from Mass Eye and Ear accepting me. I’d have gone there because it was only three years and Wilmer was five, but the Lord was directing me because the program at Wilmer was very good for someone who was leaning toward academic medicine.

JDT: And at Wilmer . . .

JLS: After one year I knew I loved ophthalmology. I was particularly impressed that Howard McCann (MD) and Harold Pierce (MD), who were board-certified internists, had given up medicine for ophthalmology.

JDT: When did you move toward neuro-ophthalmology?

JLS: Early in my residency, I began attending Dr. Frank Walsh’s Saturday morning neuro-ophthalmology conferences and Dr. Richard Lindenberg’s Monday night neuropathology conferences at the morgue of the Baltimore City Hospital. I’d be the only ophthalmology resident at the morgue. In fact, I introduced Dr. Lindenberg to Dr. Walsh. Walsh, you see, didn’t want anything to do with Lindenberg because Walsh hated Germans. As a corpsman in the Canadian Army, he’d been shot in the chest during World War I.

That’s a very interesting story in itself. Early one morning, Walsh went out to evacuate a buddy and he was hit by gunfire. Later that day, the Germans brought out mustard gas and killed hundreds of soldiers. So Walsh figured that that German soldier who shot him actually saved his life.

Anyway, Lindenberg was a big Nazi—the chief pathologist for the German Air Force—and an expert in the
pathology of hypoxia and trauma. Right after the war, the Americans persuaded him to come to America. But he didn't like the American Air Force because they didn't have enough brains—dead brains. So he came to Maryland, where there was a plentiful supply of dead brains. In due time, Walsh and Lindenberg became great friends and wrote papers together.

JDT: When you became interested in neuro-ophthalmology, who were the leaders in the field?

JLS: (Frank) Walsh in Baltimore, (Alfred) Kestenbaum in New York, (David) Cogan in Boston, (Robert) Hollenhorst, (Thomas) Hedges, and (Wilbur) Rucker at the Mayo Clinic, and (David) Harrington on the West Coast. In place of my fourth year of residency at Wilmer, I chose to spend a year's fellowship with Dr. Cogan in Boston.

JDT: What do you remember of that period?

JLS: Well, Dr. Cogan had cut his neuro-ophthalmology consults to a modest number. The neurologists didn't want to send somebody with a fresh stroke over to another building in a wheelchair. So I started making rounds with the neurologists and neurosurgeons, and the number of consults picked up. We would see every admission to their services. They would automatically call Cogan's office and tell us the names. I got a big kit up: a binocular indirect, a Risley rotary prism, a Projecto-light for fields. And with all this stuff, I'd go over there. The neurosurgeons would love it because they could get an eye consult with the patient staying in his own bed! We were seeing stroke patients with the "King Fish"—C. Miller Fisher (MD). When the patients died, he would cut the old brains and make the correlations. There was tremendous material. I wrote 13 papers that year with Dr. Cogan.

JDT: You are famous for doing your own typing of consultations. Did you do that during your fellowship?

JLS: Yes. My Daddy had me take typing lessons when I was ten years old, and I won a typing contest—66 words per minute, as I recall. When I was in medical school at Duke, I would go to lectures and write as fast as I could. I'd take those notes home at night and type them out as fast as I could. I found out later that some people got a copy of my notes and sold them to medical students all over the South. In Boston, I would see the patient, take out my typewriter, type out the consult, put the top sheet in the chart, and keep the carbons for our records. And I kept that up until I retired.

JDT: How did Cogan and Walsh differ in their approach to patients?

JLS: Walsh worked up every patient completely himself. Cogan concentrated on the pertinent parts. So I learned from Walsh how to do the whole examination and from Cogan how to get to the problem the patient is referred for.

JDT: When you returned to Wilmer for your final residency year, what were the highlights?

JLS: Well, there was Dr. Walsh's Saturday conference. Old Dr. Ford (Franklin Ford, MD, chairman of neurology) was always there. Ford was very shy—never would say anything. But he was the final arbiter of neurologic diagnoses. Everyone knew that. One Saturday, they had this about 10-year-old child, very ill, and they were all arguing about what was wrong with this child. Dr. Walsh turned to Dr. Ford and said, "Dr. Ford, you haven't said anything. What's wrong with this child?" Very quietly, Ford said, "Measles encephalitis." In his booming voice, Walsh said, "Well, Dr. Ford says it's measles encephalitis. That settles it. Next case."

The BPEI "Founding Five" (from left): Smith, John Flynn, MD, Donald Gass, MD, Ed Norton, MD, and Victor Curtin, MD, 1963. (Courtesy of Bascom Palmer Eye Institute.)
Ford never drove a car. He never left Baltimore. The story goes that a very wealthy dowager lady in Chicago once sent a telegram to Ford offering him $10,000 to come to Chicago and consult on a neurologically ill child. Ford declined the offer but told the lady she'd see the child in Baltimore for his usual fee of $25!

JDT: Why didn't you stay on at Wilmer when you finished your ophthalmology residency?

JLS: Dr. Maumenee wasn't offering anything at Wilmer, and I didn't care that much about Baltimore. Besides, at Duke they had a deal where you could make a salary and then keep 50% of what you earned. So I went to Duke. And I had no intention of leaving there. But in 1962, I came down to Miami for a meeting of the Association for Research in Ophthalmology (the predecessor of ARVO), and I met Ed Norton, whom I had known from his visits to Wilmer. Norton picked me up at the Americana Hotel and took me over to the newly built Bascom Palmer Eye Institute.

He asked me what it would take to get me down there. "Well," I said, "I'd have to have five things: a resident assigned to me full time, and four rooms—an examining room for me and one for the resident, an office for me and one for a secretary. Norton said fine. But I said I didn't have the Florida Boards. Norton handed me some old exams to practice on. So I said, "I hate to wait to get on a golf course." And he said, "I belong to a few private courses here I could get you on." A few days after I got home, I received a letter from Norton offering me everything in writing. I figured if somebody offers you all that in writing and you don't take it, you're a fool.

JDT: Why was Norton interested in you?

JLS: Norton knew Cogan, and I had published all those papers with Cogan. Besides, anyone doing anything in neuro-ophthalmology would have been recognized. Bill Hoyt (MD) and I were probably the only residents in the country interested in the field.

JDT: But why would Norton want to hire a neuro-ophthalmologist when the only faculty member he had hired was an ophthalmic pathologist (Victor Curtin, MD)?

JLS: Norton loved neuro-ophthalmology. He had had a year of neurology. And he wanted to move over to administration. He knew he needed somebody in neuro-ophthalmology full time.

JDT: So you were persuaded to leave Duke, a medical powerhouse, for the University of Miami, which wasn't even on the medical map . . .

JLS: Yes, I was unhappy with ophthalmology at Duke because it was a division of surgery. It's very hard to hire ophthalmologists when there are only five general surgeons. I tried to get them to hire Don Gass (MD), who was a year behind me in medical school at Duke, and who subsequently became "the king of the macula." They wouldn't do it. So I went to the Dean and I said, "I want you to make ophthalmology a separate department." He said he'd take it under advisement. I took (and passed) the Florida Medical Board just for insurance. Then the Dean at Duke called me in and said, "We've decided not to make ophthalmology a department just yet." I resigned on the spot. Actually, I think I did Duke a big favor by leaving, because they had to make ophthalmology a department soon after that to hire the next guy.

JDT: When you came down to Miami, what did you find?

JLS: A sparkling new institute. Good facilities. Anything I wanted. In the whole 32 years I spent at Bascom Palmer, Norton never turned me down. Duke was an entrenched bureaucracy. Miami was brand new.

Smith playing the piano to the singing of Gaby Kressly, BPEI administrator, 1966. (Courtesy of Bascom Palmer Eye Institute.)
And Norton was terrific. Some chairmen are fearful of having people underneath them who are better than they are. Norton was the exact opposite. If he needed a pediatric ophthalmologist, he wanted someone like John Flynn (MD) who was better than he was. Norton looked at ophthalmology like a garden. He was the gardener tending the beds. All I wanted was for neuro-ophthalmology to be one of the flower beds in his garden.

JDT: How did you get going at Bascom Palmer?
JLS: I started to make rounds at 7 a.m. every Monday morning with Dr. David Reynolds (chief of neurosurgery) and his team with my penlight and direct ophthalmoscope. They loved it because they had neuro-ophthalmology coming right to them. They weren’t going to send postop craniotomy patients across the street to the Bascom Palmer. But I would go with them and see their patients for nothing. What that did was build a relationship with the neurosurgeons and neurologists so they would call me when they needed help. I decided you only needed two neurosurgeons and one neurologist, and they will refer you all the patients you could ever want.

I'd go on Tuesday mornings to the neurology ward on West Wing 11 and make rounds with the ophthalmology residents and medical students. I copied Walsh's Saturday clinic. Everyone would come to that. The ophthalmology residents could learn most of neuro-ophthalmology just by attending that conference once a week for three years.

JDT: How would you describe your style of examining outpatients?
JLS: I'd spend two to three hours on each patient. I did everything myself—including color fields and peripheral fields. Everyone else would farm this out.

JDT: Why didn’t you farm out visual fields?
JLS: Because the way I was taught by Dr. Walsh was to do your own fields. I took my own history. I didn’t have a check sheet.

JDT: Didn’t the residents take histories?
JLS: The residents would do them first and then present them to me. And then I would repeat everything. I had to double check. I extended and refined their observations. I did things routinely that other doctors didn’t do.

For instance, I would do a refraction—a retinoscopy—on nearly every patient. Patients would be sent in with visual loss. The neurologist couldn’t find anything wrong, and the ophthalmologist might have done a manifest refraction. But you retinoscope them and the guy has a big 3.75 cylinder at 100 degrees and you put that up and he has 20/20. In motility cases, I’d measure their horizontal and vertical phorias. Very frequently someone would be complaining “my eyes are not comfortable,” and I learned to put maybe one base up in one spectacle and one base down in the other. I learned that it was very important if somebody had a headache and you measured him in the distance, say 3 prisms of eso, and then the guy would come back six weeks later and have 10 prisms of eso. Well, that guy was getting increasing intracranial pressure with an increasing sixth (nerve palsy) and once he got out of his fusional range he’d be seeing double and have limited abduction. So by quantitating their phorias, I could pick up a lot of motility disturbances while they were preclinical. Same way with fields. You could take a red button (Bill Hoyt used to use a red jigger stick) and have the patients compare that color on both sides of the visual field, and you could pick up a lot of defects just by color confrontation that an ordinary perimetricist might miss.

I look at it this way: the difference between a general practitioner and a superb internist is spending another hour with the patient. Same difference between a general ophthalmologist and a neuro-ophthalmologist—you can be more meticulous in an extra hour. There’s no magic to it—it’s just doing hard work, doing the job instead of sloughing it off and finessing half of it. And that’s what concerns me about the medicine of today. With the pressure to see so many patients, you’ve got to cut corners, and you’re going to miss things.

JDT: Didn’t you feel any pressure to see a certain volume of patients?
JLS: No, Norton encouraged me in every way. I asked him when I first started, “Now what do you want me to do? How much time do you want me seeing patients? How much time doing surgery? Teaching? Research? Going out of town giving lectures? And I can remember his answer right now. He said, “I don’t care what you do, just go home tired at night.” So he was smart enough to know that if he let his faculty do what they wanted to do, they would do their best.

JDT: What was your greatest joy in going to work?
JLS: Finding some condition that something could be done about, teaching the residents about that, and helping that patient. This was one of the things about ophthalmology that was better than neurology. In neurology you could make a nice diagnosis but it might be an untreatable condition. But if the guy had diplopia, I could give him prism glasses. If he had poor vision, I could give him a better refraction. If you saw a guy that they thought had sinus headaches and you found out it was migraine, why you could put him on Imidril and prevent a lot of those recurrences.

JDT: I know that your religious conversion played a large role in your life. What about that?

JLS: I went to church as a young kid every Sunday with my family because in South Carolina that was the thing to do. I was baptized in a Baptist church when I was ten, but when I came up out of that water, the only difference was that I was wet. I was not changed one iota.

At the age of 33, I became what you call "born again." If you’d have asked me before then if I believed in God and Jesus, I’d have said yes, but it was the difference between having the Lord in your head and in your heart. In 1963, I went out to the Academy (American Academy of Ophthalmology Annual Meeting) in Chicago, and I saw Jack Cooper (MD) who had been a resident with me at Wilmer. We had been good friends, but I hadn’t seen him for five years. I went to all the lectures and exhibits with him, and he was totally different. I couldn’t put my finger on it. Then he invited me to a supper of the Christian Medical Society. The speakers talked about how they did 125 cataracts a day in these camps in Pakistan and India. Very interesting. Afterwards, we were sitting in the Palmer House in Chicago and just talking and I said, “Jack, something’s different about you, and I want to know what it is.” And he said, “Well, I’ve just turned my life over to Jesus.” And I said, “Now what do you mean?” He said, “I get up in the morning and I read the Bible and I go through the day trusting the Lord, praying for my patients. Since I’ve gotten into the Bible, my practice goes better, my surgery goes better, my relationships with my family go better.” And that’s all he said. He didn’t try to get me to join anything or say anything.

Well, I came back to Miami and I knew Jack had something that I didn’t have. I just knew that. So I told my Sunday School teacher, Albert Warren, about what I’d noticed about Jack Cooper. And Warren tells me, “Well, I used to be a professional atheist. I loved to ask people questions about their faith that they couldn’t answer. I’d love to get them all shook up to destroy their faith. One day a guy asked me three questions that changed my thinking. The first one was this: ‘Will you believe that a man named Jesus Christ ever lived?’ I said ‘Well, yes, there are records.’ The second question was ‘Will you accept the fact that he was crucified?’ I said, ‘Yes, that’s a common way the Romans executed people; many Jewish people were crucified.’ So he said, ‘All right, then here’s the third question: will you accept the fact that that tomb was empty on the third day?’ I said ‘Yes, that’s the way the story goes.’ ‘All right,’ he says, ‘If you believe that, then by horse sense there are only three ways that body could have gotten out of there. One way is he could have been raised from the dead. But that’s supernatural; you don’t believe that; we’ll table that; we’ll set that over here. Only two other possibilities: either his friends or his enemies took him out. If his enemies took him, why didn’t they produce the body to destroy the idea of a resurrection? It couldn’t have been his friends who took him out of there, because most of the early believers were Jews, and they had no reason to deny the resurrection.’”

So Warren said, “I got to thinking about those points, and I got down on my knees. I don’t guess I ever had prayed, and I said, ‘If You are real, I want to know the truth. There’s a lot of weirdo stuff out there, but if You’re true, I want you to come into my life, forgive me my sins, and give me some peace.’

Now, I’d never heard the Gospel presented where intellectually I couldn’t knock a hole in it. But all this made sense to me. We had an old South Carolina preacher preaching in Miami one Sunday afternoon in October ’63, and he said, “Anyone who wants to rededicate his life to Christ, come on down here.” So I did. And I said a prayer. I didn’t see a lightning bolt go shooting by, but my life began to change very dramatically after that.

JDT: In what way?

**SPIROCHETES IN LATE SERONEGATIVE SYphilIS, PENICILLIN NOTWITHSTANDING**

By

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Frontispiece of Smith’s book on syphilis, published in 1969. (Courtesy of Bascom Palmer Eye Institute.)
JLS: The first difference I noticed was down at the Coral Reef Golf Course where I'd go play golf. I'd hear all these men cursing and blasphemy and taking God's name in vain and telling dirty jokes and all, and I was not comfortable. I don't think they had changed their language, just the ears hearing it were different. I used to like doing all that junk—run around, smoking, drinking. I gave it all up.

The next year at the Academy Meeting, a guy came up to me at the meeting of the Christian Medical Society, and he said, "What are you doing here? I took the Lancaster Course from you in 1960 or 1961, and you were the most profane instructor I ever set eyes on. You couldn't say a sentence without at least two four-letter words in them. I said, "Who you talking about? Me?" And he said, "Yeah, you." So I suppose I used to cuss like a sailor, and blaspheme, and embarrass people. If you'd asked me before if I wanted to go down to the burle-Q and see some strippers and drink some beers, I'd have said sure. If you said, do you want to go to a Bible study, I'd have said no.

JDT: How do you account for that change in psychological terms?

JLS: I can't. All I know is the Lord flew in my heart and just changed me. Frequently after somebody has a conversion, their old hell-raising buddies fall away. But there's an exception that I call the "supernatural friendliness sign." And that is my relationship with Noble David (Noble David, MD, professor of neurology, University of Miami; see accompanying interview of him in this issue). He was my buddy when I was getting drunk with him, and he is my buddy when I'm playing cello and bassoon duets with him now.

JDT: So Noble knows the Lawton Smith B.C.—"before conversion."

JLS: Yes, and here's a story you'll enjoy. There were two carousing buddies in England, and one of them came to know the Lord and became a well-known Bible expositor. The two friends found themselves in a cathedral in France. The Bible expositor goes up to the pulpit to address the congregation, and someone passes him a note written by his old carousing buddy that says, "If you get up and talk about Jesus, I'm going to get up and tell the audience about all the things you used to do." That's the kind of note you don't want to get before you start preaching, right? So the expositor gets up and says, "I just got a note from an old friend of mine in the audience, and he says that if I talk about Jesus, he's going to tell about all the things we used to do together. I just want you to know that he hasn't heard the half of it!"

Any story you might have heard about me, I could come up with one that's worse. I did everything rotten that a person could do and never thought anything about it. I was terrific on Sunday morning from 10 a.m. to 12 noon, but I was like the biggest playboy you want the rest of the time. I had fun. But since my conversion, no question I've been able to give better patient care. Somebody said you can't care for the patient unless you care about the patient.

JDT: Did religion enter your medical practice?

JLS: I started praying for patients after the examination. Let's say a woman had a four-year-old child with a chiasmal glioma. And the mother would be very distraught. They'd get ready to leave my office, and I would say, "Would you mind if I said a prayer for your daughter?" Their eyes would get big as saucers. Speechless. And I interpreted speechless as being "yes." Or they'd say, "Please do." I don't recall but once or twice in my 32 years somebody saying, "No, I don't want you to pray for me." In which case, when they left, I'd pray for them. I'd say, "Dear Lord, I pray for little Sally. If she has to be operated on, that the surgery will go well, that the anesthesia will go well, that there won't be any postoperative complications. Body and soul, financial and social, in every way I'm praying for you." That'd take about 20 seconds. Many times they would weep. And God would answer that prayer and the surgery would go well.

For Jewish patients, I would pray to the God of Abraham, Isaac, and Jacob. Once I prayed for an old Jewish man from Miami Beach. He came back a year later for a follow-up, and when the examination was over he wouldn't leave. I said, "Is there anything else I can do for you?" And he said, "Doctor, last year you prayed for me. Aren't you going to pray for me again?" He just wanted that brocha, that blessing.

I got hundreds of thank-you notes over the years of how much they appreciated that I'd said a little prayer. Everybody talks about treating the whole patient—body, soul, and spirit. In neurology, neurosurgery, and neuroophthalmology, you see patients who are frightened. They may not tell you, but they are terribly frightened. Daddy's aphasic now, or mother's getting Alzheimer's now and she can't remember her own daughter's name—all these kinds of things. I didn't try to tell them to join this church or go to that, I just wanted to pray for them that God would minister a little bit of compassion.

JDT: Did your religious zeal ever get you into trouble with patients?

JLS: I had complaints less than you can put on one hand, but sometimes I used zeal when I wasn't very wise. I'll give you the outstanding case.

During the Vietnam War, there was a young captain who began to have headaches. They thought he had papilledema, and he got evacuated all the back to Walter Reed (Army Medical Center, Washington, DC). Every time they did his fields, they got smaller. Walsh saw him at Walter Reed and thought he had optic nerve drusen. He was about to get 100% disability and discharge from the military because of field loss associated with drusen, but they sent him down to see me for another opinion. Well, he did have optic...
nerve drusen—looked like rock wool candy on both discs—but his color peripheral fields were bigger than his white fields. And it was obvious that this was functional. So I got Alan Bird (MD, London, England), who was here at the time to do the fields, and he said they were functional. John McCrary (MD) did them too, and he said they were functional.

So I sat down with the captain and said I thought this was a self-limited condition, that it would improve, and that he didn’t need to be fearful that he was going blind. Then I told him he should cast his troubles on the Lord, and I prayed for him and I gave him the Van Dusen letter, which is a Christian apologetic that the Campus Crusade for Christ uses. He went back to his congressman, showed him the literature I was giving out, and convinced him that I had gone crazy. (At least the congressman got to read the Van Dusen Letter!)

Well, the complaint came down from the congressman to the Dade County Medical Society and to the Dean of the Medical School, who passed it on to Norton. Norton called me in, and you’ll see Norton’s wisdom here. I told him the story and that Alan Bird and John McCrary had confirmed the diagnosis. Norton’s comment was “Well, I might have known it.” What had knocked the case over the center field fence was the fact that Bird and McCrary had both found the same thing. That was the end of it. It’s like old Dr. Walsh said years ago when some doctors complained that he was showing their patients at his Saturday conferences. “Doctor,” he said, “this is how I practice. I like to use these cases for teaching medical students. If you don’t want me to show them, then don’t refer them to me in the first place.” Bill Hoyt used to say that whenever a head pops up above the crowd, there’s always a thousand people with baseball bats to knock it back down. That’s the way I’ve remained all along.

JDT: As you look back, which of your professional contributions are you proudest of?

JLS: Well, this weekend (at the Bascom Palmer 40th anniversary celebration), several doctors have come up to me and said, “I want to thank you for what you taught me 25 years ago. It’s influenced my practice all these years.” Now that’s very meaningful. Scientifically, one of the biggest things I did was to get ophthalmologists to recognize that patients could have late ocular and neurosyphilis despite a nonreactive serum VDRL. And they would start doing the FTA-Abs test and find many, many patients with reactive FTAs and negative VDRLs.

JDT: How did you get into the syphilis work?

JLS: Well, that is interesting. At Wilmer, they had a guy named Bob Nelson who came down to do a medical residency, but he had six months’ spare time before his residency was to start. So he began doing experimental syphilis research with Tommy Turner, who was subsequently the
dean at Hopkins. And one night, he looked under the dark field microscope at a slide of virulent *T. pallidum* swimming and moving like mad. He put a drop of normal rabbit serum on there, and they’d keep spinning. But when he put a drop of rabbit serum from an animal that had been infected with syphilis, in short order the *T. pallidum* would be immobilized. So he invented the Treponemal Immobilization Test (TPI). It was called the Nelson Test.

I was a rube-like eye resident seeing optic atrophy and retinitis pigmentosa-like fundi, and dislocated lenses, and light near dissociated pupils, and I’d get a VDRL or RPR and it’d be negative. So I’d draw some serum and send it over to Nelson, and it’d come back positive. Then I’d talk to the patient, and he’d admit he’d had gonorrhea three times or he’d been treated with hip and arm shots of Salvarsan or bismuth back up and down the road, and I’d realize that the guy had had syphilis.

So I set up a lab and did experimental syphilis research with monkeys and rabbits for years, and wrote that book in 1969 on “Spirochetes and Late Sero-negative Syphilis—Penicillin Notwithstanding.” We found people who had been treated with penicillin who still had spirochetes. Those spirochetes could be in a dormant state, but give that patient steroids and it’s like vitamins—the organisms become clinically active.

JDT: What other contributions stand out?

JLS: Well, I’ve studied a lot of different things. Gordon Miller (MD) and I wrote the first paper in the English literature on ischemic optic neuropathy. We sent it to the AJO (American Journal of Ophthalmology) with the title of “Ischemic Optic Neuritis.” They didn’t like that title; they said we don’t know it’s a neuritis. Call it a neuropathy, they said. So we did. I think I was the first person to use the term “bull’s-eye maculopathy.” That was in a paper on chloroquine retinopathy.

Later I got interested in histoplasmosis in the retina of pigeons. I tried to dilate pigeons’ pupils with neosynephrine, tropicamide, and scopolamine, and never could dilate them. I read that pigeons have striated muscle, not smooth muscle, in the iris. So we made up some drops of curare, and that dilated the pupils beautifully. I reported that with Danny B. Jones (MD). Here’s something interesting about histo. Chickens don’t get it because their body temperature is too high. But if we would inject histoplasma intracarotid into chickens and put them in the icebox, they’d come down with beautiful granulomas in the iris, the choroid, and the retina. We reproduced the fundus picture that you see in humans.

JDT: What about other clinical work?

JLS: We did a lot on ophthalmodynamometry. They’d be putting a clamp on some guy’s carotid artery for treatment of a giant intracranial aneurysm. They’d start tightening the clamp, and we’d check for pulsations; after a certain number of turns—whammo! The pulsations would appear, so we’d tell them to back off. Then they knew they had to make that last turn very carefully—say an eighth of a turn at a time.

Another paper I’m proud of is the one on skew deviation I did years ago with Nobby David (MD). Prior to that, skew deviation was an ill-defined condition. We found that there were three groups: 1) fully comitant (same degree of vertical misalignment in all gaze positions), 2) laterally comitant (same degree of vertical misalignment only in one lateral gaze position and ortho in the other), and 3) simulating an isolated extraocular muscle weakness. So I think we made a contribution by showing the things skew could look like.

JDT: How have you occupied your time since you retired in 1994 from Bascom Palmer?

JLS: I teach a Bible study class of 15 or 20 people every Tuesday night at home (which I’ve done for over 25 years). I spend a lot of time preparing those lessons on Monday and Tuesdays. Every Saturday morning we have a men’s prayer meeting in this room—maybe 8 to 10 men. I’ve been going to Fort Lauderdale once a month to work with a black pastor, and we take out inner-city boys 6 to 16 years of age to a
Smith with Norton, the “Big Boss of the Cosmos,” at the time of Smith’s retirement, 1994. (Courtesy of Bascom Palmer Eye Institute.)

cafeteria and then show Christian videos and testimonies of successful black people.

JDT: Are the boys receptive to you?

JLS: Well, when I first started going out there 7 years ago, it was a rough group, and I was the only white face. They naturally wanted to know where I’m coming from. They had not encountered a white senior man interested in them. But after I kept coming, and paying for all their meals, they came to trust me. I stay busy. I walk an hour a day.

JDT: In the middle of the summer too?

JLS: Sure, early in the morning, before it gets hot. I go in the pool here at the house every day from May to October. I took up the bassoon in 1996. I’ve got a great teacher, the second bassoonist of the Florida Philharmonic.

JDT: You have three children?

JLS: Two boys and a girl. The oldest, Lawton Jr, is a pilot for Executive Jet, which is one of these private charter companies. He lives in Leesburg, Florida. My daughter, Polly, is married and lives in Lakeland, Florida, and my younger son, Coleman, is a pilot with Continental and lives in New Jersey.

JDT: Two pilots? How’d that happen?

JLS: The guy across the street is an old retired Eastern Airlines captain; two houses back there is an old Pan American captain. These guys would fly for two days and be here for four or five days playing volleyball. I was gone at work all day long. The children saw that the pilots were making good money and were home a lot.

JDT: What about the famous J. Lawton Smith neuro-ophthalmology audiotapes?

JLS: I did one every month for 20 years. American Board of Ophthalmology examiners have told me that, in past, virtually every candidate had prepared for the neuro-ophthalmology part of the Board with those tapes. One doctor told me “yours are the only medical tapes my wife will let me listen to in the car because she likes to laugh at the stories.”

JDT: Looking back, how would you summarize your career in neuro-ophthalmology?

JLS: I don’t think I smashed the atom into 64 equal parts. I just did careful ophthalmologic examination on sick neurologic patients by going to the wards. That is how Walsh got started on his book. He would go out to Baltimore City Hospital and make rounds with Ford on those wards filled with people who were permanently hospitalized. He’d keep a copy of his notes, a copy of the x-rays, and he’d bind it all in a notebook and put that together and that was his first edition of the book. I did the same thing, except I had access to more refined instrumentation—indirect ophthalmoscope, rotary prisms, ophthalmodynamometry, Projector-light pointer.

Now the tools are better. But a lot of ophthalmologists don’t see sick neurologic patients. So when a guy trains in neuro-ophthalmology, he should not only be in your private office with you; he should go over and see those patients on the ward.

LANGUAGE BY LAWTON

A JLS lexicon compiled by Joel S. Glaser, MD

Acey case. An interesting or unusual clinical case. Material for a potentially reportable publication. Sometimes preceded by this statement to the patient: “Lady, it is my duty to inform you that everything you are about to say or do is going to appear in the Archives of Ophthalmology.”

Ace, Big. Anyone who gets anything right, anytime (as in “you Big Ace!”).

Action totalis. Doing an examination of a neuro-ophthalmologic patient (as in “swing into action totalis”).

Avogadro’s number ($6 \times 10^{23}$). A large amount, but usually used as the reciprocal to express the extreme rarity of a condition or manifestation (as in “that case is a one over Avogadro’s number”).

Big boss of the cosmos. Ed Norton, first chair of ophthalmology department, BPEI.
Big Dog. An expert whose opinion carries weight—more weight than a Big Ace. (See also Heavy Hitter, below.)

Big ignore. What a baby or child gives you, the examining physician, after your first attempt to get the patient’s attention.

Blind dog in a meat house. Chaos among doctors working up a medical case (as in “they were runnin’ around like a blind dog in a meat house”).

Careful refraction. One that starts with retinoscopy, takes a long time, and usually ends with the discovery that the previous refraction was incorrect.

Club. A collection of experts in other specialty groups (as in “the Retina Club,” “the Strabismus Club”).

Cyclops with rotary nystagmus. A very rare case. (See Glass cage, below.)

Dead hog in the sunshine. Ultimate state of bliss (as in “Happy as a dead hog in the sunshine”).

DKAs. Doctor-killing abbreviations. Annoying, elusive medical acronyms used by other authors (not including FTA-Abs, TPI, RPR, or other Smith favorites).

Diagnosing pregnancy with the placenta in your hand. Making a diagnosis long after it was obvious.

Dockey. Affectionate greeting of another physician whose name is beyond immediate recall. Frequently used with “Now you’re talkin’, Dockey.”

Down in the country. Always applied to the practice of medicine, meaning a simpler, better way, where “treatin’ doctors,” rather than “high-powered, underwater physicians,” hold sway.

Door. Used to denote where patients go when they see a doctor who has frightened or hurt them, as after one or more lumbar punctures (as in “when you come in the front door, the patient goes out the back door”).

Eating into your brain like a rat. A preoccupying thought, a troubling idea or obsession as you are working through a medical case.

Examination. Used in this classic remark: “The doctor is interested in the first two hours of the examination; the patient is interested in the last five minutes.”

Gems. Critical and practical teaching points. Used interchangeably with Pearls; see below (as in “now this here is the gem of this case”).

Glass cage in London. Where an extremely rare condition may be found.

Heavy Hitter. Respected physician. Used interchangeably with Big Dog; see above.

Homemade sin. Always follows “Rare as ...” to denote a very uncommon condition.

Hot seat. The ophthalmic examination chair.

Joe. Exemplar (as in “Joe Cool” or “Joe Retina”).

Knock it out of the ballpark. Get it right.

Malignants. Extremely advanced (as in “nystagmus malignans”).

Massage. A thorough workup, usually excessive, expensive, and largely unnecessary (as in “she got the neurosurgical massage”).

Midnight in a coal mine. Utter darkness, used to denote very poor vision (as in “he couldn’t tell the difference between midnight in a coal mine and an atomic blast”).

Moment of truth. The instant when the diagnosis is about to be revealed.

Mmmmmmmmmmm. A sound elaborated by Smith in wide vibrato through closed lips to indicate that something interesting about a medical case has, or is about to be, revealed.

Now you’re talkin’. You finally got the answer.
Nux vomica. Superannuated therapy or tradition (as in “that went out with nux vomica and high button shoes”).

On the hoof. A live encounter, raw data.

O.V. An office visit. The ultimate truth-revealing clinical encounter; a gold standard against which all other high tech procedures pale in significance; a careful and mutually exhausting history-taking session.

Pearls. Critical, practical teaching points. Used interchangeably with Gems; see above.

Rube. An unsophisticated physician. “Rube-like” behavior is what you do when you haven’t learned . . .

Serum rhubarb. Any obscure serologic test ordered by someone else.

Smoke cleared. Always used with “when the smoke cleared” to mean the denouement, the residue, the outcome after a series of clinical events. Usually used when a clinical disaster has followed mistakes (by others).

Subaquatic workup. One characterized by excessive and usually unnecessary use of high-tech studies. Sometimes used synonymously with “underwater.” Often associated with a walletectomy, see below.

Toughy. A doctor who knows something. Used especially in reference to William Hoyt, MD (as in “Toughy Hoyt”).

Twin Smitties. High-tech equipment. (The origin is a brand of hotrod exhaust mufflers.)

Walletectomy. Part of an expensive, usually unnecessary treatment or workup.

Wheel rolled off. Desperate medical straits; a disaster, usually occurring elsewhere (as in “when the wheel rolled off, she was blind”).

Wowser. A doubter, a skeptic. Anyone demanding rigorous data before accepting a diagnosis. A “wowser malignans” doesn’t believe anything, anytime.

Zygote. Lowest rung on scale of educable individuals (as in “this is ocular motility for zygotes”).

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Noble J. David, MD, Reminisces

Jonathan D. Trobe, MD

Noble J. David, MD, always known to his friends and devotees as “Nobby,” has been a member of the round table of neuro-ophthalmologists who set the tone and ground rules for our subspecialty in the mid-20th century. He came up through the same circuit—Duke, Harvard, and the University of Miami—that prepared many of the other accomplished progenitors. Generally regarded as the most literate raconteur in a field of raconteurs, he can recount his history better than anyone. Written with customary grace and humility, here it is:

“I was born in 1927 in Jacksonville, Florida, the sixth child of Syrian immigrants. My father had come over at age 16 and later gone back and married my mother, who was in nursing school at the time. There were no trained physicians in my family, but my mother’s uncle and father were amateur medics in the small mountain village where they lived. My father had a high school education but became very fluent in English and was often a public speaker.

“My mother had apparently run out of ‘normal’ names when she got to me. I’ve long since become totally accustomed to the confusion of name reversal (David was obviously a first, not a last, name) in school, at airline and hotel desks, and in my dealings with society in general. I was never at all sure that I wanted to be a physician, although a brother ten years my senior became a pediatrician. I went through undergraduate school at Duke waiting to be drafted into the Army but was never taken because of the war’s ending. I applied to Duke Medical School, fairly certain of rejection, because I wanted to spend another year studying English and trying my hand at writing. Much to my surprise I was accepted and sternly encouraged by my father to enter medical training.

“In my first day as a medical student in the Duke Class of 1952, I was intrigued by a tall, red-headed, drawling South Carolinian who spoke in unique slang. Lawton Smith was one of a score of memorable students in that class, but it is fair to say that for four years he was usually the center of attention. I would regard Eugene A. Stead, MD, the chief of medicine, and Talmadge Peele, MD, PhD, a splendid neurologist and neuroanatomist, as the most influential amongst many fine teachers at Duke. Lawton collected “Peele’s Pearls” in a typed compendium that made the rounds as a study manual. Upon graduation, Lawton and I both ended up in as interns in internal medicine at the Grady Memorial Hospital, and after that year, both of us went to Korea as physicians in service.

“Until that time, I had only considered practicing internal medicine and returned to Duke after military discharge to resume my training. In 1957, Albert Heyman, MD, whom I had known at Grady, invited me to do a 6-month fellowship studying stroke. I was available because a cardiology fellowship had not panned out. Before long, it was clear that I was a neurologist at heart. I completed my training at Duke with a short stint with Raymond Adams, MD, chief of neurology at Massachusetts General Hospital (Harvard). I then became the chief of the neurology service at the VA Hospital in Durham for a couple of years and prepared to enter private practice.

Nobby” David as a sophomore at Duke University, 1945.
David as his alter ego, Rhett Butler, in his first year at Duke Medical School, 1948.

"Under a barrage of exhortation and suasion from the irrepressible Dr. Smith, I agreed to move to Miami in 1962 to set up a VA neurology service and to continue studies with the technique of fluorescein fundus angiography, which I had begun at Duke with Dr. Heyman. The VA hospital was in Coral Gables, a converted hotel, which has now been mercifully restored to what we know as the Biltmore Hotel. Smith and Edward Norton, MD, chief of ophthalmology at the newly opened Bascom Palmer Eye Institute, were the driving forces behind my recruitment, and I also had a small research space at the BPEI. Shortly after my arrival, Johnny Justice, our ophthalmic photographer at the Durham VA, came down to be interviewed. In the course of his stay he took some beautiful fluorescein pictures on a camera we had assembled. Justice's images fascinated Norton and vindicated Smith's extraordinary efforts to get the technique started at the BPEI.

"We did experimental fluorescein photography in monkeys, eventually developing cinematography of this contrast method. We also were the first to take infrared pictures with indocyanine dye.

"In 1968, Robert Daroff, MD, joined me at the VA and set up his studies of ocular motility. For the 12 years that he remained in Miami, I enjoyed the company of an ideal colleague and friend. His many successes have not surprised me.

"I suppose you could summarize the rest of my career as a mix of clinical teaching, patient evaluation, and some clinical studies, such as an interest in pituitary apoplexy. I saw my first patient with this fascinating disorder in 1964, and have followed the development of our understanding of this event as a clinical entity, primarily advanced by the remarkable resolution of anatomic detail provided by CT and MRI.

"I became semiretired in 1999, but still see private consultations and attend the neurology clinic at Jackson Memorial Hospital. I hope to be around long enough to sense the direction and fate of our hybrid specialty. Looking back, I wouldn't want to have missed any of it."

The following interview of Dr. David was conducted at his home in Miami on February 25, 2002.

JDT: How did you get interested in neuro-ophthalmology?
NJD: In 1960, my future as a Duke faculty member was pretty bleak. I wasn't doing anything they were interested in. But I did have an interest in fluorescein angiography. I'd learned that technique from John Hickam, MD, who had been faculty at Duke and then left to be chairman of medicine at the University of Indiana. Hickam was interested in the ocular circulation for what it would teach him about vascular reactivity to carbon dioxide and oxygen. Novotny and Alvis, who are usually credited with the discovery of fluorescein angiography, were medical students working in his lab on a summer project. Hickam left on sabbatical and told them how to get contrast pictures of the fundus. They perfected the technique. Novotny went on to become a psychiatrist and Alvis a urologist, but Hickam came to Duke in
1960 to give a talk on the technique. He showed Dr. Albert Heyman, a neurologist, and me the pictures and how to do it.

JDT: By the way, is Hickam the Hickam of “Hickam’s dictum,” the axiom you are so fond of quoting?

NJD: Yes. It stands opposite to Occam’s razor, also known as “Osler’s rule,” or “one disease to a customer.” Hickam’s dictum says that a person “can have as many diseases as he damn well pleases.”

JDT: Getting back to fluorescein angiography, would it be correct to say it was discovered at Indiana but not really applied to ophthalmology until you took it on?

NJD: Yes, it’s a long story. We had a photographer at the VA hospital in Durham named Leonard Hart who had an old Bausch and Lomb fundus camera. We put filters in it and began to take pictures. Hart had a young man named Johnny Justice running around the lab—the same Johnny Justice who later worked with Don Gass (MD) at the Bascom Palmer Eye Institute. Anyway, I was interested in seeing if we could tell papilledema from congenital disc conditions and whether we could find any difference between inflammatory, ischemic, or other types of disc conditions.

JDT: Did you find anything valuable?

NJD: No. There was nothing fundamentally different about any of the acquired optic nerve conditions. The chief of medicine at Duke—neurology was a division of medicine—was not interested in finding further research in fluorescein angiography. I owe the next move to Lawton Smith (MD).

JDT: How was that?

NJD: I had known Lawton since the beginning of our medical school days at Duke in 1948. He came back to the Duke faculty in ophthalmology in 1960 after finishing his neuro-ophthalmology fellowship with Dr. David Cogan in Boston. I was chief of neurology at the Durham VA hospital, and we would hold neuro-ophthalmology conferences—double podium stuff, Huntley-Brinkley style, two slide projectors—and everyone attended.

Lawton became increasingly chafed at the fact that ophthalmology was a division of surgery. He was looking for another position, and Norton hired him for the Bascom Palmer Eye Institute in 1962. Then Smith proselytized me. He had convinced Norton that he should bring me down to do some neurologic teaching and set up the fluorescein angiography technique.

JDT: Did you hesitate about moving to Miami?

NJD: Yes. I was highly suspicious of any Miami enterprise just because so much in a resort area is apt to bear the earmarks of quackery and sharp dealers. I didn’t know much about the University of Miami School of Medicine except that one of their graduates, Marty Liebling, had become a chief resident in medicine at the VA in Durham, and he was a very bright and able man. So I was curious. But there wasn’t much history there. The University of Miami School of Medicine opened in 1953. Florida had no anatomy law before that, you see.

JDT: Why should Norton, an ophthalmologist, want to bring down a neurologist when he had barely recruited any faculty in his own specialty?

NJD: Well, Norton had a strong interest in neuro-ophthalmology, and I think Lawton just wanted company. We may have fantasized about writing a neuro-ophthalmology textbook. Lawton and I had been joint authors on some articles—one on skew deviation, one on the corneomandibular reflex, and another on fluorescein angiography of a hemangiomia of the choroid. I took the pictures.

JDT: How did the recruitment go?

NJD: I came down to Miami and talked to Norton and to Peritz Scheinberg (MD), chief of neurology, and showed them some of the fluorescein angiography pictures. I think Norton could tell that I wasn’t sophisticated about the anatomy and physiology of the eye, which I certainly was not. But Scheinberg was looking for someone to work in his cerebrovascular disease lab, where they were studying animals and doing Fick principle studies on humans, too. I really didn’t have any interest in that. But since Norton was acting dean, once Lawton had persuaded him that I should come, he didn’t have much trouble persuading Scheinberg. Also, there also was not much going on at the Miami VA Hospital (housed in the Biltmore Hotel—seven miles away from the Medical School and Hospitals) in neurology then—just one full-time resident, supervised at a distance.

JDT: Did the salary offer come from Norton in ophthalmology or Scheinberg in neurology?

NJD: From Norton. But it didn’t sound much better than what I had made as a neurology resident. I told Lawton to forget about it. He called Norton and said, “The guy’s gotta have more oxygen.” So the offer finally got to where I figured I could do it. I was hired to start a neurology service at the VA, teach neurology, and set up the fluorescein technique. When my father heard I’d accepted the offer, he wrinkled up his nose and said, “If Sodom and Gomorrah were near Miami, the residents would come over from there to Miami on Saturday night.”

JDT: Your first impressions of Miami?

NJD: At first I was a little intimidated by the place because I’m not that much of a sharpie. Here were all these big hotels on the beach, where they would set up the Bascom Palmer Annual Neuro-Ophthalmology Symposium. At first I was self-conscious out in that social setting, but then it got to be fun. Go to an elegant hotel, live there for a couple of days, have a little resort life, meet all these interesting people—it didn’t take me long to get excited about it.

JDT: How did the job turn out?

NJD: Well, I saw private patients in the Rare Book Room of the Bascom Palmer Eye Institute Library. This was all
Norton could spare. I'd seat the patients in a library chair. I never needed to undress them. I thought you learned more from talking to them. I didn't use much equipment—a pin, a piece of cotton, a hammer, an optokinetic tape. And if I needed a slit lamp or ophthalmoscope, I could take the patient into a nearby examining room. If I said something droll while I was dictating, Reva Hurtes (the BPEI librarian then and now), sitting a few paces away, would laugh! I always felt I was something of an orphan over there seeing patients at Bascom Palmer.

JDT: When did your research get started?
NJD: Norton suggested I put in a grant to NIH to fund experimental research in fluorescein angiography. I got money approved there and separately at the VA and set to work ordering Zeiss fundus cameras. The only Zeiss camera was one that had been smuggled in from Havana by Olga Ferrer (MD). It was sitting unused in a back room at Bascom Palmer. A couple of months after I got there, I assembled my filters and I got Al Weinberg, the chief of medical illustration at the VA, to help me take the side off Olga's camera, and install the filters. Olga walked in while we were working on this dismembered camera, and I thought she would have a stroke. "What are you doing with my camera?" she said. "Olga," I said, "don't jump to conclusions. You're going to love this thing."

I could never get it to work, but Johnny Justice came down a few weeks later and got the focus right. He took a series of pictures that Norton swooned over. Everyone was set in motion. Don Gass (MD) was interested, and within a few months, they held the first fluorescein angiography conference that is still a weekly tradition at the Institute.

JDT: In what direction did the research go?
NJD: I went on to study retinal artery occlusions. The article we published (Gass and Smith were authors, too) was the first new descriptive material since von Graefe had done his very thorough original description. We saw the early filling of the retinal veins, ciliary circulation, and that dye was still flowing in the occluded central retinal artery but that it was greatly slowed. We could see sparing of the cilio-choroidal circulation.

In 1969, by the time the first International Conference on Fluorescein Angiography was held at Albi, France, I had completed most of my experimental work on fluorescein angiography—air embolism, autologous clot embolization, the effect of CO₂ and oxygen on the reactivity of the retinal vessels; and the effect of raising intraocular pressure by Dr. Tadashi Fujino's method (with a fine needle placed in the anterior chamber). With high intraocular pressure, we demonstrated the ischemic ring around the disc in the choroidal circulation. Doug Anderson (MD) got interested in this for glaucoma research.

JDT: Weren't you also the first one to perform indocyanine dye retinal angiography?
NJD: Yes. Along about 1968, my photographer, Earl Choromkos, on loan from the laboratory of research neurologist Kyuya Kogure, MD, came upon this indocyanine dye that they were using for cardiac output studies. Looking at its spectral characteristics, Choromkos wondered why we couldn't get an angiogram of the choroidal vessels unobscured by the pigment epithelium if we used infrared filters and film with this dye. So we did. First we took pictures of the surface of the monkey's brain circulation, but then we went to fundus pictures of the monkey and got those pictures that showed the choroidal pattern so well. We got some pictures in humans too, and reported this at Albi in 1969, but the amounts you needed to inject in man were too large, so after many futile attempts to make the technique clinically useful, we abandoned it. Three years ago, Larry Yannuzzi (MD) told me they were using indocyanine to distinguish wet from dry macular degeneration. They had discovered new techniques, but the principles were the same.

JDT: What about your role in carotid artery thromboembolism and the eye?
NJD: It began way back in 1957, when Dr. Al Heyman, one of the neurologists at Duke, learned that I had failed to get a cardiology fellowship (I was in training in internal medicine). He asked me if I wanted to spend six months seeing neurology patients. He aimed to collect 100 consecutive patients with stroke and characterize them as thoroughly as possible. So that became my first endeavor in neurology. It produced a paper that helped predict outcome in stroke. For instance, we showed that a well-lateralized brainstem stroke had a better prognosis. Bilateral signs raised the suspicion, I suppose, of truncal basilar involvement. And this was ominous in terms of survival.
In 1959, Miller Fisher published his observations about the fundus oculi during amaurosis fugax (and showed traveling intravascular particles). Heyman and I were very interested in his stuff. A patient of ours had had a bad stroke after carotid endarterectomy. He died, and we were able to obtain the eye, the brain, and the carotid artery, and show that the material in the carotid bifurcation, the retinal vessels, and the brain vessels was the same—cholesterol esters.

JDT: Where did that observation lead?

NJD: It further heightened suspicions that more strokes than we had previously imagined might be from emboli that came from the carotid. Some literature had sprung up tying angiographic carotid stenosis and stroke. DeBakey and others were beginning to operate on these arteries. We began to inject fluorescein into the arm vein, and two observers, each looking into one eye of the patient with an ophthalmoscope, would watch for the appearance of dye—and signal it by hitting a switch. So, we did the first arm-to-retina circulation time and reported it in 1961. You needed to have advanced carotid stenosis before you could appreciate a relative delay between the two eyes.

JDT: What else was going on here in Miami in those early years?

NJD: In 1962, when I came, there was almost no VA service in neurology. With a lot of help, especially from Dr. Scheinberg, I eventually got together a 30-bed neurology ward and a solid resident rotation from neurology and internal medicine, neurosurgery, and psychiatry. As this was...
developing, Bob Daroff (MD) came down to spend six months as a fellow with Lawton Smith in 1965. Lawton would come to the VA once a week, have rounds, and then go off to lunch. We’d show him our best cases, and he’d tune into whatever kind of research we were doing.

Shortly after that, Norman Schatz (MD) came down to spend six months with Smith. In 1966, Daroff, who was in the military, told me he’d like to come back to Miami to work with me at the VA. When Daroff got out of the army, he spent a year with Bill Hoyt in San Francisco. And when he finished, although San Francisco had offered him a position, he elected to come back here in 1968. He was my first faculty recruit. Several years later, Todd Troost (MD) joined us at the VA. In 1968, we had moved over to the present Miami VA Hospital. Small amounts of research money were easy to get then. Daroff wanted to study ocular motion. We got the money for him, and soon Lou Dell’Osso (PhD) and Larry Abel (PhD) and others joined him. By 1968, the VA neurology program had a research budget of over $500,000. We had become half the staff and research budget of the department of neurology of which we were an integral part.

JDT: How many people were doing neuro-ophthalmology at the University of Miami in those years?

NJD: Dr. Stanley Thompson has said that in the 1970s, we had the largest stable of neuro-ophthalmologists in the world: Smith, Glaser, Daroff, Troost, and me in clinical work, and a lot of others doing research. Troost left in the late 1970s for the University of Pittsburgh, and when Daroff left in the early 1980s to be chief of neurology at Case Western Reserve, Troost joined him. Troost later became chief of neurology at Bowman-Gray. Lawton retired in 1994, and Joel Glaser left the Bascom Palmer with Norman Schatz several years later. Now they are back in a part-time role.

JDT: What do you remember about the give-and-take between the Miami neuro-ophthalmologists?

NJD: There was a kind of rivalry. We were given to pranks. For instance, things usually happened at Lawton’s Saturday neuro-ophthalmology conference. It was a show you didn’t want to miss. Norton usually came if he was in town. In fact, most of the ophthalmology faculty came. Lawton ran those conferences with total influence over the course of events. He’d bring patients in, just as his mentor, Frank Walsh, had done at Wilmer. One morning, Lawton was showing a patient with a peculiar type of nystagmus. He was in the middle of his spiel when I grabbed my penlight and, while Lawton still had his hand on the top of the patient’s head, I asked if I could just peek into his throat. “Lawton,” I said, “he’s got palatal myoclonus.” And without losing a beat, Lawton continued, “I’m glad you mentioned that, because palatal myoclonus has an important place in the differential diagnosis!”

I remember a patient on Lawton’s rounds with complete abduction deficits in both eyes. We knew the diagnosis was myasthenia gravis, but we didn’t tell Lawton. Lawton looked at him and said, “These pupils aren’t equal. Now in multiple sclerosis, it is not uncommon to see unequal pupils.” While he was going on about this, a resident was sneaking in some Tensilon, and pretty soon his eye movements were completely normal! You see, Lawton noticed everything, and sometimes that was a handicap.

JDT: What was Daroff’s contribution?

NJD: He legitimized research on eye movements, particularly in the interface between experimental and clinical research. I think he was a leader—maybe the leader—in clinical research in this area. When he was getting started, he
told me how little enthusiasm the big names “up east” had about this field. This was true of neurologists from 1955 to 1970. Their eyes would glaze over when you began to talk about eye movements.

JDT: What about Lawton Smith’s contribution?

NJD: What Lawton made clear to me and to Daroff was what Cogan and Walsh had impressed on him, namely, that there were a number of pathognomonic neuro-ophtalmic signs that had not been well studied up to that time—like internuclear ophthalmoplegia and ischemic optic neuropathy. And you had to study many patients to recognize the signs—you couldn’t just come to them intuitively. Finding 95% rules in neurology is not that easy, but in neuro-ophtalmology there are a lot of phenomena that approach that in reliability.

JDT: What do you remember about Lawton Smith before his religious conversion?

NJD: I remember everything, but I can’t reveal it! Let’s put it this way: I don’t think his hypothalamus has changed, just that his superego has got control over it. He was outrageous and virtually unpredictable. As medical students, we’d go out to drive a bucket of golf balls at his invitation—he had a car and I didn’t—and we’d end up in South Carolina looking for co-eds. He’d have nicknames for everyone; he called me “Nobster the Lobster.”

He loved to pull pranks on people—I mean large pranks. He volunteered for the Air Force and was asked to look at possible assignments in Korea. There was one base right up near the parallel—K-47. And he found out that the commanding officer there was Ken Baldwin, who had been a medical school classmate of ours. Lawton had gone into the service about three days before Baldwin had. So Lawton asked the recruiting officer, “Who would be commanding officer up there if my date of entry into service is earlier than Baldwin’s?” “You would be,” he was told. So he said, “I want THAT job. And I want you to radio Dr. Baldwin that his new commanding officer will be there on the 5 o’clock gooney bird (C-43).”

Baldwin was notified that a new C.O. was coming. He spiffed up in his Class A uniform for the first time—he’d been there but a few weeks—and he came out to meet the gooney bird. As the ladder dropped, there was Lawton Smith with a big cigar wiggling in his mouth, saying “Howdy, Ken, I’m your new C.O.” Ken walked back to his tent and wouldn’t come out for about two days!

Lawton’s stories were a bit bawdy. At one of the Miami Neuro-ophtalmology Symposia, they were debating a case of “functional visual loss,” and Lawton said it reminded him of the story of a paratrooper from Fort Bragg who came in feigning blindness. His doctors couldn’t get him to follow anything; yet, his pupils reacted well. So, as Lawton tells it, they brought in a stripper, spotlighted her in a dimly lit room, and had her go through her routine in front of this paratrooper. Once she got started, they turned to the man and asked him, “What do you see now?” And he replied, “My vision is all blurry.” So one of the doctors said, “Your vision may be blurry, but your indicator is pointing back to duty at Bragg.”

Lawton’s teaching, which in the end is going to eulogize him more than his research, is synonymous with his clinical observations. And that teaching was based on strengthening memories through a strong dramatic impact—skits and things. He demonstrated that the hypothalamus, not the cerebral cortex, was the way to the hippocampus.

He was up there on stage giving the part all he had. People who regarded him as a buffoon did so at their own risk. I always envied him. His stuff used to ooze out of every pore. I watched him with an audience of ophthalmologists in Cincinnati once. He ended up rolling around on the floor. Everyone was laughing and having a wonderful time.

Lawton wasn’t the only remarkable talent. Norton was knowledgeable enough to talk about anything with you. And Curtin (Victor Curtin, MD, faculty ophthalmic pathologist at BPEI) and Gass (Donald Gass, MD, faculty retinal specialist at BPEI) also knew about neurologic disease. They were just good doctors all the way around.
Optic Nerve Protection


This transcription of Dr. Miller’s lecture to the American Academy of Neurology is an excellent state-of-the-art summary of a subject outside the immediate experience of most clinicians. Neuroprotection, neurorepair, and the use of stem cells for the restoration of sight are clearly discussed.

Neuroprotection consists mainly in the prevention of the death of retinal ganglion cells by blocking apoptosis: a physiologic, programmed process leading to cell death after optic nerve injury. Strategies that can be used to prevent apoptosis include the use of substances such as glutamate and nitric oxide inhibitors, alpha-2-adrenoreceptor agonists, nerve growth factors, and heat shock proteins, as well as vaccination with certain protocellul proteins or glycoproteins.

Neurorepair seeks to restore optic nerve function after injury. Ways in which this could be accomplished include providing a permissive environment for regeneration by counteracting the effect of substances such as the products of myelin breakdown that interfere with neurorepair or by providing external growth factors. Another experimental approach consists in activating a neuronal program of gene expression capable of inducing regeneration by means of cyclic adenosine monophosphate.

Stem cells have the potential to differentiate into retinal ganglion cells and could restore optic nerve–related visual loss after transplantation into the eye as well as by other means.

This article is the recommended starting point for an understanding of this important area of developing research.

II. Optic Nerve Inflammation


Optic perineuritis is thought to be “a form of orbital inflammatory disease in which the specific target tissue is the optic nerve sheath.” Although it may be the result of specific infections or inflammatory disorders such as Wegener’s granulomatosis, it is most frequently of idiopathic origin.

The clinical and radiologic features of 14 patients were reviewed. Eye pain, generally exacerbated by eye movement, was present at onset in all the patients. The majority of patients had visual loss consisting, most often, of paracentral or arcuate field defects and, more rarely, of diminished visual acuity. Optic disc edema was present in 10 eyes. Diagnosis was based on the presence of enhancement of the optic nerve sheath on magnetic resonance imaging.

This condition can easily be mistaken for optic neuritis. The authors discuss the distinguishing clinical features of the two conditions. Optic perineuritis affects an older age group and is characterized by a slower tempo of visual loss, a tendency to spare central vision, and an excellent response to corticosteroid treatment. Ultimately, however, the diagnosis is based on the magnetic resonance imaging findings. It is very likely that optic perineuritis is often misdiagnosed as optic neuritis. It should be considered in all patients with optic neuritis, particularly those with atypical clinical features, such as sparing of central vision and relapse after the discontinuation of corticosteroid treatment.


The finding that clinically definite MS will develop in 50% of patients with optic neuritis and magnetic resonance imaging (MRI) changes compatible with multiple sclerosis (MS), evidence that initial treatment with intravenous methylprednisolone reduces the rate of development of clinically definite MS for 2 years, and studies showing that interferon β-1a has a beneficial effect on the clinical and radiologic course of MS led to the CHAMPS study, which was designed to determine whether there is benefit in initiating treatment with interferon β-1a in patients who experience a first attack of optic neuritis, brainstem demyelination, or spinal cord demyelination and have abnormalities on MRI consistent with a diagnosis of MS.

In this multicenter study of 383 patients, there was a reduction in the rate of clinically definite MS by about 50%
and a decreased likelihood of progression of MRI lesions in patients treated with interferon β-1a.

In this article, the authors analyze separately the 192 patients in whom optic neuritis was the initial event. All patients were treated with intravenous and oral corticosteroids and were randomly assigned to receive weekly injections of interferon or placebo. The analysis yields results similar to those of the entire CHAMPS study, namely, that the rate of development of MS and the aggravation of the MRI abnormalities were significantly lower in treated patients.

The findings support the initiation of interferon β-1a treatment patients with a first episode of optic neuritis who have substantial MRI signal abnormalities compatible with demyelination.

III. Ischemic Optic Neuropathy


The purpose of this study was to discover the prevalence of recurrence of nonarteritic anterior ischemic optic neuropathy (NAION) in the same eye and to determine the possible risk factors. Recurrence was documented in 45 (7.5%) of 594 patients, with a median follow-up of 3.1 years. Thirty-two (71%) of patients with recurrence had bilateral NAION, and 4 of them had multiple recurrences in both eyes. There was no correlation between recurrence and the presence of systemic conditions such as hypertension and diabetes. The major risk factor for recurrence was nocturnal diastolic hypotension, which was greater in patients with recurrence.

Drawing on data from their previous studies, the authors state that aspirin is not beneficial in preventing NAION recurrence in the same eye or its occurrence in the fellow eye. Based on findings in this and previous studies, they emphasize the importance of avoiding the aggressive treatment of hypertension and avoiding the use of hypoten­sion-producing drugs in NAION.


Posterior ischemic optic neuropathy (PION) is uncommon relative to anterior ischemic optic neuropathy (AION). Most reports are limited to single cases. In this study, the records of 72 patients with PION examined over a 22-year period were analyzed retrospectively and, whenever possible, a follow-up determination of visual function and comorbid states was obtained. In 28 patients, the condition occurred perioperatively; in 6 patients, it was associated with temporal arteritis; in the remaining 38 patients, it was attributed to nonarteritic vascular disease. Among the patients with perioperative PION, 50% had undergone spinal surgery, and 70% of them had bilateral involvement. Patients in the perioperative and arteritic groups had the poorest visual function both at onset and during follow-up. The visual prognosis for nonarteritic PION was similar to that of patients with nonarteritic anterior ischemic optic neuropathy (NAION). The poorest prognosis was in those with a history of carotid and cerebrovascular disease.

This important study reviews the visual and systemic findings in a large number of patients with a rare condition. It draws attention to the important association of PION with surgical procedures, particularly those that involve the spine.

IV. Amaurosis Fugax


The authors describe three patients with exercise-induced visual disturbances. Patient 1, a 65-year-old man free of any known illness, experienced visual field constriction in the OD during jogging or biking. The visual disturbance would progress to complete unilateral blindness if he persisted with the exercise. A fundus photograph obtained during an attack convincingly illustrated an ipsilateral central artery occlusion. In patient 2, there was a single 30-minute episode of temporal hemianopsia in the OS after “heavy” physical activity. This patient also suffered from exercise-induced headache and abdominal pain preventable by prior administration of aspirin. Patient 3 had “graying-out” episodes in his OD on exercise. After the attacks, mild constriction of the visual field of the involved eye could be demonstrated. The attacks ceased after the administration of nifedipine.

Patient 1 is cited as evidence that visual disturbances provoked by exercise can occur in older patients. Whereas vasospasm is thought to have been the mechanism in all 3 of these cases, this was clearly established only in the first patient.

V. Temporal Arteritis


On the basis of a study of 29 patients, the authors assert that arteritic anterior ischemic optic neuropathy (AAION), like glaucoma, causes loss of the neuroretinal
ram, cupping of the optic nerve head (ONH), and parapapillary atrophy. This finding is unlike what occurs in nonarteritic ischemic optic neuropathy (NAION) and in compressive and other optic neuropathies.

The article seeks to explain these findings from a clinical, neuropathologic, and experimental viewpoint. The authors suggest that the ONH abnormalities in both AAION and glaucoma are mainly due to vascular factors. The lack of an ample physiologic optic disc cup and the much milder and more transient ischemic phenomena explain the lack of these findings in NAION.

According to the authors, the main difference in the optic disc cupping caused by glaucoma and that caused by AAION is the presence of pallor of the neuroretinal rim in the latter. The reason for this difference is not discussed. This is a thorough and thoughtful reflection on an important subject.

VI. Visual Cortex


The subject of this study was a patient with a left homonymous scotoma from an occipital cavernous angioma. Correlation of the location of the angioma as determined by MRI with the field defect reveals that none of the previously proposed maps of cortical representation of the visual field are accurate. The oldest of these maps (Holmes and Lister), according to which central vision occupies only 25% of the striate area, would situate the scotoma more peripherally. The two more recent maps, which attribute 37% (Wong and Sharpe) to 60% (Horton and Hoyt) of the striate cortex to central vision would situate the scotoma more centrally.

This paper demonstrates the value of a well-studied single case and shows that further research is required to definitively resolve the issue of the cortical representation of the visual field.

VII. Ocular Motor Phenomena


Damage to the oculovestibular pathway disrupts the normal effect of the otolithic stimulation on eye and head position and causes an ocular tilt reaction (OTR). The latter consists of a triad of vertical ocular misalignment, bilateral ocular torsion, and head tilt. The head and the superior poles of both eyes are rotated toward the hypotropic eye. The term "skew" refers to the vertical ocular misalignment, which is the most easily observed feature of the OTR.

The authors describe 6 patients in whom the ocular tilt reaction was the result of posterior fossa disease. In 5 of these patients, the ocular motility pattern was consistent with inferior oblique palsy, except for the cyclotorsion, which was in the opposite direction (the eye was exocyclo-torted) from that observed in an inferior oblique palsy. It seems likely that a significant number of cases diagnosed as inferior oblique palsy are cases of OTR.


This is a report of a patient with an isolated bilateral fourth nerve palsy from a metastasis of bronchial carcinoma to the dorsal midbrain area.

The authors state that they were unable to find a previous report in which such a palsy occurred as the sole manifestation of metastatic lung cancer. Acquired isolated bilateral trochlear nerve palsy of simultaneous onset is rare and most commonly is due to head trauma. The value of this article is to emphasize the fact that bilateral trochlear nerve palsy occurring in the absence of head trauma is likely to be due to a potentially serious structural lesion of the midline dorsal midbrain.

VII. Orbit


This is a retrospective study of the usefulness of methotrexate in the treatment of noninfectious orbital inflammation. The indication for treatment was the inability to taper corticosteroids or to tolerate their prolonged systemic use. Many of the patients had previously been treated with orbital irradiation, a few had had orbital decompression, and some continued taking corticosteroids at the same time as methotrexate. Of the 14 patients initially treated, 10 were considered to have had an adequate trial. Of the 10, most had nonspecific orbital inflammation or Graves' disease, 1 had sarcoidosis, and 1 had the Tolosa-Hunt syndrome.

Nine patients benefited from the treatment. Of these, 6 were ultimately able to discontinue methotrexate, and 5 of the 6 using corticosteroid therapy were able to cease this medication. The median duration of treatment of the nine responders was 25 months. Gastrointestinal disturbance and fatigue were the most common side effects, each affecting 50% of the 14 patients initially treated.
The limitations of the study are its retrospective nature, the small number of patients, and the heterogeneity of diagnoses and treatments. A more systematic approach is required to confirm the impression that methotrexate is an effective treatment of noninfectious orbital inflammation.

This case presentation draws attention to sclerosing orbital inflammation, an entity that may be difficult to distinguish from an orbital tumor. A 42-year-old woman had had a 6-month history of right orbital pain, lid swelling, and visual loss that failed to respond to treatment. There was restriction of OD movement with a positive forced duction test and 2 mm of right proptosis. Fundus examination revealed right optic disc edema, venous stasis retinopathy, and optic-illary shunts. Magnetic resonance imaging (MRI) showed an enhancing mass that surrounded the optic nerve and extended into the cavernous sinus, encasing the carotid artery. The extraocular muscles on the right side were enlarged. Treatment with corticosteroids did not improve the vision. A biopsy was performed to confirm a clinical suspicion of optic nerve meningioma. Three different pathologists who examined the specimen diagnosed optic nerve glioma. Histopathologic examination of a later biopsy specimen revealed the correct diagnosis. The features that initially led to the diagnosis of glioma were thought be of reactive origin.

The discussion reviews the clinical, radiologic, and neuropathologic features of sclerosing orbital inflammation and discusses the difficulty in distinguishing this entity from a tumor. Whereas the condition was initially thought to represent the end stage of orbital pseudotumor, it is currently believed to be a type of idiopathic fibrosclerosis that also affects other regions such as the mediastinum or the retroperitoneum.


Forty-two of 53 consecutive patients with moderate symptomatic Graves' ophthalmopathy (GO) were randomized to receive 20 Gy of external beam radiation to one orbit and sham therapy to the other. Six months later, the therapies were reversed. The parameters studied included the volume of the extraocular muscles and orbital fat, proptosis, range of extraocular muscle motion, area of diplopia fields, and lid fissure width. The effect of treatment was assessed by comparing the findings in the same orbit before and after treatment and between the two orbits at baseline and at 6 and 12 months.

No clinically significant difference was observed for the main outcome measures between the treated and untreated orbits at 6 months. Of marginal clinical significance was a small positive change from baseline at 12 months in the orbit treated first. In the authors' view, the value of radiotherapy in GO requires reassessment.

In an accompanying editorial (Feldon SF. Radiation therapy for Graves' ophthalmopathy: trick or treat. Ophthalmology 2001;108:1520–2), the author wondered whether the inclusion of patients with inactive disease or previous treatment with steroids may have contributed to the negative results.

VIII. Blepharospasm and Hemifacial Spasm


This retrospective study addressed the question of the duration of benefit and dosage requirements over time in patients with essential blepharospasm (BSP) and hemifacial spasm (HFS) treated with botulinum toxin. Of the 28 patients studied, 17 had BSP and 11 had HFS. The patients were treated over a 5-year period, starting in 1989. All patients had at least 6 treatments; 17 had 12 or more treatments, and 7 had more than 20 treatments.

The conclusion of the study is that the duration of benefit and dosage requirements remain stable over time for at least 20 treatments. The results were similar when the patients were analyzed as a group and when BSP and HFS were analyzed separately. These findings offer a measure of reassurance to patients with these conditions who wonder about what the future may bring. As reported by others, the duration of benefit was slightly longer in the patients with HFS (an average of 15 weeks for HFS compared with 12 weeks for BSP).

IX. Facial Nerve


This is a thorough study of lacrimation before and after the administration of botulinum toxin (Dysport) transcutaneously into the lacrimal gland of 3 patients with gustatory reflex hyperlacrimation (crocodile tears) and into the
submandibular gland of 1 patient with epiphora after the treatment of dry eyes by autologous submandibular gland transplantation to the temporal fossa.

Severity of tearing was evaluated subjectively and objectively (by means of a Schirmer test and a special tear clearance test) in the presence and absence of a tear secretion stimulus (chewing, exercise) and before and after the administration of Dysport.

In 3 of the 4 treated patients, there was marked reduction in tearing at 2 weeks. The beneficial effect persisted for 3 to 4 months, after which re-injection became necessary. Tear duct obstruction rather than inappropriate parasympathetic innervation was the cause of excessive tearing in the 1 patient who did not benefit from Dysport. Side effects were transient and consisted of upper lid ptosis in 2 patients, 1 of whom also had paresis of the superior rectus.

The findings in this small group of patients are in keeping with other positive reports on the treatment of crocodile tears with botulinum toxin. Because of the difficulties in converting Dysport units into the equivalent units of Botox, the dosage used in this study cannot serve as a guide for physicians practicing in countries where only the latter preparation of botulinum toxin is available.

**Medicine Journals**

**Reviewer:** Martin ten Hove, MD

### I. Cerebrovascular Disease


The authors describe a 49-year-old man with acute monocular blindness caused by a spontaneous dissection of the common carotid artery. The man was otherwise healthy, with no history of trauma, neck manipulation, or connective tissue disease. He did have controlled hypertension and hypercholesterolemia. The results of examination were not remarkable and consisted of upper lid ptosis in 2 patients, 1 of whom also had paresis of the superior rectus.

Although there are a few other reported cases of CRAO due to carotid artery dissection, this case differs from those reported because of the absence of associated trauma, neck or jaw pain, or significant medical history. Although the dissection is reported to be in the distal common carotid artery, the occlusion of the carotid siphon indicates that it may have extended to involve the internal carotid artery. No mention is made of the presence (or absence) of clinical features suggestive of Horner’s syndrome. The use of MRA in the evaluation of an otherwise unexplained CRAO is supported by this case.

**Westwood ME, Kelly S, Berry E et al. Use of magnetic resonance angiography to select candidates with recently symptomatic carotid stenosis for surgery: systematic review. BMJ 2002; 324:1–5.**

The current literature describes little rigorous research on the performance of magnetic resonance angiography (MRA) in evaluating cervical carotid artery stenosis. Unfortunately, there are no studies that compare conventional angiography with MRA for surgical decision making or outcomes. The authors sought to determine whether there was sufficient existing evidence to support the use of MRA as a means of selecting patients with symptomatic high-grade cervical carotid artery stenosis. The authors systematically reviewed the literature, evaluating the diagnostic performance of MRA versus conventional angiography at thresholds set by the North American Symptomatic Carotid Endarterectomy Trial (NASCET) (70 to 99% stenosis) and European Carotid Stenosis Trial (ECST) (50 to 99% stenosis). Of the 7,183 articles that were reviewed, only 26 met the main inclusion criteria, and only 8 met all the inclusion criteria. By combining the reported sensitivities and specificities, the authors plotted a summary receiver operating characteristic curve (a method described by the Cochrane Work Group for meta-analysis of screening and diagnostic tests). The point on the curve where the combined sensitivity and specificity were equal was determined (Q*).

For a diagnostic threshold of 70 to 99% carotid artery stenosis, the Q* was 99% (95% CI: 98–100). MRA technique was not a significant variable in the multiple linear regression analysis. For a diagnostic threshold of 50 to 99% carotid artery stenosis, the Q* fell to 90% (95% CI: 81–99). On the basis of these results, the authors state that MRA is highly sensitive and specific for diagnosing a 70 to 99% stenosis but caution against selecting surgical candidates with 50 to 99% stenosis using MRA alone. Although there is a trend toward improved diagnostic performance with MRA, further research is needed at this threshold. Until then, users of MRA are advised to ensure that audits are in place, including feedback from surgeons and quality control comparisons with another noninvasive imaging modality such as ultrasonography.

First ischemic stroke has a cardiogenic source in approximately one third of patients with a first ischemic stroke (and should be treated with warfarin) or are candidates for carotid endarterectomy. The rest are candidates for antiplatelet therapy, which has been shown to reduce the recurrence of stroke by 30%. Many physicians have tried to improve on this prevention rate by prescribing warfarin with little evidence-based data to support this practice. The authors investigated whether warfarin was superior to aspirin in the prevention of recurrent ischemic stroke in patients with a prior noncardioembolic ischemic stroke.

This randomized double-blind study involved 48 centers recruiting 2,206 patients over seven years. The patients were divided into two treatment groups: one receiving aspirin 325 mg daily and placebo, the other receiving a warfarin dose adjusted to achieve and maintain an INR in the range of 1.4 to 2.8. Patients in the aspirin group followed the same schedule of visits to the clinic for drawing blood, monitoring the medication, and adjusting the dose. False INR values for patients in the aspirin group were sent to the monitoring physician to ensure blinded assessments.

Patients were monitored for 2 years with monthly telephone assessments and quarterly clinical evaluations. The primary end point was death resulting from any cause, or recurrent stroke. Recurrent ischemic stroke was defined as a new lesion detected by neuroimaging or clinical findings consistent with stroke that lasted for more than 24 hours.

Overall, the end point occurred in 16.9% of patients. There were no significant differences between the warfarin and aspirin groups in time to the end point or in the number of patients reaching the end point (*P* = 0.25). Warfarin was expected to confer a small reduction in the risk of recurrent stroke; instead, it was associated with a nonsignificant 13% increase in recurrent stroke risk. Rates of major hemorrhage during the study were low in both groups, again with no significant difference between them.

This important study tells us that aspirin is a well-justified choice for the prevention of recurrent ischemic noncardioembolic stroke and that warfarin does not offer any additional benefit. For those patients taking warfarin for other established reasons, this study provides evidence of its safety.


The authors report a case of giant cell arteritis (GCA) presenting as transient vertebrobasilar ischemic attacks in an otherwise healthy 76-year-old man. The episodes consisted of 5- to 10-minute attacks of ataxia, diplopia, dysarthria, and unilateral facial weakness. He did not have any of the usual symptoms of GCA, including jaw claudication, visual loss, headache, and polymyalgia. The results of all investigations for cardiac and atherosclerotic disease were negative, including electrocardiogram, 24-hour Holter monitor, carotid Doppler ultrasonography, cholesterol, and blood pressure measurements. The diagnosis was confirmed by positive result of temporal artery biopsy and further supported by an elevated erythrocyte sedimentation rate (ESR) (70 mm/h) and platelet count (534 x 10^3 /μl).

Despite numerous case reports of stroke and transient ischemic attacks due to GCA, intracranial involvement is uncommon. This case is unique in that none of the usual GCA symptoms were present, and the diagnosis was suspected on the basis of an elevated ESR and mild thrombocytosis.

II. Headache


The author analyzed the treatment of adult patients with isolated headache who sought treatment at United States emergency departments in light of practice guidelines in the United States and Canada. Data were extracted from the 1998 National Hospital Ambulatory Medical Care Survey, which sampled all visits from 398 emergency departments in the United States over a 4-week period. The migraine headache and unspecified headache cohorts included 811,419 and 604,977 patients respectively. On average, patients received 1.8 medications from pharmacopeia of 36 drugs. The most common drugs used for the migraine cohort were meperidine (35.7%), promethazine (29.4%), IV ketorolac (16.6%), and prochlorperazine (15.6%). Parental medications were given to 85% of migraine patients. These facts need to be interpreted in light of the fact that 35% of the migraine patients reported moderate headache and only 20% reported severe headache.

The American Academy of Neurology recommends an antiepileptic (particularly prochlorperazine) plus dibhydroergotamine as the therapy of choice for aborting an acute migraine episode. The Canadian Headache Society's algorithm for the treatment of severe migraine headache states that the agent of choice is a dopamine-antagonist antiepileptic followed by dibhydroergotamine or sumatriptan. The treatment of patients in this study diverged from these recommendations in two ways. First, only one fourth of patients with migraine received a non-opioid agent as part of their drug regimen. Second, opioids were more commonly used as first-line drugs than as second-line drugs reserved for patients who do not respond to non-opioid treatment. The

The authors conducted an entertaining study designed to determine whether drawings can aid in the differential diagnosis of headaches in children. Before any formal history was obtained, 226 children (aged 4 to 19 years, mean 11.4 years) with a chief complaint of headache were asked: “Please draw a picture of yourself having a headache. Where is the pain? Are there any other changes that come with your headache that you can show me in your picture?” No leading questions were asked. With a pencil and a single piece of paper for each headache type, all children complied with the request. Two pediatric neurologists, who were blinded to the clinical history, analyzed the drawings independently. Pictures were graded as either migrainous or nonmigrainous. Specific features of the drawings that were considered to represent migraine included depiction of severe pain with a pounding/hammering quality, nausea or vomiting, sensitivity to light and/or sound, desire to sleep, headache exacerbation by exercise or movement, or clear-cut unilateral.

Overall, 57.5% of the children were given a clinical diagnosis of migraine or mixed headache with a prominent migraine component. The remaining headaches were diagnosed as nonmigraine for a wide variety of causes. Interal agreement was excellent, with a Kappa score of 0.92. The drawings had a sensitivity of 93% and a specificity of 83% when compared with the “gold standard” of the clinical diagnosis. The results were then stratified into three groups according to age. Surprisingly, there were fewer false positive and false negative results in the youngest age group.

This study adds to the growing literature on migraine art. The illustrative examples in this paper must be seen to be fully appreciated. Asking children to draw their headache is a simple and accurate adjunctive aid for headache differential diagnosis in the clinical setting. Drawings can be completed in the waiting room, with instructions given by a nurse or receptionist. For most children, this becomes an enjoyable exercise that also serves as a useful clinical adjunct.

III. Miscellaneous


Many studies have described the ocular changes and visual field changes associated with vigabatrin in the adult population. However, comparatively little information from children has been reported. The authors report ocular changes in 21 children (aged 1–16 years) who were treated with vigabatrin. The children were being treated for epileptic syndromes with infantile spasms. The vigabatrin dose varied from 25 to 114 mg/kg/day (mean 55.8 mg/kg/day) for a duration of therapy of 6 to 85 months (mean 35.7 months). Retinal changes developed in four children (19%), and optic atrophy also developed in one of these children. Visual evoked potentials (VEP) were abnormal in 16 children, 2 of whom had abnormalities before starting the drug.

All children required sedation with chloral hydrate for fundus examination and VEP testing. Visual field testing could not be performed.

The results are not surprising but support the recommendation that children receiving vigabatrin be monitored every 3 to 6 months. Evaluation should include visual field testing whenever possible; if that is not possible, sedation may be required to perform a proper funduscopic examination and VEP testing. The authors do not report electroretinogram (ERG) results because this test was not available to them. They do suggest that ERG is superior to VEP in its ability to detect vigabatrin toxicity.


The authors monitored 68 patients with isolated syndromes suggestive of multiple sclerosis (MS) (including optic neuritis) and reported the correlations between early magnetic resonance imaging (MRI) lesion volume, change in MRI lesion volume, and long-term disability. Not surprisingly, 50% of the isolated syndromes were optic neuritis. The patients were assessed at 12.5 to 16.8 years (mean 14.1 years) after diagnosis, when their mean age was 45 years. Only one patient received long-term interferon therapy. Clinically definite MS developed in 48 patients (68%).

The median EDSS score was 3.25 (with 31% of patients scoring ≥6.0). The EDSS score at 14 years correlated moderately with the change in lesion volume on MRI over
the first 5 years \( (r = 0.61) \) and the lesion volume at 5 years \( (r = 0.69) \). The change in lesion volume over the first 5 years correlated moderately with EDSS scores, but changes in lesion volume from 5 to 10 years and 10 to 14 years showed a much weaker correlation. The number of lesions on MRI at baseline correlated moderately with the EDSS score at 14 years \( (r = 0.47) \), as did the number of lesions at 5 years \( (r = 0.55) \) and 10 years \( (r = 0.45) \).

This study is an important natural history study, and similar studies are unlikely now that agents that substantially modify lesion volume on MRI are used to treat relapsing-remitting MS. The study suggests that the number of lesions and the lesion volume on MRI in patients with early MS are moderately predictive of long-term disability. Given only moderate correlation, the authors point out that MRI lesion volume alone should not be used as the sole determinant when deciding about disease-modifying treatments. Weaknesses of this MRI-based study include the change in magnetic field strength (baseline study used 0.5 Tesla, and follow-up study used 1.5 Tesla) and change in image slice thickness (10 mm at baseline and 5 mm in follow-up).


The vestibulo-ocular reflex (VOR) is augmented by the pursuit/optokinetic (OKN) system, the cervico-ocular reflex, central programming, and anticipatory intent. When the vestibular system is impaired, these mechanisms are still present and serve to minimize retinal slip and visual degradation during head movement. The authors studied the ability of central programming to augment the VOR by comparing dynamic visual acuity (DVA) during predictable (active) and unpredictable (passive) head rotation. They hypothesized that DVA would be significantly worse with unpredictable head rotation compared with predictable head rotation irrespective of the vestibular of the individual, and that subjects with bilateral vestibular loss would have the greatest decrement in DVA scores during unpredictable (passive) head rotation.

DVA was recorded in 26 subjects with normal vestibular status, 20 subjects with unilateral vestibular impairment, and 7 subjects with bilateral vestibular impairment. Vestibular loss was confirmed by clinical examination, rotational chair testing, and caloric testing. Predictable and unpredictable head movements were generated by the subject and examiner, respectively. Standardized optotypes were projected only during head rotation with velocities between 120 and 180 degrees/s.

Significant differences were found between DVA-predictable and DVA-unpredictable scores in all three groups \( (P < 0.02 \) for all three groups). The largest decrement in DVA did indeed occur in subjects with bilateral vestibular impairment during unpredictable head rotations. This is the first study to show a significant difference between VOR gain measured during active and passive head rotation in healthy subjects. The authors reason that this is because previous studies used passive head rotations that were predictable and allowed for central programming to augment the VOR. DVA can be readily used in the clinic to distinguish unilateral and bilateral vestibular loss from normal patients. This paper suggests that this test is best performed with unpredictable passive head rotations.


Thymomas occur frequently in patients with myasthenia gravis. The authors examined the association between thymoma and a second malignancy. They retrospectively reviewed 192 consecutive patients with thymoma and compared the incidence of second malignancy with that in two different “control” groups. The first control group consisted of 206 patients undergoing thymectomy for non-thymomatous reasons. The second control group consisted of 1,426 patients with nasopharyngeal carcinoma. The mean follow-up period for the three groups was 74, 72, and 70 months, respectively. A second malignancy occurred in 8% of patients in the thymoma group, 2% of patients in the nonthymoma group (OR 3.81, CI 1.05-13.81), and 2% of patients in the nasopharyngeal carcinoma group (OR 4.89, CI 2.26-10.53).

It is of interest that 73 of the 192 patients in the thymoma group and 102 of the 206 patients in the nonthymoma group had myasthenia gravis. However, the presence of myasthenia was not a significant risk factor for the development of a second malignancy. Among those in whom a second malignancy did develop, no consistent pattern of extrathyphmic sites was identified. Although the authors’ choice of a “control” group may be questioned, this paper still lends support to the recommendation that clinicians should be aware that second malignancies occur more commonly in patients with thymomas (including those who also have myasthenia gravis).
Upcoming Meetings

September 21–26, 2002
**2002 Annual Meeting of the Congress of Neurological Surgeons**
Pennsylvania Convention Center
Philadelphia, PA
Contact: info@ICNS.org

October 2–5, 2002
**Joint European Research Meeting in Ophthalmology and Vision**
Palacio de Congresos del Colegio Oficial de Médicos
Alicante, Spain
http://www.ever.be
Contact: secretariat@ever.be

October 13–16, 2002
**American Neurological Association**
Marriott Marquis
New York, NY
http://www.anetra.org/annual.htm
Contact: jori.janderson@msn.com

October 18–20, 2002
**Japanese Neuro-Ophthalmology Society**
Toshi Center Hotel
Tokyo, Japan
Contact: +81-3-3265-8211

October 20–23, 2002
**American Academy of Ophthalmology Annual Meeting**
Orlando, FL
http://www.aao.org/aaweb1/Meetings/139_1645.cfm
Contact: meetings@aao.org

November 2–7, 2002
**Society for Neuroscience Annual Meeting**
Orlando, FL
http://www.sfn.org/
Contact: info@sfn.org

February 8–13, 2003
**Frank B. Walsh Meeting**
Snowbird, UT
http://www.nanosweb.org/meetings/
Contact: (860) 586-7507 x533

March 7–10, 2003
**American Society of Neuroimaging Annual Meeting**
New Orleans, LA
http://asinnweb.org/annual/futuremeetings.html

March 28–April 1, 2003
**XXIV Pan American Congress of Ophthalmology**
San Juan, Puerto Rico
http://www.panamofla2003.org
Contact: info@paao.org

March 29–April 5, 2003
**American Academy of Neurology (AAN)**
Honoulu, HI
http://am.aan.com/future.htm

April 2–6, 2003
**American Academy of Ophthalmology Mid-Year Forum**
Renaissance Mayflower Hotel
Washington, DC
http://www.aao.org/aaweb1/Meetings/145.cfm

April 26–May 1, 2003
**Annual Meeting of the American Association of Neurological Surgeons**
San Diego, CA
http://www.neurosurgery.org/aans/meetings/index.asp
Contact: info@aans.org

April 27–May 2, 2003
**41st Annual Meeting of the American Society of Neuroradiology (ASNR)**
Washington Marriott Wardman Park Hotel
Washington, DC
http://www.asnr.org/asnr/UpcomingMeetings.htm
Contact: 630-574-0220

May 4–9, 2003
**The Association for Research in Vision and Ophthalmology (ARVO)**
Fort Lauderdale, FL
http://www.arvo.org/

June 15–18, 2003
**European Neuro-Ophthalmological Society (EUNOS)**
Göteborg, Sweden
Contact: Bertil.Lindblom@neuro.gu.se

November 5–13, 2005
**World Congress of Neurology**
Sydney, Australia