PROFILES OF THE ENDOCRINE CLINIC

A Decade of the Massachusetts General Hospital Neuroendocrine Clinical Center

BEVERLY M. K. BILLER, BROOKE SWEARINGEN, NICHOLAS T. ZERVAS, AND ANNE KLIBANSKI

Neuroendocrine Clinical Center, Neuroendocrine Unit, Department of Medicine, and Neurosurgical Service (B.S., N.T.Z.), Massachusetts General Hospital, Boston, Massachusetts 02114

Introduction: development of the Neuroendocrine Clinical Center

In 1985, the Massachusetts General Hospital Neuroendocrine Clinical Center was founded to provide a multidisciplinary approach to patients with pituitary and hypothalamic disorders. The Center was developed because of the recognition that there was fragmentation of care for patients undergoing medical treatment, surgery, or radiation therapy for pituitary and hypothalamic disorders. Although there were independent areas of expertise in neurosurgery, neuroendocrinology, radiation oncology, and neurology at the Massachusetts General Hospital as well as neuroophthalmologists at the adjacent Massachusetts Eye and Ear Infirmary, there was no coordinated program of specialty services to provide an integrated approach to patients. In addition, it was clear that innovative clinical research programs exploring the pathogenesis and treatment of pituitary disease would be facilitated by centralized patient services and a broad referral base. A partnership was, therefore, formed with neurologists and neurosurgeons who coordinated their schedules to provide a weekly unified day for out-patient consultations and multidisciplinary case reviews. Links were also established with radiation oncology for patients needing radiation therapy for sellar or hypothalamic masses, with neuroophthalmology to provide access to detailed evaluation for optic chiasm compression or involvement of the cranial nerves in the cavernous sinus, and with neuropathology and neuroradiology to coordinate access to state of the art diagnostic techniques. A major advantage for patients, particularly those traveling from other states or countries, was the coordination of consultations by all these services into a 24- to 48-h period. Experienced neuroendocrine nursing was also incorporated to provide better patient monitoring and teaching. The three major objectives of the new Center were 1) excellence in patient care, 2) establishment of a patient base for innovative clinical research studies, and 3) professional and patient education. A weekly interdisciplinary Neuroendocrine Case Conference was established as the cornerstone of coordinated patient care and physician education. This was to provide a forum for staff neuroendocrinologists, neurosurgeons, neurologists, and radiation oncologists to reach a multidisciplinary consensus for a diagnostic and therapeutic plan for each patient seen that week in the Center. Local primary care providers, endocrinologists, fellows, residents, and medical students were also invited to participate in these conferences. An office suite was designed that included patient consultation rooms, the Pituitary Test Center for performing dynamic hormone tests on site, and a conference room for formal case review.

Since its founding in 1985, the Neuroendocrine Clinical Center has grown substantially in patient volume and personnel to become a major national and international referral center for patients with pituitary and hypothalamic disorders. Initially staffed by 1 endocrinologist, 1 neurologist, and 1 neurosurgeon on 1 afternoon a week, it now is comprised of 3 weekly teaching sessions with a total of 7 endocrine fellows as well as rotating medicine and neurology residents and medical students seeing patients under supervision by 4 staff neuroendocrinologists, 1 neurologist, and 2 neurosurgeons. There are also several separate weekly staff sessions. The total volume at the inception of the Clinical Center was approximately 100 patient visits/yr; it is now well over 1000 visits annually. The most consistent reason for growth of the Center is that referring physicians believe that this type of cohesive multidisciplinary program is needed for patients with complex pituitary and hypothalamic diseases. Despite the fact that many patients come from other states or countries, permission for out of plan coverage is often obtained from insurance carriers because of the unique strengths of the Center. Many patients are referred because of the specific expertise of individual staff endocrinologists in areas such as prolactinomas, Cushing’s disease, and acromegaly. Referrals are also directed toward the expertise of the neurosurgeons, who are world-renowned for their abilities at curative transsphenoidal adenectomy with minimal morbidity. With well over 1000 transsphenoidal surgeries performed at Massachusetts General Hospital over the past 15 yr currently undergoing analysis, it is clear that the many years of experience are beneficial to patients. In addition, one of the world’s largest experiences with stereotactic radiosurgery using proton beam therapy for residual/recurrent pituitary
adenoma is now available through the Center. The expertise of neuropathologists at Massachusetts General Hospital in the diagnosis and characterization of pituitary adenomas and in pituitary pathology research also plays a key role in the high level of patient care.

The second reason for recent growth of the Center has been that it has served as a major site for the investigation of pathogenesis and the treatment of pituitary disorders. The findings that 1) the majority of clinically nonfunctioning tumors are of gonadotroph origin, 2) pituitary tumors are monoclonal, 3) inhibin subunits may play an important role in tumor phenotype and proliferation, and 4) osteoporosis is a major clinical consequence of hyperprolactinemic hypogonadism in men and women have all emerged from investigations at the Center. The Neuroendocrine Clinical Center was one of the initial sites pioneering the use of octreotide in acromegaly and has worked toward developing the availability of new dopamine agonists, such as CV205–502 and cabergoline, for prolactinomas. The Center has designed studies addressing whether adults with acquired GH deficiency should receive long term replacement of this hormone. Many physicians refer their patients to the Center to provide them with access to the most innovative diagnostic or therapeutic approaches. For example, over 100 patients with Cushing’s syndrome have undergone bilateral inferior petrosal sinus sampling at Massachusetts General Hospital.

A third reason for a recent increase in patient referrals relates to an expanding base of patient awareness groups. There are a number of groups that promote awareness in pituitary disorders, and such groups typically refer patients to major medical centers where there is the combined expertise of neuroendocrinology, neurology, neurosurgery, and radiation oncology so as to provide the most comprehensive approach to pituitary tumors.

Patterns of patient referrals

At the initiation of the Center, hyperprolactinemia was the most common referral diagnosis. The Center began at a time when it was a novel concept that medical treatment could be primary therapy for nearly all prolactinoma patients, including those with visual field abnormalities, and this was one of the pioneering approaches of the Center. However, as gynecologists and internists have become more familiar with prolactinomas, such patients have been less frequently referred to endocrinologists. Many prolactinoma referrals are now more difficult cases, such as patients who have failed medical management with bromocriptine or have other complicated issues, such as associated neuroleptic use or a cystic component to their mass. There has been a steady increase in the number of patients referred specifically because of the availability of technological procedures, such as patients with Cushing’s syndrome referred for CRH-stimulated bilateral inferior petrosal sinus sampling and patients referred for specialized proton beam therapy of pituitary or parasellar central nervous system lesions, such as meningioma, chordoma, or chondrosarcoma. An increasing number of patients have also been referred because of access to research protocols that provide newer dopamine agonists, somatostatin analog, GH, and GH-releasing peptides. The most recent year in the Neuroendocrine Clinical Center saw the largest number of referrals being from radiation oncology (to evaluate radiated patients for hypopituitarism), followed by neurosurgery, general internal medicine, and endocrinology. One of the most challenging tasks of the neuroendocrine staff has been to provide a consultation that meets the specific preference of the referring physician. The role of the Neuroendocrine Clinical Center staff in the long term care of the patient is dependent on the choices of the referring physician and the patient. Referral can be for a second opinion, for limited perioperative endocrine management in patients undergoing transsphenoidal surgery at Massachusetts General Hospital, for the development of a diagnostic and treatment plan in conjunction with the primary physician, or for long term management by the Center physicians. In the many cases referred by other endocrinologists, the Neuroendocrine Clinical Center staff feel strongly that their role should be limited to providing a second opinion or to perioperative care in the case of a hospitalized pituitary tumor patient.

Patient populations

Patients referred to the Neuroendocrine Clinical Center have a wide variety of presentations, but many elements of the neuroendocrine evaluation are similar. History, physical examination, and biochemical testing address whether there is evidence of anterior pituitary hormone excess or deficiency. The presence of posterior pituitary dysfunction also provides useful information, because a patient presenting with diabetes insipidus or syndrome of inappropriate antidiuretic hormone (SIADH) is likely to have a malignant or infiltrative process rather than a pituitary adenoma.

A typical day in a Neuroendocrine Clinical Center session included the following new patients:

A 28-yr-old dentist from South America with a classic history of acromegaly presented with headache and increased difficulty manipulating his dental instruments over the past year because of enlarging hands. He was referred to the Neuroendocrine Clinical Center by a physician in New York to undergo curative transsphenoidal surgery at Massachusetts General Hospital.

A 20-yr-old man who had recently been hospitalized in the neurosurgical intensive care unit for closed head trauma associated with diabetes insipidus. He underwent an insulin tolerance test to determine whether the steroids given for brain edema had suppressed his adrenal axis.

A 57-yr-old panhypopituitary man after craniotomy and radiation therapy for a craniopharyngioma, referred for GH stimulation testing with clonidine to determine eligibility for a clinical research study investigating GH replacement.

A 40-yr-old woman with Cushing’s syndrome (diagnosed by her neighbor who had read a magazine article) referred by her internist for evaluation and treatment.

Follow-up patients seen that day were:

A 32-yr-old woman from Connecticut 5 yr after surgery and cranial irradiation for a chondrosarcoma, evaluated on an annual basis for the development of hypopituitarism.

Three premenopausal women with microprolactinomas do-
ing well on dopamine agonist therapy.

A 27-yr-old woman with hyperprolactinemia induced by neuroleptics and a 3-mm abnormality on head magnetic resonance imaging, stable on follow-up scan.

Two patients several years posttranssphenoidal surgery for nonfunctioning macroadenomas, doing well with no evidence of recurrence clinically or radiographically.

A 34-yr-old patient with residual acromegaly after transsphenoidal surgery and radiation, under control with sc octreotide injections.

Hyperprolactinemia. The most common diagnosis seen in the Center is pituitary adenoma, accounting for 45% of cases. The major tumor subtypes are seen in Fig. 1. Hyperprolactinemia accounts for nearly half of these cases and includes idio-pathic, micro- or macroprolactinomas, and drug-induced types. Several new idiopathic/microprolactinomas are seen each week; medical treatment with bromocriptine or cabergoline is begun if the patient has hypogonadism, infertility, or clinically significant galactorrhea. Macroprolactinoma patients have historically been treated with bromocriptine, but currently many such patients are being offered participation in a new cabergoline trial because of its high rate of patient acceptance due to the low incidence of side-effects and only once a week treatment. The dose escalation in prolactinoma patients with visual compromise proceeds much more rapidly than with other patients, and visual field testing is repeated at frequent intervals to document the expected rapid improvement. Surgical intervention is used for prolactinomas when there is absence of response to medical therapy in a macroadenoma (often due to a cystic component), an episode of acute hemorrhage/apoplexy, complete intolerance to all dopamine agonists in some patients with infertility or hypogonadism, and patients taking neuroleptics who need control of a mass lesion.

Clinically nonfunctioning pituitary adenomas. Approximately 30% of patients with pituitary tumors seen at the Center have clinically nonfunctioning adenomas. Patients with these tumors typically present with symptoms due to mass effect, such as headaches or visual field loss. Others present with central hypogonadism, hypothyroidism, or hypoadrenalism, leading to the finding of a sellar mass. However, it is more common for these disorders to go undiagnosed until a mass is seen on brain imaging, with the symptoms of hormone deficiencies present in retrospect. At least half of the patients with nonfunctioning pituitary adenomas present incidentally, such as when a skull film or computed tomography scan is performed after a head injury or when sinus films are ordered, such as in a patient with recurrent sinusitis. Patients with sellar masses and no clinical evidence of acromegaly, Cushing’s disease, or prolactinoma undergo detailed hormone testing confirming that the lesion is biochemically non-functioning. The use of specialized glycoprotein hormone subunit serum assays, such as α-subunit or FSHβ can confirm the pituitary origin of sellar masses. Patients with clinically nonfunctioning macroadenomas larger than 1 cm typically undergo transsphenoidal surgery to protect the adjacent neurological structures such as the optic chiasm and cranial nerves III–VI. In many cases, large nonfunctioning macroadenomas can be completely resected, particularly if there is no lateral extension into the cavernous sinuses. Substantial recovery of bitemporal hemianopsia is seen in up to 70% of cases even if there have been long standing deficits. A typical hospital stay after transsphenoidal surgery is now 2–4 days, with outpatient sodium measurements arranged for the week after discharge to monitor for late SIADH. The morbidity rate is extremely low, approximately 1% or less for serious complications in over 1000 patients with all types of pituitary tumors (visual worsening, 0.4%; meningitis, 0.4%; cerebrospinal fluid rhinorrhea requiring repair, 1%; epistaxis requiring embolization, 0.002%). The mortality rate for both of the pituitary neurosurgeons at Massachusetts General Hospital is zero. Patients are routinely retested for recovery of pituitary function postoperatively, as many patients no longer need hormone replacement after decompression of the normal pituitary gland. Long term follow-up of patients from 1–15 yr after transsphenoidal surgery reveals a low rate of hypopituitarism directly attributable to surgery alone. Only 10% of patients who do not receive radiation after surgery require replacement of at least one hormone more than a year after surgery, and many of these patients were hypopituitary before surgery due to the compressive effects of the tumor. In contrast, after a combination of surgery and radiation, 45% of patients require adrenal replacement, and 55% require thyroid replacement.

Medical therapy is rarely used for nonfunctioning adenomas because of the lack of effectiveness in most patients; recurrences are treated with radiation and/or repeated transsphenoidal surgery. A minority of patients with α-subunit-secreting tumors may show a small degree of mass reduction with somatostatin analog therapy. Rarely, patients who are not surgical candidates because of concurrent medical problems may be treated with radiation as a primary modality. In such cases, serum hormone markers confirming a pituitary adenoma are essential for appropriate radiation dosing and management.

A number of patients are seen for “incidentalomas” with a sellar lesion of 1 cm or smaller, and these patients are
typically followed, if there is no evidence of hormone abnormalities, visual field, or cavernous sinus involvement. This includes a detailed evaluation for evidence of subtle hypersecretion from “silent” tumors, including insulin-like growth factor I (IGF-I), PRL, and urinary free cortisol levels. The first follow-up scan is performed at 3–6 months, then annually (and subsequently at increasing intervals if no change is seen), with transsphenoidal surgery performed if there is enlargement of the lesion.

Cushing’s syndrome. Sixteen percent of pituitary tumor patients seen at the Neuroendocrine Clinical Center have Cushing’s disease. Patients with Cushing’s syndrome are most often referred to the Neuroendocrine Clinical Center by endocrinologists who have already performed an evaluation and are requesting bilateral inferior petrosal sinus sampling with CRH to distinguish between pituitary and ectopic Cushing’s or are requesting a second opinion in a complex case. There has been a significant increase in the number of patient self-referrals as well. Bilateral inferior petrosal sinus catheterization is performed as an outpatient procedure by the Vascular Radiology Department and is arranged in advance so that the patient spends 24–48 h in Boston with the results typically available in 2 days. Many such patients who are confirmed to have pituitary Cushing’s subsequently undergo transsphenoidal surgery at Massachusetts General Hospital because of the high neurosurgical cure rate. Over the 18 yr since 1978, the cure rate for microadenomas, defined as profound hypoadrenalism postoperatively (urinary free cortisol, <30 µg/24 h; serum cortisol, <3 µg/dL), is 84%. Diagnostic and surgical techniques have improved, and over the past 4 yr, the cure rate for newly diagnosed Cushing’s microadenomas is 96%, with 48 of 50 patients cured. Forty-six of these were cured with a single transsphenoidal operation; 2 patients required a second operation, usually performed within a few weeks of the initial procedure. The recurrence rate since 1978 is 6%. No patients cured over the past 4 yr have yet recurred. In those Cushing’s disease patients whose long term postoperative care will be at the Neuroendocrine Clinical Center, the endocrinological focus is on providing as rapid a steroid taper as possible without inducing steroid withdrawal symptoms. The comprehensive recovery program for cured Cushing’s patients may also include coordination with physical therapy for patients with severe proximal myopathy and with psychiatry for patients with affective symptoms. Most patients are markedly improved clinically within 6 months and fully recovered by 1 yr, including intact hypothalamic-pituitary-adrenal axis function.

Acromegaly. Acromegaly represents approximately 10% of the pituitary adenomas seen at the Neuroendocrine Clinical Center. Such patients are most often referred by endocrinologists, with the goal of providing the patient with the best chance of curative transsphenoidal surgery. However, many are referred by other specialists, such as the gastroenterologist who realized that a patient with multiple colon polyps had acromegaly as their source, the otolaryngologist seeing a patient for hearing loss who noted overgrowth of palatal soft tissue, or the plastic surgeon performing a bilateral carpal tunnel release and noting fleshy palms. In addition to the standard evaluation with IGF-I and/or oral glucose suppression of GH, the Neuroendocrine Clinical Center has recently described the use of serum IGF-binding protein-3 levels as an additional diagnostic method in cases where conventional tests yield borderline results.

Transsphenoidal adenomectomy remains the primary therapeutic modality in patients with acromegaly. Using a normal IGF-I as a definition of cure, 100% of microadenomas associated with acromegaly (10 of 10) have been cured over the past 4 yr. However, most acromegalics present with macroadenomas. Over the past 4 yr, 45 of 55 acromegalics seen in the Center have sellar masses of 1 cm or greater. Sixty-nine percent of such patients were cured with transsphenoidal surgery. Among macroadenoma patients not cured surgically, over three quarters had tumor invasion of the cavernous sinus and/or sphenoid sinus and were, therefore, not considered surgically curable, but were debulked. Those patients not cured experienced a 45% decline in IGF-I from preoperative levels. There have been no recurrences among cured acromegalics.

Patients with acromegaly who are not cured because of large tumor size and/or extension into the cavernous sinus have access to radiation therapy, including conventional fractionated radiation and single dose stereotactic radiosurgery with proton beam, which minimizes the radiation to adjacent structures. With the availability of effective medical therapy, the indications for radiation therapy have become less clear, and this will be an important issue to address in the future. Because of the morbidity and increased mortality associated with acromegaly, medical therapy is administered to all patients with biochemical evidence of residual tumor after surgery, regardless of whether they have received radiation. Many patients are first given a limited (3–4 months) therapeutic trial of bromocriptine, particularly those with minimally elevated IGF-I levels postoperatively, despite its low rate of success in normalizing serum IGF-I levels (~8% in combined series), because it is available orally and costs significantly less than octreotide. For the majority of those patients with active acromegaly who do not achieve biochemical control with bromocriptine, octreotide therapy is initiated. Patients are taught sc octreotide self-injection by the Neuroendocrine Clinical Center nurse, and compliance is excellent. Patients who require more frequent dosing to achieve IGF-I normalization or headache control are offered a sc minipump for constant drug delivery. Neuroendocrine Clinical Center patients are offered access to new investigational agents as they become available; all acromegalics who initiated treatment with octreotide here will be contacted when longer acting somatostatin analogs become available for research use in the United States.

Postradiation patients. The second most frequent diagnosis group seen in the Center, representing 21% of the cases, includes patients who have received radiation therapy to the hypothalamic or pituitary region for a number of central nervous system tumors, including meningiomas, chordomas, chondrosarcomas, and other parasellar lesions. These patients are followed prospectively, from the time of radiation, to monitor the development of hypopituitarism. The
most common laboratory abnormality in the first several years after radiation is hyperprolactinemia, which develops in association with destruction of hypothalamic dopaminergic neurons. Often the first clinical symptoms are oligomenorrhea in a woman or decreased libido and impotence in a man, which respond well to bromocriptine therapy to normalize PRL levels, if the gonadotroph axis remains intact. Although hypopituitarism can occur within months of radiation, most patients develop no abnormalities for several years. There is a wide variability in the number of axes affected, with some patients developing panhypopituitarism, and others being normal or experiencing only partial pituitary deficiency up to 10 yr later. Annual evaluations in all patients with a history of parasellar radiation include cortrosyn stimulation testing, free T₄ index, menstrual history in women, and testosterone levels in men. Patients are instructed in the need for lifelong hormone monitoring after radiation therapy and in the symptoms of hypopituitarism so that they can seek attention between visits if needed.

Other neuroendocrine disorders. Miscellaneous neuroendocrine disorders comprise the remaining patients referred to the Center. Some are patients who benefit from the participation of a staff neurologist at the Clinical Center, such as those who have neurological disorders associated with endocrine dysfunction. These conditions include catamenial seizures, cata menial migraine and other headaches, and parasellar tumors, such as tuberculum sella meningiomas and cranioopharyngiomas. A final subgroup of patients seen at the Neuroendocrine Clinical Center includes the several patients a year who are referred with pituitary apoplexy, often in transfer from another hospital where a hemorrhagic sellar mass has been found on evaluation of severe headache and/or third cranial nerve palsy. Such patients are treated as neurosurgical emergencies, with high dose steroids to reduce edema and preclude acute adrenal crisis and immediate transsphenoidal decompression. Most patients experience full neurological recovery but become panhypopituitary. Recurrence of the underlying tumor, which is often necrotic on pathology, is uncommon.

Even in this clinic, which is comprised of many patients with rare diseases, there are "zebras." For example, there are several patients with unusual sellar lesions, such as granular cell tumors, dysgerminomas, and Rathke’s pouch cysts. A number of patients are followed with unusual causes of hypopituitarism, such as neurosarcomid, histiocytes, Sheehan’s syndrome, and bilateral carotid artery aneurysms. Other cases seen at the Center include lymphocytic hypophysitis in a postmenopausal woman, a case of biopsy-proven intrasellar salivary gland, and an actor who, during a fencing duel scene, sustained a rapier injury through the nares to his pituitary gland.

Geographic scope. From what geographic area are patients served? One third of patients are derived from the Boston urban area. Thirty to 45% of patients are from elsewhere in Massachusetts, and an additional 10–20% are from other parts of New England. Twelve to 20% of patients come from the rest of the United States, and approximately 7% are referred from abroad (Fig. 2).
studies of new forms of testosterone replacement are underway. Basic science studies have paralleled some of the in vitro work, addressing the in vivo tumor response to new medical therapies as well as incorporating innovative studies examining pituitary hormone regulation and tumor pathogenesis. For example, the question of whether Cushing’s disease is of hypothalamic or pituitary origin was addressed in molecular studies which showed that the majority of corticotroph adenomas are monoclonal and arise from a signal cell, implying a genetic mutation as the cause. In contrast, hyperplastic pituitary corticotroph tissue from a patient with an ectopic CRH-secreting bronchial carcinoid was polyclonal, implying a multicellular origin derived from diffuse stimulation of the pituitary by the excess CRH. Extensive cell culture secretion studies, immunocytochemical staining and molecular investigations lead to the characterization of the majority of nonfunctioning pituitary tumors as gonadotroph in origin. More recent research has included work with new pituitary peptides and detailed evaluation of somatostatin receptors. A partnership with neuropathology has also been important in exploring potential markers of nonfunctioning tumor recurrence and the role electron microscopy may play in the clinical management of patients with pituitary tumors in the future. It has become increasingly clear, using sophisticated pathological techniques, that pituitary tumors represent an extremely heterogeneous group. This information may become useful as pathological characteristics are correlated with clinical features, such as likelihood of recurrence or response to medical therapy. The past decade of research at the Neuroendocrine Clinical Center has yielded over 60 original reports and 20 reviews of neuroendocrine subjects.

**Educational initiatives**

One of the primary mandates of the Neuroendocrine Clinical Center has been education. This has been directed both at physicians and patients, as shown in Table 1.

**Endocrine fellowship training.** A major component of Neuroendocrine Clinical Center education is that it serves as an essential aspect of the Massachusetts General Hospital Endocrine Fellowship Training Program. Three weekly Neuroendocrine Clinic sessions provide the fellows a unique opportunity to follow a pituitary tumor patient from initial evaluation and diagnosis through long term care. Fellows perform a comprehensive office evaluation under staff supervision, and during the visit conduct dynamic diagnostic testing, such as cortrosyn stimulation, glucose-suppressed GH, or insulin tolerance testing. Each fellow follows his or her patients longitudinally, if the Center has primary responsibility for endocrine management, for at least a year and can choose to maintain their Neuroendocrine Clinic patients for all 3 of the fellowship years. The fellows also have the opportunity to observe their patients’ procedures, such as bilateral inferior petrosal sampling and transphenoidal surgery. When a patient has undergone pituitary adenectomy, the fellows manage the perioperative endocrine issues, such as monitoring for diabetes insipidus and/or SIADH, administering steroids, and testing the hypothalamic-pituitary-adrenal axis before discharge. If the surgery was performed for Cushing’s disease, the fellow evaluates for cure during the hospitalization, because a second transphenoidal operation is usually immediately performed in the few cases not initially cured. Patients are seen by the same fellow at the 6 week postoperative follow-up visit to ascertain whether there has been any damage to (or recovery of) the hypothalamic-pituitary-gonadal or thyroidal axes and to determine whether the tumor has been cured biochemically and/or in terms of tumor mass, depending on the tumor type. Pathology findings, including immunocytochemical staining for all anterior pituitary hormones, are reviewed. Options for adjuvant therapy (medical and radiation) are reviewed in detail with patients who have residual tumors. If the patient will be returning to a referring physician, the fellow receives instruction about communicating the perioperative history, pathology results, and long term treatment recommendations to provide a smooth transition. In addition, the weekly multidisciplinary Clinical Case Conference provides a venue for fellows, medical students, and residents to participate in a group discussion of all cases seen that week at the Center, including a review of laboratory test results and magnetic resonance imaging scans, thereby expanding their experience beyond only those cases they have seen themselves.

**Neuroendocrine conference.** A monthly Neuroendocrine scientific conference addressing current clinical and research topics in pituitary and hypothalamic diseases is attended by Massachusetts General Hospital physicians as well as endocrinologists in the community. There are two purposes of these conferences. The first goal is providing the Endocrine Fellows, residents, and primary care providers with a thorough didactic overview of neuroendocrinology; this is conducted during the first half of the academic year by having staff physicians in all divisions of the Center provide an annual lecture curriculum covering such topics as the evaluation of patients with Cushing’s syndrome, history and method of transphenoidal surgery, hypothalamic disorders, radiation of sellar region tumors, pituitary pathology, neuroophthalmological evaluation of patients with sellar masses, and sellar neuroradiology. The second purpose of the Center is to provide staff endocrinologists with a forum for current clinical and basic science research. Some of these sessions, which occur during the second half of the academic year, are conducted by members of the Neuroendocrine Clinical Center, with staff presenting their research work; others are by invited speakers, with recent topics including “Growth Hormone Releasing Peptides,” “Somatostatin Receptors: Structure and Physiology,” “Adrenal Insufficiency in H.I.V.-Associated Disease”, “Genetics and Management of

**TABLE 1. Neuroendocrine educational initiatives**

<table>
<thead>
<tr>
<th>Endocrine fellowship training</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuroendocrine clinical case conference</td>
</tr>
<tr>
<td>Neuroendocrine research conferences</td>
</tr>
<tr>
<td>Housestaff neuroendocrine elective</td>
</tr>
<tr>
<td>Neuroendocrine speakers bureau</td>
</tr>
<tr>
<td>Visiting professor/scientist preceptorship</td>
</tr>
<tr>
<td>Neuroendocrine clinical center newsletter</td>
</tr>
<tr>
<td>Physician and patient pituitary symposia</td>
</tr>
<tr>
<td>Internet services</td>
</tr>
</tbody>
</table>
Endocrine Neoplasia Syndromes,” and “Clinical Vignettes from the Sella.”

**Massachusetts General Hospital housestaff elective.** The Neuroendocrine Clinical Center offers a 2-week intensive elective course in neuroendocrinology to medical residents at the Massachusetts General Hospital. The resident attends the daily general endocrinology visit rounds, then participates in all of the fellow and staff neuroendocrine clinics during the week. Arrangements are made for the resident to attend the transsphenoidal surgeries performed during the elective course, and he/she then takes primary responsibility for the in-patient hormonal management. A syllabus and regular didactic sessions reviewing the principles of neuroendocrinology are also provided, and teaching cases, which include photographs of patients, are discussed with the staff preceptor. Special emphasis is placed on considering pituitary disorders in the differential diagnosis of patients in the medical residents’ clinics and on knowing how to evaluate properly for hypopituitarism. Because these problems are not routinely emphasized on the in-patient medical wards, participants in this elective course have been very enthusiastic about the unique experience it provides.

**Visiting physician/scientist preceptorship.** A recent addition to the Neuroendocrine Clinical Center teaching program has been a visiting physician/scientist preceptorship program. Initiated in response to requests by physicians from abroad, the visiting endocrinologist typically spends time in the Center observing patient evaluations, hearing case presentations, and attending conferences and transsphenoidal surgeries. It has been an interesting forum for exchanging information about different approaches to the evaluation and treatment of pituitary tumor patients.

**Speakers bureau and newsletter.** Two activities of the Neuroendocrine Clinical Center provide education beyond the setting of Massachusetts General Hospital and Harvard Medical School. The staff of the Center provides a speakers bureau, which has been used both nationally and internationally, offering a variety of clinical and research topics in neuroendocrinology. Some are reviews geared at a general audience, such as for Medical Grand Rounds, whereas others provide an in-depth discussion of a focused topic appropriate for endocrinologists. Speakers have also been used in a visiting professor capacity, reviewing complex neuroendocrine cases at other institutions and discussing possible approaches. Neuroendocrine staff typically provide more than 30–40 off-campus lectures regarding neuroendocrine topics annually throughout the United States. In addition, staff members have chaired scientific meetings related to neuroendocrine topics including the International Pituitary Congress and Pituitary Symposia at Endocrine Society meetings. The Center publishes an annual newsletter, mailed to physicians in New England, in which current neuroendocrine topics of interest are reviewed. Recent articles have included “Advancements in Recombinant Human Growth Hormone Replacement Therapy in Adults,” “Clinical Uses of Corticotropin-Relieving Hormone in the Evaluation of Patients with Cushing’s Syndrome,” and “Clinically Nonfunctioning Pituitary Adenomas: Characterization and Diagnosis.”

The Neuroendocrine Clinical Center is also on the internet (http://Neurosurgery.mgh.harvard.edu) at a site that contains the full text of the newsletter. Internet services include the educational material provided above and access to all service facilities and clinical research programs of the Neuroendocrine Clinical Center.

Beyond these formal teaching activities, there are also many informal interactions about patient care conducted at the Neuroendocrine Clinical Center. The neuroendocrine staff typically receives 10–25 calls each week from physicians requesting to “run a case by.” These phone requests can range from less than 1 min, such as asking where to find a particular assay or asking how to refer a patient to Boston for bilateral inferior petrosal sinus sampling, to more than half an hour reviewing detailed lab results and requesting suggestions for the next step in a specific patient’s care. The majority of such queries are from endocrinologists, but calls from general internists and gynecologists have been increasing rapidly over the past few years as physicians are under pressure to avoid subspecialty referrals.

Finally, the educational role of the Neuroendocrine Clinic has recently extended to patients, with preparation of educational pamphlets such as a “A Patient’s Guide to Acromegaly” and editing an NIH patient brochure entitled “Cushing’s Syndrome.” The Center has also served as a base for patient support groups that conduct meetings at Massachusetts General Hospital. Recently, a Pituitary Awareness Day was held at the Massachusetts General Hospital for patients and their families in conjunction with the Pituitary Tumor Network Association. Similar events have also been conducted at several other major pituitary centers in the United States. Patient education is a key aspect of the role of the neuroendocrine nurse who conducts a weekly clinic, providing direct patient teaching, such as in the use of intratestosterone or sc octreotide injections.

In summary, 10 yr of the Neuroendocrine Clinical Center at the Massachusetts General Hospital have seen it grow into an international referral center for the evaluation and treatment of both pituitary tumors and disorders of the hypothalamic-pituitary region. It has served as a major facility for clinical research as well as basic science investigations regarding the pathogenesis and treatment of pituitary tumors. The key feature of this Center is its multidisciplinary composition, with close involvement of pituitary endocrinologists, experienced pituitary neurosurgeons, neurologists, radiation oncologists, and endocrine nursing as well as availability of neuroophthalmologists to provide an integrated approach to patient care that includes access to innovative clinical research programs.