Perioperative Management for Pituitary Surgery

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Conflicts

- I have disclosed that I have NO conflicts of interest regarding this presentation
Learning Objectives

Upon completion of this session, the participant will be able to:

- Describe the perioperative anesthetic implications of patients with sellar tumors, focusing upon endocrine dysfunction.
- Make rational decisions regarding the intraoperative monitoring and anesthetic options for patients undergoing pituitary surgery.
- Anticipate and manage the postoperative complications of pituitary surgery, including hypopituitarism and posterior pituitary dysfunction.
Inquisitiveness beyond measure.
Outline

- Basic information pituitary (and sellar) tumors
- Epidemiology
- Presentation and characteristics
- Case presentation (acromegaly/gigantism):
  - Preoperative assessment
  - Intraoperative management
  - Postoperative complications
Edward R. Laws, MD
Edward H. Oldfield, MD
John A. Jane, Jr. MD
Pituitary Tumors: Epidemiology

- Represent approximately 10% of diagnosed brain neoplasms
  - Autopsy series suggest that as many as 20% of people have a tumor on post-mortem examination
  - Majority asymptomatic
- Peak incidence during the 4th to 6th decade of life
- 20% of all brain tumors at academic medical centers

Sellar Tumors in Children

- University of Pittsburgh
- 133 pediatric patients encountered from July 1999 – May 2011
- Mean age at time of surgery 12.7 years (median 14.2 years)
- Most commonly craniopharyngioma/Rathke’s cleft cyst
- Pituitary adenomas rare

### TABLE 2: Summary of the major presenting symptoms of patients with skull base tumors

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Sellar Tumors in Children

- Nemergut Database (~1000 patients over 13+ years)
  - 4.5% of patients are < 18 years
  - 1.5% of patients are < 12 years
- Most commonly craniopharyngioma/Rathke’s cleft cyst
Pituitary Tumors: Classification

- Classified by size
  - Macroadenoma: >10 mm in any dimension
  - Microadenoma: <10 mm in every dimension

- Neuroendocrine Status
  - Functioning adenoma: Produce a single, predominant hormone (70% of tumors)
  - Non-functioning: Do not produce an active hormone (30% of tumors)
  - Silent: Produce a single, predominant hormone but patients do not have related symptomatology
Pituitary Tumors: Three Presentations

- Hormone excess
  - ACTH (10-15%): Cushing’s disease
  - Growth hormone (5-10%): Acromegaly/Gigantism
  - Prolactinoma (20-30%): Hyperprolactinemia
  - TSH (<3%): Pituitary hyperthyroidism
  - LH/FSH (5%): Often functionally silent
  - Mixed
Pituitary Tumors: Mass Effects

- Local Mass Effects
  - Headache
    - Most common complaint in microadenoma
  - Visual changes (bitemporal hemianopsia)
    - Most common complaint in macroadenoma
  - Compression of normal gland and resulting anterior pituitary dysfunction
    - 70-90% patients with a macroadenoma will be deficient in at least one pituitary hormone on formal testing
    - Prolactin often increased
  - Increased ICP (relatively rare)
  - Diabetes insipidus (exceptionally rare)

Chivukula S. et al.

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Craniopharyngioma

- Craniopharyngiomas are benign neoplasms that typically arise in the sellar/suprasellar region
- Relatively rare
  - 1 – 3% of all brain tumors; 5 – 10% in children
  - ~350 new cases/year in the United States
- Occur anywhere along the infundibulum (from the floor of the third ventricle, to the pituitary gland)
Craniopharyngioma

- Three types
  - Adamantinomatous (pediatric) 90%
  - Papillary (adult) 10%
  - Mixed (have both papillary and adamantinomatous features) ~15%

- Locally aggressive
Craniopharyngioma

- Headaches and potentially raised ICP
- Visual symptoms
  - ~20% of children
  - ~80% adults
- Endocrine abnormalities
  - Short stature and delayed puberty in children
  - Amenorrhoea
- **Diabetes insipidus**
- Behavioral change and depression due to frontal or temporal extension
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Rathke’s pouch is a normal component of embryological development which eventually forms the pituitary gland.

A remnant persists as a cleft that lies within the pituitary gland.

Occasionally, this remnant gives rise to a large cyst: Rathke’s Cleft Cyst
Rathke’s Cleft Cyst

- Considered by many to be on a continuum with craniopharyngioma
- Most are asymptomatic but present similar to craniopharyngioma, albeit much less aggressively
- Rathke’s “headache”
  - Frontal Episodic headache secondary to changes in volume of cyst
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Pituitary Tumors: Incidental

- Incidental finding on intracranial imaging
  - Chronic headache workup
  - Head Injury
Mass Effect

Pituitary Tumors: Treatment (Medical)

- Medical therapy with dopamine agonists is available
  - Treatment of choice in patients with a prolactinoma (reduces symptoms and tumor size)
  - May reduce symptoms in all patients
- Other drugs are available: for example, acromegaly patients may be treated with somatostatin analogues
  - Mainly palliative—does not reduce tumor size
  - More frequently used to reduce signs and symptoms of systemic disease prior to surgery
## Medical Treatment

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<td>Cushing’s disease</td>
<td>Ketoconazole, metyrapone, metyrapone (block cortisol synthesis)</td>
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from Dunn LK and Nemergut EC Curr Opin Anaesthesiol 2013 Oct; 26(5):549-54
Pituitary Tumors: Surgical Approach

- Bifrontal craniotomy
  - Better “exposure” (optic nerves visualized)
  - Increased morbidity and mortality
  - Uncommon in 2016

- Transsphenoidal approach
  - Initially performed by Schloffer in 1906 and refined by Cushing 1910-1925
  - Less “exposure”
  - Lower morbidity and mortality
THE PITUITARY BODY
AND ITS
DISORDERS

CLINICAL STATES
PRODUCED BY DISORDERS OF THE
HYPOPHYSIS CEREBRI

BY

HARVEY CUSHING, M.D.

ASSOCIATE PROFESSOR OF SURGERY
THE JOHN'S HOPKINS UNIVERSITY
PROFESSOR OF SURGERY (SELECT)
HARVARD UNIVERSITY

AN AMPLIFICATION OF THE HARVEY LECTURE
FOR DECEMBER, 1910

325 ILLUSTRATIONS

PHILADELPHIA & LONDON
J. B. LIPPINCOTT COMPANY
Approaches to the Pituitary
1916

Transsphenoidal Surgery in the Old Days
Transsphenoidal Techniques

- Transsphenoidal
  - Endonasal
  - Endonasal endoscopic (most common in 2016)
  - Sublabial (more common in children)
- Adjuncts
  - Endoscopy
  - Frameless stereotaxy
Endonasal Approach

Nasal septum
Retraction
Operating axis

Sagittal view
Tumor in sella being removed

Sublabial Approach

Neurosurgery 2002; 51:435-44.
Pituitary Tumors: Treatment (Surgical)

- Surgery is the only treatment option that offers a potential cure
  - Success highly dependent upon experience of surgeon
  - 80 – 90% in patients with a microadenoma
  - 50 – 60% in patients with a macroadenoma
  - Post-operative radiotherapy (gamma knife, proton beam, others) may be effective against residual tumors
Craniopharyngiomas: Treatment (Surgical)

- Surgery is the only treatment option that offers a potential cure
  - Success highly dependent upon experience of surgeon
  - Post-operative radiotherapy (gamma knife, proton beam, others) almost routinely performed against residual tumor
    - Recurrence surgery alone: 30 – 50%
    - Recurrence surgery + RT: 75 – 90%
    - May be higher but series are small...

Case Presentation

Your patient is a 21 year-old man who presents for the transsphenoidal resection of a growth hormone-secreting macroadenoma. Medical history is significant for:

- Hypertension (Enalapril)
- Bilateral carpal tunnel syndrome
  - Left carpal tunnel release 3 months ago
  - Right carpal tunnel release 11 months ago
- The patient had been a high school athlete, running a 5K in 14:32, now reports significant decreases in his functional capacity.
Questions

- *Is carpal tunnel syndrome more common in acromegaly/gigantism? Why might this be important?*
- *Is hypertension more common in acromegaly/gigantism?*
- *What are the cardiac manifestations of acromegaly/gigantism?*
- *What would you expect this patient’s ECG to reveal? Echocardiogram?*
- *Does this patient require further cardiac evaluation?*
Carpal Tunnel Syndrome

- Generalized soft tissue hypertrophy can lead to numerous physical manifestations
- Hypertrophy in the wrist and hand may result in ulnar artery compression
- 50% of patients may be “radial dominant”
- As many as 90% of patients with CTS may be radial dominant with compromised ulnar blood flow
- Thus, if an acromegalic patient has a history of CTS, radial artery catheterization may have higher associated risks

Large Hands and Soft Tissue Growth
Cardiac Disease and Acromegaly/Gigantism

- The most common cause of death in untreated acromegaly is cardiovascular
  - Classically, 50% of untreated patients die before the age of 50
- Hypertension with LVH is present in about 40% of acromegalic patients
- LVH is present in about 50% of non-hypertensive acromegals

Clin Endocrinol (Oxf) 1994; 41:95-102.
Clin Endocrinol Metab 1997; 82:1047-53.
Left Ventricular Hypertrophy-1

- Echocardiography reveals tremendous increases in LV mass
  - These changes occur independently from systemic hypertension
- Stroke volume and cardiac output are preserved at rest but diastolic dysfunction may severely limit exercise capacity
- Diastolic dysfunction may even exist in the absence of LVH
- A poorly compliant LV with accompanying need for high filling pressure and long diastolic filling time
Left Ventricular Hypertrophy-2

- Evidence of RVH has also been reported (although not consistently)
- LVH and diastolic function improve following successful adenoma resection except in older patients or those with long-standing disease
  - Thought to represent interstitial fibrosis
- Treatment with somatostatin analogues has also been shown to attenuate LVH, especially in young patients
  - May be used to mitigate significant cardiovascular disease prior to surgical resection

Eur Heart J 1993;14:26-33.
Clin Endocrinol 2003; 58:169-76.
86% of patients with active, untreated acromegaly have mitral or aortic valvular abnormalities

- Most abnormalities are minor (annular calcification or leaflet thickening)
- 30% aortic regurgitation
- 5% mitral regurgitation

Valvular disease is closely related to the presence of LVH

Persists in 75% of patients despite resolution of LVH and biochemical evidence of a cure

J Clin Endocrinol Metab 2004; 89(1): 71-5.
Cardiac Disease--Miscellaneous

- Although CAD of the larger, more proximal coronary arteries is uncommon, diffuse disease of the smaller vessels has been well-described
  - Complaints of angina should be taken seriously regardless of the patients age
- Rhythm abnormalities and complaints of palpitations are common, especially during exercise
  - One case report of 17,249 PVC’s during a single day

Back To Our Patient...

- Physical examination:
  - 95 kg adult man with BP 162/90, HR 80
  - The patient has coarse facial features with mild frontal bossing
  - Chest clear
  - Heart sounds are regular
  - Airway exam reveals Mallampati III opening with intact dentition
  - The patient notes that he has recently been diagnosed with OSA but has not “gotten used to prescribed nighttime CPAP”
Questions

- What changes in airway anatomy accompany acromegaly?
- Is OSA more common in acromegaly?
- Is airway management more likely to be difficult in acromegalic patients?
- How will you intubate this patient?
- If the patient were noticeably hoarse, would it alter your approach?
Acromegalic Airway Changes-1

- Acromegalic patients display hypertrophy of the upper airway
  - Facial bones, especially the mandible become thicker
  - Soft tissues of the nose, mouth, tongue, and lips also become thicker
- Hypertrophy of the laryngeal and pharyngeal tissues
  - Reduction in the size of the glottis and patients may need a smaller ETT
Acromegalic Airway Changes-2

- Hypertrophy may result in recurrent laryngeal nerve injury
- Changes in vocal strength or frank hoarseness is strongly suggestive of laryngeal stenosis and/or recurrent laryngeal nerve injury
- Reduction in cervical spine mobility
Prognathism in Acromegaly
Acromegaly and OSA

- OSA is observed in at least 30% of female and 70% of male acromegalic patients (higher in some series)
  - Central respiratory depression of unknown etiology has also been described
- Although symptoms of OSA can persist for at least a year after curative surgery, vocal cord function returns to normal within 10 days of curative surgery

Acromegaly and Endotracheal Intubation

- Successful intubation of acromegalic patients is potentially difficult
- Messick et al. first reported an incidence of 13% with a small retrospective series in the 1970’s
- Indeed, routine tracheostomy had been historically advocated for some patients

Anesthesiology 1979; 51: 72-3.
Schmitt et al. (2000)

- Prospectively examined 128 consecutive acromegalic patients
- Defined “difficult intubation” as more than two attempts, blade change, or the use of a bougie
- Overall incidence of difficulty: 10%
- Mallampati III or IV associated with difficulty, but
- 20% of “difficult” patients were assessed as Mallampati I or II
- Unpredictable difficulty?

University of Virginia Experience

- Retrospective review of 121 acromegalic intubations between 1995 and 2001
- Defined difficulty as “failure of primary technique” (i.e. DL) and need for another, secondary technique (i.e. FOB, bougie, Fast-Trach™, etc....)
- Overall incidence of difficulty: 9.1%
- Difficulty not related to tumor size or patient gender

TABLE 3. Intubating Difficulties in Patients With Pituitary Adenomas

<table>
<thead>
<tr>
<th>Clinical Disease</th>
<th>No. of Patients</th>
<th>Difficult Intubation</th>
<th>% Difficult (90% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonfunctioning adenoma</td>
<td>345</td>
<td>9</td>
<td>2.6 (1.5–4.5)</td>
</tr>
<tr>
<td>Cushing disease</td>
<td>182</td>
<td>3</td>
<td>1.6 (0–4.2)</td>
</tr>
<tr>
<td>Acromegaly</td>
<td>121</td>
<td>11</td>
<td>9.1 (5.8–14)</td>
</tr>
<tr>
<td>Prolactinoma</td>
<td>87</td>
<td>4</td>
<td>4.6 (0.2–10)</td>
</tr>
<tr>
<td>LH/FSH secreting</td>
<td>8</td>
<td>1</td>
<td>13 (4.1–43)</td>
</tr>
<tr>
<td>Thyrotropic (TSH secreting)</td>
<td>3</td>
<td>0</td>
<td>0 (1.2–52)</td>
</tr>
<tr>
<td>Total</td>
<td>746</td>
<td>28</td>
<td>3.8 (2.8–5.1)</td>
</tr>
</tbody>
</table>

LH, lutenizing hormone; FSH, follicle-stimulating hormone; TSH, thyroid-stimulating hormone.

**TABLE 4. Mallampati Score and Difficult Intubation in Acromegalic Patients**

<table>
<thead>
<tr>
<th>Difficult Intubation</th>
<th>Mallampati 1</th>
<th>Mallampati 2</th>
<th>Mallampati 3</th>
<th>Unknown</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>No</td>
<td>39</td>
<td>60</td>
<td>11</td>
<td>0</td>
<td>110</td>
</tr>
<tr>
<td>Total</td>
<td>42</td>
<td>62</td>
<td>16</td>
<td>1</td>
<td>121</td>
</tr>
</tbody>
</table>
Secondary Techniques

- Fiberoptic bronchoscopy is more likely to be difficult in acromegalic patients secondary to soft tissue hypertrophy\(^1\)
- The Fast-Trach LMA has a low first-attempt success rate (52.6\%) and insertion was noted to be difficult secondary to the large tongue\(^2\)
- **Bougie useful in most studies**

Acromegaly

Facial changes:
- Large lips, tongue, skin changes

Bony hypertrophy:
- Prognathism,
- Thick skull, jaw, hands
- Cervical spine changes

Airway obstruction
Laryngeal narrowing
Cervical spine changes
Hypertension
Cardiomyopathy
Raynaud’s Synd
Barrel chest
Chronic renal volume increase
High adrenocorticoid output

Harvey Cushing’s First Patient

A

B
Back To Our Patient...

- After the induction of anesthesia, a lumbar intrathecal catheter is placed by the neurosurgeons
- The nasal mucosal is infiltrated with a lidocaine and epinephrine containing solution
- The patient is positioned and surgery begins
Questions

- How will you maintain anesthesia?
- Why is the mucosa infiltrated with lidocaine?
- What are the potential side-effects of nasal infiltration?
- Transsphenoidal surgeries are normally carried out with the patient in a “semi-seated” position, is venous air embolism a risk?
- Is nitrous oxide contraindicated?
- What is the purpose of the lumbar intrathecal catheter?
- Is blood loss a concern?
Maintenance of Anesthesia

- There are a broad range of acceptable anesthetics for pituitary surgery.
- After any intracranial procedure, rapid emergence is desirable.
- Especially true with transsphenoidal surgery where an exam is extremely important as the optic nerves are not visualized.
- Rapidly cleared agents have become increasingly popular.
Gemma et al. (2002)

- Investigated the use of remifentanil in patients reporting for transsphenoidal surgery
- Randomized 43 patients to undergo anesthesia
  - Nitrous oxide/isoflurane + fentanyl
  - Nitrous oxide/isoflurane + remifentanil

Table 2. Data Collected During the Study Period

<table>
<thead>
<tr>
<th></th>
<th>Isoflurane group $(n = 22)$</th>
<th>Remifentanil group $(n = 21)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical time (min)</td>
<td>96 ± 28</td>
<td>90 ± 26</td>
</tr>
<tr>
<td>Time to extubation (min)</td>
<td>14 ± 5</td>
<td>13 ± 4</td>
</tr>
<tr>
<td>Time to follow commands (min)</td>
<td>16 ± 8</td>
<td>10 ± 2*</td>
</tr>
<tr>
<td>LP$_t$ (min/h)</td>
<td>5 ± 8</td>
<td>3 ± 6</td>
</tr>
<tr>
<td>LP$_{mean}$ (mm Hg)</td>
<td>58 ± 3</td>
<td>58 ± 3</td>
</tr>
<tr>
<td>HP$_t$ (min/h)</td>
<td>14 ± 12</td>
<td>20 ± 15</td>
</tr>
<tr>
<td>HP$_{mean}$ (mm Hg)</td>
<td>91 ± 5</td>
<td>93 ± 16</td>
</tr>
<tr>
<td>Labetalol (mg/kg)</td>
<td>1.0 ± 0.6</td>
<td>0.5 ± 0.7*</td>
</tr>
<tr>
<td>Urine output (mL)</td>
<td>166 ± 188</td>
<td>131 ± 117</td>
</tr>
</tbody>
</table>

HP$_t$ = time (min/h) during which MAP was > 80 mm Hg, LP$_{mean}$, HP$_{mean}$ = mean values of MAP during the same periods, LP$_t$ = time (min/h) during which MAP was < 60 mm Hg, MAP = mean arterial blood pressure. * $P < 0.01$; † $P < 0.05$ (Bonferroni adjusted Student’s t-test).

Local Infiltration of the Nasal Mucosa

- The mucosa is infiltrated with lidocaine and epinephrine containing solutions to reduce bleeding and facilitate dissection
- Lidocaine is only present to reduce the potential for arrhythmias when such large quantities of epinephrine are utilized
  - Important consideration when Halothane was used more commonly
- Not really necessary in 2016, but still used nevertheless...

Complications of Local Infiltration

- Injection results in significant amount of epinephrine and consequent hypertension
- Pasternak et al. reported that more than 50% of patients had an increase in SBP of more than 50%
- Patients on beta-blockers may develop dangerously high blood pressures secondary to the unopposed alpha-effects of epinephrine
- Multiple case reports of ST-T changes with troponin elevations in patients with otherwise normal hearts

Pasternak et al. (2004)

<table>
<thead>
<tr>
<th></th>
<th>Cushing’s Disease</th>
<th>Acromegaly</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects (N)</td>
<td>17</td>
<td>16</td>
<td>67</td>
</tr>
<tr>
<td>Epinephrine dose (µg)</td>
<td>88 ± 49</td>
<td>93 ± 44</td>
<td>86 ± 37</td>
</tr>
<tr>
<td>Pre-injection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>115 ± 21</td>
<td>103 ± 19</td>
<td>103 ± 14</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>64 ± 13</td>
<td>58 ± 11</td>
<td>56 ± 10</td>
</tr>
<tr>
<td>HR (beats per minute)</td>
<td>70 ± 11</td>
<td>67 ± 17</td>
<td>62 ± 14</td>
</tr>
<tr>
<td>At maximum SBP postinjection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP (mm Hg)</td>
<td>174 ± 35*</td>
<td>148 ± 36*</td>
<td>168 ± 42*</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>90 ± 15*</td>
<td>77 ± 19*</td>
<td>80 ± 20*</td>
</tr>
<tr>
<td>HR (beats per minute)</td>
<td>70 ± 17</td>
<td>71 ± 20</td>
<td>64 ± 12</td>
</tr>
<tr>
<td>Net change in SBP (mm Hg)</td>
<td>58 ± 31 (0.67)</td>
<td>45 ± 28 (0.55)</td>
<td>65 ± 39</td>
</tr>
<tr>
<td>Net change in DBP (mm Hg)</td>
<td>25 ± 15 (0.54)</td>
<td>30 ± 18 (0.07)</td>
<td>24 ± 19</td>
</tr>
<tr>
<td>Net change in HR (beats per minute)</td>
<td>0 ± 16 (0.82)</td>
<td>4 ± 13 (0.32)</td>
<td>2 ± 16</td>
</tr>
<tr>
<td>Subjects with a greater than 50% increase in SBP upon intranasal injection (%)</td>
<td>53</td>
<td>50</td>
<td>61</td>
</tr>
<tr>
<td>Subjects with greater than 1 mm ST-segment changes with injection (%)</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
</tbody>
</table>

SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate.
Values expressed as mean ± SD.
There were no significant differences between either group and the control group.
P values for each group compared to “control” group expressed in parentheses for SBP, DBP, and HR.

*P < 0.05 compared to preinjection value with group.

Transsphenoidal Surgery and VAE

- The incidence of VAE in the semi-seated position for transsphenoidal surgery is reported to be 10% (using precordial Doppler).
- Incidence increases substantially with head-up angle greater than 40°.
- Nevertheless, a clinically significant VAE has never been reported in the literature nor suspected in the > 5000 cases at UVA.
- Nitrous oxide not contraindicated.

Lumbar Intrathecal Catheter

- Used to assist in the visualization of the tumor
  - CSF can be injected or removed to move the tumor up and down in the operating field
  - Air may be injected to “push” a large suprasellar tumor down and outline the tumor on intraoperative fluoroscopy
- If air is injected into the CSF, nitrous oxide should be discontinued
Anatomy

Blood Loss During Transsphenoidal Surgery

- There is the potential for significant blood loss given the proximity of the pituitary to many intracranial arteries
- Infrequent but frequently fatal complication
- In the event of injury, deliberate hypotension may assist in visualization and repair
Blood Loss During Transsphenoidal Surgery

- Mild to moderate venous “oozing” from the cavernous sinus is a more common annoyance
- In one study, bleeding not related to CVP or cavernous sinus pressure
- In the same study, bleeding related to tumor size and surgical experience

Back To Our Patient...

- After successful resection of the adenoma, a fat graft is taken from the abdomen

Questions:
- What is the purpose of the fat graft?
- Is "fat grafting" associated with increased morbidity?
- What about pain?
CSF-leaks and Fat Grafts

- Often, a fat graft is obtained from the abdomen and placed in the sella prior to reconstruction of the floor whenever a readily observable CSF-leak is present
  - Swiped with cotton such that small wisps of cotton cling to the graft
  - Thought to engender a mild inflammatory reaction that helps seal the leak
- Some neurosurgeons place a fat graft after every surgery—even if no CSF leak is present
Nemergut et al. (2005)

- The presence of an intraoperative CSF-leak results in:
  - A 3-fold increase in the post-operative diagnosis of transient DI (33.3% vs 11.3%)
  - A 3-fold increase in the need for treatment with DDAVP (22.7% vs 7.5%)
  - A 4-fold increase in the diagnosis of persistent post-operative DI (4.4% vs 0.9%)
- Likely represents a more aggressive resection; however, direct effect of fat graft itself cannot be eliminated

Flynn and Nemergut (2006)

- The presence of an intraoperative CSF-leak results in a doubling in the incidence of vomiting (11.4% vs. 5.3%)
- Mechanism unclear
  - Aggressive resection?
  - Inflammation?
  - Intracranial air?
  - Direct effect of fat graft?
- Regardless, routine prophylaxis probably indicated

Back To Our Patient...

- The patient is successfully extubated and brought to the PACU
- You are called by the PACU nurse after he puts out 1200 cc urine in two hours and complains of extreme thirst

Questions:
- Is the urine output concerning? If so, what are the likely causes?
- When and if (and how) should it be treated?
Post-Operative Polyuria--Differential

- Overzealous perioperative fluid administration
- Osmotic diuresis
  - Mannitol administration
  - Hyperglycemia
- Idiopathic acromegalic diuresis
  - Mechanism unclear
- Diabetes insipidus

ADH Secretion

- ADH is synthesized in the supraoptic and paraventricular nuclei of the hypothalamus
- Packaged, transported down the hypothalamoneurohypophyseal tract to the posterior pituitary
- In the posterior pituitary, it undergoes final maturation and is stored for future release
- The principle stimulus for ADH release is plasma osmolarity
  - A 1 – 2% increase is enough to stimulate release
- DI results from a relative or absolute deficiency of ADH
Diabetes Insipidus--Diagnosis

- Diagnostic features include:
  - Voluminous polyuria (4-18 L/day)
  - Hypotonic urine (< 300 mOsm/L or specific gravity of < 1.005)
  - Hypertonic serum and/or rising serum sodium
  - Extreme thirst
- Patients often crave “ice-cold” fluids
  - Evidence that “cold” fluids are a more powerful stimulus for ADH release

Diabetes Insipidus

- After pituitary procedures, DI can result from damage anywhere along the hypothalamus-pituitary axis
- Essentially can present in three ways:
  - Transient, self-limited DI
  - Persistent DI
  - "Triphasic" DI
    - Initial polyuric phase (like transient DI)
    - Interlude of normal urine output or "antidiuresis phase" (ADH release from degenerating neurons)
  - Permanent DI
Diabetes Insipidus--Predictors?

- Difficult to predict who will get DI
  - Total hypophysectomy leads to DI less than 50% of time (less than 33% in humans)
    - 90% of the magnocellular neurons must bilaterally degenerate to produce permanent DI
  - Damage must be high in the tract for persistent DI to occur
  - Transient DI is more common when tumor is smaller
    - Patients with larger tumors have already shifted to “hypothalamic” ADH release?

Nemergut et al. (2005)

- Diabetes Insipidus is one of the most common complications of pituitary surgery.
- At the University of Virginia, following transsphenoidal surgery the overall incidence of:
  - Transient DI is 18.3% (16.6% for pituitary adenomas)
  - Persistent DI is 2.0% (0.6% for pituitary adenomas)

Diabetes Insipidus--Treatment

- Treatment must be individualized to each patient
  - Ultimate goal is restoration of euvolemia
- Treatment with DDAVP is normally unnecessary in awake patients with intact thirst mechanisms
- DDAVP is probably only necessary when:
  - Significant discrepancy between intake and output (and/or weight loss)
  - Rising serum sodium (> 145 mEq/L)
  - Urination interferes with sleep
Diabetes Insipidus--Treatment

- Critical to avoid “overshoot” hyponatremia with DDAVP
What about pain?

- Although pituitary surgery can be very “stimulating” and associated with intraoperative hypertension
- Most patients require very little postoperative analgesia
- Pituitary has highest concentration of endogenous opioids in the CNS

Flynn and Nemergut (2006)

- At the University of Virginia
  - Median consumption of opioids in the PACU was 4 mg (morphine equivalents)
  - Increased consumption associated with later DI
  - Decreased consumption associated with a lumbar drain

Final Thoughts

- One case report of an intracranial NG tube placed 14 days after transsphenoidal surgery
- Another case report of an intracranial NG tube placed 5 days after transsphenoidal surgery
- Several case reports of intracranial NG tube placed during transsphenoidal surgery (after the tumor had eroded through the bone)

Not Good

Persistent Bony Defect

- After transsphenoidal surgery, patients have a persistent bony defect
  - Nasal intubation contraindicated
  - Placement of NG tube contraindicated
- Unclear how long defect persists
  - At least 14 days...
Summaries
Preoperative Preparation

- Hormone replacement therapy for panhypopituitarism
- “Stress dose” steroid is often unnecessary, but the prudent practitioner should be aware of the risk of absolute or relative hypocortisolism and be prepared to treat, if necessary
Monitoring

- Consider invasive arterial monitoring if BP cuff size is inadequate or in patients with significant cardiac disease.
- Acromegalic patients may have compromised ulnar blood flow. Radial arterial line should be placed with caution.
- Theoretical risk of VAE due to head up positioning. No reports of VAE-related morbidity or mortality and additional monitors (i.e. end tidal nitrogen or precordial Doppler) not typically required.
Airway Management

- Standard ETT or oral RAE are both acceptable
- Be prepared for difficult airway in acromegalic patients (Mallampati class 1 and 2 patients may be difficult to intubate)
- If macroglossia present, intubation with intubating LMA or fiberoptic bronchoscope difficult. Consider awake fiberoptic intubation.
- Consider rapid sequence induction in patients with GERD or DM and delayed gastric emptying
Maintenance of Anesthesia

- Infiltration of nasal mucosa with local anesthetic and epinephrine may cause dysrhythmias and hypertension
- Conduct anesthetic to facilitate rapid emergence. Propofol, remifentanil, or volatile anesthetics all reasonable
- Muscle relaxation to provide immobile surgical field and reduce risk of CSF leak, visual field, or vascular injury
- Injury to carotid artery may result in significant blood loss, but this is uncommon. Deliberate hypertention may facilitate repair
- Valsava maneuver may be used to check for CSF leak
Extubation

- Suction stomach and oropharynx to remove blood and irrigation fluid
- Perform awake extubation in seated position to minimize risk of airway obstruction or aspiration
Postoperative Complications

- PONV prophylaxis and treatment
- Treat headache pain with opioids, NSAIDs or acetaminophen
- Monitor serum sodium and UOP for development of DI. SIADH is rare
- Postoperative visual field testing is important as injury optic nerves may result in catastrophic loss of vision.
- Complications include cranial nerve palsy or CSF leak
- Screen for hypopituitarism and replace hormones as needed