

## GRADED REPAIR OF CRANIAL BASE DEFECTS AND CEREBROSPINAL FLUID LEAKS IN TRANSPHENOIDAL SURGERY

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**OBJECTIVE:** A graded approach to cerebrospinal fluid (CSF) leak repair after transsphenoidal surgery is presented.

**METHODS:** Patients undergoing endonasal tumor removal during an 8-year period were reviewed. Intraoperative CSF leaks were classified as Grade 0, no leak observed; Grade 1, small leak without obvious diaphragmatic defect; Grade 2, moderate leak; or Grade 3, large diaphragmatic/dural defect. Cranial base repair was tailored to the leak grade as Grade 0, collagen sponge; Grade 1, two-layered collagen sponge repair with intrasellar titanium mesh buttress; Grade 2, intrasellar and sphenoid sinus fat grafts with collagen sponge overlay and titanium buttress; and Grade 3, same as Grade 2 with CSF diversion in most cases. A provocative tilt test was performed before patient discharge to assess the integrity of the CSF leak repair. Protocol modifications adopted in 2003 included an intrasellar fat graft in Grade 1 leaks with a large intrasellar dead space, frequent use of BioGlue (CryoLife, Inc., Atlanta, GA) in Grade 1, 2, and 3 leaks, and CSF diversion for all Grade 3 leaks.

**RESULTS:** Among 668 cases in 620 patients (475 pituitary adenomas and 145 other lesions), an intraoperative CSF leak was observed in 57% of the cases: 32.5% Grade 1, 15% Grade 2, and 8.7% Grade 3. Postoperative repair failures occurred in 17 cases (2.5%), including 0.7, 3, 1, and 12% of Grade 0, 1, 2, and 3 CSF leaks, respectively. Bacterial meningitis occurred in three patients (0.45%). After protocol modifications in 2003, repair failures decreased from 4 to 1.2% ( $P = 0.02$ ).

**CONCLUSION:** A graded repair approach to CSF leaks in transsphenoidal surgery avoids tissue grafts and CSF diversion in more than 60% of patients. Protocol modifications adopted in the last 340 cases have reduced the failure rate to 1% overall and 7% for Grade 3 leaks. Provocative tilt testing before patient discharge is helpful in the timely diagnosis of postoperative CSF leaks.

**KEY WORDS:** Cerebrospinal fluid leak, Cranial base, Pituitary adenoma, Skull base, Transsphenoidal surgery

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Transsphenoidal surgery is considered safe and effective for the removal of pituitary adenomas and many other parasellar tumors (7, 20, 31, 45, 57). After tumor removal, an effective exit strategy is required to avoid postoperative cerebrospinal fluid (CSF) leak and related complications of meningitis and tension pneumocephalus. Postoperative CSF leak rates after adenoma removal are typically less than 5%, whereas higher rates are reported for extended transsphenoidal approaches (1, 6, 8, 11, 15, 20, 27–29, 38, 45). Because of the variety of tumors accessed by the transsphenoidal route, there is

a spectrum of surgical defects requiring repair. Numerous reconstruction methods have been devised with a variety of materials, including fat, muscle and fascia, vascularized mucosal flaps, vicryl patches, and collagen preparations. Buttress materials such as cartilage or bone, absorbable and nonabsorbable plates, and titanium mesh are often used (6, 9, 10, 16, 21, 37, 43, 52, 56, 57). Tissue sealants, such as fibrin glue, BioGlue (CryoLife, Inc., Atlanta, GA), and DuraSeal (Confluent Surgical, Inc., Waltham, MA), are also frequently used (9, 10, 43, 52, 56). Repairs are often further augmented with lumbar CSF diversion.

In this report, we detail our experience using a CSF leak grading and repair protocol based on two premises: 1) small CSF leaks can be repaired in a minimalist fashion, whereas larger defects require maximal and multiple measures and 2) all CSF leak repairs require a rigid or semirigid buttress to hold the repair in position. This grading system was briefly described in 2001 with our description of collagen sponge and titanium mesh for small “weeping” CSF leaks (37); we later described CSF leak rates after standard and extended endonasal approaches (16, 23, 57). Here, we detail our overall experience with this protocol and describe pitfalls and subsequent modifications that seem to have improved the success rate. To our knowledge, such a grading system for transsphenoidal CSF leak repair has not been published.

## PATIENTS AND METHODS

### Patient Population

The pituitary tumor database of the University of California, Los Angeles (UCLA) and Harbor-UCLA Medical Centers was retrospectively reviewed. All patients undergoing endonasal transsphenoidal tumor removal were identified. Operative notes and follow-up clinical notes were reviewed for demographic data, tumor pathology, CSF leak grade and repair method, and complications. All procedures were performed by the senior author (DFK). All patients had at least 3 months of postoperative follow-up. Our institutional review board approved the study protocol.

### Assessment for an Intraoperative CSF Leak

All patients underwent operation via a direct endonasal approach with the operating microscope, as previously described (16, 57). After tumor removal, a determination was made regarding whether or not a CSF leak was present, as well as its location and size. To help localize small leaks, a Valsalva maneuver was performed by the anesthesiologist to an intrathoracic pressure of approximately 30 mmHg to transiently elevate the intracranial pressure and provoke CSF egress while the intrasellar space was observed through the operating microscope or endoscope.

### CSF Leak Grading System and Repair Protocol

As previously described (23, 57), intraoperative CSF leaks were categorized based on size: Grade 0, no leak observed; Grade 1, small “weeping” CSF leak confirmed by Valsalva maneuver without a visible diaphragmatic defect; Grade 2, moderate leak with definite diaphragmatic defect; or Grade 3, large diaphragmatic and/or dural defect created as part of a suprasellar or transclival extended transsphenoidal approach (Table 1). The repair was based on the CSF leak grade as follows: Grade 0, collagen sponge only (Helistat-Collagen Hemostatic Sponge; Integra LifeSciences Corp., Plainsboro, NJ); or Instat Collagen Absorbable Hemostat; Ethicon, Inc., Johnson & Johnson, Somerville, NJ); Grade 1, a single layer of collagen sponge placed over the exposed pituitary gland, diaphragma

**TABLE 1. Cerebrospinal fluid leak grading system**

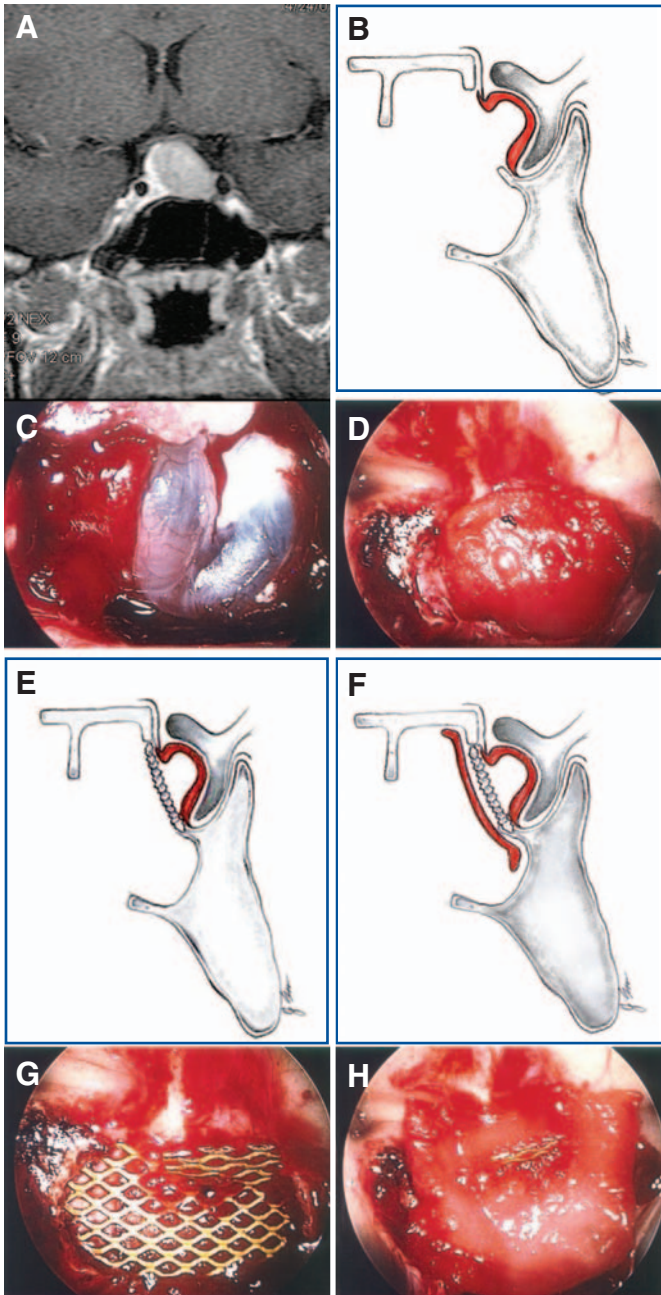
Grade of leak	Description of leak
Grade 0	Absence of cerebrospinal fluid leak, confirmed by Valsalva maneuver
Grade 1	Small “weeping” leak, confirmed by Valsalva maneuver, without obvious or with only small diaphragmatic defect
Grade 2	Moderate cerebrospinal fluid leak, with obvious diaphragmatic defect
Grade 3	Large cerebrospinal fluid leak, typically created as part of extended transsphenoidal approach through the supradiaphragmatic or clival dura for tumor access

sella and sellar dura, followed by a titanium mesh buttress (0.2-mm Micro Mesh; Stryker Leibinger, Kalamazoo, MI) wedged into the intrasellar, extradural space, followed by a second layer of collagen sponge placed over the mesh; Grade 2, intrasellar abdominal fat graft, and a collagen sponge placed over fat graft, followed by intrasellar titanium mesh buttress and additional fat placed in the sphenoid sinus; and Grade 3, same as Grade 2 repair with the addition of lumbar CSF diversion for 48 hours (Figs. 1 and 2; Table 2).

In all repairs, the titanium mesh was placed over the collagen sponge and not directly on the dura. The mesh was cut and shaped to the appropriate size, including a small handle so that it could be maneuvered into the intrasellar extradural space in either a transverse or cephalad-to-caudal direction. Care was taken to trim sharp edges off the mesh and ensure that there was no encroachment on the optic canals or cavernous sinus. In Grade 1 and 2 repairs, the mesh was wedged transversely so that 1 to 2 mm of mesh extended under the bone edge along each cavernous sinus (Figs. 1 and 2). For Grade 3 repairs after a suprasellar extended transsphenoidal approach, the mesh was wedged from the inferior lip of the sellar bone to the anterior superior bony defect in the posterior planum.

An additional concern in Grade 3 leaks is the possibility of intradural graft migration because there is typically a large diaphragmatic and/or dural defect through which the fat graft and collagen may migrate. Thus, in assembling the graft, it is important to have portions of the fat and collagen extending out extradurally on at least two sides of the defect (typically, bilaterally) so that when the mesh is placed in the extradural bony defect, it holds the fat and collagen against the edges of the bony and dural defect, thereby preventing intradural graft migration.

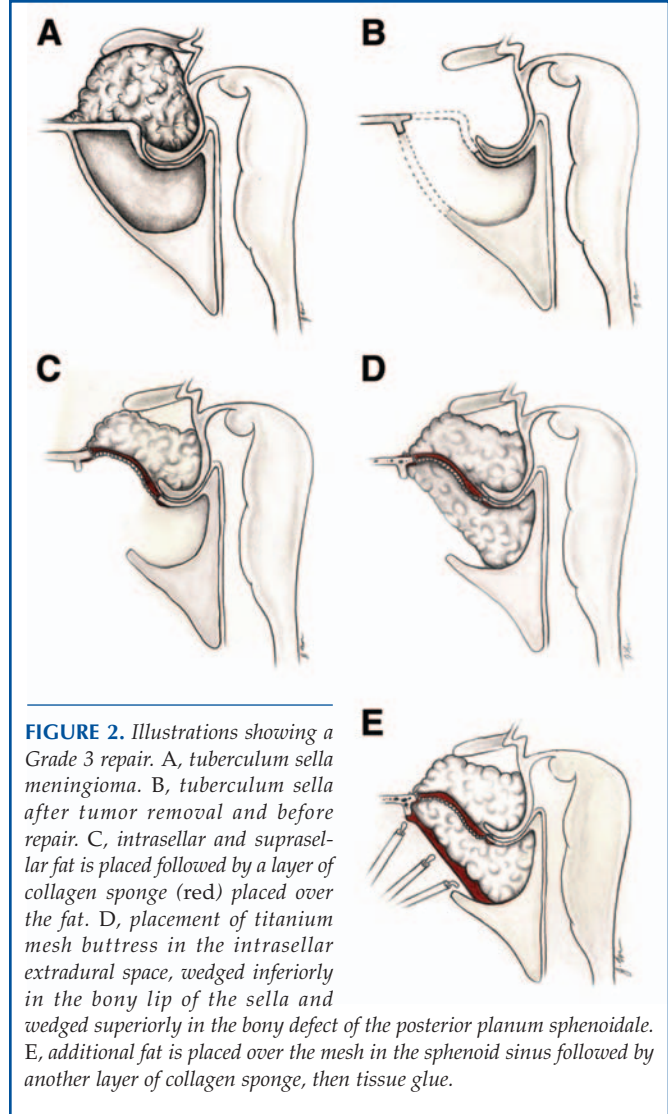
For all Grade 1, 2, and 3 repairs, after the mesh was positioned in the intrasellar, extradural space, a Valsalva maneuver was performed to ensure that CSF was not streaming around the repair and that the mesh did not dislodge. If there was a persistent leak, the repair was revised by adding more fat or collagen. If the mesh dislodged, a new piece that is slightly wider or taller was configured.



**FIGURE 1.** Intraoperative photographs and illustrations showing a Grade 1 repair. A and C, the first layer of collagen sponge is placed over the exposed normal gland and diaphragma sella. B and D, a piece of malleable titanium mesh (0.2 mm thick) (red) is cut to the appropriate shape. E and G, placement of titanium mesh (red) buttress in intrasellar extradural space wedged side-to-side. F and H, the second layer of collagen sponge (red) is placed over the mesh.

**Repair Protocol Modifications**

In operations performed after October 2003, a thin layer of BioGlue was applied on the outer collagen layer to reinforce most Grade 1 leak repairs. Similarly, in Grade 2 and 3 leaks,



**FIGURE 2.** Illustrations showing a Grade 3 repair. A, tuberculum sella meningioma. B, tuberculum sella after tumor removal and before repair. C, intrasellar and suprasellar fat is placed followed by a layer of collagen sponge (red) placed over the fat. D, placement of titanium mesh buttress in the intrasellar extradural space, wedged inferiorly in the bony lip of the sella and wedged superiorly in the bony defect of the posterior planum sphenoidale. E, additional fat is placed over the mesh in the sphenoid sinus followed by another layer of collagen sponge, then tissue glue.

BioGlue was applied on the outer layer of collagen to prevent construct migration within the sphenoid sinus. BioGlue is a quick-setting tissue epoxy comprised of bovine serum albumin and glutaraldehyde and applied through a long applicator tip for transphenoidal surgery (19). Additionally, in all Grade 1 leaks with a large intrasellar dead space after tumor removal, a fat graft was placed, similar to a Grade 2 repair, and the closure was reinforced with BioGlue over the outer layer of collagen sponge. Finally, in all Grade 3 leaks since July 2003, a lumbar drain was routinely placed; before that time, CSF diversion was used inconsistently. Nasal packing was used in the first 104 cases but not in the last 564 cases.

**Postoperative Surveillance for CSF Leaks**

In patients with an intraoperative CSF leak, a computed tomographic (CT) or magnetic resonance imaging (MRI) scan is typically performed on postoperative Day 1 or 2. All patients

**TABLE 2. Cerebrospinal fluid leak repair protocol**

Grade of leak	Current repair method
Grade 0	1) Collagen sponge
Grade 1	1) Collagen sponge (intrasellar fat graft if large dead space present after tumor removal) 2) Titanium mesh buttress (intrasellar, extradural) 3) Second layer collagen sponge over mesh 4) Tissue glue to hold repair in position
Grade 2	1) Intrasellar fat graft 2) Collagen sponge over sellar dura 3) Titanium mesh buttress (intrasellar, extradural) 4) Additional fat in sphenoid sinus 5) Tissue glue to hold repair in position
Grade 3	1) Intrasellar fat graft 2) Collagen sponge over sellar dura 3) Titanium mesh buttress (intrasellar, extradural) 4) Additional fat in sphenoid sinus 5) Tissue glue to hold repair in position 6) Lumbar cerebrospinal fluid diversion for 48 hours

have a provocative tilt test performed before hospital discharge to assess for rhinorrhea. While sitting up, patients are asked to tilt their head down with the nose in a dependent position for approximately 30 seconds. A repair failure with CSF rhinorrhea is typically obvious, manifested as a persistent watery drip from one or both nostrils, whereas thicker, mucous-like drainage does not constitute CSF rhinorrhea. For patients who had a Grade 3 leak with CSF diversion, the lumbar drain was closed for 6 to 8 hours before the tilt test. If no rhinorrhea was seen with the tilt test, the lumbar drain was removed. For patients with a positive tilt test, a head CT scan was generally performed to evaluate for new or worsening pneumocephalus, and the patient was either returned to surgery for reoperation or lumbar CSF diversion was initiated.

### Data Analysis

Rates of repair failure and meningitis were compared between various groups (different grades, different pathologies, different time periods, etc.) using Fisher's exact test.

## RESULTS

### Cohort Characteristics

From July 1998 through June 2006, 620 patients (59% women; median age, 46 yr; age range, 5–86 yr) underwent endonasal tumor removal, for a total of 668 operations (Table 3). Of these patients, 100 (16%) had more than one operation, either a previous surgery at an outside hospital (by a sublabial, transseptal, or transcranial approach) or repeat surgery at UCLA. Extended transsphenoidal approaches (suprasellar, transclival, cavernous sinus, or combined) were used for parasellar pathologies in 80 patients.

**TABLE 3. Pathologic diagnoses of 620 patients undergoing transsphenoidal surgery<sup>a</sup>**

Pathology	No. of patients
<b>Pituitary adenoma</b>	475
<i>Endocrine inactive</i>	257
<i>ACTH secreting<sup>b</sup></i>	90
<i>Prolactinoma</i>	73
<i>GH secreting (acromegaly)</i>	52
<i>TSH secreting</i>	3
<b>Non-adenomatous lesions</b>	145
<i>Rathke's cleft cyst</i>	46
<i>Craniopharyngioma</i>	23
<i>Chordoma/clival mass</i>	20
<i>Meningioma</i>	19
<i>Other parasellar tumors<sup>c</sup></i>	37

<sup>a</sup> ACTH, adrenocorticotropic hormone; GH, growth hormone; TSH, thyroid-stimulating hormone.

<sup>b</sup> Including 86 cases of Cushing's disease and four cases of Nelson's syndrome.

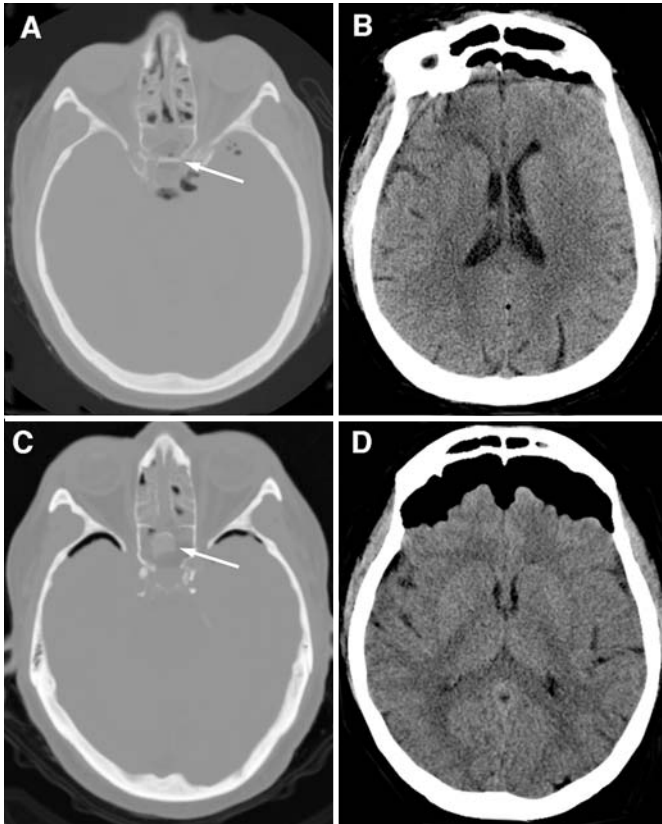
<sup>c</sup> Including arachnoid cyst, cholesteatoma, epidermoid/dermoid cyst, Ewing's sarcoma, fibrous dysplasia, gangliocytoma, giant cell tumor, hemangiopericytoma, histiocytosis, inflammatory lesion, lymphocytic hypophysitis, mucoepidermoid carcinoma, optic glioma, pituitary cyst or pseudocyst, malignant tumor metastases (breast carcinoma and non-Hodgkin's lymphoma, neuroendocrine carcinoma, schwannoma, squamous cell and undifferentiated carcinomas, sphenoid sinus carcinoma, and pituitary sarcoïdosis).

### Intraoperative and Postoperative CSF Leaks

Of all procedures, 378 (56.6%) had a recognized intraoperative CSF leak, including 217 Grade 1 (32.5%), 103 Grade 2 (15.4%), and 58 Grade 3 (8.7%) leaks (Fig. 3; Table 4). Postoperative CSF leak repair failures occurred in 17 cases (2.5%), including seven Grade 1 (3%), one Grade 2 (1%), and seven Grade 3 (12%) repairs (Table 4). There were also two (0.7%) postoperative leaks in patients without a recognized intraoperative leak (Grade 0). The failure rate for Grade 3 leaks (12%) was greater than for all other grades combined (1.6%;  $P = 0.0003$ ), and the failure rate for Grade 0 leaks (0.7%) was less than all other grades combined (4%;  $P = 0.005$ ). The failure rate was highest in meningioma cases (21%) compared with 2% in adenoma cases ( $P = 0.001$ ) and 3% in craniopharyngioma cases ( $P = 0.067$ ; Table 5).

All postoperative CSF leak repair failures were detected before patient discharge from the hospital, including more than 50% that were detected as a result of the provocative tilt test. Eleven repair failures were treated with a reoperation and six with lumbar CSF diversion for 2 to 3 days.

There was one additional patient who had a delayed CSF leak diagnosed 17 days after surgery and who was not included in the total count of repair failures because the leak emanated from a site distant from the sellar repair. He had a Grade 1 leak repair, a negative tilt test, and no intracranial air observed on a postoperative CT scan before discharge. At the time of reoperation, he was found to have CSF rhinorrhea emanating from a small bony and dural defect in the ethmoid roof



**FIGURE 3.** CT scans demonstrating titanium mesh dislodgement shortly after surgery for removal of a tuberculum sellae meningioma. A and B, early postoperative CT scans showing the proper placement of the mesh (arrow) in the intrasellar, extradural space, with small degree of pneumocephalus. Repeat CT scans several hours later, after emesis and rhinorrhea, showing displacement of the titanium mesh (arrow) into the sphenoid sinus (C) and an increase in pneumocephalus (D).

that was not recognized at his original surgery and that likely resulted from a fracture associated with septal mobilization. This defect was repaired uneventfully without meningitis or other sequelae.

**Meningitis and Other Repair-related Complications**

There were three cases (0.45%) of bacterial meningitis (Table 4). One patient with an adenoma and no observed leak (Grade 0) had a postoperative leak on tilt testing and developed *Enterococcus faecalis* meningitis. Another patient with a Grade 3 leak after debulking of a parasellar epidermoid tumor developed a postoperative leak and *Escherichia coli* meningitis. A third patient had a Grade 3 leak after biopsy of an optic glioma and had no postoperative leak but developed *E. faecalis* meningitis after hospital discharge. All three patients received antibiotics and recovered without sequelae. Overall, the meningitis rate after Grade 3 leaks (3.4%) was greater than for all other Grades combined (0.16%;  $P = 0.021$ ).

Two patients with meningiomas treated early in the series had excessively large intrasellar and suprasellar fat grafts that

**TABLE 4.** Intraoperative cerebrospinal fluid leak rate, repair failures, and meningitis<sup>a</sup>

CSF leak grade	Intraoperative CSF leaks (%)	Repair failures (%)	Meningitis (%)
Grade 0	290 (43%)	2 (0.7%)	1 (0.3%)
Grade 1	217 (33%)	7 (3%)	0 (0%)
Grade 2	103 (15%)	1 (1%)	0 (0%)
Grade 3	58 (9%)	7 (12%)	2 (3.4%) <sup>b</sup>
Totals	668	17 (2.5%) <sup>c</sup>	3 (0.45%)

<sup>a</sup> CSF, cerebrospinal fluid.

<sup>b</sup> Meningitis rate highest for Grade 3 leaks compared with all other grades combined ( $P = 0.021$ ).

<sup>c</sup> The overall repair failure rate of the recognized 378 intraoperative leaks (combining Grades 1, 2, and 3) was 4%.

caused chiasmal compression. Both were taken back to the operating room for revision, which led to a new CSF leak in one (included in the total count of 17 postoperative leaks). Both patients showed improvements from their preoperative visual status to normal. The two most recent Grade 3 repair failures were both patients who had dislodgement of the titanium mesh buttress from its original placement at surgery after repeated bouts of emesis in the recovery room; both patients were promptly returned to the operating room with placement of a slightly longer buttress (Fig. 4). One patient had delayed dislodgment of mesh that she expectorated uneventfully almost 2 years after surgery. There were no neurovascular complications related to placement of the titanium mesh.

**Repair Failures with Time and Relative to Protocol Modifications**

In procedures performed through October 2003 ( $n = 328$ ), there were 13 repair failures (4%) versus four failures (1.2%) in the 340 subsequent procedures ( $P = 0.02$ ; Table 6). The use of BioGlue and the routine use of an abdominal fat graft for Grade 1 leaks with a large dead space were both implemented at approximately this time. Before this time, 111 Grade 1 leaks occurred with six postoperative failures (5.4%). After adopting

**TABLE 5.** Intraoperative and postoperative cerebrospinal fluid leaks by pathology

Pathology	No. of procedures	Intraoperative leaks (%)	Repair failures (%)
Pituitary adenoma	503	270 (54%)	10 (2%)
Rathke's cleft cyst	49	33 (67%)	0 (0%)
Craniopharyngioma	30	27 (90%)	1 (3%)
Meningioma	19	13 (68%)	4 (21%) <sup>a</sup>
All others <sup>b</sup>	67	35 (52%)	2 (3%)

<sup>a</sup> The failure rate was highest in meningiomas cases compared with adenoma cases ( $P = 0.001$ ).

<sup>b</sup> These two repair failures occurred in patients with Grade 3 leaks with an optic glioma and a parasellar epidermoid tumor.

these protocol modifications, 106 Grade 1 leaks occurred (of these, 41 were repaired with the addition of a fat graft) with only one postoperative failure (0.94%;  $P = 0.07$ ). This one failure was in a patient in whom the repair protocol was not strictly followed; no titanium mesh buttress was placed and only collagen sponge and BioGlue were used. In all cases following the protocol, there were no repair failures of Grade 1 intraoperative leaks during this period compared with a 5.4% repair failure rate before this time ( $P = 0.02$ ). There was also a reduction in the rate of Grade 3 failures after the change in protocol (17.9% before versus 6.7% after;  $P = 0.18$ ). Since October 2003, the overall number of patients repaired without use of a fat graft or lumbar drain was 64%.

## DISCUSSION

### Summary of Experience

In 620 patients treated with endonasal transsphenoidal tumor removal, a graded CSF leak repair strategy based on the size of the leak has been used. The overall postoperative CSF leak rate was 2.5%, with the highest repair failure rate (12%) observed in patients with Grade 3 leaks. Meningitis occurred in 0.45% of patients. Three protocol modifications implemented in 2003 have reduced the overall failure rate since that time to approximately 1%.

### Intraoperative and Postoperative CSF Leak Rates

For pituitary adenomas, the intraoperative CSF leak rate ranges from 6 to 60% (3, 8, 10, 22, 37, 49, 53, 57). With extended approaches for suprasellar tumors, the intraoperative CSF leak rate approaches 100% because of the necessity of large bony and dural openings (13, 15, 17, 18, 24, 35, 36). In our series, a relatively high rate of intraoperative leaks (57%) was observed,

which may be explained, in part, by the routine use of a Valsalva maneuver to better localize the leak site and to identify small (Grade 1) leaks that might otherwise go undetected. Additionally, this series contains a large number of extended transsphenoidal procedures with large (Grade 3) CSF leaks.

Postoperative CSF leak rates after standard microscopic or endoscopic transsphenoidal approaches range from 0.3 to 14% but are generally less than 5% (8, 12, 13, 24, 25, 37, 54, 57). For extended transsphenoidal approaches, the failure rate is higher, ranging up to 65%; in most series, however, it ranges from 9 to 21% (13, 15–17, 28, 29, 35, 36, 54). Bacterial meningitis after transsphenoidal surgery is closely related to the incidence of postoperative CSF leak and ranges from 0.5 to 14% (6, 12, 25, 35). Fortunately, tension pneumocephalus is not common after transsphenoidal surgery and occurs in fewer than 0.5% of cases; it is often precipitated by lumbar CSF diversion in the setting of an inadequate cranial base reconstruction (5, 50, 51).

### Materials and Methods for CSF Leak Repair

Numerous techniques have been described for cranial base repair after transsphenoidal surgery (2, 4, 8, 9, 12, 13, 16, 21, 30, 31, 33, 34, 37, 39–41, 44, 46–48, 52, 53, 55, 57). Although the methods may vary, the same key principles apply. In general, a material to prevent CSF egress is used (e.g., fat, muscle, fascia, or collagen sponge) in conjunction with a rigid or semirigid buttress for mechanical support (e.g., septal cartilage, nonresorbable plates of silicon, polymers, titanium, or bioabsorbable materials such as vicryl). Tissue sealants and CSF diversion have been variably used (9, 10, 19, 42, 43, 52, 56).

The repair materials used in this series include collagen sponge, abdominal fat, titanium mesh, tissue glue, and, in some cases, CSF diversion. Collagen seems to be effective as a dural substitute because it provides scaffolding for fibroblast ingrowth and stimulates the coagulation cascade and platelet aggregation. When effectively compressed against the dura with a buttress, a watertight barrier is formed (37, 39, 46, 47, 55). The advantage of fat over muscle or fascia is that it can be harvested from a lower quadrant or periumbilical incision, which is generally less painful than a thigh incision. When compressed with a buttress, fat effectively fills the intrasellar dead space and sphenoid sinus and helps stop CSF egress.

Titanium mesh has been used as the buttress material in our repairs since we began using the endonasal approach because septal bone or cartilage is not taken in the approach. The advantages of titanium are that it provides relatively rigid support to hold the repair in position and prevents graft migration into either the sphenoid sinus or the intradural space by holding the graft against the edges of the bony and dural defect; it is malleable and easily configured to the bony defect; it is inert with minimal risk of infection; and it is easily visualized on CT and MRI scans, allowing its location to be easily confirmed (2, 13, 16, 37, 57). The major disadvantages of titanium mesh are that there is a risk of injury to neurovascular structures during deployment, although this complication has not occurred to date. It can also be difficult to remove at reoperation, and it can

**TABLE 6. Repair failures before and after October 2003**

Time period	No. of procedures	Repair failures (%)
Through October 2003		
Grade 0	137	1 (0.7%)
Grade 1	111	6 (5.4%)
Grade 2	52	1 (1.9%)
Grade 3	28	5 (17.9%)
All grades	Total n = 328	13 (4%)
After October 2003 <sup>a</sup>		
Grade 0	153	1 (0.7%)
Grade 1	106	1 (0.9%)
Grade 2	51	0
Grade 3	30	2 (6.7%)
All grades	Total n = 340	4 (1.2%) <sup>a</sup>
Total	668	17 (2.5%)

<sup>a</sup> A significant reduction in the postoperative CSF leak rate was seen for all grades combined ( $P = 0.02$ ).

dislodge into the sphenoid after the operation, as occurred in one patient. Newer absorbable biosynthetic materials may ultimately prove preferable to titanium mesh as a buttress (8, 9, 33, 34, 40, 41, 48, 52).

Regarding tissue glues, we have not been overly impressed that such adhesives are able to stop a CSF leak per se but have been more convinced that such substances, particularly BioGlue, can help prevent migration of the repair construct because it lends a degree of relative rigidity to the construct when applied over the collagen sponge (19, 43). It seems likely that BioGlue or other semirigid sealants can be used alone without a buttress in certain types of CSF leak repairs, although the success rate of this more minimalist and perhaps riskier technique remains unproven.

Lumbar CSF diversion, which increases the overall invasiveness of the procedure, seems to be helpful only for the largest Grade 3 defects, which are typically associated with extended approaches with large suprasellar or transclival dural openings. As our series and others have shown, meningiomas with large dural-based attachments are probably the most challenging to repair because the dural defect after tumor removal is relatively extensive and often cauterized at the edges (16, 28). A potential alternative to a lumbar drain is the use of acetazolamide to diminish CSF production for 48 to 72 hours after surgery (26, 32). Although this offers a simple, nonsurgical treatment, its effectiveness has not been confirmed.

### Graded Repair of CSF Leaks and Protocol Evolution

Although we originally used only a two-layer collagen sponge repair with titanium mesh for Grade 1 leaks and observed no repair failures in our first 20 patients (37), we subsequently had six repair failures with this method, all performed in patients who had a large intrasellar dead space after removal of a macroadenoma. Therefore, we added an intrasellar fat graft to fill the dead space in this subset of Grade 1 leaks. Since then, there has been only one failure in a Grade 1 leak closed in this fashion. For Grade 2 and 3 leaks we occasionally observed migration of fat grafts from the posterior sphenoid sinus into the anterior sphenoid sinus. We have since placed BioGlue over the outer collagen sponge layer to stiffen the construct and prevent migration. Finally, in Grade 3 leaks, we did not initially use lumbar drainage in all cases. After postoperative CSF leaks in two patients with tuberculum sellae meningiomas who did not have a lumbar drain placed initially but whose leaks resolved with CSF diversion for 48 hours, we began to include CSF diversion for all Grade 3 leak repairs (13, 16).

Three protocol modifications instituted in 2003 seem to have lowered the repair failure rate in Grade 1 and 3 leaks: 1) an intrasellar fat graft for Grade 1 leaks with a large dead space, 2) BioGlue to reinforce and hold the construct in position, and 3) CSF diversion for all Grade 3 leaks. In the future, more frequent use of the endoscope to better visualize suprasellar diaphragmatic defects may lessen the failure rate. Semirigid but moldable buttress materials and better tissue sealants may also provide watertight constructs that are more effective.

Although retrospective, these results suggest that a graded repair protocol based on leak size is useful because almost 80% of patients have no leak or only a small Grade 1 leak. By tailoring the closure to the leak size and using our current protocol, almost two-thirds of leaks can be effectively repaired without use of tissue grafts or CSF diversion. Couldwell et al. (14) recently confirmed that an extensive repair is not necessary in patients without an intraoperative leak.

### Postoperative Surveillance for CSF Leak

Detecting a postoperative leak before a patient is discharged home is essential to reduce risks of meningitis and tension pneumocephalus. A postoperative protocol of imaging and provocative tilt testing may explain, in part, the low rate of meningitis and absence of tension pneumocephalus in this series. Although the tilt test is relatively unsophisticated, we have found it useful and predictive in identifying patients with obvious postoperative leaks. In contrast, although the  $\beta$ -2 transferrin test is a more definitive test for CSF than the tilt test, this assay is not performed in most medical centers and specimens must be analyzed at an outside laboratory, with results not available for at least 2 to 3 days, which, in most instances, is too long to wait for a patient who may have an active leak (58). Thus, we propose that the use of the tilt test plus CT or MRI scanning to identify new pneumocephalus and confirm repair stability is the most rapid, reliable, and practical method for identifying an early postoperative CSF leak. Two patients in this series had early imaging after extended transsphenoidal procedures showing that the mesh had dislodged; both had prompt repairs as a result of the imaging.

### Treatment of Postoperative CSF Leaks

Once a patient has a postoperative CSF leak, timely and appropriate treatment is indicated. If CT or MRI scans show that the buttress has dislodged or that there is appreciable new pneumocephalus, reoperation is indicated. Use of lumbar CSF diversion alone should be avoided in this situation because it may provoke tension pneumocephalus (5, 50, 51). However, if there is no intracranial air and the buttress is in a good position, most leaks will resolve with 48 hours of lumbar CSF diversion without surgical revision. Such patients should be monitored for new pneumocephalus, ideally with a repeat CT scan within 24 hours of starting CSF drainage.

## CONCLUSIONS

A graded repair protocol for intraoperative CSF leaks after transsphenoidal surgery seems to be effective and helps minimize the invasiveness of the procedure for patients with no intraoperative leak or a small CSF leak. Using this approach, more than 60% of patients can avoid autologous tissue grafts and lumbar CSF diversion. The overall repair success rate has increased with time, as the protocol has been refined. However, there is still a relatively high failure rate for large (Grade 3) leaks, which will hopefully improve in the future. These results

also suggest that delayed CSF leaks and meningitis can be avoided by routine screening measures that include early post-operative imaging and use of the provocative tilt test before patient discharge from the hospital.

## Disclosures

Daniel F. Kelly, M.D., has consulting agreements with Mizuho America and Cryolife. Mizuho and Cryolife had no input into the design and results of this study or the production of this article.

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## COMMENTS

The authors have described a grading system for the types of cerebrospinal fluid (CSF) leaks seen in transphenoidal surgery. There is some value to this, as we cannot consider a few drops of CSF seen coming from the interface of the pituitary gland and arachnoid the same way we would consider a situation with a large hole in the arachnoid. They are very different and often require different types of repair. Neither can be assumed to be the same as the opening created in extended transphenoidal tumor resections. Therefore, categorizing the different leaks to evaluate the success of repair is worthwhile.

The repair method presented is just one approach this team finds successful. There can be many variations on this theme. I agree that most small leaks (i.e., grade 1 or even grade 2) do not require a lumbar

drain for diversion of CSF. For larger leaks, I like a lumbar drain; however, once placed, I prefer it remain in place for four to five days rather than 48 hours recommended by the authors. The use of the collagen sponge has been presented by this team before and is certainly one good possibility; however, there are many others. I prefer a small amount of fat and a small piece of bone from the vomer, even in a very limited transnasal opening. It is relatively easy to find a small piece of bone, except perhaps in reoperations. In that setting, I use biodegradable plates to buttress the fat, which works well with an extremely low (<1%) failure rate.

In my opinion, the exact closure type is a personal preference; however, the idea that leaks must be looked for with valsalva maneuver, postoperative positioning, and imaging is important. I also find it valuable to obtain a computed tomography scan on postoperative Day 1 in patients with a significant intraoperative leak as a baseline for intracranial air that can then be followed with serial scans if necessary. This makes certain that air is not being sucked into the intracranial compartment.

Leaks from standard adenoma surgery are usually relatively easy to manage, although there are occasional challenges. The extended procedures are always a challenge to seal, and it is heartening to see the leak rate more than halved in the latter half of this series.

**Kalmon D. Post**

*New York, New York*

In this report, Esposito et al. review their management of CSF leaks after transphenoidal cranial base surgery. The authors present a scheme of management based on the degree and extent of the CSF leak and cranial base defects. Although the classification of the CSF leaks by the authors may be fairly rigid, there is a continuum of pathoanatomic possibilities in this regard, and it is nevertheless intuitively correct. It makes sense that larger cranial base defects and greater breeches in the dura and arachnoid require more complex closures.

In regard to the closure technique described by the authors, I suspect that the improvement they observed in their results after modifying the technique in 2003, was related to obliteration of the dead intrasellar space by placing the graft inside the sella. I agree with the concept of buttressing the graft; however, I disagree with the concept of challenging the repair with the provocative tilt test. A repair that does not work will declare itself without provocation. In contrast, we advise our patients not to stoop or bend forward for about two to three weeks postoperatively.

Our closure technique and technique for preventing a CSF leakage has been described previously (1). We think one can avoid a significant number of CSF leaks in pituitary macroadenomas by not opening the anterior sella dura all the way up toward the planum to avoid opening the anterior arachnoid recess that may be occluded by the tumor. Instead, only open it up as the tumor is decompressed and/or removed. In regard to the closure technique, it has been our practice to occlude the dead intrasellar tumor bed space with an autologous abdominal fat graft in practically every case. In larger defects, abdominal fascia is applied first, followed by the fat graft admixed with pulverized surgical. If possible, we prefer to sandwich the dura opening between the intrasellar fat graft and a flattened-out extradural fat graft. The entire construct is then secured by a buttressing bone graft, which is preferably placed snugly between the dural and bony windows of the exposure. The bone used is either a posterior septal graft, or in larger defects, appropriately fashioned cortical bone from an iliac allograft. This technique effectively occludes the anterior arachnoid recess from where a significant number of leaks originate. In patients with an overt intraoperative CSF leak, the remaining gaps in the bony buttress are covered with calcium phosphate bone substitute paste. Depending on the extent

of the cranial base defect and the degree of CSF leak, we may use biologic fibrin glue to cover the construct, and/or place a lumbar drain for three to five days. This is decided on a case-by-case basis. Using this technique, we have reduced the incidence of our postoperative CSF leaks that require re-operation to well below one percent.

**Ivan S. Ciric**  
Evanston, Illinois

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1. Ciric I, Rosenblatt S, Zhao JC: Transsphenoidal microsurgery. *Neurosurgery* 51:161-169, 2002.

**T**his report by Esposito et al. concerns CSF leak repair, which is one of the main problems of transsphenoidal surgery. A classification of CSF leak is proposed to tailor repair of the leak grade. I appreciate the method which may contribute to reducing this complication, selecting the most effective surgical behavior under different circumstances. However, we should not be satisfied with the actual 2.5% of repair failure, and to further reduce these percentages, the authors are to be encouraged in the work of analysis and criticism necessary to improve the protocol. In this spirit, I would like to make some observations.

I agree that a using buttress to hold the graft in place to prevent its migration is important. However, I am not convinced by the suggested material, such as the titanium mesh, which, as the authors stated, could potentially be dangerous and difficult to remove. I believe the only viable material that may provide a lasting repair is an autologous graft, such as abdominal fat, fascia lata, mucoperiosteum and bone. I would like to moderate the authors' estimation of the value of provocative tilt testing because it could be a source of error. If the CSF leak is mainly posterior to the rhinopharynx, the test may be falsely negative. On the contrary, a false positive may owe to lacrimal or mucosal secretion col-

lected and arising from the sinuses. Therefore, and particularly in some doubtful cases, to confirm that the liquid obtained is CSF, a Beta trace protein or a Beta two transferrin test on the collected samples is mandatory. Our laboratory, which is surely not as technologically advanced as the UCLA laboratory, analyzes the Beta trace protein 1 and gives a definitive answer in one to two hours. Possibly, the problem is not the difficulty of performing the test but the absence of requesting it.

**Giorgio Frank**  
Bologna, Italy

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1. Reiber H, Walther K, Althaus H: Beta-trace protein as sensitive marker for CSF rhinorrhea and CSF otorhea. *Acta Neurol Scand* 108:359-362, 2003.

**T**his is a credible summary by a respected and experienced neurosurgical group describing the UCLA experience with repair of CSF leaks after transsphenoidal surgery. Their thoughtful repair strategy based on stratifying the degree of leak provides results similar to what are generally reported in the literature by experienced pituitary surgeons. In my own experience, little distinction is made between Grade 1 and 2 leaks and a collagen dural substitute placed intradurally and extradurally followed by a fat graft, which is usually sufficient for patients with simple leaks. Unlike the authors, I have not found it necessary to routinely use a buttress or BioGlue. With an overt leak, I add a spinal drain for two to three days to the postoperative regimen. My personal results have not been subject to the same rigorous retrospective analysis, but anecdotally have a comparable complication rate despite the omission of buttresses and BioGlue.

**Jeffrey N. Bruce**  
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