Advances in the management of CSF rhinorrhoea

Andrew C Swift, Patrick Foy

Cerebrospinal fluid fistulae are under-diagnosed, difficult to locate and often clinically silent. They are potentially lethal and carry a long-term cumulative risk of meningitis. They should be fully investigated and treated aggressively. Current endoscopic techniques combined with intrathecal fluorescein dye enable most defects to be located and sealed with minimal morbidity.

Cerebrospinal fluid (CSF) rhinorrhoea carries the risk of meningitis and is therefore an important symptom to recognize. However, the diagnosis and localization of the CSF leak can be difficult, and there is a significant risk of morbidity and mortality with conventional treatment. Advances in imaging and endoscopic techniques are improving the management and the outcome of CSF rhinorrhoea (Jones and Becker, 2001).

PHYSIOLOGY OF CSF

CSF circulates in the subarachnoid space and forms a protective fluid cushion for the brain and spinal cord. Most CSF is produced by the choroid plexus in the lateral, third and fourth ventricles, and about a third is formed from ventricular ependyma. The average volume in adults is 150 ml, and the rate of production is relatively constant at 500 ml/day with a pressure of 60–150 mmH_2O (Ow et al, 1999). An increase in the volume of CSF relative to the brain volume is known as hydrocephalus, and this can be classified as non-obstructive (communicating with the subarachnoid space) or obstructive (non-communicating) according to the cause.

HISTORICAL ASPECTS

A frontal craniotomy with an extradural or intradural approach is still the standard method of repair of an anterior fossa CSF leak in many neurosurgical centres. This surgical approach, particularly in the acute post-traumatic phase, has a significant morbidity (10.3%) and mortality (2.6%) (Eljamel, 1991). Postoperative problems include anosmia, epilepsy, retraction damage to the frontal lobes and infection. Transfacial approaches for repair of a CSF leak were described in the 1940s and included an external ethmoidectomy for access to the anterior fossa and a trans-septal approach to the sphenoid sinus. Advances in imaging of the brain and skull base and the development of endoscopic sinus surgery have gradually changed the management of this troublesome problem.

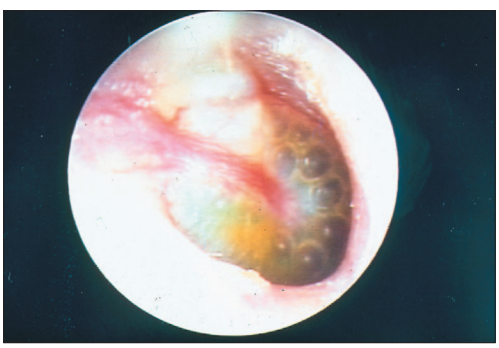
CLASSIFICATION AND AETIOLOGY

A breach of the dura may result in a CSF leak. CSF rhinorrhoea can occur from anywhere in the central anterior skull base or from a defect in the middle cranial fossa via the middle ear and Eustachian tube (*Figure 1*).

Approximately 70% of CSF fistulae reported in the literature present with CSF rhinorrhoea and just less than 30% have CSF otorrhoea (Eljamel, 1991).

Eljamel's review of 253 cases is the largest UK series and showed that head injury was the most common cause of a CSF fistula (74.3%) followed by surgery of the paranasal sinuses, cranium or pituitary (15.3%) and other non-traumatic conditions (10.4%) (Eljamel,

Figure 1. Fluoroscein-stained CSF seen through the right tympanic membrane in a patient with a skull base fracture.



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1991) (*Table 1*). Within the non-traumatic group, CSF leaks were often classified as 'spontaneous', but with improved diagnostic methods the actual cause, such as a small meningocele or a meningoencephalocele, can usually be identified and truly idiopathic leaks are now rare (Har-El, 1999).

It is important to appreciate that CSF leaks can present many years after a skull fracture.

WHAT ARE THE RISKS OF CSF RHINORRHOEA?

It had previously been assumed that the risk of meningitis would disappear when the CSF leak dried up; therefore, to avoid the morbidity of a craniotomy, the fistula should be allowed time to heal spontaneously. Approximately 30% of leaks cease within 3 weeks, and surgery could then be considered for the leaks that persisted. It was not until 1991 that a better understanding of the natural history of CSF leaks and the cumulative risk of meningitis was appreciated (Eljamel, 1991). It was noted that the risk of meningitis continued even when there was no obvious clinical evidence of a CSF leak: the dural defect in such cases had not healed sufficiently to form an effective mechanical barrier to prevent intracranial bacterial infection (*Figure 2*).

This evidence suggests that all patients should be considered for surgical repair even when the CSF leak appears to have stopped. This goal is becoming attainable with advances in endoscopic sinus surgery, which allow exploration and repair with minimal morbidity. The authors recommend an active policy of detection, exploration and repair of anterior fossa dural defects.

DETECTION OF CSF LEAKS

Clinical findings

The classic history of a CSF leak is a unilateral intermittent watery nasal discharge when the head is in a dependant position. Some patients describe the fluid discharge as tasting salty. However, the leak may be minimal or infrequent, making confirmation of the diagnosis difficult. Also, in patients who have had a head injury, the true diagnosis may be a pseudoleak. Such patients will give a history of a watery nasal discharge with exercise or emotion, and the fluid originates from the nasal mucosa as a result of autonomic dysfunction. A watery discharge from the nasal mucosa can also occur after nasal trauma and confuse the true diagnosis.

Biochemical tests for CSF

Traditionally, the glucose content of a watery nasal discharge has been used to diagnose a CSF leak, but this is far too unreliable to be of any real practical use. The best investigation to confirm a true CSF leak is to test for the protein beta-2 transferrin (Nandapalan et al, 1996). This test is now available in most large hospitals in the UK. Beta-2 transferrin is detected by electroimmunophoresis and is specific to CSF and perilymph. Occasionally, there is a similar protein in the blood and therefore a parallel control blood sample should be tested at the same time as the nasal fluid. A sample as small as 0.3 ml fluid is sufficient, but even this may be difficult to obtain in patients with subclinical leaks or in patients who are being ventilated in an intensive care unit after head trauma.

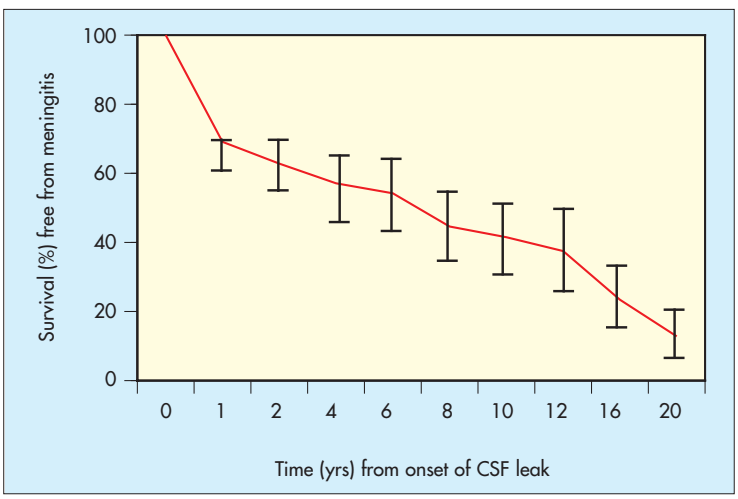
Imaging techniques

Historically, plain radiographs and tomography of the skull base were used to detect bony defects, indicating the site of the fistula. This approach was not very accurate or reliable and radioisotope tracer studies were disappointing. Advances were made with high-resolution coronal and axial computed tomography (CT) scanning aided by

TABLE 1.
Causes of CSF rhinorrhoea

Trauma	Skull fracture (affecting middle or anterior cranial fossa)	
	Penetrating injuries of frontal sinus, ethmoid sinus or orbit	
	Surgical trauma	Trans-sphenoidal pituitary surgery
		Skull base surgery or sinus surgery
Non-traumatic	Meningocele or encephalocele	
	Skull base erosion by tumour (e.g. prolactinoma, meningioma)	
	Idiopathic dehiscence	
	Raised intracranial pressure	

Figure 2. The cumulative risk of developing meningitis following a CSF leak. From Eljamel (1991).



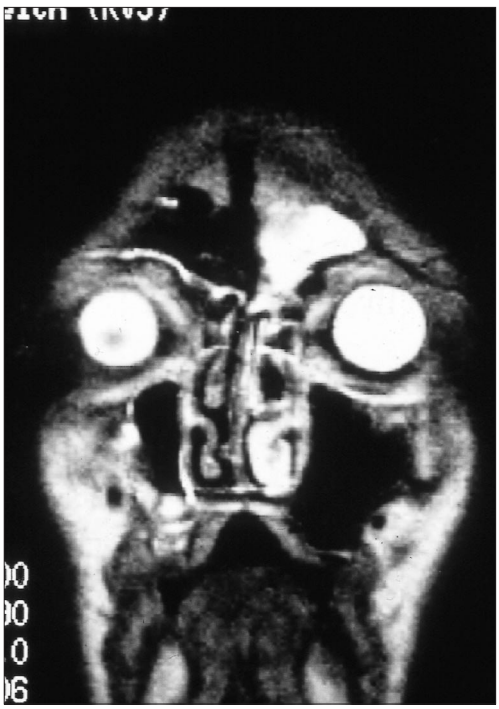


Figure 3. T2-weighted magnetic resonance imaging scan showing CSF leak into the left frontal sinus from an external penetrating injury.

intrathecal injection of water-soluble contrast agents, such as metrizamide and iohexol.

Magnetic resonance (MR) scans have also been shown to be helpful in detecting the site of a CSF leak, and T2-weighted images will demonstrate CSF as a high-intensity signal (*Figure 3*). New generation MR scanners will detect flowing CSF and may well become the investigation of choice. A combination of CT and MR currently gives the best guide as to the site of the leak and any associated pathology and is the authors' preferred method of imaging (Shetty et al, 1998).

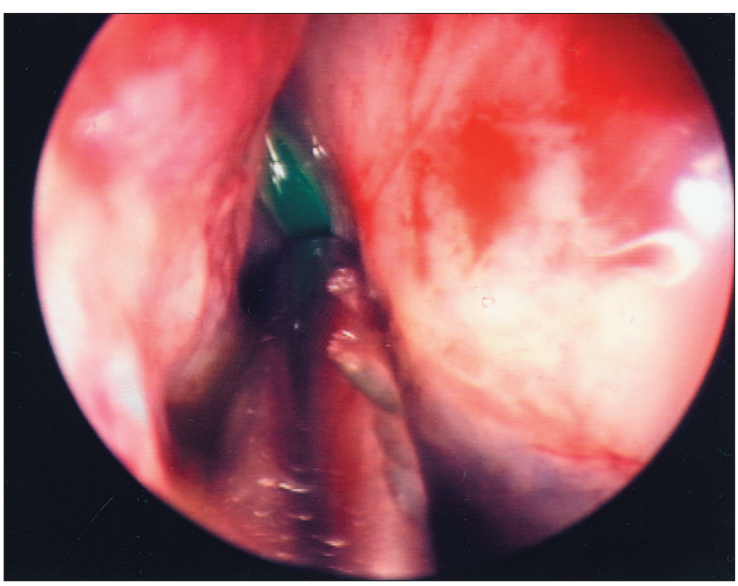


Figure 4. Fluorescein-stained CSF in the right spheno-ethmoidal recess.

Intrathecal fluorescein

A small quantity of very pure fluorescein injected intrathecally via a lumbar puncture with a narrow gauge needle will stain the CSF a fluorescent yellow. The technique is carried out by withdrawing 10 ml of CSF, adding 1 ml of 5% fluorescein (or 0.5 ml 10% solution) and slowly re-injecting the fluid intrathecally.

The technique can either be done before simple nasal endoscopy to confirm the diagnosis of an active CSF leak, or before endoscopic exploration of the anterior skull base. Fluorescein takes about 5 days to clear from the CSF, and patients should be warned that during this time, their urine will be stained yellow.

Fluorescent, yellow-stained fluid is diagnostic of a CSF leak and endoscopic exploration will enable the site to be localized (*Figures 4* and *5*). Another advantage of intrathecal fluorescein is that it can be seen through a thin dural defect that is not actively leaking at the time of the investigation. A blue light with or without a red filter can enhance the appearance of a minimal leak (*Figure 6*).

Confirmation of a sub-clinical minimal CSF leak may be aided by placing small, labelled,

Figure 5. Fluorescein-stained CSF from a leaking meningocele in the right sphenoid sinus.

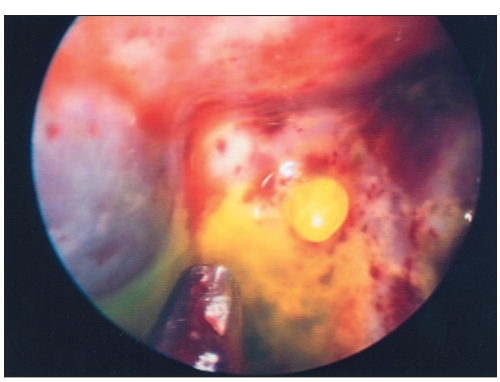
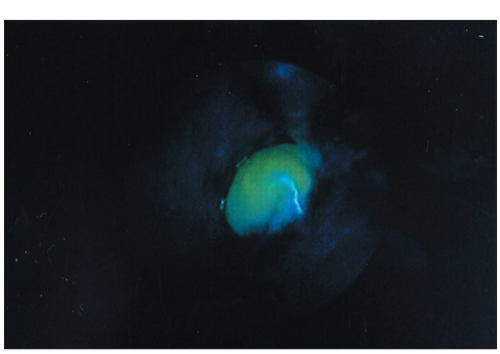


Figure 6. Enhancement of fluorescein-stained CSF by a blue filter in a patient with a small meningocele of the right posterior ethmoid sinus.



tagged neurosurgical patties in specific sites in the nose for several hours before sending for fluorescein electrophoresis. However, the authors have not found this test to be particularly useful.

Intrathecal fluorescein is extremely sensitive at detecting even the most minimal of leaks, and although early reports quoted complications, these are extremely rare with the modern day purified preparations of fluorescein. None of the complications in the early reports were permanent, but they did include numbness and weakness of the legs, generalized seizures, opisthotonus and cranial nerve deficits (Moseley et al, 1978).

MANAGEMENT OF CSF LEAKS

Prophylactic antibiotics

The use of antibiotics in the management of CSF leaks always gives rise to debate. On the one hand, it has been argued that antibiotics do not give any protection against the development of meningitis and that they may actually encourage antibiotic-resistant bacteria to cause meningitis, which then becomes more difficult to treat (Eljamel, 1993). However, a meta-analysis has shown that antibiotics do confer a small advantage in preventing meningitis (Brodie, 1997). It is the authors' view that antibiotics are indicated if there is any history that suggests chronic sinus disease in patients who have CSF leaks from acute head trauma, but they are not recommended for routine use.

Indications for surgery

Although many CSF leaks will stop spontaneously, there is a cumulative risk of meningitis of about 10% per year (Eljamel, 1991). Endoscopic surgery will facilitate exploration of the anterior skull base and repair of a leak with minimal morbidity, and the sense of smell is usually preserved if present before surgery (Marshall et al, 2001).

It is the authors' belief that all patients with a recent or active CSF leak should undergo endoscopic exploration after intrathecal fluorescein.

When to operate

Because of the cumulative risk of meningitis, the ideal time to operate is as soon as possible after the onset of the leak. However, this may not be possible in patients with head trauma until the acute brain injury or other major injuries have had time to recover.

Exploring the ethmoid endoscopically shortly after a skull base fracture will predispose the patient to bleeding and an unclear view of the skull base because of the inflammatory healing response. The authors therefore prefer to wait 3–4 weeks before undertaking such surgery.

Techniques of repair

Nearly all CSF leaks from the anterior skull base can be repaired endoscopically after injecting fluorescein intrathecally into the CSF. Once the site of the leak has been confirmed, the surrounding mucosa should be removed and the defect sealed by a graft that is fixed in position by fibrin glue (Tiseel, Immuno AG, Vienna, Austria). Various successful graft tissues have been described and include fat, muscle or fascia from a distant site, such as the thigh, or middle or inferior turbinates from the nose. Defects in the sphenoid are best dealt with by obliterating the sinus with fat. Occasionally, a rapid leak that is difficult to control may be managed by inserting a lumbar CSF drain for a few days after surgery.

Extensive skull base defects may be more suitable for external repair by craniotomy.

SPECIFIC OR DIFFICULT MANAGEMENT PROBLEMS

CSF leaks after head injuries

In patients with head trauma, the leak may be from either the anterior or middle cranial fossa, the latter presenting via the Eustachian tube. It is therefore important to examine the tympanic membranes with an endoscope to exclude fluorescein staining before exploring the skull base if a leak is suspected (*Figure 1*).

If the leak is from the frontal sinus, fluorescein-stained CSF may be seen running as a track from the frontal recess. Alternatively, an endoscope can be passed directly into the frontal sinus via an external frontal trephine. However, the authors have not found this to be as useful as first expected.

A suspected defect in the frontal sinus would require a formal external exploration via an osteoplastic flap. Since this is a much more extensive procedure, surgery is limited to patients with a proven, persistent leak. Whether there is a similar cumulative risk of meningitis from such injuries is not known. However, if a fracture line is undisplaced, it is unlikely that a residual dural defect will remain, and meningitis will therefore be unlikely. Unfortunately, there are no clear answers to this dilemma at present.

CSF leaks after sinus surgery

With the increased recognition of chronic sinus disease and the subsequent increase in endoscopic sinus surgery, there will inevitably be an increased chance of damaging the skull base. The reported incidence of this complication is

low and estimated to be 0.5% in the UK (Cumberworth et al, 1994).

If a leak is seen at the time of surgery, the defect should be sealed immediately with a graft – nasal mucosa or a section of inferior turbinate is ideal for this. However, if there is extensive sinus disease, a leak may be difficult to recognize. It is possible that such defects may remain unrecognized unless the leak persists or an intracranial complication ensues.

If a leak is suspected in the postoperative period, a high-resolution coronal CT scan should be obtained, and if possible, fluid should be collected for beta-2 transferrin analysis. Endoscopic exploration after intrathecal fluorescein should be considered as soon as possible.

The spontaneous CSF leak

A small proportion of CSF leaks are spontaneous. However, with the increased visual imaging that is possible with fine nasal endoscopes and the use of fluorescein to detect the true site of a leak, a precise diagnostic cause can be recognized in most cases. Such leaks are usually the result of a small meningocele or encephalocele or, particularly in the elderly, an idiopathic dehiscence in the anterior skull base.

Recurrent meningitis

A history of recurrent meningitis should lead the clinician to suspect that there is a defect in the skull base until proved otherwise (Schick et al 1997). It is, however, important to confirm whether the meningitis is bacterial since there are rare instances in which aseptic recurrent meningitis can occur (Mollaret's syndrome).

Management of leaks from pituitary tumours

Some surgeons routinely repair the defect at the time of trans-sphenoidal pituitary surgery, but others reserve a repair for those patients with a persistent leak.

Patients with large prolactinomas may develop iatrogenic fistulae after being treated with dopamine agonists. Prolactinomas are benign but cause local bone destruction. They respond to bromocriptine, but as their size decreases, bony defects that are 'plugged' by the tumour open up, leading to a CSF leak into the sphenoid or posterior ethmoid. Transnasal endoscopic repair should therefore be coordinated with their medical management and should only be performed after tumour shrinkage has been achieved (Leong et al, 2000).

KEY POINTS

- Unrepaired CSF fistulae have a lifelong risk of meningitis, irrespective of the time of onset, duration or aetiology of the leak.
- The 'survival free from meningitis' has been shown to be less than 42% at 10 years after a CSF fistula.
- Meningitis after a CSF fistula has a mortality of 4.7% and a total morbidity of 58.4%.
- Craniotomy and closure of a dural fistula has a mortality of 2.6% and a postoperative morbidity of 10.3%.
- Advances in imaging, endoscopic sinus surgery and the use of intrathecal fluorescein have considerably improved the management, morbidity and mortality of patients with a CSF fistula.
- Every patient with a CSF leak should be considered for surgical repair.

CONCLUSIONS

The management of CSF leaks from defects of the anterior skull base has advanced considerably over recent years, and endoscopic techniques of repair are now well established and have the advantage of low risk and morbidity. Injecting fluorescein intrathecally before endoscopy or exploration is an extremely sensitive way of detecting a CSF leak and of tracing the site of the defect. The long-term goal of repairing a defect is to minimize the risk of subsequent meningitis. HM

Conflict of interest: none.

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