Section of Laryngology

President G H Bateman FRCS

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President's Address

Experiences with Cerebrospinal Fluid Rhinorrhœa Arising from the Pituitary Fossa

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These cases are rare and no surgeon has much experience in this field. They can be divided into two groups: those arising during surgical transsphenoidal hypophysectomy and those arising as a result of disease or nonexcisional trauma to the pituitary fossa.

Any surgeon performing transsphenoidal hypophysectomy is faced in the great majority of cases with a cerebrospinal fluid (CSF) leak from the diaphragma sellæ. This is normally controlled at operation by filling the empty pituitary fossa with a free muscle graft which is held in place by packing the sphenoid with ribbon gauze impregnated with some antibiotic. If any technical error has been made a cerebrospinal rhinorrhœa will begin when the pack is removed; this happens with increasing rarity as the surgeon gains experience. In my first 50 cases it occurred six times but only once in my next 100 cases. It remains, however, as a possible complication of the operation: it is relatively easily cured. The cause is faulty application and retention of the graft in the pituitary fossa, which provides a good vascular bed which heals well.

The treatment, therefore, is exposure of the pituitary fossa under general anæsthesia, repositioning of the muscle graft and repacking the sphenoid for a further seven days. The combined nasal, septal and ethmoid approach that I use provides an easy method of exposure of the pituitary fossa: a long, 3·5 inch, Killian nasal speculum is inserted into one nostril and the mucosa of the anterior wall of the sphenoid is stretched between the tips of the blades and the mucosa is torn with a blunt dissector; the pituitary fossa is then immediately beyond the tips of the speculum and the necessary manipulation is easily carried out. These post-operative cases have always been easily and effectively treated and present no unexpected problem.

The other class arise either as the result of the implantation of irradiated material into the pituitary fossa – and this is the kernel of the problem – or as the result of disease of the pituitary of which I have experience of 2 cases, one a pituitary abscess and the other a chromophobe adenoma of the pituitary which had been treated some months previously by partial transfrontal hypophysectomy followed by telcradiation of the pituitary fossa.

Post-radioactive-implantation CSF Rhinorrhœa

Many cases are treated by yttrium implantation into the pituitary and only a very small proportion develop CSF rhinorrhœa; in spite of this, I have treated 7 cases and, though this is not a large number, I have learnt some lessons from them; as I believe this experience is unusual, I propose to describe in detail some cases and then record the conclusions I have reached and the lessons I have learnt.

Case 1 Housewife, aged 58

I first saw this patient in 1958, with acromegaly which had been diagnosed years previously; she was managed medically until in 1958 she was suffering from intense, prolonged and crippling headaches, with considerable blurring of her vision, accompanied by contraction of her visual fields. Her physician referred her to a neurosurgeon who, on account of her general condition, advised against transfrontal hypophysectomy and suggested she be referred for consideration of implantation of pellets of yttrium 90 to destroy the pituitary function and shrink the tumour. It was a big tumour.

At that time I was treating multiple metastases of mammary carcinoma by destruction of the pituitary by implanting yttrium 90 into it after

surgical exposure of the anterior aspect of the pituitary fossa by the nasal transseptal approach. I had no experience with pituitary tumours at that time, but the patient's life was miserable and it was forecast that she would soon be blind if no effective treatment could be devised. After consultation with the radiotherapist at St Thomas's Hospital I agreed to treat her and we decided to implant five pellets, distributed throughout the bulk of the pituitary tumour.

On June 13, 1958, when the sphenoid was opened, the anterior bony wall of a very large pituitary fossa was exposed. It had been decided to make five puncture holes, disposed as are the pips of a 5 domino, and to introduce one yttrium rod into each puncture. The bony wall was thin and easily punctured with an antrum trocar. Four of the punctures were dry, but the upper right puncture leaked CSF quite briskly. The yttrium rods were inserted (Fig 1). The depth of the

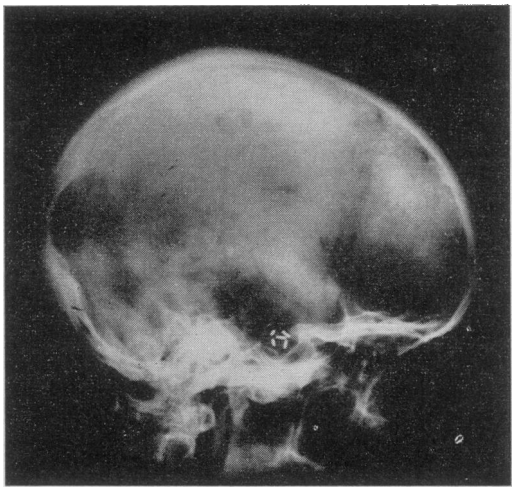

Fig 1 **Case 1** *Lateral X-ray after insertion of yttrium, showing position of rods*

implantation of the rods had to be monitored with an image intensifier. Five days later, June 18, CSF rhinorrhœa became obvious and the diagnosis could not be escaped; I hoped it would recover spontaneously but it showed no signs of improving; after about three weeks meningitis developed. This was rapidly cured by appropriate medical treatment but I was persuaded to become active. When the dura is punctured in a mastoid operation the CSF leak ceases unless a bone chip lies in the puncture: I therefore thought this might be the cause and explored the sphenoid; I found that the leak was occurring only at the puncture which had leaked at operation and that there was a bone chip hinged into the puncture. I elevated and removed the chip, and put some gelatin sponge over the hole. My hopes of curing the rhinorrhœa were unfounded: it continued unabated. Two and a half weeks later I re-explored the sphenoid and packed the hole with Horsley's wax; this made no improvement and the situation seemed insoluble. At both these operations there had been no bleeding and no sign of healing of the bone of the pituitary fossa.

At the beginning of September, ten weeks after the implant, the rhinorrhœa was continuing and, as a result of much discussion with many surgeons of varying specialties, I decided to see if a muscle graft would cure the rhinorrhœa. To cure the rhinorrhœa was by now very important, for the patient's vision had improved enormously and her headaches were much improved. On September 8 I re-explored the sphenoid and removed the anterior bony wall of the pituitary fossa: there was greyish, avascular, amorphous tissue in the fossa, which was removed; also any of the dead yttrium rods which appeared were removed. I curetted the cavity until the walls of the cavity were pink and bleeding. I then took a muscle graft from the sternomastoid and filled the cavity – it took a lot of muscle to fill the cavity and I had to reopen the neck wound to get more muscle before I had filled it. I packed the sphenoid with bipp gauze to hold the muscle graft in place. A week later I removed the gauze and, to my delight, the rhinorrhœa did not start again. She has remained well, without headaches and with normal vision, until the present, seven years later; she has to take cortisone and thyroxine but is otherwise normal.

I was impressed in my management of this case with two things. The first was that once a post-radiation CSF rhinorrhœa is established there appears to be no prospect of spontaneous recovery. The second was that even after three months the inside of the pituitary fossa was remarkably avascular, which should not cause any surprise because the dose of irradiation in these cases is very high: it is something of the order of 20,000 to 50,000 rads at the periphery of the gland and we are all familiar with the change in healing capacity caused by a tumour dose of 5,000 to 6,000 rads used in the treatment of carcinoma of the larynx.

In May 1959, in Copenhagen, I was shown, with others, in Professor Riskaer's clinic, a surgical method of transsphenoid hypophysectomy. This was a great excitement, because by then I had been working on suppression of pituitary function for four years and was still looking for a satisfactory surgical method of

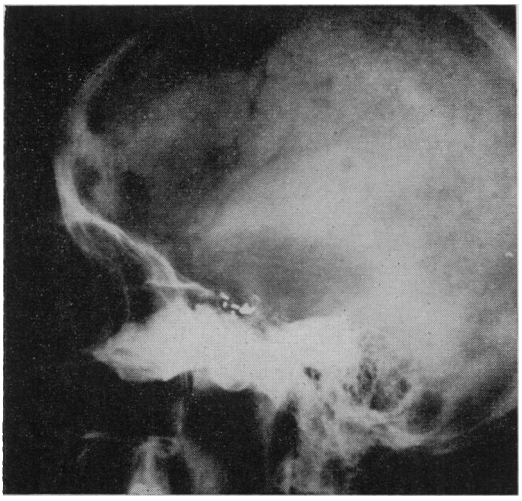

Fig 2 **Case 2** *Lateral X-ray of patient in September 1960, showing burr holes of frontal exploration and yttrium rods in the pituitary fossa*

ablation. I started using this surgical method in the summer of 1959, confident that, with the muscle graft, I could control any CSF rhinorrhœa that I might cause.

The next case I encountered was not truly one of this series, but she was part of my education:

Case 2 Woman, aged 41 in December 1953 when she had a left radical mastectomy for carcinoma of the breast.
August 1954: Bilateral oophorectomy.
August 1957: Carcinoma right breast – local mastectomy.
November 1957: Yttrium implant into the pituitary for secondaries; transfrontal approach; secondaries were not controlled nor was the patient hypophysectomized.
April 1958: Second yttrium implant (nasal).
December 1958: Third yttrium implant (nasal). Secondaries were controlled and she was well until May 1960, eighteen months later, when minor epistaxis began. This increased. The following transfusions were needed for the epistaxis: July 1960, 3 pints; 23.8.60, 6 pints; 13.9.60, 5 pints.

At this stage I was asked to help and, on September 17, 1960, there was an epistaxis needing 2 pints transfusion of blood.
17.9.60: At exploration, hæmorrhage from right cavernous sinus was identified and a muscle graft was inserted (Fig 2).
30.9.60: Examination under anæsthesia; the muscle graft appeared partially adherent so the pack was left out; bleeding started again in the recovery room; repacked.
1.10.60: Examination under anæsthesia; Oxycel packed over the graft and held in place with a bismuth subgallate pack.
17.10.60: Examination under anæsthesia; some bleeding – repacked.
21.11.60: Examination under anæsthesia; repacked.
28.11.60: Examination under local analgesia; gelatin sponge put in and repacked.
5.12.60: Examination under local analgesia no bleeding; no pack.
12.12.60: Because of minor epistaxes – examination under anæsthesia; bleeding from the right wall of the pituitary fossa; repacked.
19.12.60: Examination under anæsthesia; fresh muscle graft inserted and packed.
29.12.60: Examination under anæsthesia; Muscle graft in place – bleeding beside it; repacked.
1.1.61: Epistaxis.
3.1.61: Epistaxis.
6.1.61: Examination under anæsthesia. Plugs removed. Massive hæmorrhage. Repacked. Peripherally pulseless for ten minutes. Rapid blood transfusion caused recovery but she had a hemiplegia. It was clear that this was arterial hæmorrhage.
15.1.61: Epistaxis.
16.1.61: Epistaxis.
20.1.61: Pack removed – massive hæmorrhage – repacked. Respiration ceased one hour later.

Autopsy showed erosion of right internal carotid artery into the pituitary fossa. Four months' struggle had taken place to no avail. This case is not strictly in this series but, being an escape of fluid from an irradiated pituitary fossa, an unsuccessful but instructive and prolonged attempt was made to cope with it.

The next case came to me six months later:

Case 3 Man, aged 52, with acromegaly
He was treated elsewhere, on June 16, 1961, with an yttrium implant (Fig 3). Cerebrospinal fluid leaked

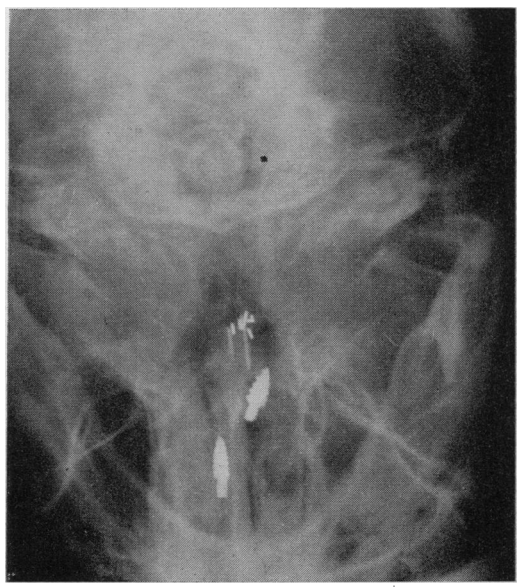

Fig 3 **Case 3** *Shows the large number of yttrium rods and the two screws which had been used in an attempt to control the CSF rhinorrhœa*

from the right needle hole, so a screw was put into the defect in the bony pituitary wall. However, CSF rhinorrhœa developed post-operatively. On July 4, 1961, an attempt was made to put a screw into the left hole. The CSF drip continued. He was referred to me.

On 31.7.61, six weeks after the implant, I removed the screws and some of the yttrium rods and put a muscle graft into the avascular pituitary fossa (Fig 4). It was held in place with a sphenoidal pack. The leak started again when the pack was removed so, on 11.8.61, an examination under anæsthesia was done and the muscle graft was seen to be partly adherent; it was repositioned and repacked. On 21.8.61 the pack was removed and there was no further leak.

He was discharged without a leak but almost immediately the rhinorrhœa began again and he developed signs of meningitis. This was treated effectively and on 15.9.61 a further muscle graft was prepared and inserted. The pack was removed after ten days and there has been no further trouble.

I believe the trouble here was that I put in the graft too soon after the implant: the graft put in after six weeks failed, while the graft put in after twelve weeks was successful.

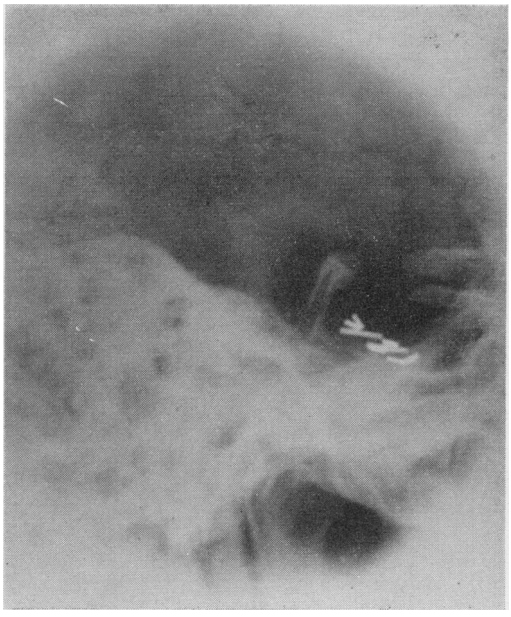

Fig 4 **Case 3** *Lateral view after the first attempt to cure the rhinorrhœa. The screws and some of the rods have been removed*

Case 4 A man, aged 60, had suffered from pituitary insufficiency for five years and, over the past year, had suffered from intermittent CSF rhinorrhœa and recurrent meningitis. It was assumed that the leak came from the pituitary fossa and he was referred to me (Fig 5).

27.1.61: The sphenoid was explored and the sinus and its mucosa appeared normal. The wall of the pituitary fossa was thick and was removed to expose the dura

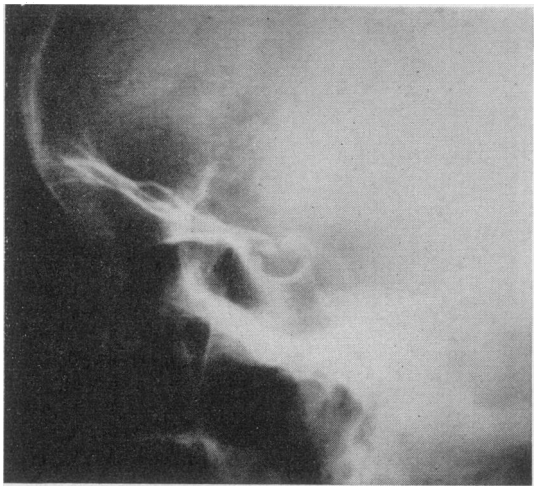

Fig 5 **Case 4** *Lateral X-ray of the skull. The patient had a pituitary abscess*

covering the pituitary. The dura was seen to pulsate but no CSF leak could be detected. The dura was thickened and was incised with a diathermy knife. There was no CSF leak from the pituitary fossa. The contents of the pituitary fossa oozed out of the incision as a yellowish-white viscous material looking like pus or necrotic tissue. No normal pituitary tissue was seen. As I did not know the nature of the material filling the pituitary fossa it was sent for microscopy and no muscle graft was put into the fossa. Histology: necrotic eosinophilic cells and foamy macrophages with a few polymorphonuclear cells. Necrotic tissue.

3.2.61: A muscle graft was inserted into the pituitary fossa, since when there has been no further CSF leak.

This is what is described as a pituitary abscess but, though I could not define the CSF leak at operation, evacuating the pituitary fossa and grafting it with muscle cured his rhinorrhœa and his liability to meningitis.

Case 5 A man, aged 52, had Cushing's disease. On September 14, 1962, yttrium was implanted in his pituitary fossa. In December 1962 he developed CSF rhinorrhœa. On March 8, 1963, I put a muscle graft in his pituitary fossa and the leak stopped. He returned to Asia and follow up is not available.

Case 6 A woman, aged 62, had an yttrium implant elsewhere in September 1959 for carcinoma of the breast. In January 1960 a muscle graft was put in the pituitary fossa and the CSF rhinorrhœa which had started the previous October was controlled. The operation was four months after irradiation.

Case 7 A woman, aged 68, had multiple metastases from a carcinoma of the breast. In June 1961 yttrium was implanted into her pituitary at another hospital. Persistent CSF rhinorrhœa followed and, on November 13, 1961, I put a muscle graft into the pituitary fossa. The rhinorrhœa ceased but she died of her carcinoma in December 1961. The operation was five months after irradiation.

Case 8 A man, aged 30, was diagnosed as having Cushing's disease in 1959. In 1962 he had a bilateral adrenalectomy; the disease was uncontrolled and, on June 26, 1962, an yttrium implant was done. The disease was still uncontrolled and, on August 3, 1962, a further yttrium implant was done. CSF rhinorrhœa followed the second implant; the puncture was screwed but the rhinorrhœa continued. I was persuaded to put in a muscle graft on September 7, 1962, one month after the last implant. This was apparently successful but, one month later, the rhinorrhœa restarted. On October 20, 1962, a further muscle graft was put in but, on the removal of the pack on the ninth day, the rhinorrhœa began again, so the next day a further operation was done and a third muscle graft was put in on October 30, which was successful. The third muscle graft was put in nearly three months after the yttrium implant. I think there has been no recurrence since then; the patient went back to Australia and I have no recent news of him but, in this case, no news almost certainly means that the rhinorrhœa has not started again.

Case 9 A woman, aged 51, was diagnosed as having acromegaly in 1960, and was treated with a course of deep X-ray therapy. The acromegaly persisted and, on July 10, 1964, an yttrium 90 implant into her pituitary was done. Three months later a cerebrospinal rhinorrhœa began. In December 1964 she developed a breast abscess and intracranial symptoms which might have been a pituitary abscess. She was treated with chloramphenicol and recovered, but the rhinorrhœa continued; it appeared to be coming from the right sphenoid so, in March 1965, a screw was put into the bore hole on the right through which the yttrium had been implanted. The CSF leak continued. In May 1965 she developed meningitis. This was treated and cured but the rhinorrhœa continued. Meanwhile she was apparently cured of her acromegaly. She was referred to me and was admitted on June 28, 1965. On July 2, 1965, the pituitary fossa was exposed through the sphenoid. The screw was lying in fibrous tissue and there appeared to be no bony wall of the pituitary fossa in the right sphenoid, though a very fragile bony wall still existed in the left sphenoid. The screw was removed and a rod was seen in the fibrous tissue; the rod was removed and a cavity created by stretching the hole in which the rod had been. Another rod was removed. The third rod was seen but only intermittently, as it was lying in the diaphragma and was flapping back and forth with respiration. There was a deficiency in the diaphragma through which cerebrospinal fluid was pouring. No pituitary recognizable as such was either seen or removed and no tissue was removed from the pituitary fossa. A muscle graft taken from the right vastus intermedius was inserted and packed in place. The CSF rhinorrhœa was controlled and the patient developed diabetes insipidus. The pack was removed on the tenth postoperative day and there has been no recurrence of the rhinorrhœa. The graft was put in one year after the yttrium implant and took with no trouble.

It is very hard to understand why this patient should have developed diabetes insipidus after the muscle graft, when no tissue was removed from the pituitary fossa, but not when her pituitary fossa had been subjected to a very large dose of β radiations.

Case 10 A man, aged 41, was found to have a pituitary tumour, a chromophobe adenoma, in 1964. He had a transfrontal hypophysectomy and the enlarged pituitary fossa was emptied as far as possible in July 1964: the diagnosis of chromophobe adenoma was confirmed histologically. His pituitary fossa was treated with teleradiation and, in October 1964, his symptoms had been cured and he had no sequelæ of his surgery or radiation. In December 1964, five months after operation and three months after completion of his radiotherapy, his nose began to drip; it was winter and it was some time before it was realized that he had developed a cerebrospinal rhinorrhœa. He was treated with various drugs in the hope that the rhinorrhœa would cease but, after three months, he developed meningitis, which was treated and cured; the rhinorrhœa persisted. He was referred to me and, on May 25, 1965, I exposed the sphenoids through the nasal septum and the right ethmoid. The anterior bony wall of the pituitary fossa had largely disappeared and, in relation to the right sphenoid, the capsule of the pituitary looked ragged and torn; CSF was leaking through it. The pituitary fossa was opened up: it was full of CSF and the diaphragma was deficient; on its floor were small islands of whitish tissue which were removed, and histologically showed chromophobe adenoma cells. A piece of the capsule of the gland was excised and showed fibrous tissue with a few degenerate chromophobe adenoma cells enmeshed in the fibrous tissue. A muscle graft was inserted to fill the cavity, the sphenoid being packed with neomycin ribbon gauze. The pack was removed ten days later and there has been no recurrence of his rhinorrhœa. Immediately after operation he developed a copious polyuria and polydipsia which needed control with Pitressin Tannate; he did not develop diabetes insipidus when he had his transfrontal hypophysectomy in July 1964. I did remove some pituitary tissue and this may be the cause; but in the previous case I removed some dead yttrium rods but no pituitary tissue, yet she also developed diabetes insipidus.

The onset of diabetes insipidus after transsphenoidal hypophysectomy seems to be unpredictable and unexplained. It is usual but not invariable after hypophysectomy when a normal pituitary is removed, as in carcinoma of the breast. At first I thought that when removal was incomplete there was no diabetes: this was not supported by post-mortem findings. I then thought that it was perhaps dependent on the manner in which the stalk was torn; this is largely a matter of chance beyond the control of the surgeon. But in neither of the last two cases of rhinorrhœa that I have described was the stalk seen; in the last patient, who had a transfrontal hypophysectomy ten months before my operation, the remains of the stalk should have been well

outside my reach. As far as I am concerned the incidence of diabetes insipidus after transsphenoidal hypophysectomy is usual, but unpredictable and unexplained.

Nine cases of cerebrospinal rhinorrhœa from the pituitary fossa have been described. Seven of them occurred after yttrium pellets had been inserted in the pituitary fossa for a variety of reasons: 3 for acromegaly; 2 for Cushing's disease; and 2 for multiple metastases from carcinoma of the breast. There were thus 3 cases with an enlarged pituitary fossa and 4 with a normal-sized fossa. There were 5 cases with an abnormal pituitary gland and 2 cases with a normal gland. In addition to this there was one patient whose pituitary had been operated on without damage being done to the natural barrier between the pituitary fossa and the sphenoid sinus; in the final case there had been no surgical or radiological treatment to the pituitary to cause or assist the breakdown of the natural barrier between the contents of the pituitary fossa and the subarachnoid space on the one hand and the sphenoidal sinus on the other.

Patients who have not been subjected to intense local irradiation present no really difficult problem in treatment. Transsphenoidal exposure of the pituitary fossa, emptying the fossa and insertion of a muscle graft can be expected to cure the condition. It can be treated as soon as it is diagnosed.

Patients who have had intense local irradiation are difficult to treat because the reduction of the blood supply caused by the irradiation interferes with healing. The factor is well recognized in neck surgery, where the dose to which the neck has been exposed is much lower than the dose to which the periphery of the pituitary fossa has been exposed. I have not been successful in curing the CSF leak within two months of the implantation of the irradiated material. The earliest success I have had has been eleven weeks after irradiation commenced. In future I shall try to avoid operating till three months after the implantation.

These cases have been a very considerable worry but increasing experience is reducing the worry because results are becoming predictable to some extent. We can predict that a muscle graft will fail to take and the rhinorrhœa will recur if the graft is put in less than ten weeks after the insertion of the irradiated material. Probably the very large dosage used in some of these cases means that a longer interval is needed than after the more ordinary dosage. Two of these cases had had more than one implantation of yttrium. It is only now, seven years after my first case, that I can undertake treatment of these cases with reasonable confidence of a successful outcome.

[The second part of the President's Address, 'On editing the *Journal of Laryngology*', will be published in that journal.]