TRANS-SPHENOIDAL HYPOPHYSECTOMY

By G. H. BATEMAN* (London)

I BECAME interested in attempted destruction of the pituitary with a trans-sphenoidal operation in 1955, when Professor J. B. Kinmonth of St. Thomas' Hospital was investigating the possibility of relieving patients with diffuse carcinomatosis secondary to carcinoma of the breast.

Oscar Hirsch first performed trans-sphenoidal hypophysectomy through the nasal septum in 1907 and has since operated on more than 350 patients. These cases were all cases of tumour of the pituitary and he supplemented his surgical excision with local implantation of radium. He has a high proportion of long term cases and this is a satisfactory method of treatment in his hands.

The problem of hypophysectomy in the treatment of diffuse carcinomatosis is different. In this case it is necessary to destroy the function of the normal pituitary and this demands the removal of the whole pituitary, or at least an operation so complete that there is no macroscopic pituitary tissue in the sella turcica at the end of operation. Normal pituitary tissue is highly radio-resistant and the optic nerves and chiasma are in close relation to the sella and therefore destruction of the pituitary by irradiation in any form sets a difficult problem of dosage if damage to vision is to be avoided.

I started using the trans-septal approach to the sphenoid to attempt surgical hypophysectomy in 1955, but I was unable to perform a total hypophysectomy in any case (Table I). I therefore changed to the

TABLE I.

TRANS-SEPTAL HYPOPHYSECTOMY

March-August 1955
12 Cases—None successful

implantation of irradiated gold grains, using the same surgical approach (Table II). I treated eighteen cases with this method and vision was seriously affected in two cases. I changed to using irradiated yttrium

TABLE II.

RADIO-ACTIVE GOLD IMPLANTS

February-August 1956
18 Cases

No clinical improvement	11
Clinical remission	7

(Vision was affected in two of these cases)

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pellets and reported the results of treatment of twenty-two cases at the Royal Society of Medicine in May, 1959. Meanwhile, other rhinologists had been improving techniques for surgical trans-sphenoidal hypophysectomy and I should specially mention Escher, Riskaer and Hamberger. They have all contributed to the development of what appears to be a satisfactory operation. In May 1959, I saw a trans-sphenoidal hypophy-

TABLE III.

RADIO-ACTIVE YTTRIUM IMPLANTS

Total 22 Cases	
Carcinoma of the breast	20
11 had a clinical remission	
1 remission lasted four years	
Pituitary tumours	2
Clinical relief in both cases	

sectomy performed in Professor Riskaer's clinic in Copenhagen and it appeared that the problems of dissecting the pituitary from the sella had been solved. If this were really so it seemed to me a much more satisfactory method of destroying the pituitary function than any form of local irradiation.

Escher uses the trans-ethmoid approach; Riskaer also uses this approach and Hamberger uses the trans-antral approach. Both of these methods give satisfactory exposure of the cavities of the sphenoidal sinuses and of the pituitary fossa projecting into the sphenoid, but with neither approach is it easy to determine the midline. The use of the binocular operating microscope is of great value in monitoring the dissection of the pituitary and it is very difficult to use the microscope with the trans-antral approach.

The microscope can be satisfactorily used with the ethmoid approach, but this relatively small access to an operation site about three inches deep has to serve the following functions:

(1) illumination of the field

(2) vision

(3) allow access for the suction end

(4) allow access for the dissector.

In order for all these things to be done at the same time the suction end and the dissectors have to be bent so that the operator's hands are not in the way of the light or the vision. This restricts the movements and interferes with the sense of touch. After using the ethmoidal approach in some cases and then, inspired by Hamberger, the trans-antral approach, I have developed a technique using both the trans-septal approach and the trans-ethmoid approach. It is this combined surgical technique that I propose to describe.

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Selection of Cases

The ear, nose and throat surgeon does not select the cases. Cases are referred to him for operation and he can either operate or refuse.

The absolute contraindications for operation are:

(1) extremely poor pneumatization of the sphenoid

(2) gross nasal sepsis. I have not yet encountered this

(3) gross evidence of secondary deposits in the liver with jaundice

(4) a moribund patient. Patients will recover surprisingly after operation and I only refuse patients who are expected to die in a few days.

Pre-Operative Investigations

Radiography of the skull. A true lateral radiograph of the skull and a submento-vertical view of the sphenoids are necessary to obtain the required information about the anatomy of the sphenoid and the degree of pneumatization.

The features to be looked for are the degree of pneumatization, the relative size of the two sphenoids, the disposition of the intersphenoid septum and the septa transversales and the thickness of the bony wall of the pituitary fossa. Lateral tomograms help in this latter estimation.

The nose should be inspected for sepsis and the state of the nasal septum.

Blood count, chest X-ray and similar investigations will probably have been done by the referring surgeon or physician.

Operation

General anæsthesia with a cuffed oral endotracheal tube is used. Fluothane provides very satisfactory operating conditions. Paralysis and intermittent positive pressure respiration is to be avoided because of the bleeding from venous sinuses caused by the positive phase.

The patient is placed supine on the operating table and the head of the table is raised. The patient is towelled in the ordinary way for nasal operations. The eyelids on both sides are sewn together so that risk of a corneal abrasion is minimized.

The nose is painted by the surgeon with 25 per cent. cocaine paste. This ensures a relatively bloodless field and allows the surgeon to make a detailed examination of the nasal anatomy. The line of the incision in the right orbit is injected so as to reduce the hæmorrhage when the orbital incision is made later in the operation.

Septal operation

An incision is made on to the presenting end of the septal cartilage and submucous dissection performed on both sides of the septum. This

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dissection is continued back across the vomer to the anterior aspect of the sphenoids exposing the bony wall on both sides. Enough of the septal skeleton is removed to permit an unobstructed view of the anterior bony walls of both sphenoids. A special long (three inch) Killian nasal speculum is needed to obtain good exposure. It is now possible to break through into the sphenoid sinus on either side of the central buttress of the alae of the vomer. This buttress is now grasped by Luc's forceps and avulsed. Rarely this bone may be so strong that it cannot be avulsed and in these cases it must be cut above and below with an osteotome. Both sphenoids are now opened and the anterior bony wall of the sphenoid can be extensively removed with sphenoidal punch forceps.

The intersphenoid septum is now removed with Luc's forceps and it may be necessary to remove the septum transversalis. The cavity of the two sphenoids is now widely exposed and the bulge of the pituitary fossa can be identified. The mucosa of the sphenoidal sinus is completely removed. This reduces the bleeding and prevents the constant annoyance of the mucosa blocking the sucker.

The cavity of the sphenoid is now packed through the nasal septum with a strip of two inch ribbon gauze.

Ethmoid operation

On the right side the orbital plate of the ethmoid is now exposed with the incision ordinarily used for the external ethmoid operation. The orbital periosteum is elevated on the medial aspect of the orbit and the anterior ethmoid vessels are identified. These are coagulated with diathermy and cut. A self-retaining retractor is put into the wound. The ethmoid cells are then broken into and exenterated. The nasal mucosa covering the ethmoid is not torn and is preserved intact. The removal of the cells is continued inwards along the bony floor of the anterior cranial fossa and the sphenoid is opened. The direction of the cavity is backwards, inwards and downwards. The sphenoid is recognized immediately because it is packed with ribbon gauze and the hesitation that can be caused in identifying a large posterior ethmoid cell is avoided. The edges of the ethmoid cavity are cleaned and a good view of the sphenoid is obtained by displacing the right lateral nasal wall medially. The sphenoidal pack is removed and the pituitary fossa defined. The midline can be accurately defined by re-introducing a long Killian nasal speculum into the nasal septum. The septal crest of the maxilla marks the midline with accuracy. A straight instrument will now define the midline on the pituitary bulge.

The next step is to make a breach in the bony wall of the pituitary fossa. In most cases this can be done with a long handled small mastoid curette. If, however, the bone is demonstrated to be thick in the pre-operative tomograms the breach is best made with a bone cutting burr

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driven by an electric motor. The straight access to the pituitary fossa obtained by the septal approach enables an ordinary straight dental handle to be used and the work to be monitored through the ethmoid incision.

I normally place a blunt flat probe through this defect along the floor of the pituitary fossa and confirm its position with a lateral X-ray in the theatre.

The defect in the bony wall is now enlarged by using special punch forceps so that the dura of the whole of the anterior wall of the pituitary fossa and part of the fundus is exposed. It is usually possible to see the cavernous sinus on each side and the anterior communicating sinus in the upper part of the defect through the exposed dura. There is sometimes a venous sinus visible over the fundus of the fossa.

The Zeiss operating microscope is now brought into use. The stand is placed near the patient's left shoulder and the arm comes across the patient's head. The surgeon sits on the right side of the patient's head and the assistant sits at the head of the table. The tutor eye piece is in the left side of the microscope and directed towards the assistant. The microscope is used through the ethmoid incision. A bent insulated sucker end is put on the sucker tubing and a diathermy end with only a short exposed end is fitted. I find the end developed by St. Mary's Hospital for submucous diathermy of the inferior turbinate entirely satisfactory for this purpose. Using the six times magnification the dura of the pituitary fossa is brought into focus. Suction is used in the surgeon's left hand through the ethmoid incision and the diathermy is inserted through the septal incision and a cruciate incision is made in the dura. This is extended in each direction as far as is possible whilst yet not opening a venous sinus. There are two distinct layers of the dura and it is most important to incise both layers.

When both layers have been incised the pituitary gland will bulge slightly through the incision. Dissection of the pituitary from its capsule is now commenced. The Tumarkin double-ended mastoid dissector is a good instrument for this stage. As the pituitary is freed from its capsule it tends to bulge more through the incision. This dissector frees the anterior part, the floor and the lateral aspects of the gland. Olivekrona devised a left- and right-sided pituitary dissector. These have been modified for trans-nasal use by Angell James. These Angell James dissectors are now used to complete the dissection of the lateral and superior aspects of the gland. At this stage the gland will bulge out of the incision even more and the greyish diaphragma will be seen. A rather more curved flat dissector is now used to complete the dissection of the posterior aspect of the gland which will now be freely mobile within the sella, being attached only by the stalk of the pituitary.

The pituitary is now grasped by forceps and avulsed. I have not yet found or devised any entirely satisfactory forceps for this purpose. Long

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nandle baby Henkel's forceps are reasonably satisfactory for this purpose. If the dissection has been entirely satisfactory the fossa will now appear empty.

Not infrequently there are small remnants seen in the fossa and these are now dissected free and removed. The diaphragma bulges down into the fossa and the stump of the stalk is seen lying in this. When the gland is removed there is a copious flow of cerebrospinal fluid and often some bleeding. This soon stops. The sella and the sphenoid are now packed, through the septal incision, with two inch ribbon gauze. This controls the cerebrospinal fluid leak and the bleeding.

A muscle graft is now obtained. Following Hamberger's technique, I obtain this from the vastus intermedius in the right thigh. A three inch incision is made about six inches above the patella, the fascia lata is incised and the muscle exposed. A piece of muscle, 1-inch by ½-inch by ½-inch, is excised. It is smaller than this when it is removed from the body. The muscle, fascia lata and skin are sewn up and the wound dressed.

A piece of muscle big enough to fill the sella turcica and overflow into the sphenoid is prepared.

The surgeon now returns to the microscope and removes the packing from the pituitary fossa which is again inspected. If the inside of the cavity is free of pituitary remains the muscle graft is now inserted and tucked firmly into the pituitary fossa. This is somewhat difficult because the sucker cannot be used while the muscle graft is loose as the graft will disappear up the sucker, and the graft tends to stick to the forceps. However, with patience, the graft can be satisfactorily placed in position.

It is now packed into place with two inch ribbon gauze wrung out in a Neomycin solution. This pack is introduced through the septal incision and the sphenoid is tightly filled with it. The septum itself is not packed, but one end of the gauze is brought out through the septal incision and cut off about one inch outside the incision. This one inch is tucked into the fossa navicularis of the nasal vestibule where it can be found when required. The nasal cavities are thus quite clear at the end of the operation. The right lateral nasal wall is now displaced laterally again into its normal position. The retractor is removed from the orbital incision which is sewn up.

After Treatment

The after treatment from a surgical point of view is minimal. The orbital stitches are removed on the fifth day. The pack from the sphenoid is removed on the ninth day. This is done in the ward without anæsthesia or premedication. The end of the pack is found in the right nasal vestibule. A firm grip on it with artery forceps is obtained and it is pulled. After initial resistance the pack comes out very easily and with very slight pain. There may be a little bleeding from the septal incision for an hour or two.

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I always give the patients sulphadiazine by mouth from the time of operation till the pack is removed. I also give them penicillin by injection for the same period.

Endocrine Management

Cortisone therapy

On the morning of the day before operation an injection of Cortisone acetate, 100 mgms. is given.

Early on the day of operation a further injection of Cortison acetate, 100 mgms., is given and followed by an injection of hydrocortisone hemisuccinate, 100 mgms., four hours pre-operatively.

Post-operatively an intravenous saline drip is set up and in this is given 4 grams sulphadiazine and, if necessary, hydrocortisone, 150 mgms.

The day after the operation, Tab. Cortisone, mgm. 25, is given by mouth three times daily and reduced to twice daily in one week.

Thyroid is given by mouth starting two weeks after operation. The assumption is that the thyroid will cease to function in the hypophysectomized patients, and they are therefore treated as though they had had a total thyroidectomy.

In diabetes hypophysectomy alters the diabetic state very considerably. The patient becomes much more sensitive to insulin and has to be stabilized again after operation. These patients can easily be put into a hypoglycæmic state, and it is a common experience to find that the insulin needs are very greatly reduced.

Complications of Operation

Immediate hæmorrhage

There may be troublesome hæmorrhage from the dural sinuses in relation to the pituitary fossa. In particular there may be little room between the anterior communicating sinus and the sinus over the fundus of the gland. The hæmorrhage from these sinuses is not severe and is not a danger to life, but it may be enough to make it impossible for the surgeon to see what he is doing.

It has been necessary in two cases to divide the operation into two stages on this account. The bleeding is completely controlled by packing the sphenoid with ribbon gauze wet with a penicillin solution. This packing can be left for one week and when it is removed the field is dry and the operation can be completed without difficulty and without restarting the hæmorrhage.

Cerebrospinal rhinorrhœa

When the sphenoidal pack is removed on the ninth day cerebrospinal rhinorrhœa may commence. If this is allowed to continue indefinitely an

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infective meningitis is almost inevitable. In addition a patient with cerebrospinal rhinorrhœa feels light-headed, has headaches and is unwell, and the continual soaking of pillows and clothes is very unpleasant. Occasionally this will cure itself in the first two or three days, but I do not leave it untreated longer than this. The cause is inaccurate placing of the muscle graft at the primary operation, or, possibly, displacement of the graft when the pack is removed.

With the double approach I use the management of this post-operative complication presents no difficulties. The patient is anæsthetized and a long Killian nasal speculum is inserted into one of the nostrils. The nasal septum can be pushed out of the way, because of the previous submucous resection of the septum, and the mucosa of the anterior wall of the sphenoid can be stretched between the tips of the blades of the speculum. The mucosa is torn with a blunt dissector and the pituitary fossa is immediately beyond the ends of the speculum. The situation can now be assessed. It is usual to find that the muscle graft is partly in the pituitary fossa and partly displaced into the sphenoid. It is replaced in the pituitary fossa and is packed into place with a strip of two inch ribbon gauze in the sphenoid. There have been six cases in this series.

The ribbon gauze is removed on the seventh to ninth day, depending on whether the seventh or eighth day falls on a Sunday. In every case so far this has been successful in curing the rhinorrhœa. It therefore follows that the cerebrospinal rhinorrhœa is the result of faulty placing of the muscle graft in the first place. It is quite understandable that this should happen, even though the surgeon realizes the risk, because there is often hæmorrhage after the pituitary is removed and a sucker cannot be used while there is a muscle graft in the area to be cleared by suction.

Meningitis

Meningitis is a possible complication of this operation. It is surprisingly rare. By force of circumstance we have to nurse our cases at St. Thomas' in the open ward as single-bed wards are not available. The patients are therefore exposed to the risks of cross infection encountered in the open ward. In spite of this I have only had three cases of infective meningitis in the post-operative period. All were controlled, very rapidly, with antibiotic therapy. One, a diabetic, then developed a cerebral thrombosis and died of this one month later. It is surprising that more cases did not develop meningitis. In the same period there were three cases of infection of the wound in the thigh made to obtain the muscle graft. None of these three developed meningitis.

Damage to the eye

It has been suggested that wide exposure of the sphenoid through

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an orbital incision would be likely to cause blindness because of stretching of the optic nerve. This has not happened.

Intracranial hæmorrhage

Two cases have occurred. One was a surgical error and should not be repeated. The anterior cranial fossa was opened and the anterior cerebral artery was torn. The patient died of subarachnoid hæmorrhage.

In the other case the diaphragma sellæ was invaded by a secondary carcinomatous deposit and tearing through this at operation caused a subarachnoid hæmorrhage from which the patient died thirty-six hours after operation.

Polyuria and polydipsia

This is a common sequel to the operation, but it is not inevitable. It would appear that it is caused by damage to the floor of the third ventricle when the pituitary stalk is avulsed. The assumption is that if the stalk tears at the level of the diaphragma there is no polyuria, but if it is avulsed from its origin in the floor of the ventricle the damage to the floor causes polyuria. It can be controlled by once daily injections of Pitressin Tannate. When the nose has recovered from the operation Pitressin snuff can be substituted for the injections. After three to six months the water balance returns to approximately normal and the use of Pitressin can be discontinued.

Results

The time has now come to assess the results of this operation. Table IV shows the total experience to the end of July 1961.

TABLE IV.

SURGICAL HYPOPHYSECTOMY

July 1959-July 1961

70 Cases

Type of case treated

Carcinoma of the breast	35
Diabetic retinopathy..	23
Pituitary tumours	7
Carcinoma of prostate	1
Cerebrospinal rhinorrhœa	4
(Referred from other hospitals)	

I have no series of brilliant successes to put before you. But in estimating the success of the operation it is necessary to have some idea of the state of the patients subjected to operation. The carcinoma of the breast series consists of thirty-five cases. With very few exceptions all were bedridden because of bone secondaries or lung secondaries. Most patients had both types of secondary tumour. Without treatment it was extremely unlikely that any of these patients would get home alive and all conventional forms of treatment had failed. If any patient left hospital

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and went home to resume her household duties it was something of a miracle. The patients were drawn from all over the south of England, and my shortage of beds is such that, as soon as the patient had recovered from operation and the risk of post-operative complications was passed, the patient was transferred back to the hospital whence she came. If she died in our hospital I knew about it. If she died in the hospital to which she was transferred I was informed. But if she got back home to the care of her own doctor it is quite possible that I might not be told if she died, or if she continued to be alive and active.

Therefore, I know about all the immediate deaths in hospital and they are recorded. I know about the St. Thomas' Hospital patients, but I do not know about all the patients who were referred from elsewhere and who got back to the care of their own doctors.

With this background I have traced twenty-nine out of the thirty-five cases of carcinoma of the breast subjected to operation. I have classed as bad results patients who died in hospital or who never resumed normal activities. I have classed as fair results patients who survived the operation and recovered sufficiently to go home and resume normal activities for up to six months after operation. I have classed as good results all cases who went home and resumed normal activities and were still well and active after six months from the operation.

Classified in this way the twenty-nine cases followed up are divided into:

eleven bad, six fair and twelve good cases.

TABLE V.

RESULTS OF SURGICAL HYPOPHYSECTOMY

Carcinoma of breast—35 cases	
Insufficient information	6
29 cases—traced	
Good	12
Fair	6
Bad	11

The best result I have is alive and active two years after operation. She is still doing her own housework. Before operation she was bedridden with shortness of breath due to lung secondaries.

These apparently discouraging results must be viewed against the background of the type of case referred for operation. It takes seven to ten days to process a patient for operation. Several patients, looking little worse than the patients who reached operation, died of their disease during the processing period. It is therefore remarkable that any patient is alive three months after being referred to me, and very few would have been alive at this time without operation. There is no doubt that hypophysectomy produces some result in some patients. Also it must be realized that the operation does not subject the patient to severe pain and suffering.

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The post-operative discomfort is minimal and the most noticeable feature is a "black eye", which disfigures some of the patients for about ten days after operation.

Diabetic Results

Twenty-two cases with severe diabetic retinopathy have been subjected to operation. They were therefore all patients with long standing diabetes and many of them had other evidence of diabetic arterial disease. They were therefore not selected as good subjects for operation. The reason for operation was to attempt to preserve some vision in patients whom the physicians considered to be doomed to total loss of vision in a short time. This time could be measured in months.

Twenty cases have been successfully operated on and these cases are all drawn from the diabetic clinic at St. Thomas' Hospital. They are being carefully followed up in the diabetic clinic and by the ophthalmologist. Ultimately a detailed report on these patients will be published by the physician in charge of the diabetic clinic. This present report of the results must be regarded as an interim and incomplete report.

Last week all the doctors involved in the treatment, investigation and management of the diabetic retinitis cases met at St. Thomas' Hospital to assess the experiences of the twenty cases we have treated. The cases were operated on between December 1959 and August 1961. The longest follow up is therefore twenty-six months, and the shortest six months. The following facts emerged at this meeting:

Mortality

One patient died as a direct result of surgery. He died of a coliform meningitis on the ninth day, having appeared well until twenty-four hours before his death. However, seven of the remaining nineteen patients have died since operation of conditions which commonly cause death in long standing diabetics with vascular disease.

(1) Cerebral thrombosis	Six weeks after operation
(2) Renal failure	One month after operation
(3) Acute depression, attempted suicide, heart failure	Two months after operation
(4) Coronary infarct	Three months after operation
(5) Chronic renal disease, liver biopsy, hæmorrhage	Six weeks after operation
(6) Coronary infarct	Four months after operation
(7) Coronary infarct	Twelve months after operation

The mortality of these patients has therefore been 40 per cent., during the period of up to two years after operation. Even though only one of

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these deaths is directly attributable to the operation we are left with a very strong impression that successful hypophysectomy increases the risk of diabetics dying of the conditions which are the normal causes of death in diabetes. Perhaps it is significant that there have been three deaths from coronary infarct and none of the patients under review has had a coronary infarct and recovered.

Morbidity

This is the most striking fact that emerged at the meeting last week. All the patients come from the diabetic clinic at St. Thomas' and they come back to the hospital when they are ill. They are seen by the senior resident medical staff and it is these doctors who drew our attention to the fact that hypophysectomy is a cause of serious morbidity in diabetics. They do not get ill more often after operation than before, but when they do get ill they become serious medical emergencies and are at serious risk of death unless skilled and informed medical help is immediately available. An attack of diarrhœa will, for example, cause a serious collapse within two or three hours. The blood pressure will fall alarmingly, they become hypoglycæmic; but they do not become pale and they do not sweat. They do not get the normal peripheral vascular reactions to a fall of blood pressure. They need emergency treatment with hydrocortisone, intravenous infusions and perhaps glucose. In fact, if they go away from the doctors who know them there is grave risk of their dying because the clinical picture presented is so bizarre. Many of these patients have had to be admitted as emergencies on more than one occasion for this sort of reason. Provided they obtain appropriate emergency treatment they make a rapid and complete recovery within one or two days.

Vision

All these patients received treatment because their vision was rapidly deteriorating and there was a real threat of total blindness within a short time. All have been carefully followed up in the ophthalmic department. In nine of the surviving twelve patients there is accurate and recent information on the state of the vision. Of these eighteen eyes: five are better; five the same; and eight are worse than before operation.

This at first sight seems encouraging for none are blind. However, the retinopathy has not been abolished in any case and in no case can the ophthalmologist say that what has happened to the eye is outside the ordinary natural history of the disease. There is, therefore, no convincing evidence that the vision of any single patient has been significantly improved or preserved as a direct result of the operation.

We therefore decided to discontinue hypophysectomy in the treatment of diabetic retinitis on the grounds that there is no convincing evidence of amelioration of the retinitis to compensate for the disadvantages of successful hypophysectomy in these patients.

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This is a very brief report of the follow up of these patients, and it is proposed that the physicians will report the cases in full and give details of the individual cases when the reports are complete.

In the first months of our experiences we thought we were helping these patients. Often there was dramatic improvement in the vision in the immediate post-operative period. This, however, happens in diabetic retinitis without hypophysectomy, as part of the natural history of the disease, and the state of the vision at any moment is not an accurate means of assessing the progress of the retinitis. Fluctuations of the state of vision of the patient must not be regarded as a sign of success of hypophysectomy in controlling the retinitis.

Pituitary tumours

In addition to removal of normal pituitaries this surgical method can be used for the treatment of pituitary tumours and for the treatment of the complications of the implantation of irradiated material, usually yttrium, into the pituitary.

I have treated seven cases of pituitary tumour. There has been one surgical death, but it is doubtful if the pituitary is totally removed in any of these cases. However, this may not be important as the symptoms are relieved and the operation does not cause lasting disability in these patients. It does not cause the morbidity that hypophysectomy causes in the diabetics.

Complications of Irradiation with Yttrium

Cerebrospinal rhinorrhœa

I have treated four cases, one being a case treated with the yttrium implant by myself. These cases present no great technical difficulty. The sphenoid is opened by the septal route. The sphenoid is widely opened and the punctures in the pituitary fossa can be easily detected. These are joined together and the dura of the pituitary fossa incised. Any yttrium pellets which are present are removed and the necrotic pituitary tissue is curetted from the pituitary fossa. If possible the granulating surroundings of the necrotic gland are exposed. A muscle graft is now prepared and the fossa filled with muscle. This is packed into place with Neomycin ribbon gauze. This controls the rhinorrhœa. I think it wise to wait for two months after the implantation of the yttrium before putting in the muscle graft because before this the reaction to irradiation will prevent the graft from taking.

I was also asked to treat a patient with severe hæmorrhage from the cavernous sinus. This was the result of radio-necrosis and occurred two years after the implantation of yttrium. I was unable to cure this patient as the muscle graft would not take in the irradiated pituitary fossa. We were able to control the bleeding and keep her alive until the carotid artery also was eroded as the result of radio-necrosis.

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Conclusion

This operation offers some hope to patients who otherwise have no hope of relief of their symptoms or disease.

In *carcinoma of the breast* the bone and lung can become painless and inactive and fractures will heal. The duration of this remission is variable; the longest I have had is four years in a case treated with yttrium. About half the patients treated obtain a worth while remission.

In *diabetic retinitis* there is no convincing evidence that hypophysectomy causes an amelioration of the retinitis and there is evidence that successful operation renders the patient much more liable to alarming illness than he was before. We no longer feel justified in recommending operation.

In *pituitary tumours* effective relief of the symptoms can be obtained, though it is doubtful if complete excision is ever achieved. Cases, rejected as inoperable by the neuro-surgeons, have been successfully treated.

Cerebrospinal rhinorrhœa caused by the implantation of radio-active material into the pituitary fossa has been successfully treated.

In *carcinoma of the prostate* where control by stilbœstrol has been lost a further remission can be obtained by hypophysectomy.

Possible further applications of the operation which are under consideration at present are in the treatment of malignant exophthalmos and of idiopathic cardiac hypertrophy.

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