PANEL DISCUSSION

Hypophysectomy

Chairman: Mr. B. H. COLMAN (Oxford)

Panel: MR. S. H. RICHARDS (Cardiff)
MR. G. DALTON (Birmingham)
PROFESSOR A. P. M. FORREST (Edinburgh)
MR. P. HARRIS (Edinburgh)
Mr. W. M. S. IRONSIDE (Halifax).

Mr. Colman: It is exactly sixty years since Chiari operated on the pituitary via the trans-sphenoidal approach to decompress pituitary tumours. Today hypophysectomies are performed for a variety of reasons and the majority are done by otolaryngologists. At this meeting it is hoped to discuss the causes of failure and the problems which arise from hypophysectomy rather than the successes. Firstly, we would like to discuss the advantages of the various approaches to the pituitary fossa.

Mr. Harris: It is an honour, as a neuro-surgeon, to be included in this panel. In 1889 Horsley was the first to use the sub-frontal intra-cranial approach to the pituitary and two years later he used the subtemporal approach. Hirsch in 1909 first described the trans-sphenoidal operation and in 1911 reported his twelve successful cases. Harvey Cushing also used this route, but ten years later changed to the trans-frontal procedure. There are now four routes commonly used, the trans-cranial, the trans-sphenoidal, intra-cranial stalk section, and various stereo-tactic procedures.

Mr. Colman: Which cases do you feel should be performed by neuro-surgeons? Presumably those with supra-sellar extensions. Is it not sometimes a little difficult to get down into the pituitary fossa by a trans-cranial approach?

Mr. Harris: All cases really! The great majority of my pituitary surgery though is other than by the trans-cranial route.

Mr. Richards: I had a case of acromegaly with extension of the tumour downwards into the body of the clivus. This would surely be very difficult to approach trans-cranially.

Mr. Harris: Mr. Richards' cases would be approached by the trans-clivus approach. All patients with evidence of visual impairment or cerebral involvement should be operated on by the trans-cranial approach.

https://doi.org/10.1017/S0022215100074818 Published online by Cambridge University Press

These cases should all be thoroughly investigated with angiograms and tomographic air studies to assess the exact extent of the tumour before operation.

Mr. Colman: Should E.N.T. surgeons be doing air encephalograms to avoid operating on cases with supra-sellar extension?

Mr. Harris: Unless the clinician has full neuro-radiological facilities there may be some risk in these.

Professor Forrest: Effective treatment for acromegaly depends on performing a total hypophysectomy. Surely trans-cranial hypophysectomy only decompresses the chiasma and does not produce a total removal.

Mr. Harris: If there is no visual disturbance they can be treated by a proton beam.

Mr. Colman: Most E.N.T. surgeons approach the sphenoid via the ethmoids, the trans-antral approach may also be used, but is this not a deep dark hole?

Mr. Ironside: This approach was learnt from Hamburger. There is no problem of access and visualization is excellent.

Mr. Dalton: Lack of pneumatization of the sphenoid does not interfere with the trans-sphenoidal approach as long as one has radiographic control. The inter-sinus septum on the sub-mento vertical radiograph is an essential landmark when opening the pituitary fossa.

Professor Forrest: Lateral tomograms through the sella are also very helpful to show these septa and aid localization.

Mr. Harris: Surely a contraindication to the trans-sphenoidal approach is any chronic infection of the sinuses.

Mr. Richards: Sinus infection may be cured and then the operation performed. Quite a high proportion of acromegalics have either infection or polyps in the ethmoids.

Mr. Colman: There are various methods of destroying or removing the pituitary. The majority will remove it by excision but Yttrium implants are often used.

Professor Forrest: Yttrium is a β emitter which causes local intense radiation and necrosis of the pituitary without spread outside the fossa. The route for insertion since 1955 has been via trans-nasal cannulation. The complications are visual damage, diabetes insipidus, C.S.F. rhinorrhoea and meningitis and IIIrd nerve palsy. To get good localization and fixation of the Yttrium, the rod is fixed into a stainless steel screw which is screwed into the anterior wall of the pituitary fossa. One is introduced into each side. The great advantage is the rapid post-operative recovery. In 387 operations the mortality was

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3 per cent. Complications were, meningitis 5 per cent, rhinorrhoea 5 per cent. One per cent of which was permanent and required packing with muscle, 2 per cent visual defects, and 4 per cent occular palsies.

Mr. Ironside: It is impossible to obtain 100 per cent destruction with this method and multiple small sources were used to try to get more complete destruction. Eight to eleven beads, 1 × 2 mm. were implanted. The complication rate was very high though, with a 73 per cent morbidity and it was given up in preference to the trans-antral removal of the pituitary.

Mr. Colman: Does Yttrium implant require careful timing and a nearby source?

Professor Forrest: It does depend how near one is to Harwell. There is only an hour or so to play with and the activity must be measured locally before insertion. A standard dose of 10 m.curies is used in the two rods in cases of breast cancer.

Mr. Harris: Yttrium is a useful technique. If the fossa is large, however, the exact dose must be worked out carefully.

Cryo-surgery has also been used. The size of the lesion produced may be tailored depending on the size of the probe, the length of cooling and whether re-cooling is done. Neuro-surgeons are used to producing tailored stereotactic cryo-lesions within the brain for other reasons.

Mr. Richards: The disadvantage of Yttrium implants for tumours is that the size of the gland itself is not known. X-rays show only the size of the fossa and not any lateral extensions, so it is impossible to calculate the dose.

Mr. Colman: Most people in the audience would destroy the gland by removing it. This does have problems, however, for example, bleeding.

Mr. Richards: Total removal is a very important goal to try and achieve. A bloodless field produced by hypotension is most helpful to achieve this.

Mr. Harris: The commonest reason for hypophysectomy apart from tumours is progressive diabetic retinopathy. If the gland is excised or even the stalk sectioned, the patients will be very ill and the diabetes very unstable and therefore, slower destruction produced by Yttrium is preferable.

Mr. Colman: Mr. Richards, do you put clips on the inter-cavernous sinuses to attempt to reduce bleeding?

Mr. Richards: The inter-cavernous sinuses limit access. It is, however, very difficult to put clips onto these sinuses.

Mr. Colman: How do you deal with an enormous inter cavernous sinus then?

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Mr. Dalton: Pack it and return two weeks later.

Professor Forrest: What is the average blood requirement for trans-sphenoidal hypophysectomy?

Mr. Colman: One to two pints.

Mr. Dalton: Blood loss is only 20–50 ml. with hypotension to 50 mm. Hg.

Mr. Colman: The vast majority of these operations are done for breast cancer. One of the problems is how to select which cases will benefit.

Professor Forrest: Results show that trans-cranial hypophysectomy gives better results than adrenalectomy and oophorectomy, which in turn is somewhat better than trans-sphenoidal hypophysectomy or Yttrium implants. Pre-menopausal patients should be given a trial of steroids and then have an oophorectomy before hypophysectomy is considered. Post-menopausal women should have adequate hormonal therapy first. The discriminant test does give some indication of the possible effectiveness of operation but it is a multifactorial problem. Jensen has recently claimed excellent prediction rates by examining the tumour cell to see whether that cell can bind oestrogens. Those that do will respond much better to adrenalectomy or hypophysectomy.

Mr. Ironside: We tend to depend on the referring surgeons for selection but it is often on clinical grounds. Patients with bony metastases do better than those with skin lesions, those with lymph nodes being intermediate.

Mr. Harris: I would agree with Professor Forrest that intractable pain is a definite indication as is early spinal paresis. Visceral metastases do not do well.

Mr. Dalton: Cases which are just post-menopausal at the time of diagnosis have a much better response than those several years post-menopausal irrespective of age.

Mr. Colman: One can say that roughly one-third will get an objective remission, another third will have subjective improvement, and the rest will not respond at all.

Mr. Dalton: Out of 103 patients, 40 had objective remission at three months, either reduction in the size of the lesion or freedom from pain.

Mr. Harris: At the present state of knowledge, one has to treat patients with all types of advanced breast cancer, irrespective of its distribution.

Mr. Colman: What about those cases with broken-down lesions on the chest wall?

Mr. Harris: Healing has been observed with all types of lesions. Liver metastases tend to do badly however, because they are so advanced when first detected.

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Professor Forrest: With strict objective assessment one only gets a 20 per cent remission rate, particularly if one accepts Hayward's criteria of no regression of under six months duration being worthwhile.

Mr. Colman: The matter of judging results is very difficult, and one must not only consider the increased length of survival but the quality of life these patients have. Do pathological fractures benefit?

Mr. Ironside: They tend to do very well.

Professor Forrest: Pathological fractures tend to heal if they are plated anyway, but of course these patients have disseminated disease and need some form of systemic therapy.

Mr. Colman: More patients are now being referred with acromegaly and Cushings disease.

Mr. Richards: Fourteen cases of acromegaly have had trans-sphenoidal hypophysectomies, 11 had ethmoidal polyps, 3 had extensions of the tumour into the clivus, 3 into the sphenoid sinus, and 3 into supra-sellar region. The latter were easily removed once the gland had been taken out of the fossa.

Mr. Harris: Did any of these patients have visual disturbances pre-operatively?

Mr. Richards: One. The visual acuity improved after operation.

Professor Forrest: The first patient who had a Yttrium implant in 1956 was an acromegalic with large central scotomata. These improved and vision is still normal. So procedures from below can improve the vision.

Mr. Richards: Acromegaly should be treated before visual disturbances develop.

Mr. Harris: They normally are, but if the pituitary is enormous the patient should have an intra-cranial procedure.

Mr. Richards: Probably the best objective measurement of regression is change in shoe size. All 11 out of the 14 cases who have been done for a long enough time have noticed this.

Mr. Colman: Do they have to have new dentures, too?

Mr. Richards: Seven wore dentures and five have had to buy new ones.

Mr. Colman: Is the gland usually soft and easily removed?

Mr. Richards: The glands often have a soft central portion which can be sucked out and then the shell can be dissected. If the gland is of normal size it is dissected out in one piece, to ensure total removal.

Professor Forrest: It is important to do a complete removal and this can be assessed with growth hormone assay. Mr. Richards' results were little better than ours with Yttrium. People doing this operation must assess the completeness of their own technique.

Mr. Richards: About one-third of patients both post-hypophysectomy and after Yttrium implants had normal levels of growth hormone.

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Three year follow-up of these hypophysectomies has shown normal or near normal levels of growth hormone. Recent work has shown that there is definitely active pituitary tissue in the roof of the naso-pharynx from which growth hormone has been assayed.

Mr. Colman: Cushings disease is also being seen more often. There are two types of disorder—those with supra-renal disorders and those with primary pituitary abnormalities.

Mr. Dalton: There is also one other type of Cushingoid patient who has a carcinoma, usually in the bronchus. This carcinoma produces an A.C.T.H.-like substance. It is important to make sure the patient has the pituitary type of Cushings before performing hypophysectomy. The Endocrinologist selects the patients by the dexamethasone suppression test. This suppresses the plasma cortisol levels in those with pituitary Cushings but not the other types. There is no X-ray evidence of enlargement of the sella to differentiate the cases.

Mr. Colman: Does the hypertension associated with Cushings make the operation more difficult?

Mr. Dalton: No, but there have been two deep vein thromboses and one extra-occular palsy which was thought to be vascular in origin. One advantage of excision over implantation is that one has material for histological examination and six cases had adenomas and two with focal hyperplasia. All these cases have been assessed by an independent Endocrinologist. One failed to remit, three had partial recovery only and the other seven returned to normal. In one, an adenoma was removed, the rest of the gland remained and she subsequently became pregnant and lactated.

Mr. Harris: When using the stereotactic approach either for implantation or freezing a biopsy is taken. These patients also do very well with radiotherapy.

Mr. Richards: It has been shown that only one-third of Cushings respond to radiotherapy.

Professor Forrest: The results of adrenalectomy, which has been performed for many years, are very good, and until good five-year figures are produced for hypophysectomy, adrenalectomy will continue to be the operation of choice.

Mr. Dalton: Does not adrenalectomy stimulate the pituitary to produce cysts and increase its activity?

Professor Forrest: Certainly it may. Nelson's syndrome.

Mr. Colman: Is hypophysectomy used for carcinoma of the prostate?

Mr. Ironside: Approximately half of the cases of carcinoma of the prostate treated with hypophysectomy appear to have worthwhile remissions, but they are more difficult to assess objectively.

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