PITUITARY ABLATION BY ⁹⁰YTTRIUM IMPLANTATION FOR ADVANCING DIABETIC RETINOPATHY*

A PRELIMINARY REPORT

BY

J. F. CULLEN, P. HARRIS, J. W. TURNER, A. A. DONALDSON, J. F. MUNRO,
AND L. J. P. DUNCAN

*From the Departments of Ophthalmology, Neurological Surgery, and Radiodiagnosis, University of Edinburgh,
and the Diabetic Department, Royal Infirmary of Edinburgh*

THE indications for pituitary stalk section in advancing diabetic retinopathy have been discussed in a previous communication (p. 393). Pituitary insufficiency can also be induced by implantation of ⁹⁰yttrium into the pituitary gland, a procedure first used in the treatment of advanced malignant disease (Forrest, Blair, and Valentine, 1958; Forrest, Blair, Brown, Stewart, Sandison, Harrington, Valentine, and Carter, 1959), and later adopted by Fraser, Joplin, and Steiner (1962) and Joplin (1964) for the treatment of diabetic retinopathy. We report our initial experience with this technique.

Properties of ⁹⁰Yttrium and Dosage

Where complete ablation of the normal gland by means of radiation is desired, ⁹⁰yttrium is agreed to be the material of choice because of its intense but localized beta radiation. Having a half-life of sixty-four hours, its effective radio-activity lasts about two weeks, during which period a gradual reduction of pituitary activity is induced. The aim is to give not less than 100,000 rads to any part of the gland. The diaphragma sellae should receive as small a dose as possible, and no more than 10,000 rads should reach the adjacent nervous structures, i.e., the optic nerves, chiasma, and the third cranial nerves. Improperly placed rods or excessive radiation may damage the diaphragma and cause cerebrospinal fluid to leak into the fossa and thence out through the trocar and cannula holes into the nose.

Pre-operative Assessment

All patients were assessed in the manner already described for pituitary stalk section (Cullen and others, 1965). In addition, nasal and throat swabs were cultured and radiographs taken of the paranasal sinuses. Clinical, bacteriological, or radiological evidence of upper respiratory tract infection precluded operation. The

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size of the pituitary fossa was determined by radiographic studies, using a standard technique; from these measurements the physicist determined the radio-activity of $^{90}\text{yttrium}$ required for each patient.

FIG. 1.—Method of insertion of $^{90}\text{yttrium}$ rod on stainless steel screw.

Operation

General anaesthesia was induced and transverse skin incisions made at a pre-determined point, usually near the osseo-cartilaginous junction of the nasal bones. Using two image intensifiers, one anteroposterior and one lateral, the trocar and cannula were then inserted and guided to the anterior part of the floor of the pituitary fossa, which was punctured and a threaded hole made, using a special rod and screw. The gland capsule was then perforated by a special stilette and the rod of $^{90}\text{yttrium}$, on its stainless steel screw, was screwed into position, thus minimizing the risk of cerebrospinal fluid leaking through the trocar and cannula hole (Fig. 1). The same procedure was carried out on the opposite side, the two rods being placed parallel to the diaphragma. Swabs were taken from each sphenoidal sinus, into which liquid bacitracin (2 ml.) was then instilled, the nasal wounds were sprayed with bacitracin and closed with two stitches. A simple dressing was applied and final check radiographs taken (Fig. 2). The patient was allowed up the next day.

Post-operative Management

Patients were immediately started on replacement doses of cortisone acetate. Other hormone replacement therapy was given as required and insulin doses adjusted according to the appropriate blood and urinary glucose estimations. The long-term problems of insulin hypersensitivity, diabetes insipidus, and adrenal insufficiency were managed as if the patients had undergone pituitary stalk section.

FIG. 2.— ^{90}Y trium rods and screws in position (Case 3). *Top*, Right lateral, *Bottom*, Submento-vertical, view.

TABLE
DETAILS OF 10 PATIENTS UNDERGOING ⁹⁰YTTTRIUM IMPLANTATION FOR DIABETIC RETINOPATHY

Details	Case 1	Case 2	Case 3	Case 4	Case 5
Age in years	50	54	22	40	26
Sex	M	M	F	F	F
Duration of Diabetes (years)	11	14	10	20	22
Insulin Requirements	26 Lente	22 PZI 14 Sol.	32 PZI 16 Sol.	36 PZI 16 Sol.	40 PZI 32 Sol.
	None	10 PZI 6 Sol.	18 PZI	6 PZI 4 Sol.	12 PZI 10 Sol.
Renal Function	Poor	Poor	Good	Good	Slightly impaired
Duration of Visual Symptoms (years)	1	3	1	4	2
Visual Acuity	R.E. Pre-operative	H.M.	6/18	6/18	H.M.
	R.E. Post-operative	H.M.	6/9	6/9	6/24
	L.E. Pre-operative	C.F.	6/18	6/12 pt	6/18
	L.E. Post-operative	C.F.	6/9	6/18	6/9
Main Features of Retinopathy	Secondary neovascularization	Secondary neovascularization	Primary neovascularization	Secondary neovascularization	Secondary neovascularization
	Vitreous haemorrhages	Vitreous haemorrhages	Vitreous haemorrhages	Vitreous haemorrhages	Vitreous haemorrhages
	Secondary neovascularization	Secondary neovascularization	Primary neovascularization	Secondary neovascularization	Secondary neovascularization
	Vitreous haemorrhages	Vitreous haemorrhages	Vitreous haemorrhages	Vitreous haemorrhages	Vitreous haemorrhages
Duration of Diabetes Insipidus	None	None	4 mth.	3 mth.	6 mth. severe
Complications	Rhinorrhoea	Died—Meningitis	—	—	—
Duration of Follow-up	1 year	4 wks. Post-operative	1 year	10 mth.	9 mth.
Result	Arrested		Improved	Improved	Improved

TABLE—continued

Details	Case 6	Case 7	Case 8	Case 9	Case 10
Age in years	35	49	32	62	44
Sex	F	F	M	F	F
Duration of Diabetes (years)	14	19	18	1	20
Insulin Requirements	40 PZI	24 Sol.	68 PZI	None	24 PZI
Post-operative	12 PZI	16 Sol.	8 Sol.	None	16 Sol.
Renal Function	Impaired	Good	Good	Good	8 Sol.
Duration of Visual Symptoms (years)	1	0.5	1	1	Poor
Visual	6/12 pt	6/6	6/9	C.F.	6
R.E. Pre-operative	N 5	N 5	N 5	C.F.	N 5
R.E. Post-operative	6/12 pt	6/6	6/9	C.F.	6/12
L.E. Pre-operative	6/12 pt	6/36	H.M.	6/18	6/12
L.E. Post-operative	6/12 pt	6/18	H.M.	6/18	H.M.
Main Features of Retinopathy	Secondary neovascularization Vitreous haemorrhages	Venous changes Haemorrhages and micro-aneurysms	Primary neovascularization Vitreous haemorrhages	Secondary neovascularization Vitreous haemorrhages	Secondary neovascularization
Duration of Diabetes Insipidus	Primary neovascularization	Secondary neovascularization	Secondary neovascularization Vitreous haemorrhages	Secondary neovascularization Vitreous haemorrhages	Secondary neovascularization Vitreous haemorrhages
Complications	None	4 mth. mild	1 mth. mild	None	None
Duration of Follow-up	8 mth.	7 mth.	7 mth.	Rhinorrhoea	—
Result	Improved	No change	Improved	2 mth.	1 mth.
				Improving	Too early

Results

The Table summarizes the medical and ophthalmological details of the ten patients operated upon. Three patients (Cases 1, 2, and 10) failed to satisfy the medical criteria as laid down for pituitary stalk section because of advanced renal disease. One patient (Case 2) failed to satisfy the ophthalmological criteria. Case 9 is exceptional in that she was not insulin-dependent. None of the patients was disturbed by the operation and diabetic and metabolic control were straightforward. Diabetes insipidus developed insidiously rather than acutely. Case 2 was discharged from hospital two weeks after implantation apparently well, but was re-admitted five days later in coma and died of a fulminating leptomeningitis. Post-mortem examination showed complete destruction of the pituitary gland without undue necrosis. Since then all patients have received prophylactic antibacterial therapy for one month starting two days pre-operatively and have remained in hospital during this period. Two patients (Cases 1 and 9) developed rhinorrhoea and this was so troublesome in Case 1 as to require further operative intervention. A number of patients have complained of general lethargy and loss of self-confidence lasting up to several months post-operatively.

In Case 7 satisfactory pituitary ablation has not been achieved, although the $^{90}\text{yttrium}$ was well positioned in a small pituitary fossa. It is proposed to repeat the procedure. In the other patients a significant fall in insulin requirements has occurred, suggesting satisfactory pituitary ablation, although the results of the thyroid stimulating hormone and gonadotrophin assays have yet to be evaluated. In these patients the improvement in vision and in the retinopathy was comparable to that achieved by pituitary stalk section, but developed less rapidly. (See Figs 3 to 7.)

FIG. 3.—Case 1, right eye. Before, and six months after, operation.

Discussion

Cases 1 and 2 had both been assessed for pituitary stalk section and rejected. They were operated upon only because they insisted on surgery, despite being told that no benefit was likely.

The early ophthalmological results are encouraging, but it will be some time before the long-term effects can be assessed. In spite of the unfortunate post-operative death of Case 2, we believe that $^{90}\text{yttrium}$ is a simpler and potentially

FIG. 4.—Case 3, right eye. Before, and one year after, operation.

FIG. 5.—Case 3, left eye. Before, and one year after, operation.

FIG. 6.—Case 5, left eye. Before, and seven months after, operation.

FIG. 7.—Case 6, right eye. Before, and six months after, operation.

safer method of inducing pituitary insufficiency in diabetics than either formal hypophysectomy or stalk section. It may therefore be justifiable to operate on older patients, those with more advanced renal disease, and those whose retinopathy has not yet progressed to the stage of fibrosis. However, we still consider that surgery is contra-indicated before subjective evidence of visual deterioration has occurred.

Summary

⁹⁰Yttrium implantation provides an alternative method for pituitary ablation in the treatment of advancing diabetic retinopathy. The principles involved are discussed, the radiological and operative techniques are described, and the preliminary results of ten patients so treated are given. This method would appear to be the treatment of choice in most diabetics requiring pituitary ablation.

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