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PITUITARY ABLATION BY ^{90}YTTRIUM IMPLANTATION FOR ADVANCING DIABETIC RETINOPATHY*

A PRELIMINARY REPORT

BY

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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 ^{90}yttrium 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 ^{90}Yttrium and Dosage

Where complete ablation of the normal gland by means of radiation is desired, ^{90}yttrium 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}yttrium required for each patient.

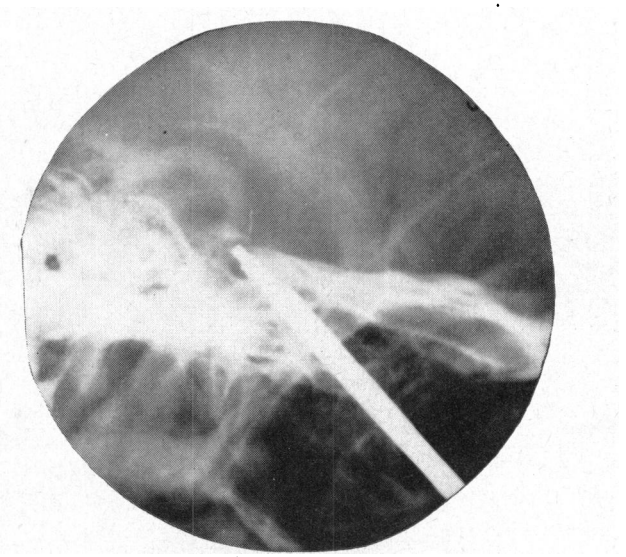

FIG. 1.—Method of insertion of ^{90}yttrium rod on stainless steel screw.

Operation

General anaesthesia was induced and transverse skin incisions made at a predetermined 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}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.

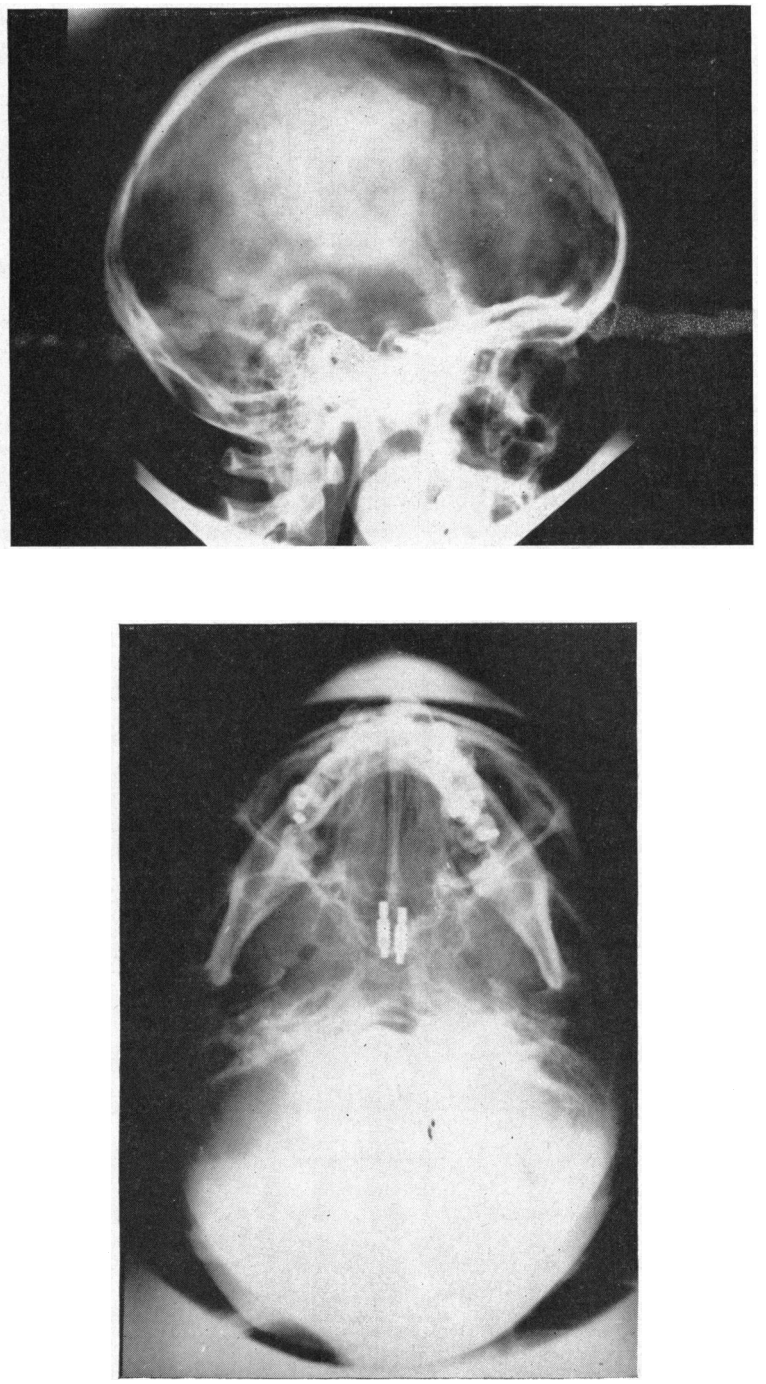

FIG. 2.—^{90}Yttrium rods and screws in position (Case 3). *Top*, Right lateral, *Bottom*, Submento-vertical, view.

TABLE

DETAILS OF 10 PATIENTS UNDERGOING ^{90}YTTRIUM 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	Pre-operative	26 Lente	22 PZ1 14 Sol.	32 PZ1 16 Sol.	36 PZ1 16 Sol.	40 PZ1 32 Sol.
	Post-operative	None	10 PZ1 6 Sol.	18 PZ1	6 PZ1 4 Sol.	12 PZ1 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	C.F.	H.M.	6/18 N 6	6/18 N 5	H.M.
	R.E. Post-operative	C.F.	H.M.	6/9 N 5	6/9 N 5	6/24 N 36
	L.E. Pre-operative	6/60 N 24	C.F.	6/18 N 6	6/12 pt N 6	6/18 N 8
	L.E. Post-operative	6/60 N 24	C.F.	6/9 N 5	6/18 N 5	6/9 N 5
Main Features of Retinopathy	R.E.	Secondary neovascularization Vitreous haemorrhages	Secondary neovascularization Vitreous haemorrhages	Primary neovascularization Vitreous haemorrhages	Secondary neovascularization Vitreous haemorrhages	Secondary neovascularization Vitreous haemorrhages
	L.E.	Secondary neovascularization Vitreous haemorrhages	Secondary neovascularization Vitreous haemorrhages	Primary neovascularization	Secondary neovascularization Vitreous haemorrhages	Secondary neovascularization 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 Pre-operative	40 PZI 20 Sol.	48 PZI 24 Sol.	68 PZI	None	24 PZI 16 Sol.
Insulin Requirements Post-operative	12 PZI 4 Sol.	48 PZI 16 Sol.	24 PZI 8 Sol.	None	12 PZI 8 Sol.
Renal Function	Impaired	Good	Good	Good	Poor
Duration of Visual Symptoms (years)	1	0·5	1	1	6
Visual Acuity R.E. Pre-operative	6/12 pt N 5	6/6 N 5	6/9 N 5	C.F.	6/12 N.5
Visual Acuity R.E. Post-operative	6/12 pt N 5	6/6 N 5	6/9 N 5	C.F.	6/12 N 5
Visual Acuity L.E. Pre-operative	6/12 pt N 5	6/36 N 14	H.M.	6/18 N 14	H.M.
Visual Acuity L.E. Post-operative	6/12 pt N 5	6/18 N 14	H.M.	6/18 N 14	H.M.
Main Features of Retinopathy R.E.	Secondary neovascularization Vitreous haemorrhages	Venous changes Haemorrhages and micro-aneurysms	Primary neovascularization Vitreous haemorrhages	Secondary neovascularization Vitreous haemorrhages	Secondary neovascularization
Main Features of Retinopathy L.E.	Primary neovascularization	Secondary neovascularization	Secondary neovascularization Vitreous haemorrhages	Secondary neovascularization Vitreous haemorrhages	Secondary neovascularization Vitreous haemorrhages
Duration of Diabetes Insipidus	None	4 mth. mild	1 mth. mild	None	None
Complications	—	—	—	Rhinorrhoea	—
Duration of Follow-up	8 mth.	7 mth.	7 mth.	2 mth.	1 mth.
Result	Improved	No change	Improved	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}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.)

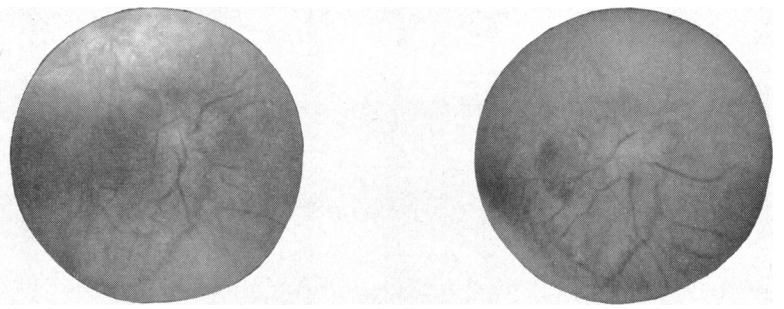

FIG. 3.—Case 1, right eye. Before, and six months after, operation.

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}yttrium is a simpler and potentially

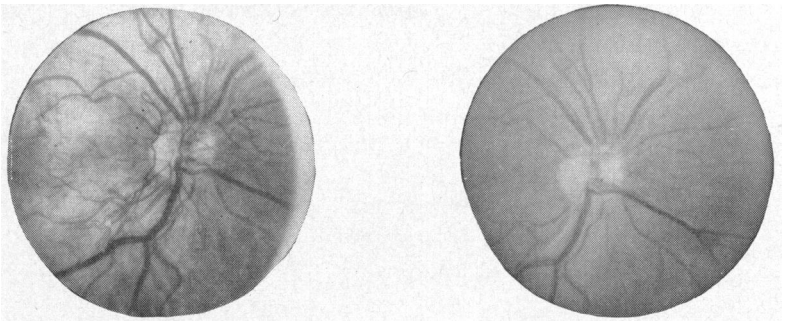

FIG. 4.—Case 3, right eye. Before, and one year after, operation.

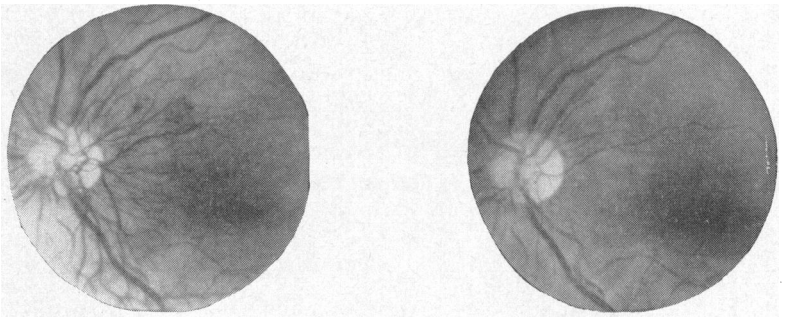

FIG. 5.—Case 3, left eye. Before, and one year after, operation.

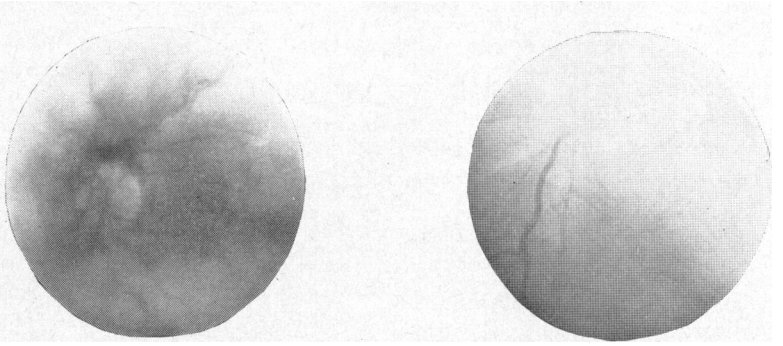

FIG. 6.—Case 5, left eye. Before, and seven months after, operation.

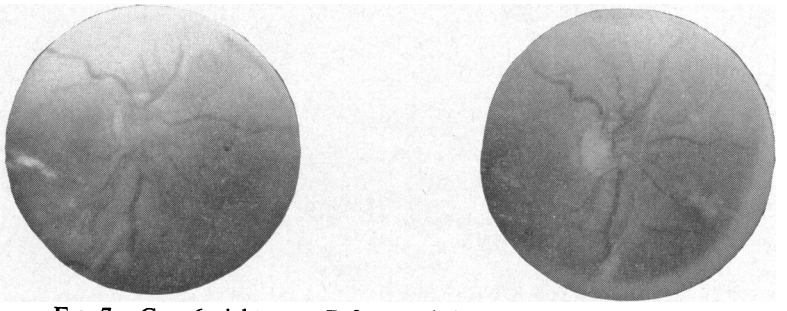

FIG. 7.—Case 6, right eye. Before, and six months after, operation.

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

^{90}Yttrium 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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