

# Efficacy of Cryotherapy in Retinoblastoma

A. C. B. MOLTENO

## SUMMARY

Five cases of retinoblastoma treated by freezing are reported. From these cases it appears that a single freeze-thaw cycle will destroy all tumour and that with suitable instruments it is possible to destroy tumours involving up to 30% of the volume of the globe without causing blindness.

*S. Afr. med. J.*, 50, 1089 (1976).

Freezing of retinoblastoma, which was first reported by Lincoff *et al.*<sup>1</sup> and later by Rubin,<sup>2</sup> has been shown by histological examination to cause complete destruction of tumour in treated areas.<sup>3</sup> In this article I report the effect of freezing 5 tumours which involved between 1% and 60% of the volume of the eye in respective cases.

## PATIENTS AND METHODS

### Patient Selection

In 1 patient (1% lesion) the diagnosis was presumptive, since the patient's brother had a retinoblastoma. In the remaining 4 patients the diagnosis was proved by histological examination of the more involved eye, which had been removed.

Cryotherapy was indicated when the tumour recurred after radiotherapy in 1 patient and in patients in whom lesions were untreatable by other means, owing to size, or extension into the vitreous cavity.

### Principles and Treatment

Treatment was planned to freeze and thaw the whole tumour mass twice only, to minimise the danger of severe haemorrhage. The smaller lesions were treated with a standard cryoprobe used for retinal detachment work and which can form an iceball 5 mm in radius. For larger lesions a cryoprobe designed by the author was used. This instrument was cooled to a temperature of  $-89^{\circ}\text{C}$  by the evaporation of nitrous oxide through a sintered bronze filter and was provided with a set of interchangeable applicators to provide iceballs of increasing size up to approximately 12-mm radius.<sup>4</sup>

### Case Reports

**Case 1.** The first patient was a 5-year-old boy whose brother had a retinoblastoma. At routine examination of the family an elevated yellow nodule was detected in the mid-periphery of the nasal side of the patient's retina.

Although the lesion seemed inactive, it was frozen trans-conjunctivally, and promptly disappeared, to be replaced by a pigmented chorioretinal scar. There has been no recurrence so far after 4 years.

**Case 2.** The second patient was a boy whose right eye was enucleated, because of retinoblastoma, when he was 6 months old. This was followed by radiotherapy to the posterior segment of the remaining eye, both orbits, optic nerves and the chiasma (cobalt-60, 3 600 rads fractionated over 6 weeks).

At 11 months of age two yellow nodules, situated in the posterior pole near the upper nasal vessels, appeared in the left eye. These slowly enlarged and ultimately coalesced to form a slightly raised mass, approximately one disc diameter across. Examination 2 weeks after two freeze-thaw cycles at  $-89^{\circ}\text{C}$  showed that the lesions had disappeared. A pigmented chorioretinal scar developed slowly over the following 3 months and there has been no recurrence to date (3 years later).

**Case 3.** A 3-year-old boy presented with a staphylo-matous right eye. After enucleation the eye was found to be filled by a tumour. An endophyte type of retinoblastoma, which involved about 20% of the volume of the eye and extended 6 mm into the vitreous cavity, was seen in the left eye. Radiotherapy and chemotherapy with tri-ethyl melamine were undertaken, and cryopexy was attempted by means of overlapping applications with a cryoprobe giving an iceball of 5-6-mm radius.

The initial transscleral cryotherapy destroyed most of the tumour and was well tolerated. However, since the iceball did not extend far enough into the vitreous, the tumour was frozen again 2 weeks later and the iceball grown so as to include all vitreous deposits.

The second cryopexy was followed by considerable vitreous reaction and a temporary exudative detachment

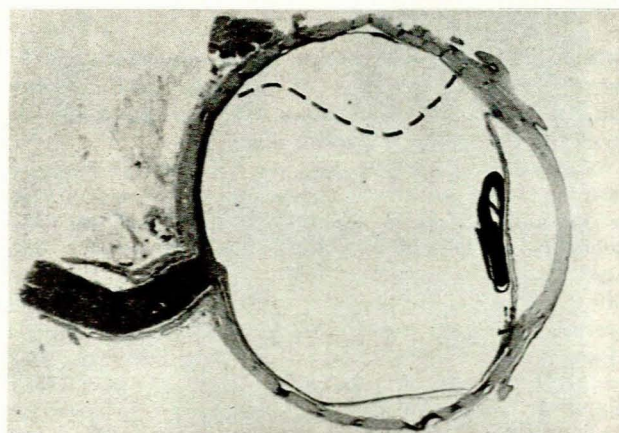


Fig. 1. Case 3. Section through treated left eye to show destruction of tumour — former extent shown by altered vitreous outlined (H and E  $\times 4$ ).

Department of Ophthalmology, University of Stellenbosch and Tygerberg Hospital, Parowvallei, CP

A. C. B. MOLTENO, M.B. CH.B., F.R.C.S.

Date received: 16 September 1975.



of the retina. However, histological examination of this eye at autopsy 5 months later demonstrated complete destruction of the tumour in the area which had been frozen, as well as a tiny deposit of actively growing tumour in the area, which had been irradiated but not frozen (Figs 1 and 2). The remainder of the eye was histologically intact.

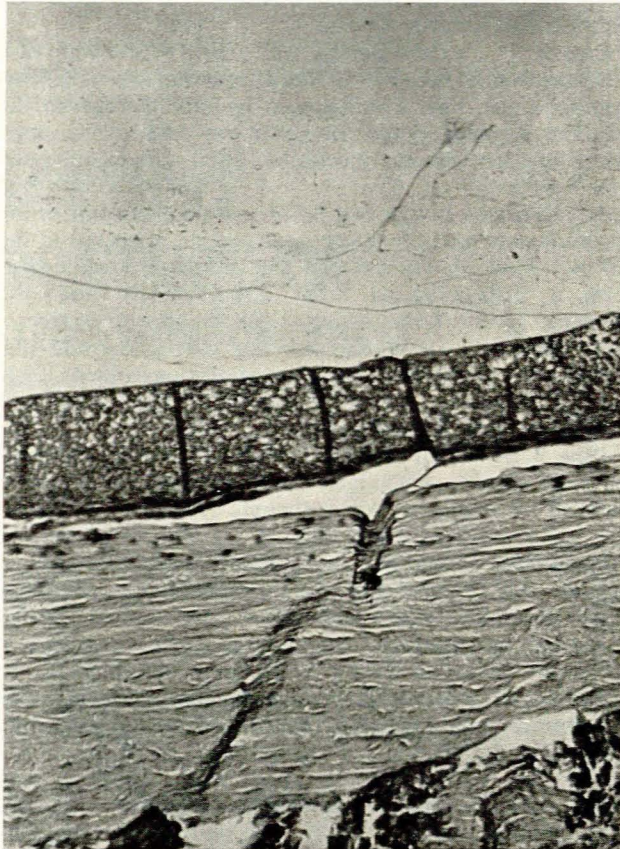


Fig. 2. Case 3. Section through irradiated but not frozen 'retinoblastoma in situ' (H and E  $\times 120$ ).

**Case 4.** A 3-month-old male infant presented with bilateral symmetrical masses of exophyte retinoblastoma which involved the nasal halves of both retinas and encroached onto both optic discs (Fig. 3).

After enucleation of the right eye, the presence of retinoblastoma was confirmed. Radiotherapy to both orbits was commenced and the lesion in the left eye was completely frozen by four overlapping applications of a large curved cryoprobe cooled to  $-89^{\circ}\text{C}$ . Freezing was continued until the iceball had engulfed the surface of the tumour and extended to include the nasal half of the optic nerve.

Examination under anaesthesia 2 weeks later revealed a residual tumour and cryotherapy was repeated and extended to include a suspicious area below the macula.

After the second cryopexy the child became blind, with a shallow total detachment of his retina. However, vision of 6/60 returned when the retina became re-attached after 3 weeks, while examination under anaesthesia revealed

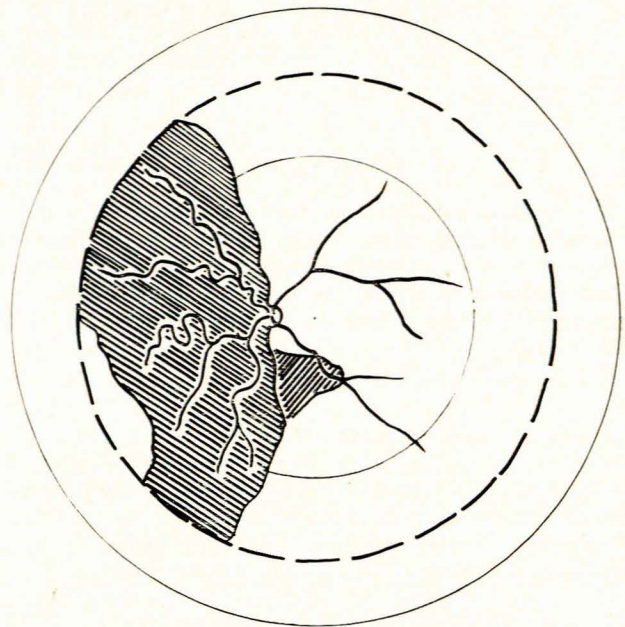


Fig. 3. Case 4. Extent of tumour in the left eye.

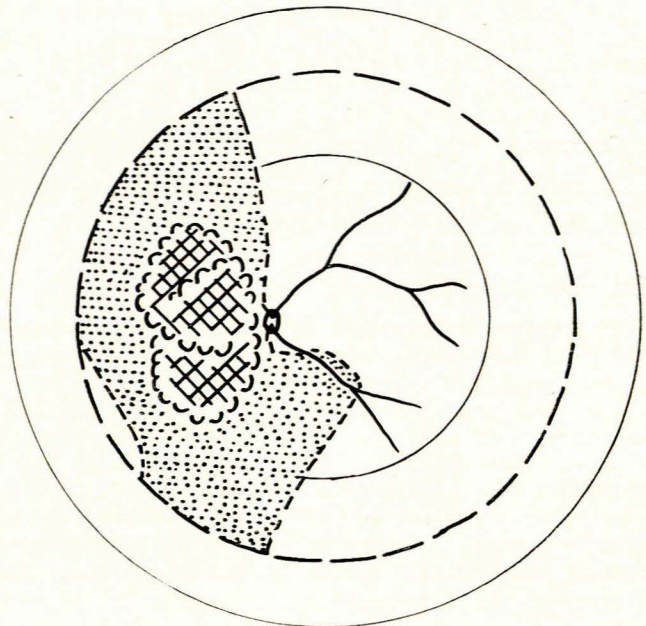


Fig. 4. Case 4. Drawing of treated left eye after  $3\frac{1}{2}$  years, showing chorioretinal atrophy (stippled) and sponge-like calcified tumour matrix (cross-hatched).

extensive chorioretinal atrophy surrounding the calcified framework of the tumour (Fig. 4).

At 3 years of age a radiation cataract developed and was aspirated; however, the calcified remnant and the fundal picture have remained unchanged  $3\frac{1}{2}$  years after the initial treatment.

**Case 5.** A  $2\frac{1}{2}$ -year-old boy presented with a fungating



retinoblastoma in the right orbit (removal of the eye was done elsewhere). A large exophyte tumour occupied approximately 60% of his left eye, which still retained a small amount of vision (Fig. 5). Radiotherapy and chemotherapy were commenced and the tumour was frozen in one procedure by a single application of a cryoprobe to each of the three main tumour masses. A temperature of  $-196^{\circ}\text{C}$  was obtained by using liquid nitrogen to form a large iceball.

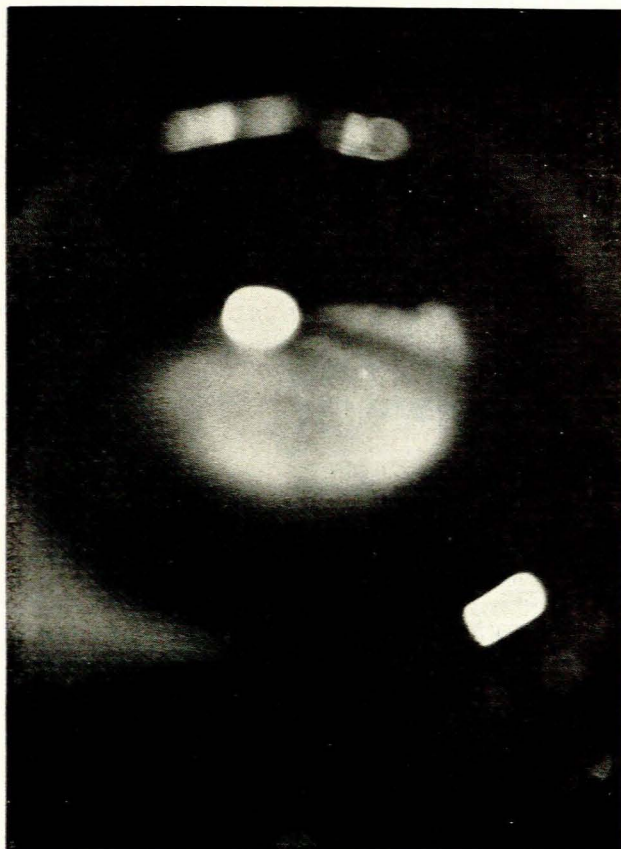


Fig. 5. Case 5. Left eye with pupil dilated to show tumour mass.

There was considerable postoperative reaction and, although the anterior segment and lens remained clear, no fundal detail could be seen and all vision was lost. When no improvement occurred after 2 months, the eye was enucleated, but the child died of widespread metastases 3 months later.

Histological examination of the eye revealed a normal anterior segment with complete destruction of all tumour and a gliotic mass of totally detached retina attached to an optic nerve, which, while showing histological signs of atrophy, was not involved by tumour (Fig. 6).

### DISCUSSION

Patient 5, in whom each portion of the tumour was frozen once only, demonstrates that a single freeze-thaw cycle kills

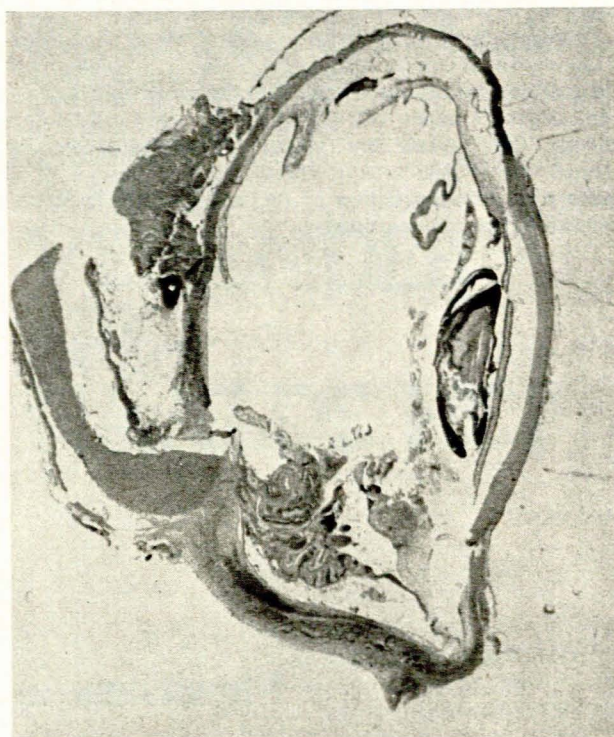


Fig. 6. Case 5. Section through left eye (H and E  $\times 4$ ).

all retinoblastoma cells. The presence in patient 3 of active tumour in an irradiated area that was not frozen, and the destruction of recurrent tumour after radiotherapy in case 2, demonstrates that radio-insensitive lesions were destroyed.

Repeated cryoprobe applications cause haemorrhage and care was taken to avoid freezing any portion of the tumour more than three times; however, re-treatment of residual tumour after an interval of 2 weeks provoked a much more severe reaction than initial intervention (cases 3 and 4). Thus the ideal technique is probably to engulf the entire tumour by a single iceball once only. This is possible when the tumour involves less than 30% of the volume of the globe.

Conventional radiotherapy is limited by the fact that anoxic tumour deposits (i.e. vitreous seedlings) are radio-resistant while radiation damage to the lens and retinal vessels limits the dose that can be given. Stallard's technique,<sup>5</sup> of placing radioactive plaques on the sclera over the tumour, can destroy tumour deposits which occupy up to 50% of the volume of the globe, but two operations are required to insert and remove the source, while the tumour responds slowly over a period of months. The very high doses which are given may cause occlusion of retinal veins or arteries.

Cryotherapy is rapidly effective, so that the success or otherwise of the treatment can be decided within 4-6 weeks. Furthermore, there is no possibility of delayed radiation damage which may destroy sight years later.

On the basis of the cases presented I consider it justifi-



fiable to withhold prophylactic radiotherapy to an uninvolved second eye, while cryotherapy alone is indicated in lesions which can be completely frozen at a single operation without destroying vision (30% or less of the eye).

In larger tumours (40-50% of the eye) cryotherapy destroys the tumour but vision will probably be lost through retinal detachment; consequently radiation, which causes a slower destruction of the tumour, may well be a preferable form of treatment.

I should like to thank the trustees of the Willem Goosen Trust Fund for financial support.

#### REFERENCES

1. Lincoff, H., McLean, J. and Long, R. (1967): *Amer. J. Ophthalm.*, **63**, 389.
2. Rubin, M. L. (1968): *Ibid.*, **66**, 870.
3. Moltano, A. C. B., Griffiths, J. S., Marcus, P. B. and Van der Walt, J. J. (1971): *Brit. J. Ophthalm.*, **55**, 492.
4. Moltano, A. C. B. and Luntz, M. H. (1968): *S. Afr. med. J.*, **42**, 1201.
5. Stallard, H. B. (1948): *Brit. J. Ophthalm.*, **32**, 618.

## Physicians and Sex Therapy

DOMEENA C. RENSHAW

### SUMMARY

The physician's role in sex therapy is discussed. Problems of sexual dysfunction and guidelines for physicians who wish to engage in sex therapy are set out briefly.

*S. Afr. med. J.*, **50**, 1092 (1976).

Should physicians be concerned about developments in the field of the new sex therapy? Who should comment on the standards, the therapists and the recipients of sex therapy? Should there be a separate subspecialty, and if so, under whose aegis? Who will protect a most vulnerable public from potential malpractice?

In every culture, the 'medicine man' has been the repository of ultimate intimacies. To whom does any person tell the size and shape of a stool, the colour and flow of menstrual blood, the force and feeling of urination? And now, with equally comfortable professionalism, the physician of the 1970s must ask about early morning erections, duration of coital penetration, masturbatory activity, aversion or preference for oral or anal sex, details of early childhood sexual experiences, current patterns of sexual signals and also about additional couplings. These facts

are all as essential to a holistic medical history as the details of contraception or social stresses.

In no other area of medicine does the true meaning of 'doctor', namely 'teacher', show such close application as in the field of sex therapy. It is here that persons who have sex problems have a need to know, to sort out what confusions they may have, and to be taught accurate medical and scientific facts of human sexual exchange by those adequately trained and authorised to do so, namely physicians.

### ORIGINS OF MODERN SEX THERAPY

It was not until 1966 that scientific and objective data about the human male and female sexual response patterns from the authoritative St Louis sex laboratories became widely available to the layman as well as the medical profession.<sup>13</sup> Since Masters and Johnson published *Human Sexual Inadequacy*<sup>13</sup> in 1970, almost 4 000 'sex clinics' have been established in the United States. Dr Masters estimates that less than 100 of these offer quality therapy by reliable professionals. As with marriage counsellors, sex counsellors may sell services without a licence or the fear of challenge, and with little more than good will. The public is highly vulnerable; particularly those persons seeking the relief of acute sexual and marital problems.<sup>16</sup>

Not all medical schools in the USA offered formal courses on human sexuality to medical students during 1975, so that even recent graduates have a critical need for education and clinical experience in the fundamentals of normal male and female sexual responses, as well as

Sexual Dysfunction Clinic, Department of Psychiatry, Loyola University Stritch School of Medicine, Maywood, Illinois, USA

DOMEENA C. RENSHAW, M.B. CH.B., Associate Professor

Date received: 28 October 1975.