Effects of fast neutrons on the eye

A preliminary communication

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Patients with advanced tumours of the head and neck have been treated with fast neutrons from the Medical Research Council's cyclotron at Hammersmith Hospital for the last 5 years. In 62 per cent of the first hundred cases there was complete regression of the tumour and in only two cases did the tumour recur (Catterall and Vonberg, 1974). The effects of these 7.5 MeV neutrons on the normal tissues which are unavoidably irradiated have also been studied and, in the relatively short period of follow-up available, these effects have been entirely acceptable in skin, mucous membranes, and bones in the great majority of cases. The ophthalmic changes seen in relation to the doses received are described in this paper.

The patient

Altogether 28 patients received a measurable dose of neutrons to the eyes.

All the tumours were locally extensive and in ten cases involved the bony orbital cavity. Eleven were localized to the nasopharynx or were salivary gland tumours without bone involvement, and seven patients received treatment for glioblastoma multiforme. A total of 52 eyes received a measurable dose of radiation and were examined. In these patients, 47 eyes received fast neutrons and were given radical x-ray therapy.

The extent of these tumours required relatively large volumes of tissue to be treated and this included the whole of one eye in ten cases. Where there were apparently no distant metastases at the start of treatment the full dose of 1555* rads of neutrons was given in twelve treatments over 26 days to the eye on the involved side without shielding. The contralateral eye was given as little radiation as possible. The exact dose received by each eye was carefully calculated by means of isodose

curves constructed for each area of all beams of radiation used. These doses were checked during treatment by the measurement of the activation induced in aluminium pellets placed over the inner and outer canthi and the centre of the eyelids.

Method

In most cases patients were seen before treatment so that any pre-existing ocular conditions could be noted and excluded from the results given in the present study. The interval between examinations varied from a week to several months; the minimum follow-up period was 28 days and the maximum 2 years from the start of radiation. The majority were seen at intervals up to at least 6 months.

Patients were questioned about symptoms before each examination. Visual acuity was tested on a Snellen chart at 6 m with distance correction if worn, and a detailed examination of the eye and ocular adnexa was carried out using standard ophthalmological apparatus and methods. Pupils were dilated with a short-acting mydriatic and lenses examined by focal and retroillumination. Photographs were taken of optical sections of the lens using the apparatus described by Brown (1972). Abnormalities of the eye and lids were noted and scored on a points system which will be described in detail elsewhere.

Results

The results are summarized in the Table and the dose effect on various regions of the eye is shown in the Figure.

A measurable dose of neutrons (20 rads or more) was received by 37 eyes. Those receiving less than 85 rads were unaffected. Some of the eyes (see Table), which received between 85 and 220 rads showed eye lid erythema and oedema, tear fluid and oil excess, and punctate epithelial keratitis within 60 days of the first treatment. In the next 120 days some patients complained of blurred vision, eye irritation, and epiphora, and conjunctival oedema appeared. All these symptoms and signs were reversible and vision was not permanently affected.

*This 1555 rads has been reported as 1440 rads in previous papers. The change followed an examination of dosimetry technique by physicists at the Hammersmith Hospital, Glasgow, Washington DC, and Houston, Texas. To facilitate comparison between these centres, the Hammersmith rad has been decreased in value by 8 per cent. The amount of radiation actually received by the patient is the same. All other doses in this paper have been corrected.

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FIGURE Anatomy of eye and its adnexa related to dose of neutrons required to cause significant clinical effect

Eleven eyes received 220–860 rads; these produced additional effects, which were incompletely reversible in the lids, lacrimal apparatus, and cornea. These effects included lid distortion, stenosis and ectropion of the lacrimal puncta, tear oil deficiency, and precorneal drying, which occurred within 60 days of the first treatment. They proceeded in some eyes to loss of cilia, meibomian gland obliteration, mucous discharge, conjunctival telangiectasia, and reduced corneal sensation. In all eyes in this group there was incomplete resolution with some permanent reduction in vision.

Six eyes received 860–1510 rads, which produced severe effects followed by little resolution and a significant permanent reduction in vision. These eyes showed the changes found in the lower dose groups and in addition some proceeded to conjunctival keratinization, cataract, and retinal telangiectasia, which appeared between 60 days and 12 months after the first treatment.

Seven eyes received more than 1510 rads, which produced severe ocular damage, with such additional features as corneal erosions which were reluctant to heal and corneal stromal ulceration. These eyes did not retain useful vision and three required enucleation.

The cataracts which developed consisted of small collections of granules in the posterior subcapsular region of the lens with some minor anterior subcapsular changes. But in two eyes in the highest treatment group rapidly maturing cataracts occurred in association with corneal ulceration.

Pre-existing ocular disease was observed in several patients at their preliminary examination. The findings included naso-lacrimal duct obstruction, proptosis, corneal anaesthesia, keratoconjunctivitis sicca, cataract, and optic atrophy, and have been subtracted from the results of the examinations after treatment.

Discussion

The eyes of a group of patients receiving fast neutrons have been examined in detail, but insufficient data on x -ray effects have been obtained to make comparisons between the two types of radiation. However, the literature on the effects of x irradiation on the eye in man has been reviewed by Merriam, Szechter, and Focht (1972), and it is evident from the literature and from our own observations that the effects of neutron radiation are similar to those of x irradiation.

Neutron radiation produced loss of cilia, erythema of the eyelids, injection of the conjunctiva, and mucopurulent discharge. These were not serious but other potentially severe effects were observed on detailed ophthalmological examination. Significant among these were varying degrees of corneal epithelial damage ranging from fine punctate epithelial keratitis to total epithelial loss which could lead to corneal destruction. Destruction of the meibomian glands of the eyelids eliminated the oily secretion, an important component of the tear film, and corneal drying and epithelial damage occurred. The action of the eyelids in protecting the cornea was also impaired by distortion of the lid margin and by keratinization of the tarsal conjunctiva which abraded the cornea. When these changes occurred in conjunction with a reduction in corneal sensation the patient developed severe corneal ulceration but in spite of this remained free of symptoms.

It is of obvious importance to the radiotherapist and the ophthalmologist to know what dose of radiation does long-term harm to the eye. Many of the signs and symptoms are transient or of little consequence, but others, in particular corneal ulceration, are significant. While it is probable that our study gives an accurate impression of the incidence of the side-effects of neutron radiation up to about 6 months after the start of treatment, it is probable that the incidence of late complications such as cataract may be higher than is shown in this study. Such cataracts as have been seen were of little consequence except in two eyes with severe corneal ulceration.

It appears that patients whose eyes have received a high dose (1080 rads or more) may have a biphasic response with an initial peak of symptoms

Table *Effect of neutron radiation on the eye*

<i>Dosage (rads)</i>	<i>Eyes treated (No.)</i>	<i>Clinical effect</i>	<i>Description</i>	<i>Eyes affected (No.)</i>	<i>Result</i>
< 85	10	Nil	Nil	Nil	Nil
85-220	13	Minor	Symptoms		Complete resolution
			Blurred vision	2	
			Irritation	2	
			Eyelid		
			Erythema	12	
			Oedema	2	
			Tear film		
			Fluid and oil excess	5	
			Epiphora	5	
			Conjunctiva		
			Injection	6	
			Cornea		
			Punctate epithelial keratitis	2	
220-860	11	Moderate	Symptoms		Incomplete resolution
			Discomfort	5	Some permanent reduction in vision
			Eyelid		
			Distortion	5	
			Loss of cilia	6	
			Meibomian gland obstruction	8	
			Lacrimal puncta		
			Stenosis	5	
			Ectropion	7	
			Conjunctiva		
			Telangiectasia	5	
			Tear film		
			Pre-corneal drying	6	
			Mucus excess	5	
			Debris excess	6	
			Oil deficiency	2	
			Cornea		
			Reduced sensation	2	
860-1510	6	Severe	Conjunctiva		Little resolution
			Keratinization	3	Significant reduction in vision
			Lens		
			Cataract	2	
			Retina		
			Telangiectasia	2	
1510+	7	Destructive	Cornea		Severely defective vision or complete loss of eye
			Erosion	3	
			Ulceration	3	
			Iris		
			Atrophy	1	
			Lens		
			Cataract	3	
			Eye enucleated	3	

and signs at 28 days followed by a remission and a further more severe peak at about 2 months.

Conclusion

Because of the considerable individual variation in

response it is, at this stage, only possible to relate changes to wide ranges of doses given. The most sensitive structures of the eye were in the anterior segment and these appeared to be more in need of protection than the lens.

The study is being continued to acquire sufficient

data to establish more accurately the dose-response relationship and to determine the end-result after an adequate period of follow-up.

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