Cryotherapy of proliferative sickle retinopathy, II: triple freeze-thaw cycle

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SUMMARY Complete closure of retinal neovascularisation due to proliferative sickle cell retinopathy was achieved in 28 ‘sea fans’ (areas of neovascularisation) in 9 eyes of 9 patients by means of a triple freeze-thaw technique. However, 2 eyes developed subsequent rhegmatogenous retinal detachments, presumably related to vitreous traction on necrotic retina. We therefore recommend photocoagulation as the best treatment of proliferative sickle cell retinopathy. If opacities in the media prevent photocoagulation, a single freeze-thaw cycle is preferable.

Persons with sickle cell anaemia (haemoglobin SS), sickle cell B thalassaemia (haemoglobin S-Thal), and especially sickle cell haemoglobin C disease (haemoglobin SC) develop vasoproliferation from the retina into the vitreous. Left untreated, these areas of neovascularisation (sea fans) may progress to vitreous haemorrhage, tractional retinal detachment or rhegmatogenous retinal detachment (Goldbaum, 1971). Photocoagulation with the xenon arc or argon laser has been used to destroy neovascular tissue (Goldbaum and Acacio, 1973; Goldbaum et al., 1977). For successful photocoagulation the media must be sufficiently clear over the feeding vessels to allow the photocoagulation beam to form a sharp image in the retina. Vitreous haemorrhage or other opacities in the media can prevent successful photocoagulation. Furthermore, photocoagulation has known complications such as haemorrhage (Goldbaum et al., 1977), choroidal ischaemia (Goldbaum et al., 1976), and chorido-vitreal neovascularisation (Galinos et al., 1975; Goldbaum et al., 1977). A previous paper from our clinic relates our experiences with a single freeze-thaw cycle of transconjunctival cryopexy in the treatment of proliferative sickle retinopathy (Lee et al., 1975). Thirteen sea fans in 10 eyes of 6 patients were treated. Four of these 13 sea fans (31%) were still patent, though markedly attenuated, after treatment. None of the attenuated sea fans has bled in the 3 years since the cryopexy.

Several authors have reported successful treatment of retinoblastomas and vascular tumours, such as retinal angiomatics, with repeated freeze-thaw techniques (Hale and Christensen, 1968; Amoils and Smith, 1969; Welch, 1970; Watzke, 1973; Watzke, 1974). With this in mind an attempt was made to improve our previous cryotherapeutic results in proliferative sickle retinopathy by employing a triple freeze-thaw cycle.

Materials and methods

Between February 1974 and July 1974 every third eye of the patients seen at the Sickle Cell Eye Clinic of the University of Illinois Eye and Ear Infirmary that required treatment for proliferative sickle cell retinopathy and any eye in which sea fans could be identified but were partially obscured by vitreous haemorrhage were selected for triple freeze-thaw cycle cryotherapy. A total of 28 sea fans in 9 eyes of 9 patients were treated. The patients’ ages ranged from 16 to 53 years, with a mean of 30 years. Seven patients had haemoglobin SC, 1 had haemoglobin SS, and 1 had haemoglobin AS (all confirmed by quantitative haemoglobin electrophoresis).

Before treatment each patient received an eye examination with measurement of best corrected visual acuity, slit-lamp examination, and a detailed retinal drawing with indirect ophthalmoscopy and scleral depression. Fluorescein angiography confirmed the patency of the sea fans to be treated. In eyes in which vitreous haemorrhage made identification of a sea fan difficult or uncertain, fluorescein angioscopy with a Wratten 47 blue filter on an
indirect ophthalmoscope was performed to locate
the telltale green vitreous cloud of fluorescein over-
lying each sea fan.
Each treatment was performed either with a
carbon dioxide probe or a fluorocarbon probe, each
adjusted for maximum cooling. The intense cryo-
pexy was painful with topical anaesthesia. Hence
1% lignocaine was injected subconjunctivally in the
quadrant to be treated, or a retrobulbar injection
was given. The cryoprobe was applied to the globe
directly over the site of the smaller sea fans, which
were then treated with a triple freeze-thaw that
totally encompassed the area of neovascularisation.
Larger sea fans were first treated with a triple freeze-
thaw cycle to the feeding vessels. The cryoprobe
was then moved to adjacent sites until the entire sea
fan had been covered (Fig. 1).
Each transconjunctival cryopexy lesion was
monitored by indirect ophthalmoscopy. The probe
was positioned to indent the desired area. The iceball
was allowed to grow until the treated vessels were
incorporated. The end point was a hazy appearance
of the vessels to be treated within the iceball as if
they were being viewed through frosted glass (Fig.
2). The process was repeated two additional times
at each site of application. It is important to note
that, when the vessels to be treated stood out
brilliantly in relief against the white background of
the iceball, the iceball had not yet reached the
vessels and the end point had not yet been achieved.
When vitreous haemorrhage was present and the
view of the sea fan was obscured, the end point
was more difficult to identify and had to be esti-
mated.
Twenty-four or 48 hours after treatment and again
several weeks later fluorescein angiography was

Fig. 1 Technique of triple freeze-thaw cryopexy. For a
small sea fan (A) a single site was treated. For a some-
what larger lesion (B) the feeding vessels were treated
first, followed by freezing of the lesion itself. For a large
sea fan (C) the feeding vessels were treated and then
multiple applications were made to cover the entire lesion

Fig. 2 Endpoint of treatment corresponded to
incorporation of vessels within the iceball with a 'frosted'
appearance to the vessels.
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Results

After this intense cryopexy there was often considerable transient conjunctival chemosis. Blood vessels in the conjunctiva were sometimes occluded 24 to 48 hours after the treatment. After a week the conjunctiva appeared normal. No abnormalities in muscle balance were induced.

After the triple freeze-thaw applications each of the sea fans was engorged and appeared purple against a background of pale oedematous retina (Fig. 3). Fluorescein angiography 24 or 48 hours later showed non-perfusion of the treated sea fan (Fig. 4); all 28 sea fans were closed and have not reperfused over a 3-year period of observation (Fig. 5, Table 1).

In 2 of the 3 eyes with vitreous haemorrhage (Cases 2 and 4) the vitreous cleared spontaneously over the next 6 months. One patient (Case 5) with a dense central vitreous haemorrhage failed to clear over a 6-month period, though there was no evidence of rebleeding. Vitrectomy and subsequent lens extraction returned the visual acuity to 20/20 with a soft contact lens.

Two of the patients (Cases 1 and 8) developed local rhegmatogenous retinal detachments shortly after treatment. These detachments were successfully treated by scleral buckling with cryopexy. In both these eyes a retinal hole appeared to have been pulled open by vitreous traction on retina made necrotic by the triple freeze-thaw cryopexy.

Discussion

Multiple freeze-thaw cycles have certain theoretical advantages in the destruction of tissue over a single freeze cycle. Zacarian (1977) showed that 2 freeze

Fig. 3 Appearance of treated sea fan 1 day after cryopexy

Fig. 4 Fluorescein angiography 1 day after treatment shows absence of perfusion

Fig. 5 Fluorescein angiography some weeks later again shows absence of perfusion of treated lesion
cycles are far more lethal to suspended HeLa cells than a single cycle, and he concluded that a period of incomplete thaw permitted 10% more cells to remain viable than did a complete thaw between freezes. In experimental retinal cryopexy lesions in albino rabbits Amoils (1969) noted that a triple freeze-thaw cycle potentiated vascular damage and accelerated and intensified the exudation, stasis, and thrombosis present in such lesions. He showed that with a triple freeze-thaw technique the vascular stasis became marked within 20 minutes and involved larger choroidal veins and arteries throughout the lesion. Petechiae, presumably secondary to minute ruptures of the capillary walls, were noted on the surface of retinal angiomas and retino-blastomas treated with a triple freeze-thaw cycle, but in no case did bleeding extend into the vitreous.

In the current study complete closure of 28 sea fans was achieved with a triple freeze-thaw cycle. Unfortunately 2 of the 9 eyes treated by this method developed retinal detachments. From our experience with photocoagulation, single freeze-thaw cryopexy, and triple freeze-thaw cryopexy we consider that photocoagulation is the safest and preferred treatment for closing the circulation to a sea fan. We have discontinued triple freeze-thaw cryopexy because of the occurrence of the 2 retinal detachments. The vitreous traction that is almost invariably present with proliferative sickle retinopathy makes triple freeze-thaw cryopexy too risky. When vitreous or lenticular opacities prevent photocoagulation, but allow identification and partial visualisation of sea fans, single freeze-thaw cryopexy is an acceptable alternative to photocoagulation. Though single freeze-thaw cryopexy is not 100% effective in closing treated sea fans, none of the attenuated sea fans that were not totally closed has bled after treatment (Lee et al., 1975).

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References


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**Table 1 Triple freeze-thaw cryotherapy of proliferative sickle retinopathy**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Haemoglobin type</th>
<th>Age at time of treatment (years)</th>
<th>Eye treated</th>
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<th>Pre-op. visual acuity</th>
<th>Final visual acuity</th>
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<td>1</td>
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<td>20/30</td>
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