

PERSONAL PRACTICE

Initial experience of screening for retinopathy of prematurity

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The initial results of the Multicenter Trial of Cryotherapy for Retinopathy of Prematurity (ROP) in the USA,¹ published in 1988, showed a significant reduction in the number of visual complications in babies treated with retinal cryotherapy for stage 3 'threshold' disease. These results were the first real evidence that treatment could improve the outcome in ROP. Based on the results and recommendations of that study, we set up a screening service for ROP based at the Mersey regional neonatal intensive care unit. This unit comprises 24 cots, of which seven have been designated as being for infants who require ventilation. In practice these numbers are often exceeded. The purpose of this paper is to describe the service which started in April 1989.

Screening programme

Our aim was to screen all infants of birth weight below 1500 g and/or less than 32 weeks' gestation. Babies born at 26 weeks' gestation and under were first examined at 32 weeks after conception. Others all had a first eye examination by the time they were 7 weeks old, and in many cases it was before that. All infants were then examined every two weeks. If no ROP was detected by term, when the retinal vessels have normally reached the ora serrata, the babies were discharged. All babies who developed ROP continued to be reviewed by one of us (DIC) until there were either definite signs of regression or treatment by cryotherapy was indicated. Infants with mild ROP and those in whom regression occurred were reviewed until they were 3 years old, first at three monthly and then at increasing intervals. Orthoptic assessment, refraction, and retinal examination were performed. Infants who were treated with cryotherapy were seen more frequently because of an increased risk of developing high myopia, amblyopia, or strabismus. We intend to continue to follow up these children.

All neonatal units in the Mersey region were contacted and informed of the ROP screening service. They were invited to refer those babies who met the screening criteria to our unit for retinal examination if such a service was not already being provided by their local ophthalmology department. The offer was taken up by two hospitals in a neighbouring region and five of the seven nurseries which are located in the Mersey region, but outside Liverpool. One of us (DIC) already provided an ophthalmological service to the three nurseries in Liverpool.

During the two years of this study three babies were unfit to travel for screening. None had been previously nursed on our intensive care unit. On those occasions one of the authors (DIC) examined the babies in their respective neonatal intensive care unit.

Retinal examination is carried out as follows. The pupils are dilated with 0.5% cyclopentolate and 2.5% phenylephrine eyedrops, and ophthalmoscopy performed with a 28 dioptre lens. A lid speculum and scleral indentation is used to facilitate examination of the retinal periphery. Clinical findings are recorded in accordance with the recognised classification system.² All babies are monitored with a pulse oximeter and an electrocardiograph during the screening procedure. Most babies are examined on the neonatal intensive care unit in a converted isolation room modified by the fitting of blackout curtains. Those who were too ill to be moved were examined in their incubators. In these cases the view of the retina is less good because there is more light in the room. It is also more difficult to get the baby into an optimal position. In spite of these difficulties, these have often been the sickest babies with the worst disease, and even though the quality of the examination is less good, a quick look for 'plus' disease is possible.

Results of the screening programme

Between April 1989 and April 1991, 204 babies completed the screening programme, of whom 44 were transferred from other hospitals; 103 (51%) had developed ROP. Seventy five of the 91 babies (82%) born at 28 weeks' gestation or less developed ROP, while 28 of 104 babies of 29-31 weeks' gestation (27%) developed ROP. The incidence of ROP by gestation is shown in fig 1. All babies under 27 weeks' gestation developed ROP. Fifty two (87%) of the 60 babies with a birth weight of less than 1000 g developed ROP whereas 51 (35%) of the 144 babies of birth weight greater than 1000 g developed ROP. All 13 babies of birth weight below 750 g developed ROP (fig 2).

The worst stage of disease seen in either eye of the 103 babies with ROP is shown in table 1. Three babies were bilaterally blind due to retinal detachment (stage 4/5) when they were first examined by an ophthalmologist. Their clinical details are shown in table 2. This was at the start of the screening programme and they had been considered to be too ill for ophthalmological examination. We now make strenuous efforts to

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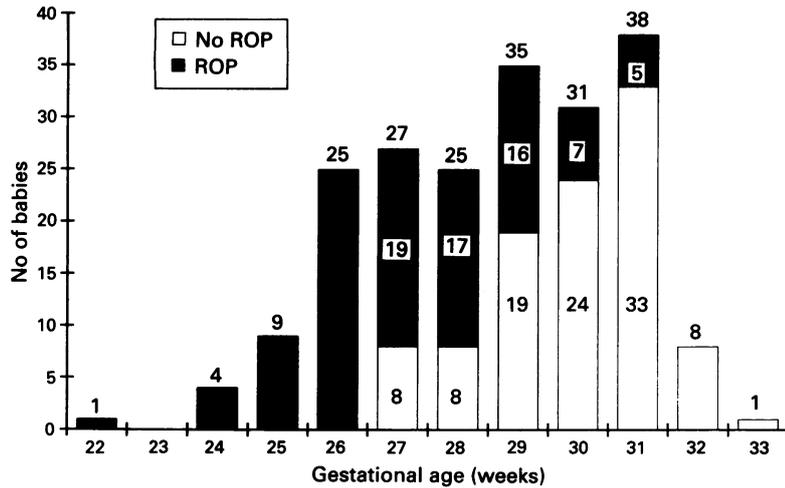


Figure 1 Incidence of ROP by gestation.

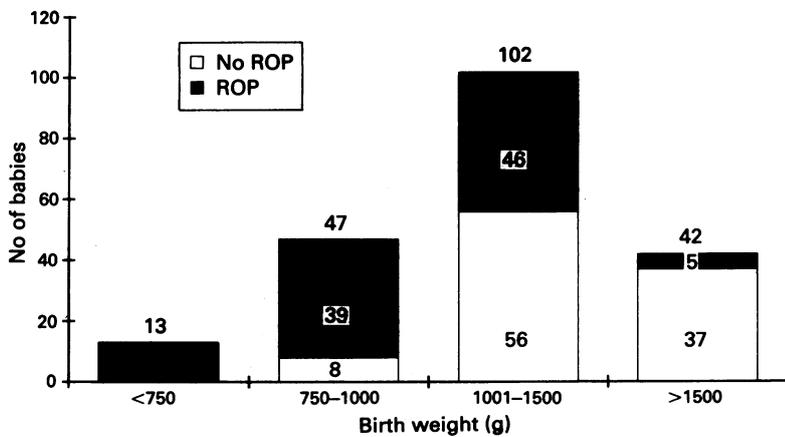


Figure 2 Incidence of ROP by birth weight.

review infants on time and the problem has not arisen since.

As all cases of stage 1 and stage 2 ROP regress spontaneously we have grouped these babies together and compared them with those whose worst stage of ROP was stage 3-5, plotted against gestational age (fig 3) and birth weight (fig 4).

Minor changes in heart rate occurred relatively frequently during scleral indentation, but there were no serious bradycardias. The major complication noted during ocular examination was apnoea. This occurred in three infants: one experienced recurrent apnoeic attacks both before and after the screening procedure; a second had chronic lung disease which subsequently required home oxygen; and the third baby was found to be anaemic (haemoglobin concentration 80 g/l) and a further examination after transfusion was uncomplicated.

Table 1 Worst stage of ROP achieved by either eye

	No of babies	Birth weight (g)		Gestation (weeks)	
		Median	Range	Median	Range
Stage 1	24	1271	595-1660	29	26-31
2	44	1022	580-1606	27	24-31
3	25	860	450-1460	26	22-29
4/5	10	812	664-1480	26	24-29

Table 2 Clinical details of three infants who had retinal detachment when first examined by an ophthalmologist

Gestation (weeks)	Birthweight (g)	Age first examined (weeks)	ROP stage
24	668	14	Bilateral 5
25	664	13	Bilateral 4
29	1480	24	Bilateral 5

Treatment by cryotherapy

Thirty eyes (16 babies) had stage 3 'threshold' disease and were treated with retinal cryotherapy. The median gestational age of these babies was 26 weeks (range 24-29 weeks), median birth weight was 813 g (range 622-1460 g), and median postnatal age at the time of treatment was 78 days (range 66-106). The treatment was performed on the neonatal unit with a paediatric senior house officer and neonatal nurse in attendance. The babies were intubated, ventilated, and nursed under an overhead heater. They were paralysed with pancuronium, and fentanyl (15 m/kg) was given for analgesia. Twenty six eyes were treated with a retinal cryoprobe to be avascular retina (average applications 37), four eyes were treated with the modified hammerhead cryoprobe. If necessary the conjunctiva was incised to allow better access of the cryoprobe over the avascular retina.

No anaesthetic complications occurred. Three eyes developed ocular complications: two were found to have a 1 mm overgrowth of conjunctival tissue onto the peripheral cornea, which was visually insignificant and occurred in one case despite conjunctival suturing; another baby was found to have suffered a small vitreous haemorrhage, temporal to the macula, at the time of the first post-treatment examination.

The outcome of treatment was regression of the disease in 21 of the 30 eyes, while seven eyes progressed to retinal detachment, and two eyes had retinal folds involving the macula. Three of the treated babies became bilaterally blind and were placed on the blind register. Subsequently, two of these three babies died as a result of other systemic illness unrelated to the ocular treatment. A further baby died with failed surgery in one eye, the other eye having been successfully operated on.

The estimated costs of this service are described below. This should not be considered to be a rigorous costing exercise. We have purposely left out the cost of the paediatric registrar and senior registrar, and the extra secretarial time required, because the people were already employed to work on the neonatal unit.

The initial capital costs for establishing this service was approximately £6000 for the purchase of the equipment. This included a cryotherapy machine, cryoprobes, an indirect ophthalmoscope, and lenses for the retinal examination. It did not include the cost of the pulse oximeter or a heart rate monitor.

The revenue costs of running such a service in terms of consultant ophthalmologist's time and extra nursing may be expressed as follows. Liverpool Maternity Hospital is a level 3 regional neonatal intensive care unit ventilating around 200 babies each year. This amounted to 2198 ventilator days in 1990 and 1894 ventilator days in 1991. At that hospital, one consultant oph-

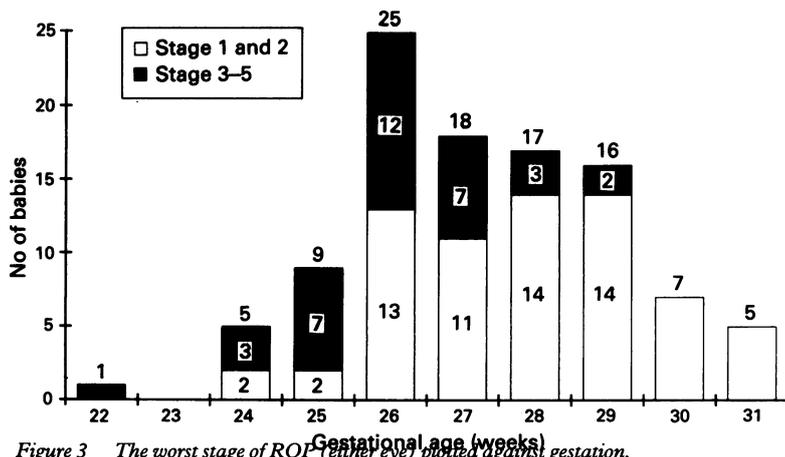


Figure 3 The worst stage of ROP (either eye) plotted against gestation.

thalmologist needed one notional half day (NHD) each week for screening. A further 1 NHD was needed for long term follow up of babies born prematurely at that hospital. This is carried out at the local eye hospital. A third NHD was required for treatment. A senior registrar in ophthalmology rotates through this service, but is considered supernumerary. An additional three half days of nursing time were needed for the service.

So that other neonatal units can determine their requirements for ROP screening based on the workload in their own unit, the revenue costs have been expressed in terms of the number of ventilator days per year. We calculated that the provision of the service required 1.2 NHDs of consultant ophthalmologist's time and 4.8 nursing hours each week per 1000 ventilator days per year. The average cost for the ambulance service to transfer the babies from the district general hospital to the central hospital was £15 per journey (£0.58 per mile and £18 per hour). No extra nurses were employed for this.

Discussion

One hundred and three (50%) of the 204 infants who satisfied the inclusion criteria for screening, that is who were below 32 weeks' gestational age and/or weighed less than 1500 g at birth and who completed the screening programme, developed ROP. This figure is similar

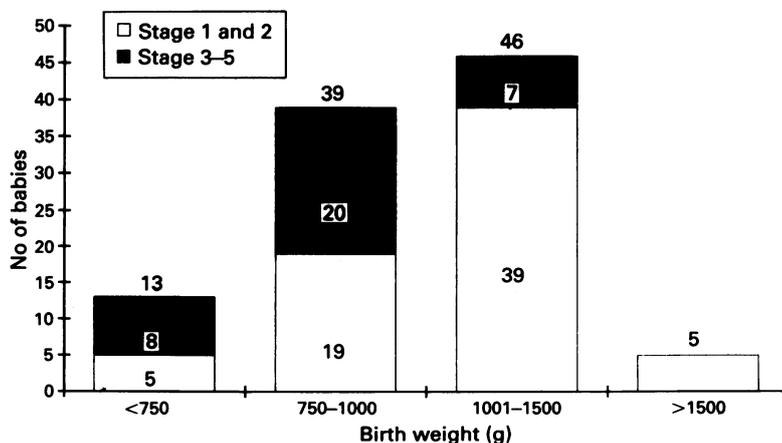


Figure 4 The worst stage of (either eye) plotted against birth weight.

to other published series,^{3,4} but somewhat higher than the figure of 32.6%⁵ reported in a recent study from the Hammersmith Hospital, London. Different inclusion criteria and examination techniques may account for the different rates of ROP found. We used a lid speculum and scleral indentation. This allowed us to examine the peripheral retina in greater detail than the method used by the Hammersmith group.

ROP was more likely to occur in the more immature infants (82% of those born at ≤ 28 weeks) and in those with a lower birth weight (87% of those born < 1000 g). In particular, the more serious and vision threatening stages of ROP—that is, stages 3–5—were seen in the more preterm infants (table 1). Twenty five babies (24%) developed stage 3 ROP, which is similar to or slightly higher than previous studies^{3,5-7} and 10 babies reached stage 4/5 (nearly 10%). Figures 3 and 4 show that the severer stages of ROP are more common with decreasing birth weight and gestational age. Six out of 13 (46%) of babies born weighing under 750 g and nine out of 47 (19%) of babies weighing between 750–1000 g developed stage 3 threshold disease or worse. Such a high incidence of severe stage ROP is a matter of concern and is under investigation at present.

In 1988, the preliminary results of the randomised cryotherapy trial for stage 3 threshold ROP found that treatment reduced the likelihood of an unfavourable outcome from 43% for untreated eyes and 22% for treated eyes.¹ An unfavourable outcome was defined as 'posterior retinal detachment, retinal fold involving the macula, or retrolental tissue'. However, a more definitive follow up report from that same trial, published in 1990, found an unfavourable outcome in 51% of untreated eyes as against 31% for treated eyes.⁸ Our results of cryotherapy treatment are more in line with the second of these reports. Nine of the 30 treated eyes (30%) in our group had an unfavourable outcome after cryotherapy.

Despite the apparent reduction in unfavourable outcome after cryotherapy, the relatively high proportion of cases that went on to retinal detachment is a cause for concern. Recently published results of cryotherapy for stage 3 ROP, performed earlier than the 'threshold' disease definition used by the Multicenter Trial of Cryotherapy for ROP^{1,8,9} found that retinal detachment occurred in only 1.25% of 79 treated infants.⁹ We feel that delay in cryotherapy by even a short time once threshold disease has been reached may be prejudicial to the outcome.

Complications during screening and treatment were fairly uncommon, mostly related to the stimulation of the oculocardiac reflex due to ocular manipulation and the administration of the eye drops.^{10,11} No anaesthetic complications occurred during or after the retinal cryotherapy procedure. A vitreous haemorrhage was noted in one eye at the first post-treatment retinal examination. This complication has been reported to occur in up to 20% of treated eyes,⁸ and may be due to the disease process itself rather than to the treatment.

We have presented the costs of the service in terms of the workload of the neonatal unit, the initial capital costs for equipment and the revenue consequences. Any attempt to cost blindness would be extremely difficult and would have to take into account the emotional as well as the financial costs involved for both the patients and parents.¹² Nevertheless a North American study has estimated that cryotherapy for ROP gives a 20 to 60 million dollar net savings to the Federal budget for each annual birth cohort of 25 000 premature infants (<1500 g), depending upon the assumptions made about lifetime costs of blindness.¹³

We conclude that screening for ROP should be available for all infants born at less than 32 weeks' gestation and weighing less than 1500 g, and that this should be performed by a trained ophthalmologist. If ROP of stage 3 or worse is detected, we recommend that treatment should be performed at a regional centre, where appropriate expertise will have been developed.

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