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From our own correspondent

Effects of premature exposure to light: a credibility struggle

The construction of credibility is ... simultaneously an outcome of competing forces [to say what the world is like] and a marker of the thickening of social ties [within which knowledge can be reliably exchanged].[1]

Does *ambient* light play a causal role in the pathogenesis of retinopathy of prematurity (ROP)? We need to confess, sadly, that this simple question has not yet been answered to the satisfaction of all concerned. The query was first posed 55 years ago (!) by Theodore Terry in his initial reports describing the strange new disorder.[2,3] The recent report of 'no significant difference in outcome' in LIGHT-ROP (a multicentre randomised controlled trial of light reduction involving a total of 409 high-risk premature infants)[4] has been followed by angry outbursts.[5] 'We predicted the report would be a whitewash, because [the study] was flawed,', said the founder of a group of parents of ROP-blinded children. 'The infants were not fitted with protective goggles for hours,' said another parent, pointing to the delay in enrolling eligible babies [since informed consent was required before enrolment; the study protocol permitted delays of up to 24 h after birth].[a] 'We didn't need any study to see that babies did better when shielded from light,' a neonatal nurse declared.

Several months before the LIGHT-ROP report was published, Phelps and Watts conducted a meta-analysis[6] for a Cochrane Review of the evidence then extant in clinical trials of early light reduction to prevent ROP. Eight relevant studies were identified in a search of the medical literature in the 5-decade interval from 1942 to 1997, but only two of these fulfilled the reviewers' pre-search criteria for methodological rigour.[7,8] Although the results from the two acceptable studies were 'inconclusive', the analysts anticipated that the outcome in the multicentre LIGHT-ROP study would weigh-in more convincingly than those in any previous parallel comparison.

[a]The dogged use of *post hoc* argument, based on anecdotal evidence without concurrent controls, reminds me of Richard Peto's story of the quack who advocates mountain climbing for the cure of cancer. A number of patients with 'incurable cancer' are assembled at the foot of the mountain and assured that those who climb to the top will live a long time. Some die even before attempting the climb, and the quack, with a sigh of heartfelt grief, says: 'If only they had come earlier.' Another group of patients die halfway up the mountain; but they of course did not complete the treatment, so they could not hope to benefit. A small residual percentage of patients reach the top of the mountain, and they may live for a number of years, confirming, yet again, the benefits of fresh alpine air and vigorous exercise.

The LIGHT-ROP trialists foresaw that their study would be criticised because of the above-noted delay in placing the light-reducing goggles. Consequently, they examined the results in a subgroup of 47 infants enrolled within 6 h after birth. Again, there was no evidence of a treatment effect: 'Infants who had goggles placed early had a 65 per cent incidence of retinopathy of prematurity, compared with 52 per cent in the control group.'

An editorialist predicted,[9] very perceptively, that despite the negative results in LIGHT-ROP (the largest and the most carefully crafted study of premature light exposure conducted so far), the debates about this issue will continue interminably. As Engelhardt and Caplan have noted,[1] it is unrealistic to assume that complex disputes can be resolved solely by an appeal to concrete evidence. The view that a controversy can be settled is based on the shaky assumption that there is 'prior agreement on (1) how to acquire evidence relative to the dispute, and (2) how to reason with the evidence to resolve the controversy.' And, they point out, 'perceptions about stakes in a controversy are themselves a problem when the stakeholders in the debate belong to different communities with different appreciation of the disputed evidence...or to competing social groups with opposing political and ethical agendas.' Additionally, Epstein argues,[10] 'the notion that any *one* clinical trial can be ''definitive'' misses a fundamental point: a study's conclusiveness is not a given; it is a negotiated outcome. The extent to which closure is achieved...depends crucially on the capacity of actors to present themselves as credible representatives or interpreters of scientific experiments – to ensure that others trust their evaluations and will fall in behind them.'

Does *early* light exposure have an adverse effect on the development of visual function – quite *apart* from any influence on the course of ROP? In all the arguments about a possible relationship between light and the risk of ROP, there has been little or no discussion about the possibility of an independent pathogenic influence. The second question is timely, I believe, because in developed countries ROP is no longer the most frequent cause of severe visual impairment in children under 5 years of age. For example, retinopathy accounts for only 6% of all children on the Oxford Register (born between 1984 and 1992) with severe vision loss.[11] Now we need to pay special attention to 'cortical visual impairment' (CVI), because it is the most frequent condition associated with blindness in early childhood. Over one-quarter of the pre-school children on the register with severe visual loss are classified under the CVI heading. A search for possible co-determinants of CVI (light exposure, for example) seems reasonable.

Infants enrolled in LIGHT-ROP were examined biweekly by indirect ophthalmoscopy until the post-conceptional age of 44 weeks; and a complete ophthalmological examination was carried out by a 'masked' examiner 6 months after 'term' (as calculated from conceptional age). Further examination of vision as these children grow older might provide an opportunity to gather circumstantial evidence for or against the notion of a harmful non-ROP effect

of early exposure to light. And there is a similar opportunity for extended follow-up of negative results at 4–6 months (corrected age) in a more recent small trial of light reduction.[12] Of course, any interesting associations found in these 'fishing expeditions' would need to be tested prospectively in future trials to develop a convincing causal argument.

The full story, I suspect, has not yet been told. It would be ironic if the 'single-causers,'[b] who never wavered in their belief that bright ambient light in neonatal special care units is harmful, were right all along – but for the wrong reason!

WILLIAM A. SILVERMAN
Greenbrae, CA, USA

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[b] In this myopic view of the natural world, the uninspired mantra is 'one disease, one cause, one cure (a magic bullet)'.[10]