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Retinopathy of prematurity in Brazil: an emerging problem

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The tragedy of blindness from retinopathy of prematurity (ROP) does not arise from a lack of knowledge about the disease. Based on results of large multicenter trials,[1,2] we know when sight-threatening acute retinopathy is most likely to develop, we know that babies at risk are usually in hospital under medical care, and we have treatments currently available that have been proven effective in markedly decreasing visual morbidity. Nevertheless, blindness due to ROP is an emerging reality in many countries as survival rates of very premature babies improve. This is of particular importance in countries with medium levels of human development (as defined by the UN Development Program Index)[3] in which the number of neonatal intensive care units is increasing rapidly and effective detection and treatment programs are not yet in place. Prevention of blindness from ROP requires a complex series of interactions that must be carefully choreographed. The paper by Fortes Filho et al.[4] in this issue of Jornal de Pediatria highlights many important issues regarding the detection of sight-threatening disease.

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The impetus for starting ROP screening programs usually comes from concerned physicians, both neonatologists /pediatricians and ophthalmologists, who begin to see sporadic cases of blindness due to ROP in young children as smaller and smaller premature babies survive. These concerned individuals set out to increase awareness in the medical community that the disease is occurring in the population and that its detection and treatment are important. Fortes Filho et al. report that the importance of ROP blindness as a public health issue was established in Brazil with a 2002 ROP workshop that was jointly sponsored by national organizations of ophthalmology and pediatrics, as well as nongovernmental organizations. The workshop attendees determined that basic demographic data on which babies were blind due to the disorder were not available. Such data are essential when implementing a screening program. The attendees also acknowledged that data were not available on the prevalence of visual impairment due to ROP in the community, that few screening programs existed, and that different criteria were being used when programs did exist. Based on the expert opinion of those attending the workshop, guidelines were established to determine which babies should be screened, the timing of those examinations, what techniques were appropriate for use in screening, and how the findings of the screenings would be recorded. Each of these components is essential for establishing an effective ROP screening program.

Fortes Filho et al. examined babies who had birth weights of ≤ 1,500 g and/or gestational age of ≤ 32 weeks and who survived to the time of the initial screening at 6 weeks. Over a 4-year period in a single hospital, they examined 300 babies and found that 6% of these developed ROP severe enough to require treatment. This disease incidence is in accord with the large multicenter trials in the United States, though these trials enrolled babies only up to 1,250 g birth weight.[1,2] This,

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however, probably reflects a high level of neonatal care in their hospital. A word of caution is warranted here. Fortes Filho et al. have just begun the work of implementing effective ROP screening in Brazil since they report their experience in a single nursery. Other nurseries in Brazil need to report their screening results, since, based on experience in other countries,[5] it is relatively common for larger babies to develop blinding disease as neonatal services are extended to the broader community.

For the nursery data presented from Porto Alegre, the birth weight (BW) and gestational age (GA) criteria selected for screening are in general agreement with those currently recommended in countries with high levels of human development.[6-8] It is noteworthy that no babies with larger BW or greater GA developed sight-threatening ROP in the nursery in Porto Alegre, but these findings are not generalizable to all nurseries in countries with middle levels of human development. This was emphatically documented by Gilbert et al.[5] in *Pediatrics* 2005, when the investigators determined the birth weight and gestational age of babies who developed blindness or sight-threatening ROP in large number of countries with low, moderate and high development rankings. Using the UK guidelines of < 1,500 g and/or < 32 weeks gestation, they found that almost all babies (99.6%) in countries with high development rankings were within these guidelines, while more than 12% of babies with potentially blinding ROP in low or moderate development rankings would not have been examined if the UK guidelines had been generally applied.

As more data are collected on ROP from other nurseries in Brazil, the ROP screening guidelines, at first determined by expert opinion, can be modified using an evidence base. The parameters for birth weight and gestational age can then be set wide enough to include babies at risk for developing sight-threatening ROP, but not so broad that the physicians responsible for performing screenings are overwhelmed with numbers of babies to be examined. For example, in a large nursery in Peru, during a 1-year period, the ophthalmologist would have to screen 112 babies under the birth weight and gestational age criteria similar to those recommended in Brazil, but, based on his/her experience and according to the blindness observed in larger, more mature babies, guidelines were set that include babies up to 2,000 g birth weight and 33 weeks gestation. This increases the screening burden in that nursery by more than twice, but these larger babies are still developing serious disease (personal communication, L Gordillo, 2006). ROP screening guidelines should not be considered immutable, as change may be required as a better understanding of the prevalence of serious disease in the neonatal units is acquired. This is emphasized by the recent revision of the 2006 US guidelines that lowered the gestational age guideline from 32 weeks or less to 30 weeks or less.[6] Indeed, it may be appropriate to develop guidelines within each neonatal unit that differ from national guidelines, but there may well be bureaucratic, political, and legal obstacles to such individualized guidelines.[9]

Another critical point in which ROP screening programs break down is in getting the baby in for a follow-up examination. In the Fortes Filho et al. report, the only child reported to progress to blindness was not brought by his parents for follow-up appointments. This is tragic since the timely treatment would likely have prevented this outcome. The caregivers need to make sure that parents or guardians are aware of and understand the critical importance of timely follow-up and, indeed, there may well be a case for keeping some babies in hospital until the time for developing serious disease is past. It is essential that the ophthalmologists and the neonatologist/pediatricians involved with the baby's care develop guidelines that ensure outpatient follow-up appointments are made and attended.

Still, with the best of intentions and care, some babies will be blinded from ROP. They may not have been screened appropriately and we must develop alternative methods for detection of disease. Here, telemedicine offers promise for extending services where ophthalmology expertise may not yet be available.[10,11] Some babies may have received timely treatment, but still progressed to retinal detachment and blindness. Despite the failure of the healthcare system to prevent their blindness, these children deserve our best efforts to educate and integrate them into society as much as they are able. This will require cooperative efforts among parents, the medical community and governmental institutions.

References

1. Multicenter trial of cryotherapy for retinopathy of prematurity. Three-month outcome. Cryotherapy for Retinopathy of Prematurity Co-operative Group. Arch Ophthalmol. 1990;108:195-204.
2. Early Treatment for Retinopathy of Prematurity Cooperative Group. Revised indications for the treatment of retinopathy of prematurity: results of the early treatment for retinopathy of prematurity randomized trial. Arch Ophthalmol. 2003;121:1684-94.

3. United Nations Development Programme. Human development report. New York: Oxford University; 2005.
4. Fortes Filho JB, Barros CK, da Costa MC, Procianoy RS. Results of a program for the prevention of blindness caused by retinopathy of prematurity in southern Brazil. J Pediatr (Rio J). 2007;83:209-16.
5. Gilbert C, Fielder F, Gordillo L, Quinn G, Semiglia R, Visintin P, et al. Characteristics of infants with severe retinopathy of prematurity in countries with low, moderate and high levels of development: implications for screening programs. Pediatrics. 2005;115:e518-25.
6. Section on Ophthalmology American Academy of Pediatrics, American Academy of Ophthalmology, American Association for Pediatric Ophthalmology and Strabismus. Screening examination of premature infants for retinopathy of prematurity. Pediatrics. 2006;117:572-6. Erratum in: Pediatrics. 2006;118:1324.
7. Guidelines for screening examinations for retinopathy of prematurity. Canadian Association of Pediatric Ophthalmologists Ad Hoc Committee on Standards of Screening Examination for Retinopathy of Prematurity. Can J Ophthalmol. 2000;35:251-2.
8. Retinopathy of prematurity: guidelines for screening and treatment. The report of a Joint Working Party of the Royal College of Ophthalmologists and the British Association of Perinatal Medicine. Early Hum Dev. 1996;46:239-58.
9. Quinn GE. What do you do about ROP screening in "big" babies? Br J Ophthalmol. 2002;86:1072-3.
10. Ells AL, Holmes JM, Astle WF, Williams G, Leske DA, Fielden M, et al. Telemedicine approach to screening for severe retinopathy of prematurity: a pilot study. Ophthalmology. 2003;110:2113-7.
11. Fielder AR, Gilbert, C, Quinn G. Can ROP blindness be eliminated? Biol Neonate. 2005;88:98-100.

RIX4414 (Rotarix™): a live attenuated human rotavirus vaccine

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Rotaviruses are recognized as the single most important cause of severe infantile gastroenteritis worldwide. On a world scale, rotaviruses are estimated to be responsible for over 600,000 deaths annually.[1,2] For these reasons, rotaviruses have received a high priority as a target for vaccine development.[3] Incorporation of an effective rotavirus vaccine into the infant immunization schedule in developed countries could reduce hospitalizations due to dehydrating diarrhea in young children by 40 to 60%.[4] More important, the worldwide use of such vaccine could decrease the total number of deaths caused by diarrhea by approximately 10 to 20%.[1,4]

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Transmission of rotaviruses occurs by the fecal-oral route, providing a highly efficient mechanism for universal exposure that has circumvented regional and national cultural practice differences. The symptoms associated with rotavirus disease typically are diarrhea and vomiting accompanied by fever, nausea, anorexia, cramping, and malaise that can be mild and of short duration or produce severe dehydration.[5,6] Severe disease occurs primarily in young children, most commonly among those aged 6 to 24 months. Approximately 90% of children in both developed and developing countries experience a rotavirus infection by the time they reach 3 years of age.[5]

Initial efforts to develop a rotavirus vaccine relied largely on the use of a single animal strain to create a live attenuated oral vaccine that would provide protection from severe disease. Because efficacy results were inconsistent, these attempts were modified to include multi-component

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