Red Reflex Examination in Neonates: The Need for Early screening

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Children are a priority in “Vision 2020,” the World Health Organization's global initiative for the prevention of avoidable visual impairment [1]. Congenital cataract is the leading cause of preventable childhood partial sight or blindness [2] – both by primary prevention, for example, through a rubella immunization program, and by secondary prevention depending on early screening of the pupillary red reflex. Given that the optimal time to remove a dense congenital cataract in an infant and initiate optical treatment appears to be age 4 to 6 weeks [3], screening to ensure prompt early treatment is essential for improving visual outcome [4]. Newborn screening for media opacities, comprising examination of red reflex, is widely accepted. The red reflex test uses transmission of light from an ophthalmoscope through all the normally transparent parts of a subject's eye. Any factor that impedes or blocks this optical pathway will result in an abnormality of the red reflex. Corneal opacities, aqueous opacities, iris abnormalities, cataracts, vitreous opacities, and retinal abnormalities including tumors or chorioretinal colobomata, may produce abnormalities or asymmetry of the red reflex [5].

Screening newborns with the red reflex test is widely accepted. The American Academy of Pediatrics [6] and the British Paediatric Association [7] currently recommend red reflex assessment as a component of the eye evaluation in the neonatal period and during all subsequent routine health supervision visits. The purpose of this policy statement is to minimize the risk of delay in the diagnosis of serious vision-threatening or life-threatening disorders. Despite these worldwide recommendations, there are large variations in the implementation of red reflex examination [8-12]. In the UK, less than half the cases in the 1995–1996 cohort of congenital and infantile cataract were detected by screening examinations at age 8 weeks or less [8]. Similarly, a recent study of infantile cataracts in the United States showed that 38% were diagnosed after age 6 weeks [9]. Reporting their 10 year experience in a single regional ophthalmology center, Sotomi et al. [10] showed that none of the 27 infants with congenital cataracts was diagnosed by the newborn screening examination. Six of 8 infants who were diagnosed before 3 months of age had a good visual outcome in contrast to only 3 of 19 diagnosed after 3 months. Considering that this practice was not evaluated prospectively, it is not clear whether the low detection rate is the result of non-compliance, inadequate technique, or low sensitivity of the red reflex test as a screening tool.

In this issue of IMAJ, Eventov-Friedman and colleagues [14] report a single-center clinical experience following implementation of the red reflex test as part of the newborn physical examination. During the 2 year study period, of 11,500 newborns who were screened with red reflex examination, 12 were referred to ophthalmology consultation due to suspected abnormal red reflex. In 5, the diagnosis of congenital cataract was confirmed, giving an incidence of 4.3 per 10,000 newborns. Based on routine notification systems for monitoring congenital anomalies in the USA and Europe, the current annual birth prevalence of congenital or infantile cataract has been estimated to be approximately 1 per 10,000 of the total number of births. The British Congenital Cataract Interest Group reported a cumulative incidence of congenital and infantile cataract of 2.29 per 10,000 by age 1 year [13]. In comparison to these findings, the reported incidence in the current study is higher, suggesting a high detection rate. However, in the absence of follow-up or national surveillance for the diseases, the incidence and sensitivity of red reflex have yet to be determined.

The positive predictive value (42%) that was shown here, after a short period of implementation, is also higher than that shown elsewhere [15], yet over-referral is unavoidable in the effort to detect infants with congenital media opacities.

The authors included in their report a survey of all Israeli neonatal departments on the implementation of the red reflex test in the newborn examination, showing that until December 2008 only 12 of 26 neonatal departments routinely assessed the red reflex prior to discharge. The disparity between the incidence of congenital cataract in the current study and the 0.68 cases per 10,000 newborns reported to the Israeli registry of congenital anomalies during the years 2000–2008 (personal communication) should encourage neonatologists to implement this screening.
for early diagnosis of eye pathology. The Israel Neonatology Association guidelines for routine red reflex examination in newborns published in July 2009 [16] constitute the first step for improving the quality of red reflex screening. However, more specific guidance regarding the purpose and content of red reflex examination and the promotion of programs for training all involved in its management are required. In addition, there is a need for repeated examination before age 6 weeks. In all infants with a family history of retinoblastoma or cataract, neurologic or metabolic disorders, and microphthalmia or eyelid hemangioma, consultation with an experienced ophthalmologist should be emphasized.

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References

Activin A or Tie2 signaling ameliorates osteolytic bone disease

Bone metastases are a common feature of many advanced-stage cancers and are among the most painful and debilitating complications. Tumor cells alter bone tissue by unbalancing the bone remodeling process that occurs naturally throughout adult life. In the context of osteolytic (bone-destroying) metastases, this disruption occurs through an enhanced production of osteoclasts (the cells that resorb bone) – or through a suppressed production of osteoblasts (the cells that build bone). The molecular mechanism by which tumor cells alter the abundance of these cell types is the subject of two recent studies using mouse models of cancer. Vallet et al. (Proc Natl Acad Sci USA 2010; 107: 5124) found that multiple myeloma cells cause bone marrow stromal cells to secrete activin A, which is a member of the transforming growth factor-β family of cytokines and which inhibits the differentiation of cells into osteoblasts. In independent work on breast cancer-associated bone disease, Min et al. (Cancer Res 2010; 70: 2819) found that Tie2, a receptor tyrosine kinase that is expressed at high levels in breast cancer, is also expressed in bone marrow cells that normally differentiate into osteoblasts and is in fact required for osteoblast production. Inhibition of either activin A or Tie2 signaling with soluble decoy receptors led to the amelioration of osteolytic bone disease, suggesting that these two molecules may be useful therapeutic targets.

Eitan Israeli

“Men occasionally stumble over the truth, but most of them pick themselves up and hurry off as if nothing ever happened”

Sir Winston Churchill (1874-1965), British politician known chiefly for his leadership of the United Kingdom during World War II. He served as Prime Minister from 1940 to 1945 and again from 1951 to 1955. A noted statesman and orator, Churchill was also an officer in the British Army, a historian, writer and artist, and laureate of the Nobel Prize in Literature,