#### **REFERENCES**

- 1. Pediatric Tuberculosis Collaborative Group. Targeted tuberculin skin testing and treatment of latent tuberculosis infection in children and adolescents. Pediatrics. 2004;114(4 pt 3);1175-1201
- 2. Driver CR, Valway SE, Cantwell MF, Onorato IM. Tuberculin skin test screening in schoolchildren in the United States. Pediatrics. 1996;98:
- 3. Mohle-Boetani JC, Miller B, Halpern M, et al. School-based screening for tuberculosis infection: a cost-benefit analysis. JAMA. 1995;274:613-619
- 4. Centers for Disease Control and Prevention. Guidelines for using the QuantiFERON-TB test for diagnosing latent Mycobacterium tuberculosis infection. MMWR Recomm Rep. 2003;52(RR-2):15-18
- 5. Fruth U, Young D. Prospects for new TB vaccines: Stop TB Working Group on TB Vaccine Development. Int J Tuberc Lung Dis. 2004;8:151-155

# **Supporting Vulnerable Preschool** Children: Connecting the Dots **Before Kindergarten**

orty-one years ago, the infant son of President John F. Kennedy died at Children's Hospital in Boston after being born 5.5 weeks prematurely and weighing 2.1 kg.1 At that time, there were no regional systems of maternal transport and neonatal care, no National Institute of Child Health and Human Development or program projects supporting research in developmental biology, no screening for genetic disorders that cause mental retardation, no Head Start programs, and no laws ensuring that children with challenges would have the supports required to succeed in school and the community. Three decades later President George H.W. Bush, who had lost a daughter to leukemia and had a son who struggled with reading, convened a conference of governors from all 50 states. These leaders unanimously agreed on a most ambitious goal that by 2000 all children who entered kindergarten would be ready to learn.2 Now in a decade of revolutionary advances in molecular, developmental, and systems biology, we as a pediatric community face 2 major challenges. First, how can we ensure that developmental and behavioral supports exist for families after benefiting from advances in pediatric care? Second, how can we ensure that young children in families struggling with poverty access quality health and preschool developmental supports?<sup>3</sup>

The study by Roth et al<sup>4</sup> in the September issue of *Pediatrics* builds on advances of regionalization of Florida's nurseries, collaboration between health professionals and social scientists to link information on birth certificates to subsequent school success, and policy initiatives of the Chiles Center for Healthy Mothers and Babies. Of the 120 554 children born in 1990–1991 with links to kindergarten data, biomed-

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ical risk included 0.3% with birth weights of <1000 g, 0.7% with birth weights of 1000 to 1499 g, 6.1% with birth weights of 1500 to 2499 g, and 1.3% with congenital anomalies. These medical conditions contributed \$19 300 000 to extra kindergarten costs. The social risks were much higher: 37% were born into poverty, 28% had parents who did not complete high school, 15% had teen mothers, and 7% had less than optimal prenatal care. These social risk factors were responsible for almost \$129 000 000 in extra kindergarten educational resources. It is tragic that at this time <1 in 3 children in poverty had access to Head Start. Similarly, there are major gaps for children in poverty with all degrees of low birth weight to accessing comprehensive early intervention services.<sup>5</sup>

In an era of debates about health and educational reform, this study has an important lesson to teach: poverty is not a developmental enhancer. If we are going to test all elementary school children, we must also release report cards that examine gaps in accessing quality medical homes and home visiting, early intervention, early start, and early childhood programs. We must work together to connect the dots of biopsychosocial supports that will allow all children in 2010 to enter kindergarten healthy and ready to

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#### REFERENCES

- 1. Blair WM. 2d Son born to Kennedys; has lung illness. New York Times. August 8, 1963;P1
- 2. Goals 2000: Educate America Act of 1994. Pub L No. 103-227, 20 USC §§5801 et seq
- 3. Shonkoff JP, Phillips D, eds. From Neurons to Neighborhoods: The Science of Early Child Development. Washington, DC: National Academy Press; 2000
- 4. Roth J, Figlio DN, Chen Y, et al. Maternal and infant factors associated with excess kindergarten costs. Pediatrics. 2004;114:720-728
- 5. Msall ME, Tremont MR, Ottenbacher KJ. Functional assessments of preschool children: optimizing developmental and family supports in early intervention. Infants Young Child. 2001;14:46-66

# Management of Hyperbilirubinemia: Quality of Evidence and Cost

ABBREVIATION. AAP, American Academy of Pediatrics.

ernicterus is associated with early hospital discharge, reduced concern about jaundice in otherwise healthy newborns, and breastfeeding.<sup>1–3</sup> To compensate for early discharge, the Amer-

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ican Academy of Pediatrics (AAP) recommends that newborns be seen by a qualified health professional by 5 days of age (see "Recommendation 6.1.2" in ref 4). Providing this rapid follow-up to the estimated 70% of all infants now discharged before 48 hours of age would probably cost more than \$10 million to prevent 1 case of kernicterus, as Suresh et al<sup>5</sup> describe in this issue of *Pediatrics*. Here I address 2 questions: (1) Is the evidence sufficient to justify the recommendation? (2) Is the cost too high?

Of the 30 recommendations on the management of hyperbilirubinemia for which the AAP guidelines indicated "evidence quality," none were in the highest category ("well-designed, randomized, controlled trials or diagnostic studies on relevant populations"4(p308)), 10 were in the lowest category ("expert opinion, case reports, reasoning from first principles" 4(p308)), and 15 were in the next to the lowest of the 4 possible categories (see "Appendix 1" in ref 4 for further definition of evidence categories). We still don't know the incidence of kernicterus, whether it is rising, or how neonatal hyperbilirubinemia can best be managed in healthy infants who face early discharge. In addition to rapid follow-up of all infants, options include predischarge serum or transcutaneous bilirubin on all infants (see AAP "Recommendation 5.1.1" in ref 4), either postponing discharge for those whose bilirubin exceeds a threshold value or requiring that they receive a home visit (see below) within 2 days that would include a repeat bilirubin, and additional visits or readmission as necessary. A randomized, controlled trial comparing these or other options for the likelihood of reducing peak bilirubin, or some other short-term proxy outcome for kernicterus, is badly needed.

The recommendations were also based on a literature review requested by the AAP. The review concluded that "there is no strong evidence to suggest neurologic abnormalities in children with neonatal bilirubin levels higher than 20 mg/dL when followed up to 7 years of age."6 That is not to say that the association between hyperbilirubinemia and kernicterus does not exist. Rather, it indicates that the vast majority of infants with hyperbilirubinemia do not develop neurologic abnormalities. In an accompanying commentary, Ip et al<sup>7</sup> noted that 2000 newborns with a total serum bilirubin ≥20 mg/dL (a higher concentration than the cutoff in the AAP recommendations) would have to be treated to prevent 1 case of kernicterus if its incidence is 1 in 100 000. Ip et al concluded that "hyperbilirubinemia, in most cases, is a necessary but not sufficient condition to explain kernicterus."7(p263) A randomized, controlled trial similar to the one mentioned above could also be used to examine factors that contribute to high peak values and early signs of acute bilirubin encephalopathy (see "Appendix 1" in ref 4).

Questions also arise about the efficacy of phototherapy. In a Kernicterus Registry study,<sup>8</sup> 74 of 81 infants who developed kernicterus received phototherapy. At least 7 of the 14 infants seen by age 4 or 5 days after early discharge, in accord with the AAP's recommendation, would have received phototherapy. Reports of other cases of kernicterus vary

in the effects of phototherapy on behavioral and neurologic outcomes.6

The cost to prevent 1 case of kernicterus by a rapid follow-up of all healthy newborns is >1000 times higher than the cost per quality-adjusted life-year gained by introducing tandem mass spectrometry into routine newborn screening, and the false-positive/true-positive ratio of predicting kernicterus by bilirubin testing is 80 times higher. Nevertheless, the introduction of tandem mass spectrometry into newborn screening is still debated, partly on the basis of cost.<sup>10</sup> Thus, implementing the recommendation for rapid follow-up of early-discharged infants seems exorbitantly expensive. However, there are 2 reasons why this might not be the case. First, the recommendation for follow-up within 48 hours of nursery discharge is multipurposed. Suresh et al<sup>5</sup> concede that they did not include other benefits that might result from rapid follow-up in their analysis. For rapid follow-up, a home visit by a nurse has advantages over a visit to a pediatric office; maternal as well as infant health can be assessed. Moreover, noncompliance will be higher with an office visit. 11 At present, probably no more than one third of healthy infants are seen within 2 days of discharge. Low-income families, who are at greatest risk of postnatal problems, are overrepresented in the group without rapid follow-up.<sup>12</sup>

Second, some parents and health care providers will be unwilling to allow 1 case of kernicterus to occur if it could be prevented regardless of the cost or of forgoing alternative policies that could benefit a larger number of infants. 13 If we could be confident that implementing the AAP's recommendation of rapid follow-up for all early-discharged infants had the highest yield per dollar in preventing kernicterus, then investing in it might be justified. I lack that confidence.

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#### REFERENCES

- 1. Bhutani VK, Johnson LH. Newborn jaundice and kernicterus—health and societal perspectives. Indian J Pediatr. 2003;70:407-416
- 2. Ebbesen F. Recurrence of kernicterus in term and near-term infants in Denmark. Acta Paediatr. 2000;89:1213-1217
- 3. Hansen TW. Kernicterus: an international perspective. Semin Neonatol.
- 4. American Academy of Pediatrics, Subcommittee on Hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics. 2004;114:297-316
- 5. Suresh G. Cost-effectiveness of strategies intended to prevent kernicterus in newborn infants. Pediatrics. 2004;114:917-924
- 6. Ip S, Chung M, Kulig J, et al. An evidence-based review of important issues concerning neonatal hyperbilirubinemia. Pediatrics. 2004;114(1). Available at: www.pediatrics.org/cgi/content/full/114/1/e130
- 7. Ip S, Lau J, Chung M, S et al. Hyperbilirubinemia and kernicterus: 50 years later [commentary]. Pediatrics. 2004;114:263-264
- 8. Johnson LH, Bhutani VK, Brown AK. System-based approach to management of neonatal jaundice and prevention of kernicterus. J Pediatr. 2002:140:396-403
- 9. Schoen EJ, Baker JC, Colby CJ, To TT. Cost-benefit analysis of universal tandem mass spectrometry for newborn screening. Pediatrics. 2002;110:

- Holtzman NA. Expanding newborn screening: how good is the evidence? IAMA. 2003;290:2606–2608
- Worsley J. Hyperbilirubinemia guidelines and unintended harms [letter]. Pediatrics. 2004;114:In press
- Galbraith AA, Egerter SA, Marchi KS, Chavez G, Braveman PA. Newborn early discharge revisited: are California newborns receiving recommended postnatal services? *Pediatrics*. 2003;111:364–371
- 13. Newman TB. The power of stories over statistics. *BMJ*. 2003;327: 1424–1427

## **International Pediatric Congress**

ABBREVIATIONS. UNICEF, United Nations Children's Fund; UN, United Nations; HIV, human immunodeficiency virus; AIDS, acquired immunodeficiency syndrome.

hild survival (and the overall health and wellbeing of children) lies at the heart of everything the United Nations Children's Fund (UNICEF) does. We believe every child has the right to grow to adulthood in health, peace, and dignity. We share this vision and mission uniquely with pediatricians and the national organizations that represent them at the 24th International Pediatric Congress. Here I summarize UNICEF's current perspective on the work to be done. Active participation by the global pediatric community as allies can hasten achievement of our shared goals.

Our commitment to child survival is as old as UNICEF. In the 1940s and 1950s, UNICEF provided food and basic health interventions to children in war-torn countries; in the 1960s and 1970s, UNICEF expanded its work into virtually every developing nation in which children's lives were at risk; in the 1980s, UNICEF helped inspire a global child-survival "revolution"; and in the 1990s, UNICEF led efforts to help the world achieve its first set of global goals focused on the health and well-being of children.

The United Nations (UN) Secretary General's report on progress in reaching the World Summit goals was the evidence base for determining the new goals at the 2002 UN Special Session on Children. The report revealed that the 1990 World Summit for Children target of reducing the child mortality rate to <70 deaths per 100 000 live births (or a one third reduction, whichever resulted in a lower rate) by the

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Carol Bellamy is the Executive Director of UNICEF. Prior to joining UNICEF, Ms. Bellamy was Director of the United States Peace Corps. Having served as a Peace Corps volunteer in Guatemala from 1963 to 1965, she was the first former volunteer to run the organization, which works in more than 90 countries.

The 24th International Pediatric Congress, held in Cancun, Mexico, on August 15–21, 2004, brought together 7000 pediatricians from every continent. An International Pediatric Congress, organized by a host country selected under the auspices of the International Pediatric Association, occurs every 3 years. The American Academy of Pediatrics is 1 of more than 100 national pediatric organizations that constitute the International Pediatric Association. This commentary summarizes Dr Bellamy's speech at the opening session of the International Pediatric Congress.

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year 2000 was achieved in only 5 of the 53 highest burdened countries (with mortality rates >100 per 100000 live births in 1990), and a global decline of only 10% was achieved, compared with the 33% required to achieve the summit target.

Today UNICEF has 5 priorities, all of which focus on saving children's lives and improving their chances of becoming productive citizens. The UNICEF priorities, immunization, early childhood development, girls' education, human immunodeficiency virus [HIV]/acquired immunodeficiency syndrome [AIDS] prevention, and care and child protection, underpin the Millennium Development goals endorsed at the 2000 UN Millennium Assembly. They are also central to the program of action adopted by the nations of the world at the UN Special Session on Children in 2002.

In an effort to provide special support to achieve the Millennium Development goal on child survival (to reduce the mortality rate among children <5 years old by two thirds by 2015), UNICEF is hosting a new Child Survival Partnership. The partnership has a 2-pronged strategy. First, the partnership encourages better use of existing resources; second, it advocates for additional resources to scale up programs for child survival at global and country levels.

As pediatricians know, a number of factors contribute to the persistent child mortality rate. More than 10 million totally preventable child deaths still occur every year. Some are the direct causes of illness (eg, pneumonia, acute respiratory infection, diarrhea, measles), and others are affected by indirect causes such as conflict, marginalization, and HIV/AIDS. Malnutrition and a lack of safe water and sanitation are factors contributing to more than half of these deaths.

Six million children could be saved annually by basic, cost-effective measures such as vaccines, anti-biotics, micronutrient supplementation, insecticide-treated bed nets, and improved breast-feeding practices and oral rehydration therapy. We know what it takes to improve child health and survival, but millions still die because they lack access to these basic services

There is ample evidence of what works, but health and nutrition systems are faced with major implementation constraints. The public health environment has changed dramatically, and a number of new issues challenge child survival and well-being:

- Inequity and marginalization (eg, geographic, socioeconomic, cultural, gender) are increasing.
- Decentralization policies have not always been effective in channeling resources to the poorest communities
- The complexity of health and nutrition situations (eg, over- and undernutrition, epidemiologic transitions, emerging drug resistance) is increasing.
- The impact of HIV/AIDS has reversed the mortality gains achieved during the 1980s.
- Health financing has increased globally but is fragmented in a number of separate, sometimes competing initiatives.

## Management of Hyperbilirubinemia: Quality of Evidence and Cost

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