Outcomes in CAH: Need for Evidence-Based Estimates

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We appreciate the many efforts of the CARES Foundation, Inc. on behalf of children with CAH and recognize that the death of even one child with this preventable outcome is a tragedy. Preventive programs and policies can be most effectively developed on an evidence-based foundation, and the available data support our conclusion that infant mortality in classical CAH is $\leq 4\%$ in North America and Europe. Additional supporting data come from a recent study of stored blood spot specimens for unexplained infant deaths in Austria and the Czech Republic that found about one fifth as many cases of CAH as had been expected on the basis of expert opinion [1]. Out of more than 2 million births during a 13-year period, there were 3 *unexplained* deaths due to CAH, or 2% of the expected number of children with CAH.

We agree with Ms. Leight that there should also be a systematic study of a sample of *all* infant deaths to determine the frequency of death due to CAH. As stated in our article: 'One way to ascertain such deaths in cohorts not screened for CAH at birth is to retrieve stored dried blood spot filter paper cards for children who died in infancy or early childhood and test for the presence of CAH, including analysis of *CYP21* mutations specific for SW-CAH.' We would be pleased to collaborate with CARES Foundation, Inc. to identify other research needs as well.

The statement that among children born in United States jurisdictions that screened for CAH in 2006 'Over 56% of presumed cases of CAH went undetected' is incorrect. The sensitivity of newborn screening for classical CAH is extremely high, essentially 100% for salt-wasting CAH [2]. The 'National Newborn Screening and Genetics Resource Center records' cited by Ms. Leight come from the US National Newborn Screening Information System (NNSIS) database to which states voluntarily report data and which is regularly updated [3]. The NNSIS as of April 6, 2007, included a total of 150 children born in 2006 with confirmed classical CAH. Because a number of states had either not yet reported data or reported incomplete data for CAH diagnoses in 2006, the ultimate number will be substantially larger. NNSIS data for 2005 included 180 children confirmed with classical CAH born in 30 states with a total of 2.8 million births that were screened for CAH, or 1 in 15,700 births.

We share Ms. Leight's concern about the plight of children with CAH born in low-income countries, among whom the rate of mortality is likely to be quite high. On the other hand, the most cost-effective approach to reducing CAH mortality in such countries needs to be carefully considered along with the availability of treatment following identification of CAH. This requires data on outcomes with and without screening. Migeon and Donohoue

[4] suggested that 'limited health care funds would be more appropriately spent to further increase the awareness of the problem through education rather than to screen all newborns'. Our study indicates that many, perhaps most, CAH-related deaths can be prevented through heightened clinical awareness and prompt treatment.

References

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- 2 Votava F, Torok D, Kovacs J, Moslinger D, Baumgartner-Parzer SM, Solyom J, et al: Estimation of the false-negative rate in newborn screening for congenital adrenal hyperplasia. *Eur J Endocrinol* 2005;152:869–874.
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- 4 Migeon CJ, Donohoue PA: Adrenal disorders; in Kappy MS, Blizzard RM, Migeon CJ (eds): *The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence*, ed 4. Springfield, Thomas, 1994, pp 717–856.