

dence and trust to serve the multicultural population health care needs of the people living in the United States. Data collected from the studies of pediatrics genetics specialists and genetic counselors show that the majority are Caucasian.<sup>5,10</sup> Another important element is the location of genetics specialists. Because many genetics specialists are concentrated in academic medical centers and research institutions in major cities and suburban areas, patients and consumers residing in smaller cities or rural areas will have limited access to genetics specialists or comprehensive genetic care.

The future of genetics in science and medicine is bound to be exciting and revolutionary. However, the fate of genetics specialists and their future role(s) remain to be determined. A comprehensive workforce assessment will allow the genetics community to take a closer look at themselves and, it is hoped, provide an opportunity to shape their fate and the future of the specialty that will benefit all involved.

## Disclaimer

Data cited in this letter were collected in support of a comprehensive analysis of genetics issues by the HHS Secretary's Advisory Committee on Genetic Testing. However, the views expressed here are solely those of the authors and do not reflect the views or position of SACGT, ASHG, or the Center for the Advancement of Genomics.

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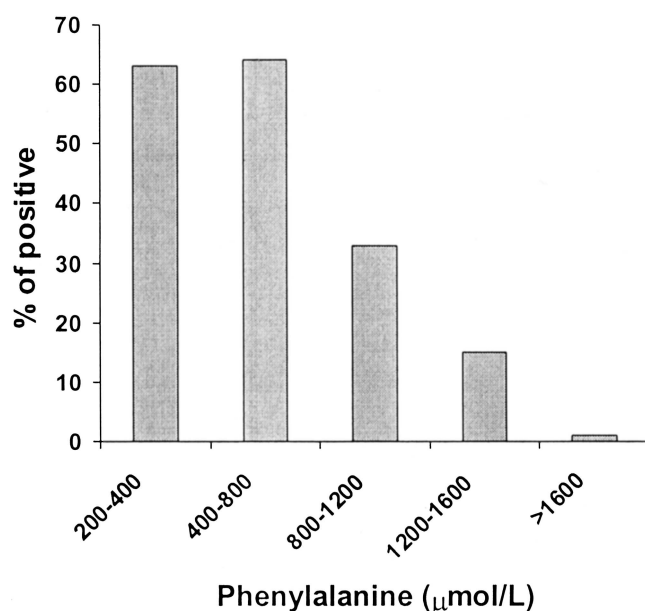
## Tetrahydrobiopterin control in phenylketonuria

*To the Editor:*

In patients with phenylketonuria (PKU), blood phenylalanine concentration during childhood is the major determinant of cognitive outcome. Adolescents and young adults generally do not comply with recommendations for the monitoring and control of phenylalanine concentrations,<sup>1</sup> and two thirds of pregnant women in the United States did not follow the diet before becoming pregnant.<sup>2</sup>

Recently it has been shown that some patients with PKU respond to the loading test with 6R-tetrahydrobiopterin (BH<sub>4</sub>) by lowering plasma phenylalanine concentrations and that these patients can be treated with BH<sub>4</sub>.<sup>3</sup> BH<sub>4</sub> is the natural cofactor of aromatic amino acid hydroxylases, and particular mutations in the phenylalanine hydroxylase gene may affect enzyme stability or its affinity for the BH<sub>4</sub>. We recently found that more than 60% of patients with plasma phenylalanine concentrations between 400 and 800  $\mu\text{mol/L}$  respond to BH<sub>4</sub> challenge and that the best results can be obtained with doses of 20 mg/kg body weight (Fig. 1).<sup>4</sup> Oral supplementation with 10 mg BH<sub>4</sub>/kg reduced plasma phenylalanine concentrations below 360  $\mu\text{mol/L}$  in most patients with mild forms of phenylalanine hydroxylase deficiency (Phe < 1200  $\mu\text{mol/L}$ ) and increased phenylalanine tolerance in some patients with classical PKU (Phe > 1200  $\mu\text{mol/L}$ ).

Our findings show the importance of the BH<sub>4</sub> loading test in the diagnosis of BH<sub>4</sub>-responsive variants and open new prospects for the treatment of PKU and mild hyperphenylalaninemia. Replacement of the low-phenylalanine diet with the commercially available BH<sub>4</sub> (Schircks Laboratories, Jona, Switzerland) may significantly improve compliance in adolescents and young adults



**Fig. 1** Percentage of patients with different degrees of hyperphenylalaninemia who responded to 6R-tetrahydrobiopterin challenge (20 mg/kg body weight) by lowering plasma phenylalanine levels by at least 30% within 8 hours.

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with PKU variants and may solve some barriers that prevent control of blood phenylalanine levels in pregnant women with PKU. Thus BH<sub>4</sub> may be a practical, but not inexpensive, alternative to control PKU.

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