



CLAIRE ALTMAN HEINE FOUNDATION, INC.
dedicated to identifying carriers of SMA

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To the Editor:

The ACOG Committee on Genetics recently issued a Committee Opinion on Spinal Muscular Atrophy (SMA).ⁱ As the Executive Director of the Claire Altman Heine Foundation (CAHF), a private nonprofit advocacy organization dedicated to implementing pan-ethnic carrier screening for SMA, I feel compelled to correct a factual error contained within the Opinion and to comment on the recommendations contained therein.

The Opinion had an error in the description of the natural history of SMA; it incorrectly identified Type II SMA as the most common phenotype. In fact, Type I SMA is both the most severe form of the disease and the most common. Approximately 60 to 70% of individuals diagnosed with SMA are affected by Type I, with onset of disease symptoms before six months of age and death from respiratory failure within the first 2 years of lifeⁱⁱ. Type II SMA is the second most common form of SMA, affecting 20 to 30% of diagnosed individualsⁱⁱⁱ. Type II has an onset of disease symptoms after 6 months of age, individuals never achieve the ability to stand or walk unaided and frequently have significant respiratory issues, and lifespan is variable, but typically Type II children survive past 4 years of age. Type III SMA, the least common form, is milder; most Type III children are ambulatory and have a normal lifespan.^{iv}

With regard to the substance of the Opinion, one issue that the Committee suggests must be addressed prior to recommending pan-ethnic SMA carrier screening is the development of education materials. I agree that education for both patients and primary obstetrician-gynecologists is a priority in any successful screening program. It is for this reason that advocacy groups such as CAHF have spent significant time and resource developing educational information that is available for both patients and physicians free of charge in print or on-line (www.preventsma.org). Commercial labs have developed similar educational materials that also are readily available.^v Additionally, the American College of Medical Genetics is in the process of developing its



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own educational materials for both patients and physicians regarding SMA carrier testing, laboratory assay standards, and result reporting.

Concerning the Opinion's comparison of SMA to Tay-Sachs and Sickle Cell, many geneticists would find Cystic Fibrosis (CF) the more appropriate comparison.^{vi} SMA is the second most common lethal autosomal recessive genetic disease after CF and the leading cause of inherited early childhood mortality.^{vii} Both CF and SMA are relatively common, impact all ethnic groups, and have a common inheritance pattern. Additionally, carrier testing offers a risk reduction for both disorders and each has a variable phenotype/genotype correlation.

Using CF as a comparison may provide answers to some of the questions asked by the Committee with regard to patient preference for carrier screening. The NIH funded eight projects before recommending a carrier screening program for CF. These studies have broader application to principles considered in any genetic screening program (including SMA) and it would seem redundant and wasteful to repeat them. Some of the findings for CF that are directly applicable to SMA are: a high interest in screening following educational intervention, optimal practices for testing (setting, timing, education, consent and counseling), and the importance of a broad educational effort.^{viii} In 2005 ACOG decided to offer CF carrier testing to all patients regardless of ethnicity.^{ix}

Finally, published data from academic and industry research show the carrier frequency of SMA to be 1:35 in the Caucasian population, 1:41 in Ashkenazi Jewish population, 1:53 Asian population, 1:66 in the African American population, and 1:117 in the Hispanic population.^x Following the example of CF, it would seem the time has come for pan-ethnic population based SMA carrier screening.^{xi} Given ACOG's current threshold for carrier frequency of a disease and screening recommendations, at a minimum SMA carrier testing for SMA must be offered to the Caucasian and Ashkenazi Jewish populations.^{xii}

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ⁱ Spinal muscular atrophy. ACOG Committee Opinion No. 432. American College of Obstetricians and Gynecologists, *Obstet Gynecol* 2009; 113:1194-6.

ⁱⁱ Prior, T. ACMG Practice Guidelines Carrier screening for spinal muscular atrophy. *Genet Med* 2008 10:11:840-842.

ⁱⁱⁱ Meldrum C, Scott C and Swoboda K. Spinal muscular atrophy genetic counseling access and genetic knowledge: parents' perspectives. *J Child Neurol* 2007;22:1019-1026.



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^{iv} Wang CH, Finkel RS, Bertini ES, Schroth M, Simonds A, Wong B, Aloysius A, Morrison L, Main M, Crawford TO, Trela A, and Participants of the International Conference on SMA Standard of Care. 2007. Consensus Statement for Standard of Care in Spinal Muscular Atrophy. *J Child Neurology* 22: 1027-1049.

^v Genzyme Genetics www.mytestingoptions.com.

^{vi} Smith M, Calabro V, Chong B, Gardiner N, Cowie S and du Sart, D. Population screening and cascade testing for carrier of sma. *European Journal of Human Genetics* (2007) 1-8

^{vii} Simic G. Pathogenesis of proximal autosomal recessive spinal muscular atrophy. *Acta Neuropathol* (2008) 116:223-234.

^{viii} Consensus statement No. 106 . Genetic testing for cystic fibrosis. 1997 April 14-16;15(4);1-37 NIH Consensus Statement Online at <http://consensus.nih.gov/1997/1997GeneticTestCysticFibrosis106html.htm>.

^{ix} Update on carrier screening for cystic fibrosis ACOG Committee Opinion No. 325. American College of Obstetricians and Gynecologists, *Obstet Gynecol* 2005;106:1465-8.

^x Hendrickson BC, C Donohoe, VR Akmaev, EA Sugarman, P Labrousse, L Boguslavskiy, K Flynn, EM Rohlf, B Allitto, C Sears, T Scholl. SMN1 allele frequencies in the major ethnic groups within North America. "In Press" in the *Journal of Medical Genetics* June 2009 and published 58th Annual Meeting of the American Society of Human Genetics, Philadelphia, PA, October, 2008 (Poster).

^{xi} Update on carrier screening for cystic fibrosis. ACOG Committee Opinion No 325. American College of Obstetricians and Gynecologists, *Obstet Gynecol* 2005;106:1465-8.

^{xii} Prenatal and preconceptional carrier screening for genetic diseases in individuals of eastern european and jewish descent. ACOG Committee Opinion No. 298. American College of Obstetricians and Gynecologists, *Obstet Gynecol* 2004;104:425-8.