



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

June 2009

The Claire Altman Heine Foundation's Formal Response to the ACOG Genetics Committee Opinion on Carrier Screening for Spinal Muscular Atrophy

The American College of Obstetricians and Gynecologists' (ACOG) Committee on Genetics concludes in a "Committee Opinion on Spinal Muscular Atrophy" published in the May 2009 issue of *Obstetrics & Gynecology* that "preconception and prenatal screening for SMA is not recommended in the general population at this time."ⁱ The Claire Altman Heine Foundation (CAHF) respectfully disagrees with and opposes the Committee's recommendation and disputes several of the premises and assertions on which it is based.

Broadly, ACOG's Committee bases its opposition to pan-ethnic carrier screening for SMA on three flawed and/or incomplete suppositions. It states that: (1) pilot studies specific to SMA have not been completed to determine patient preference and best practices relative to patient counseling; (2) educational materials for patients and professionals have not been developed; and (3) a threshold for widespread screening has not been addressed by public policy professionals. The Committee's reliance on these assumptions results in a conclusion that is misguided and inconsistent with existing ACOG protocols relative to pan-ethnic carrier screening. Additionally, the Opinion itself is internally inconsistent. Specifically, the Committee:

- Fails to consider existing pertinent pilot data that is broadly relevant to patient preference and best practices for pretest and posttest education and counseling;
- Overlooks existing patient and professional educational materials developed and/or under development by various sources;
- Unilaterally and arbitrarily imposes metrics for implementing widespread screening that excludes nearly every genetic disorder and currently existing genetic test;
- Patently makes no mention or consideration of Cystic Fibrosis (CF), the most directly relevant genetic disorder to SMA with regard to pan-ethnic carrier status and for which ACOG has recommended population-based carrier screening since 2002ⁱⁱ;
- Ironically does not apply to pan-ethnic carrier screening for SMA the very criteria for consideration of a candidate condition identified by ACOG in the Opinion; and
- Places ACOG at odds with the American College of Medical Genetics (ACMG), which issued new practice guidelines in November 2008 that recommend offering SMA carrier testing to all families, regardless of race or ethnicity.ⁱⁱⁱ



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ACOG's assertion that "there have been no studies to date to determine patient preferences" is misguided. Several studies have been conducted over nearly two decades that examine patient preference with regard to carrier screening, including studies funded by the National Institutes of Health (NIH) from 1991 – 1995 relative to CF.^{iv} In general, these studies have demonstrated that the vast majority of Americans welcome carrier screening and the knowledge such screening provides. While it is true that no studies have been conducted specific to SMA carrier screening, the existing studies have broad application to principals relative to any genetic screening program, including SMA. It would be redundant and wasteful to repeat these studies.

CAHF is supportive of pilot studies and the ongoing refinement and improvement of the SMA carrier screening test and pretest and posttest protocols. In fact, CAHF has advocated for four years for federally funded SMA carrier screening pilot studies and presently funds a nearly completed pilot study at the Ohio State University in Columbus to address specific, targeted challenges.^v The large scale, comprehensive pilots recommended by ACOG are unnecessary. CAHF agrees with ACMG that there is sufficient data from over a decade of carrier screening in the SMA community to responsibly commence pan-ethnic SMA carrier screening while smaller scale, targeted pilot studies are continued.^{vi}

CAHF agrees with ACOG that "development of appropriate educational materials for both patients and primary obstetrician-gynecologists" is a prerequisite to a pan-ethnic prenatal screening program for SMA. ACOG should be pleased to learn that such materials already exist.^{vii} Advocacy groups such as CAHF have spent significant time and resources developing educational materials that are widely available in print and online and have been widely distributed to both patients and physicians free of charge. Commercial laboratories such as Genzyme have developed similar educational materials that are distributed as protocol to all patients and providers who participate in their ongoing and successful SMA carrier screening efforts. Additionally, ACMG is in the process of developing its own educational materials for patients and physicians regarding SMA carrier screening, laboratory assay standards, and result reporting.

ACOG states that "the question of what threshold for carrier frequency any disease must meet to be considered for widespread screening has never been formally addressed by genetics and public policy professionals." While this statement is technically factual, it fails to convey that a dialogue on this very issue is ongoing among various stakeholders. Several thought leaders at the NIH, ACMG, and elsewhere have been informally contemplating for several years the feasibility of whether and how to implement a system for evaluating candidate conditions for pan-ethnic carrier screening.^{viii} It is noteworthy that ACOG did not identify as a barrier the lack of a formal process for considering candidate conditions for pan-ethnic carrier screening in its 2002 endorsement of pan-ethnic carrier screening for CF (or any genetic disease it currently recommends for carrier screening)^{ix}.



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ACOG references “carrier frequency” as the appropriate metric to be considered by geneticists and public policy officials in considering candidate conditions. While carrier frequency is important, used exclusively it is an incomplete and imprecise measure for ascertaining the need for pan-ethnic carrier screening from a public health and public policy perspective.^x An equally important metric is the impact of a disease on mortality.

While SMA has a carrier frequency less than that of CF, for example, the disease is much more severe; it is the leading genetic cause of death in infants under the age of two.^{xi} The impact of SMA on mortality is at least comparable to and likely is greater than that of CF, for which ACOG recommends pan-ethnic carrier screening.^{xii} If SMA, the leading genetic killer of infants under the age of two, does not meet the criteria for pan-ethnic carrier screening, then it is likely that no disease or disorder could pass muster.

ACOG indicates that pan-ethnic carrier screening for SMA should wait until cost effectiveness analysis specific to SMA can be investigated. While ACOG is correct in stating that such research has not been conducted to date, this is a curious and unfair barrier to erect. CF is the only genetic disease currently recommended for screening for which any cost analysis research has been published, and this single study, published in 1998, states that carrier screening for CF would have to fall to \$100 to equal the averted costs of CF patient care.^{xiii} However, over a decade later, CF testing still significantly exceeds \$100 and yet ACOG continues to recommend CF pan-ethnic carrier screening. Thus, ACOG appears to be holding SMA to an entirely different and significantly more demanding threshold that is contradictory and inequitable.

ACOG also implies concern over the sensitivity and specificity of the SMA carrier screening test. However, ACOG acknowledges that the SMA test has 95% sensitivity and nearly 100% specificity^{xiv} that is well within professionally acceptable rates per medical geneticists and public policy experts and significantly superior to CF carrier screening, which has a sensitivity of less than 90% and possibly as low as 80%.^{xv} The functionality and performance of the SMA carrier test is robust and well vetted and has never previously come under question. In fact, the SMA community has successfully utilized the test for well over a decade with very good results.

Lastly, the ACOG recommendation is internally inconsistent. The Opinion lays out five criteria for which a candidate disease should meet before widespread screening is instituted:

- (1) The disease significantly impairs health in the affected offspring;
- (2) There is a high frequency of carriers in the population to be screened;
- (3) Technically and clinically valid screening methods are available to the population, and screening is cost-effective;
- (4) Testing is voluntary, and informed consent and pretest and posttest counseling are available and effective; and



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- (5) Fetal testing is available for couples whose screening results are positive and reproductive options are readily available in a time-sensitive manner.

SMA meets every one of these criteria:

- (1) The disease is the leading genetic cause of death in infants under the age of two;
- (2) Its carrier frequency in certain populations (e.g., in Caucasians 1 in 35^{xvi}) is comparable to CF and it is, in general, the second most common recessive genetic disease after CF;
- (3) A well-vetted clinical test has existed for over a decade and currently ongoing pilot studies are nearly completed;
- (4) Comprehensive educational brochures are readily and widely available to assist in both pretest and posttest counseling; and
- (5) Several options exist for carrier couples, including sperm and/or egg donation, pre-implantation genetic diagnosis (PGD), and adoption.

While CAHF appreciates the ACOG Committee on Genetics consideration of and focus on SMA carrier screening, CAHF believes that the Committee's Opinion is inconsistent and its conclusion misguided. CAHF looks forward to working with ACOG and the other stakeholder groups, such as NIH, ACMG, and the National Society of Genetic Counselors (NSGC) to continue a dialogue towards implementing practice guidelines for pan-ethnic SMA carrier screening.

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

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

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

^{iv} 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>.

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^v United States Cong. Senate. Committee on Appropriations. Departments of Labor, Health and Human Services, and Education, and Related Agencies Appropriations, 2009. 110th Cong., 2nd Sess., 2008. S. Rpt. 110-410. Washington: GPO: 2008.



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