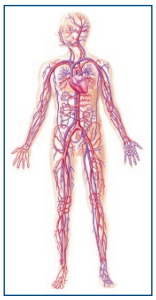
Highlights of This Issue

Prenatal Screening: Coercion and Eugenics or Options and Choices?

This month we feature several articles that touch upon general themes regarding prenatal screening and the ever present shadow cast by the memory of eugenics over our field. In the first commentary, Edward and Linda McCabe (page 708) explore prenatal screening for Down syndrome and ask when such screening crosses the line from service to coercion.

In an accompanying commentary from the California State Prenatal Screening Program, Flessel and Lorey (page 711) describe California's program and take issue with some of the conclusions of McCabe. We also feature an original article by Van Riper et al. (page 714) addressing family-provider interaction surrounding Down syndrome and an article by Anderson et al. (page 744) that examines the communication of Down syndrome screening results and physician numeracy.

These topics can be uncomfortable to discuss. A natural tension exists in a heterogeneous and free society like ours where large groups of individuals do not share fundamental values. The fact that genetics finds itself continually at the center of such controversies is a testament to the power that our field has harnessed. As that power grows, so too will the ethical conundrums which confront us. The only way to deal fairly with such issues is through open dialogue. We hope that *Genetics in Medicine* will continue to be a forum for airing conflicting views and arising at consensus.



Ehlers-Danlos Syndrome Type IV: Genotype Phenotype Relationships

Leistritz et al. shed light on genotype phenotype relationships in EDS Type IV on page 717. The vascular type of EDS is of considerable clinical concern due to the risk of arterial and viscus rupture. In this article the investigators report on the histories of 54 patients from 19 families and compare the nature of their collagen 3α1 mutation. Compared to individuals with missense or exon skipping mutations it was found that null mutations were associated with a longer life span, an almost 15 year delay in the age at first complication and complications limited to vascular events. These data are of considerable potential clinical utility as they will assist our patients in understanding the likely natural history of their condition, may inform the diagnostic process and ultimately may influence surveillance recommendations.

News Briefs

Giving credit where credit is due

There has been much criticism of the DTC genetic testing industry from many quarters, including this one. My basic premise remains that (thus far) such testing is by and large of little demonstrable value in any clinical or practical sense and that purveyors of such testing should not misrepresent this fact with misleading advertising. However, 23andMe has also touted its potential as a novel engine for genetic research and a recent publication in *PLoS Genetics* validates the potential of their endeavor in this realm. By teaming up with Parkinson Disease (PD) foundations and support groups, the company recruited a large number of PD cases for participation in a novel research effort. The disease status of cases was ascertained through online questionnaires and a large set of controls was recruited through the existing 23andMe customer database.

The investigators identified two novel loci associated with PD and replicated 20 previously discovered genetic associations, demonstrating the validity of their approach. Moreover, this study was able to place a lower-bound estimate of PD heritability at 0.27, implying that only a small fraction of the genetic etiology of PD has been identified.

Impressively, this study recruited 3,426 cases of PD in about 18 months, representing the largest genome-wide association study of PD conducted on a single cohort to date, validating the investigators' approach to rapid recruitment via the internet.

While some caveats apply (such as control and study populations undeniably skewed towards the high end of the socioeconomic scale) this study is an important and welcome validation of claims by the top echelon of DTC genetics companies that their resources may be fruitfully turned towards tackling important research questions. While I remain skeptical of the implicit clinical claims of these companies, I am delighted that they may be showing the research community a new model by which to pursue genetic research.

Highlights of the *AJHG* More Genetic Heterogeneity

In this month's *AJHG*, Rivière et al., report that hereditary sensory and autonomic neuropathy type II (HSANII), can result from mutations in the *KIF1A* gene.

A subset of HSANII had previously been shown to result from mutations in *FAM134B* and *WNK1*. Using a yeast two-hybrid screen, they found that the axonal transporter of synaptic vesicles, *KIF1A*, interacts with *WNK1*. Moreover, genome-wide homozygosity mapping identified homozygosity spanning the *KIF1A* gene locus. Sequencing of *KIF1A* in a series of 112 unrelated patients with related features revealed truncating mutations, implicating mutations in *KIF1A* as a rare cause of HSANII.

This study provides insight into the molecular pathogenesis of HSANII, reveals further genetic heterogeneity and highlights the potential biological relevance of alternative splicing in the peripheral sensory nervous system.