Highlights of This Issue

Fabry Disease

This month's *GIM* features three articles addressing various aspects of the treatment of Fabry disease (OMIM #301500). Watt et al. (page 703) report on quality of life in patients treated with agalsidase beta (71 men and 59 women) who were followed for at least two years. The investigators demonstrated improvement in both of the study's measures, which evaluated physical and mental components of well-being. Men that had baseline measures below average demonstrated the most dramatic improvements. A particularly welcome finding was that the magnitude of response by Fabry patients was comparable to, or greater than, the published effects of various treatments for multiple sclerosis, rheumatoid arthritis, central neuropathic pain, and Gaucher disease. As might be expected, while quality of life measures improved in both sexes, beneficial effects were more pronounced in men. Such studies of efficacy and clinical utility are important, especially as genetics seeks to take its place among other medical specialties focused on treatment and successfully arguing for adequate reimbursement.

Two other articles in this month's issue also focus on Fabry disease. Lidove et al. (page 668) executed a comprehensive review of the medical literature to explore the effects of enzyme replacement, and an original report by Mehta et al. (page 713) propose a series of therapeutic and symptomatic goals for use in setting the expectations of enzyme replacement therapy and for assessing response in the treatment of Fabry disease.

Risks and Benefits of Genomic Testing

If genomic testing is to become commonplace in medical practice it will need to be evaluated for clinical benefit and prove itself worthwhile just like any other medical intervention. Moreover, there is a general perception that such tests are inadequately regulated and there are increasing calls for a risk-stratified approach to the regulation of genetic testing. Indeed, the FDA has recently voiced its intention to develop a regulatory scheme to be implemented in the context of genetic testing. Given the current landscape an article by Veenstra et al. (page 686) is a timely addition to the literature. In this article, the authors present a risk-benefit framework for assessing the health-related utility of genomic tests incorporating approaches from a variety of established fields including decision science, outcomes research, and health technology assessment to develop a framework from which to work. The development of such a framework should accelerate the utilization and evidence development of genomic tests that pose low risk and offer plausible clinical benefit, while discouraging premature use of tests that provide little benefit or pose significant health risks compared to usual care. A commentary by Khoury et al. (page 680) expands and explores this issue further.

News Briefs

Growing Complexity

A recent report in *Nature* (Published online 29 September 2010) gives us a glimpse of the vast complexity underlying a highly visible human trait: height. The authors (all 292 of them!) reported a multinational study in which almost a quarter million individuals were analyzed for genes that contribute to stature. They identified 180 loci which appear to influence height. Strikingly, these 180 different regions of the genome explain only about 10% of variation in height. This study is a tour de force from a technical standpoint and points the way towards dissecting the genetics of common disease, as well as other important human traits. However, there are sobering lessons inherent in this study as well. It starkly reinforces what should by now be a rather obvious lesson: genetics is complex. This complexity presents a monumental challenge as we attempt to harness genomic knowledge toward better health. If a common trait like height is influenced by hundreds of loci, the same may well be expected for common diseases. Moreover, it should also be remembered that height is a classic multi-factorial trait i.e. many environmental influences likely interact with the myriad genes now beginning to be identified to create a stunningly complex picture.

Highlights of the *AJHG*

Autism spectrum disorders (ASDs, OMIM #209850) are both clinically and genetically heterogeneous, describing a range of behaviors that involve varying degrees of impaired language development, socialization, and interests. Microarray-based comparative genomic hybridization techniques have documented numerous copy number variations in individuals with ASD. In this month's *AJHG*, Rosenfeld et al. examined the yield of abnormal microarray-based comparative genomic hybridization findings from a series of individuals who had been referred for testing due to a clinical diagnosis of autism spectrum disorder. The team also examined the presence of autistic features among 151 additional individuals who were tested for indications other than ASD, but who had genomic alterations overlapping those found in cases referred for ASD. Of 1,461 individuals referred for testing due to ASD, significant abnormalities were reported in approximately 11.6% and included alterations in novel candidate genes such as *SNTG2, SOX5, HFE,* and *TRIP38*. These results suggest that CNVs represent one of multiple factors contributing to the ASD phenotype. Such CNVs are unlikely to be ASD-specific but rather result in a more general impairment of neurodevelopment.