IN THIS ISSUE

Caution urged in reporting noninvasive prenatal screening results to patients

see page 234

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Prospective parents who are told there is a 99% chance their fetus is affected by trisomy 18 are likely to react very differently than those being told that the actual likelihood of trisomy 18 is less than 60%, based solely on the result of noninvasive prenatal testing (NIPT). A clinician not savvy in basic statistics could perhaps be excused for assuming a test specificity of 99.9% means the test is nearly foolproof. But that's not the case if the condition in question is relatively rare. This issue is of particular importance for NIPT results, which, because of the relatively low prevalence of the conditions sought by the test, still must be confirmed by direct cytogenetic studies. The critical difference between test specificity and the more important positive predictive value (PPV) is illustrated in the report in this issue by physician–scientists at the Quest Diagnostics Nichols Institute. The research team examined the results of cytogenetic follow-up tests ordered after a positive NIPT for the trisomy 21, 18, and 13 in 109 consecutive specimens from several NIPT providers in California. They found a true-positive rate of 93% for trisomy 21, 64% for trisomy 18, and only 44% for trisomy 13. The authors explain that the low figures can be accounted for by the statistical prevalence of the abnormalities in the women undergoing testing. Even if the test specificity were 99.9%, the PPV for diagnosing these three trisomies would be much lower, as borne out by the figures presented here. The authors urge education of clinicians about the important difference between published specificities and the more important statistic of PPV, particularly in light of recent data suggesting that positive NIPT results are in some cases not being followed up with cytogenetic studies. The authors stress that NIPT is a screening test, not a substitute for invasive prenatal diagnosis, and thus should properly be referred to as NIPS. —*Karyn Hede, News Editor*

Study links subset of mutations with aortic events in Marfan syndrome patients

see page 177

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Among the many possible mutations in the fibrillin-1 (*FBN1*) gene causing Marfan syndrome, the subset comprising truncations and splicing disruptions may be associated with more severe aortic events. In this issue, Baudhuin et al., of the Mayo Clinic, Rochester, Minnesota, present data suggesting that truncating and splicing events are associated with early aortic events such as aortic dissection and aortic surgery. The study examined the clinical records for 179 consecutive Marfan syndrome patients referred to the Mayo Clinic over a four-year period. The findings contradict the current understanding that patients with these mutations actually have a milder course of disease. The authors speculate that clinicians may have thought these patients are less affected because they often have fewer outward manifestations of the disease as judged by the generally accepted clinical criteria (Ghent nosology criteria). By contrast, the current study showed that of patients who had an early aortic event, all (12/12, <30 years) or nearly all (20/21, <40 years) had a truncating or splicing variant. In addition, the researchers observed that aortic dissection or surgery occurred at a younger age in patients with a truncating or splicing variant (median age, 29 years) as compared with other types of mutations (51 years). The findings suggest that Marfan syndrome patients with *FBN1* truncating and splicing variants should be followed closely to prevent potentially catastrophic aortic events. —*Karyn Hede, News Editor*

NEWS BRIEFS

American history as seen through a genomic lens

Yuri Arcurs/Hemera/Thinkstock

Americans' curiosity about their genetic heritage has helped reveal wider patterns of genetic mixing among distinct ethnic groups in North America, demonstrating how genetics can contribute to a better understanding of ancient and even relatively recent historic events. Scientists at Harvard Medical School and the consumer genetic testing company 23andMe (Mountain View, California) parsed the genetic data of 23andMe customers and combined that information with responses to survey questions about ethnicity and racial identity to create maps of the genetic landscape of the United States. Based on anonymized data from more than 160,000 consenting customers, the study traces the lingering genetic stamp of events such as the forced movements of Native Americans, Spanish colonization, and the aftermath of the slave trade. The data, published in the 8 January 2015 issue of the *American Journal of Human Genetics*, buttresses our understanding of these historic events and identifies newly revealed patterns such as the tendency of individuals with even small amounts of African-American ancestry to self-identify as African-American. Individuals who self-identified as of European ancestry had little evidence of interracial mixing