IN THIS ISSUE

From the *New York Times Sunday Magazine* to *GIM*…

see page 51

©iStockphoto.com

The Enigma decoding machine used during World War II.

The National Institutes of Health (NIH) Undiagnosed Diseases Program (UDP) has garnered considerable attention in the medical and lay communities, having been featured, for example, on the cover of the *New York Times Sunday Magazine* in 2009. *GIM* is delighted to publish the first systematic analysis of that program's experience over its first two years. Study participants were selected in a rigorous process to characterize and assess the possibility of determining the etiology of their enigmatic disorder. Each accepted participant was extensively phenotyped, and a subset of participants and selected family members were subjected to an integrated set of genomic analyses, including high-density single-nucleotide-polymorphism arrays and whole-exome and whole-genome analysis. From 1,191 medical records reviewed, 326 patients were accepted for the program, of whom 160 were admitted directly to the NIH clinical care center. Of this group, 53% had neurological disorders and 47% were children. Diagnoses were reached in 24% of patients on clinical, biochemical, pathological, or molecular grounds. Twenty-one diagnoses involved rare or ultra-rare diseases, and two new disorders were discovered. The UDP addresses an important need, and its substantial reliance on emerging genomic technologies highlights the importance of our field as genomics increasingly informs medical practice.

Newborn screening: making hard calls

see page 129

©iStockphoto.com

Decisions regarding which disease entities should be included in newborn screening (NBS) are difficult. The task is further complicated by advances in technology that have enabled NBS for a multitude of inborn errors. In this issue, Petros proposes a framework for use by public health practitioners as they struggle with these decisions. This framework expands on the now classic Wilson-Jungner criteria with the addition of 11 criteria specific to NBS. A calculation that the author refers to as the pNBS (proposed (or prototype) newborn screening) decision score is used to quantify results and rank candidate disorders. The scoring system designates phenylketonuria, cystic fibrosis, and Pompe disease for inclusion but suggests that Krabbe disease not be screened for at this time. This proposed framework should assist policy makers in making difficult NBS decisions and can be seen as a valuable first step toward revisiting the Wilson-Jungner criteria in a new era of medicine.

NEWS BRIEFS

GIM's new publishing partner!

nature publishing group

You'll notice changes this month to *Genetics in Medicine*, the foremost shift being that we are now being published by Nature Publishing Group (NPG). The selection of NPG by the College was a long and involved process given that a great many publishers vied to be the new home for *GIM*. In the end, the board of the ACMG felt that NPG was the best publisher for the College's official journal given NPG's small size and its intense focus on quality, two attributes that also apply to the ACMG.

We look forward to a productive relationship with NPG; we share a tangible sense of excitement about the direction that genetics and genomics is taking as our field becomes increasingly critical to the practice of medicine. We will continue to do our best to bring to both the genetics and the broader medical community word of the most significant and exciting advances in our field.

The genetics of dengue fever

©iStockphoto.com

Dengue fever is a particularly dreadful infectious disease and, after malaria, the most common mosquito-borne infection in the world. The symptoms of dengue can vary from a mild flu-like illness to a lethal disorder characterized by extremely high fever and increased vascular permeability. What determines whether an individual develops the mild or severe form of the disease has thus far been largely a mystery, although epidemiologic studies have suggested a role for underlying genetic factors. Now, researchers have begun to dissect the underlying genetics of this disorder. A genome-wide association study comparing almost 5,000 controls with more than 1,700 infected individuals identified two polymorphisms that appear to predispose to the severe form of dengue infection. One polymorphism, in the *MICB* gene, appears to play a role in immune response; the other gene implicated, *PLCE1*, may be involved in vascular permeability, a major clinical feature of severe dengue fever. The work, published recently in *Nature Genetics* (2011;43:1139–1141), was carried out by a multinational team of researchers from Singapore, Vietnam, and the United Kingdom.