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The shape of things to come

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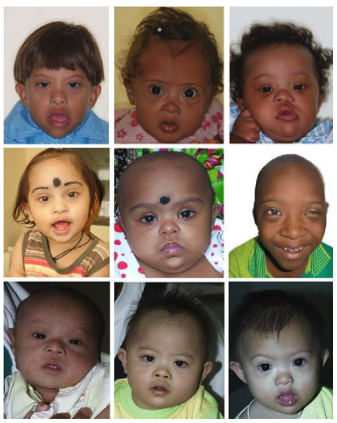

If humans come in a myriad of shapes and sizes, why do clinical diagnostic guidelines often not reflect that diversity? That simple question led a group of medical geneticists experienced in working in multicultural settings to compile such a resource, now available freely online (http://research.nhgri.nih.gov/atlas) and described here. The Atlas of Human Malformation Syndromes in Diverse Populations catalogs genetic syndromes and includes photographs of affected patients of various ethnicities. Registered users can search by phenotype, syndrome, ethnicity, and genetic diagnosis. The goal, according to the organizers at the National Human Genome Research Institute, is to provide a tool to clinicians in underresourced countries with few local medical geneticists available for consultations. The photos in this online resource have not previously been published and were obtained directly from clinicians throughout the world. The authors point out that although genomic medicine is rapidly expanding globally, its impact has not been felt in the underresourced countries where 80% of people live and 90% of births occur. In an accompanying review, Koretzky *et al.* ponder the ethical questions surrounding selection and portrayal of individuals in the atlas. They review the complex and sometimes troubled history of medicine and race politics and evaluate the ethical risks attendant with making identifiable pictures of individuals, many of whom are children with intellectual disabilities, available online. —*Karyn Hede, News Editor*

New clinically significant genetic variants found in Ehlers–Danlos syndrome

see page 1119

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A next-generation-sequencing (NGS) approach has revealed new, clinically actionable genetic variants in patients diagnosed with Ehlers–Danlos syndrome (EDS), the highly heterogeneous group of overlapping disorders of connective tissue. The new NGS panel, developed by a team including the National EDS Diagnostic Service in London, and reported in this issue, identified seven new pathogenic or likely-pathogenic variants that required clinical follow-up. Because EDS is associated with a high risk of life-threatening complications, including arterial aneurysm or rupture and bowel perforation, accurate diagnosis is paramount. The investigators developed an NGS panel that covers not only genes linked to EDS but also related genes with overlapping clinical manifestations. They recruited 177 unrelated patients referred to the National EDS Diagnostic Service with suspected EDS. Investigators were blinded to previous genetic testing results. The NGS panel identified all 22 pathogenic variants in collagen genes that had previously been sequenced using classical methods. Importantly, it also identified four additional potentially pathogenic variants in collagen genes not previously selected for sequencing and four additional variants in genes associated with risk of aortic rupture. The test also revealed 22 variants of uncertain significance. The results may help guide development of new genetic testing for EDS diagnosis. —*Karyn Hede, News Editor*

NEWS BRIEFS

Schizophrenia may have emerged after human–Neanderthal evolutionary split

The Neanderthals may have lacked the facile mind for language we modern humans enjoy, but they may also have been spared certain mind-altering disorders, such as schizophrenia. It appears that genetic changes that help define modern humans may also play a significant role in the development of the hallucinations and delusions that characterize schizophrenia. A recent genetic analysis that compared data from genome-wide association studies of people who have schizophrenia with Neanderthal genomic information revealed that risk loci were more likely to be found in regions that diverged from the Neanderthal genome. The study, published in the journal *Biological Psychiatry*, included an analysis of loci associated with evolutionary markers. The findings suggest that several of these gene variants related to cognitive processes have undergone selection. According to senior author Ole Andreassen from the University of California, San Diego, and the University of Oslo, Norway, schizophrenia may be a "side effect" of advantageous gene variants related to the acquisition of human traits such as language and complex cognitive skills. These variants may also have increased our propensity to developing psychoses. "Our findings suggest that schizophrenia vulnerability rose after the divergence of modern humans from Neanderthals," said Andreassen in a supplementary report released by the journal, "and

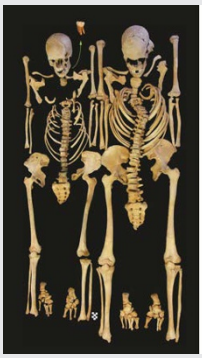
Prehistoric/©Getty Images

NEWS BRIEFS *(continued)*

thus support the hypothesis that schizophrenia is a by-product of the complex evolution of the human brain." —*Karyn Hede, News Editor*

The plague: it's ba-ack

In the complex and intertwined history of human disease, few organisms inspire fear like the infectious bacterium *Yersinia pestis*. History serves notice that plague, now confined to a few reservoirs of endemic disease, could re-emerge without warning. *Y. pestis* has been causing documented pandemics throughout human history. The Justinian pandemic in the sixth to eighth centuries AD was the first such recorded, but the extent of disease and geographical reach are not well understood. Now, a genomic sequencing effort has produced a high-quality *Y. pestis* sequence that offers insight into its evolutionary history, its key mutational changes in virulence-associated genes, and possibly its potential for re-emergence. Investigators based



Staatssammlung für Anthropologie und Paläoanatomie München

Archäologische Staatssammlung München

in Munich, Germany, extracted genetic material from the tooth pulp of skeletons buried in the sixth century in an early medieval settlement, Altenerding, in southern Germany, near Aschheim, the source of an earlier sequenced plague genome from the same pandemic. The more recent sequence, published in the journal *Molecular Biology and Evolution* in September 2016, reached much higher coverage than the earlier sequencing effort, allowing investigators to correct 19 false-positive mutations reported in the published draft genome, as well as to identify 30 new mutations. Their findings point to a bacterial source with low genetic diversity in a rural region of southern Germany in the sixth century, as the two genomes extracted in the region were nearly identical. Future investigations may reveal the range of the outbreak and enable investigators to trace the path of the disease and its transmission rate. The investigators also suggest that comparing the genome structure of historical *Y. pestis* strains to those of extant strains and to that of the related soil- and water-borne organism *Yersinia pseudotuberculosis* could offer insights into key evolutionary changes, such as those in virulence-associated genes, through time. In addition, the results could inform preparation for a public health emergency, as plague is classified as a re-emerging infectious disease with reservoirs on nearly every major continent. —*Karyn Hede, News Editor*