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Family history highly predictive of mutations in HCM

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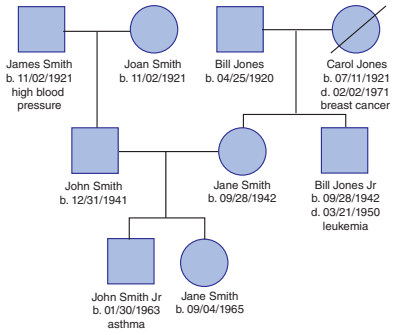

The risk of sudden death in individuals with hypertrophic cardiomyopathy (HCM), particularly young athletes, is alarmingly high. But only about half of patients with a clinical diagnosis ever receive a definitive genetic diagnosis. In a 10-year analysis of Australian HCM patients published in this issue, Ingles and colleagues from three major specialized cardiac genetic clinics in Australia found that a genetic diagnosis is much more likely in patients with a family history of HCM than in those without such a history. Of those with an established family history of HCM, 102 (72%) received a definitive diagnosis, compared with 36 (29%) of patients with no family history. The mutation-detection rate for those with a family history of HCM increased to 89% among individuals with family members who had died suddenly. The authors identified causative mutations in 10 genes, with *MYBPC3* and *MYH7* accounting for more than 50% of cases. They note that the large difference in mutation-detection rate has direct clinical relevance because patients can be more appropriately counseled regarding their likelihood of receiving a genetic diagnosis based on their family history. The results may also assist in developing an algorithm to assess HCM patients' risk of heart failure or sudden death. *—Karyn Hede, News Editor*

High-throughput techniques speed genetic diagnosis of FH

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Despite the high risk of heart disease and early death that comes with inherited high cholesterol levels, three of four people in England carrying familial hypercholesterolemia (FH) gene mutations are unaware they have the disorder. Current genetic testing is costly, and few take advantage of it. A recent yearlong study now reveals that benchtop sequencing of known FH genes has high sensitivity and offers an affordable option for screening patients in a clinical setting. The research team, from Imperial College, London, studied a group of patients referred for genetic screening by a lipid clinic and compared the results with those for a validation group of patients with a known FH molecular diagnosis. The researchers studied two systems: a targeted sequencing protocol and a PCR-based array system with a more limited sequencing capacity. Both methods detected all cases in previously diagnosed patients, with the exception of two cases involving large deletions and duplications that were missed in the PCR-based system. The mutation-detection rates among new patients with definite (66%) and possible (26%) FH were comparable to those reported in published studies. The researchers report that the PCR-based system was much faster—handling 96 samples per day—and less expensive to run, and they suggest that PCR-based screening may be an affordable option for clinical screening of large numbers of patients with suspected FH, allowing more at-risk individuals to be identified and treated. *—Karyn Hede, News Editor*

NEWS BRIEFS

Researchers withhold gene sequences of potentially deadly botulinum toxin


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Citing fears of use in biological warfare, researchers who discovered a potent new form of botulinum toxin have selectively withheld gene sequences needed to replicate it in the lab. The new toxin, discovered by a research team at the California Department of Public Health, was isolated from an infant. The research team was unable to neutralize the toxin with any known antisera, which simultaneously proved its status as a new toxin and made it a dangerous public health hazard. Facing an ethical dilemma, the research team decided to withhold key gene sequences in their description of the new toxin. In two papers appearing in the *Journal of Infectious Diseases* in October 2013, the research team described the first new botulinum neurotoxin reported in more than 40 years and explains that, until an effective antitoxin can be developed and shown to be effective, the gene sequence will remain sealed. Three accompanying commentaries discuss the fascinating history of the discovery of *Clostridium botulinum* in the late nineteenth century and its evolutionary diversity as well as the inherent tension between the closely

NEWS BRIEFS *(continued)*

held principle of openness in science and the growing specter of biological warfare with the attendant concerns for national security. This will surely not be the last time this issue is faced by the scientific community, and it's worth evaluating these case studies of delicate ethical balancing acts between maintaining scientific freedom and safeguarding public health.
—Karyn Hede, News Editor

Science and public health suffer under US shutdown

As the US government shutdown painfully demonstrated, the US scientific and public health enterprise has become vulnerable to the capriciousness of Congress. The shutdown caused permanent damage to countless research endeavors that will cost millions in lost productivity, to say nothing of the human cost. One of the widely publicized human costs, with immediate impact, affected the National Institutes of Health (NIH) Clinical Center, where desperately ill patients were turned away as clinical trials were shut down. The NIH had become a convenient political backdrop for grandstanding politicians attempting to cherry-pick which government functions qualify as "essential."

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After some in Congress complained, the NIH reopened the shuttered ClinicalTrials.gov database, allowing at least some trials to resume enrollment. The image of children being turned away from potentially lifesaving treatment was enough to get the Clinical Center partially reopened. Other, less immediately visible, scientific and medical research projects languished out of the spotlight. The NIH has told researchers that they can continue their research until their current grant money runs out. But perhaps the most disturbing turn of events is that the budget fight has rendered the NIH a politically expedient poster child, a status that doesn't bode well for the future stability of research funding. *—Karyn Hede, News Editor*