

DR. ACKERMAN: Well, hello. Good afternoon. My name is Mike Ackerman, and I'm one of the pediatric cardiologists at the Mayo Clinic in Rochester, Minnesota. And I'm the director of Mayo's long QT syndrome clinic and the Windland Smith Rice Sudden Death Genomics Laboratory. And I'm affiliated in the departments of Medicine, Pediatrics, and Molecular Pharmacology and Experimental Therapeutics.

And I'm really pleased and delighted to share with you my thoughts on our recent publication in the October issue of *Mayo Clinic Proceedings*. And our work was entitled *Unexplained Drownings and the Cardiac Channelopathies: A Molecular Autopsy Series*. And over the course of the last 12 years, we've received cases from medical examiners offices, forensic pathologist offices, coroners, of unexplained drownings that caught their attention, for whatever reason. And so this was a survey and a molecular genetic testing, if you will, a molecular autopsy, of 35 such unexplained drownings that we received in our laboratory.

Now, it's important to note that, during the same time, there were probably over 10,000 drownings that took place in the United States. In the subset that we received-- and we don't know what motivated these medical examiners and coroners to send them to us, whether it was their Quincy-like investigation, or CSI-like investigations that made them concerned that this wasn't like an ordinary drowning, from inability to swim, or alcohol, or other explanations for why that individual drowned. These 35 cases bothered these medical examiners enough to reach out to a research laboratory like ours at the Mayo Clinic and ask to see whether or not one of these genetic heart rhythm diseases that we spend a great deal of time studying, like long QT syndrome or catecholaminergic polymorphic ventricular tachycardia, CPVT, might be the root cause for that tragic drowning.

And so over those 12 years, we received 35 such unexplained drownings. And what we found when we did our mutation spell checker, looking through, looking for mutations in the genes that give rise to long QT syndrome or CPVT-- basically a collection of genetic heart rhythm abnormalities where the heart is genetically programmed to spin electrically out of control into a potentially lethal rhythm, heart rhythm disturbance-- we found that 30% of those submitted drownings had a putative long QT syndrome or CPVT causative mutation. In other words, almost one third of these drownings that were submitted for molecular autopsy had a potential genetic explanation for their drowning.

Now, this does not suggest, and should not be used to suggest, that up to 30% of all drownings-- in other words, the 1,000 drownings that occur in the United States each year-- are genetic in origin or due to genetic heart rhythm abnormalities, like long QT syndrome or CPVT. What it should suggest, however, is that there should be some questions asked. Because what we found was, among the 28 swimming-triggered drownings, we had mutations found in about 30% of the case. But in almost 60% of the women who drowned while swimming did we find mutations, compared to only 15% of the male drowning victims.

The second thing we observed is that we found mutations in up to half of those cases where that drowning victim had a personal history of a previous event that went unrecognized, undiagnosed. In fact, we had one individual who had a previous near-drowning before the ultimately fatal drowning episode. Or these individuals who had a positive mutation for a genetic heart rhythm abnormality, they had a positive family history that was there, it was elicited, but the connections weren't made, a diagnosis wasn't made in these individuals. In fact, there were two drowning victims that had other relatives die of a drowning in years before their ultimate drowning.

And so what we are seeing is, drowning deserves a second look to ask the question, was this the sentinel event of a genetic heart rhythm abnormality like long QT syndrome or CPVT? Or was this simply a drowning, like so many drownings are? Whether it was inadequate attention, or inability to swim, or alcohol-- many reasons. Most drowning is not genetic. But those drownings where it didn't make sense-- it was a good swimmer, she was a good swimmer, she had fainted the year before in track, or there's a family history of previous unexplained cardiac arrest-- those should be warning signs that should prompt suspicion to say, wait a second, this might not be one of those ordinary drownings. Maybe instead, this drowning is an expression of a potentially lethal-- in this case, ultimately lethal-- genetic heart rhythm condition.

By asking those questions, that can have a significant impact. Because, of those drowning victims who are found to be mutation positive, we went on and did genetic testing of the rest of the family and found several individuals who were positive, who they then could be treated and have the outcome that was experienced tragically by their deceased drowning victim, the relative, not occur. Whether on land or in sea. That we could have their disease correctly diagnosed, correctly treated. Because these diseases-- these genetic heart rhythm diseases, that are potentially lethal-- are highly, highly treatable. So when we know they're there, we should be able to prevent sudden death from happening.

And so one of the things that we would encourage medical examiners, and forensic pathologists, and coroners out there is not to just dismiss drowning too quickly, and say, oh, she didn't know how to swim. But to ask those questions. And ask and see, were there any other suspicious spells, faints, collapses, seizures that had happened in that person's life before their drowning? Is that drowning victim related to anybody where there's been an unexplained sudden death before the age of 50? Where there's been an unexplained car accident? Why did that uncle go off the road? Or why were there a series of spells in relatives?

And if there are yeses to any of those questions, to then take the next step. And to make sure that the decedent's family, the deceased drowning victims family, is informed of the possibility of doing further investigations even after that tragic death has occurred. That we can do a cardiac channel molecular autopsy and search for a genetic cause. And in doing so, then find the potential answer that could save another family member's life.

It's also important for that family of a drowning victim to ask those questions and to delve into it a little bit more. And perhaps they themselves, if there were signs or signals before that drowning took place of a potentially lethal heart condition present, that they themselves get checked out by having an electrocardiogram to look for long QT syndrome. Having a treadmill stress test to look for CPVT. Because as we saw in this study-- motivated for a variety of reasons from these medical examiners offices, but at least among these 35 unexplained drowning victims-- we found a genetic root cause in about 30% of those individuals.

SPEAKER 1: We hope you benefited from this presentation based on the content of *Mayo Clinic Proceedings*. Our journal's mission is to promote the best interests of patients by advancing the knowledge and professionalism of the physician community. If you're interested in more information about *Mayo Clinic Proceedings*, visit our website at www.mayoclinicproceedings.org. There, you will find additional videos on our YouTube channel, and you can follow us on Twitter. For more information on healthcare at Mayo Clinic, please visit www.mayoclinic.org. This video content is copyrighted by Mayo Foundation for Medical Education and Research.