Learning to Care for Those in Harm's Way

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Scientists unearth major clues to mysterious Guam disease

Bethesda, Md. – Researchers from the Uniformed Services University (USU) have shed light on a fatal neurodegenerative disease that has long afflicted the native Chamorro people living on Guam – a unique and mystifying disorder that has baffled scientists for decades. Their new collaborative study published March 20 is the first to find that this disease – ALS/parkinsonism-dementia complex (ALS/PDC), or as it is known on Guam, lytico-bodig – involves the accumulation of prions, abnormally formed proteins which can spread in the brain and impair its structure and function. This discovery could not only help better understand this unique and mysterious illness, but others like it, such as Alzheimer's disease, ALS (Lou Gehrig's disease) and Parkinson's disease.

The study, published in the Proceedings of the National Academy of Sciences, was led by Dr. Stanley Prusiner at the University of California, San Francisco (UCSF), in collaboration with USU. For decades, lytico-bodig was uniquely seen among inhabitants of Guam. At the height of its epidemic, it led to more than 10% of the adult deaths on the island. Clinically and pathologically, the disease has unusual and complex characteristics which combine aspects of Alzheimer's disease, Parkinson's disease and ALS. The mysterious disease develops in adulthood and progresses to death within several years. It is not seen elsewhere in the world, though there is a similar disease that has been described in an isolated rural region of Japan, explained Dr. Dan Perl, a professor of Neuropathology at USU who has been studying this disease for more than 30 years.

Early on, lytico-bodig was believed to be a hereditary disorder, since it was unique to the native population living on this Pacific island. However, that theory proved incorrect since migrants from the Philippines who had moved to Guam began to develop the disease after having lived on Guam for more than 20 years, Perl said. In addition, new cases of the disease have also drastically decreased over the last several decades. This dramatic disappearance of the disorder also suggests that it could not be hereditary in nature since genetic diseases do not disappear this rapidly in an at-risk population.

Knowing that a better understanding of this disease may lead to answers for other similar diseases, Perl collaborated with Prusiner to study brain specimens obtained from individuals who had died of the disease. The scientific team used newly-developed highly sensitive and specific assays to look for the presence of prions, which are proteins that can transmit their misfolded shape onto normal variants of the same protein. Prusiner won the Nobel Prize in Physiology or Medicine in 1997 for his seminal work characterizing prions and their involvement in brain diseases. In this study they found the diseased brains from Guam contained high concentrations of two proteins, tau and beta-amyloid, that had

become prions and thus added lytico-bodig to a growing list of prion-related neurodegenerative disorders.

Guam has been a US Territory since 1898 and its inhabitants are U.S. citizens. The island also possesses major U.S. Air Force and Navy bases and, because of its unique location in the western Pacific, Guam has continually served as a critically important strategic location for the U.S. military.

“We’re excited about these findings, which, although they do not explain the underlying cause of the disorder, they do provide answers for how the disease spreads through the brain and produces its devastating effects on brain function. The findings reported here could have a significant impact on both civilian and military health care through further research and ultimately provide answers to why this disease has been endemic to Guam. It could also lead to a better understanding of the nature of other similar neurodegenerative diseases seen elsewhere in the world,” Perl said.

Funding for this study, “Guam ALS-PDC is a distinct double prion disorder featuring both tau and Aβ prions,” was provided by grants from the National Institutes of Health (AG002132) and the Defense Health Agency (HU0001-17-2-0029).

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