Effect of chronic exposure to chemicals used as weapons, pesticides under study

April 18 2012

Dr. Alvin V. Terry Jr., pharmacologist at the Medical College of Georgia at Georgia Health Sciences University studies organophosphates, which are proven, rapid killers of people and pests that can also produce chronic disabilities such as problems with learning and memory, headaches and pain. Credit: Phil Jones, GHSU photographer

Soldiers in war zones and farmers tending their fields can have in common chronic exposure to chemicals that impact their nerves.

In large doses these agents, called organophosphates, are proven, rapid killers of people and pests that can also produce chronic disabilities such as problems with learning and memory, headaches and pain, said Dr.

Alvin V. Terry Jr., pharmacologist at the Medical College of Georgia at Georgia Health Sciences University.

A Department of Defense grant is helping him document the less understood – and probably more common - consquences of low-dose exposure for long periods.

"The use of these chemicals is like making the Faustian bargain," said Terry. "They are great for enhancing farming productivity and getting rid of vector-born illnesses like malaria and yellow fever, but they are almost ubiquitious in our environment." Conceding the last thing he wants is to encourage elimination of useful agents, he hopes instead that a prospective look at their cumulative toll will help identify ways to stop the ill effects.

"Once we have identified there is a problem and we know the mechanism, we have a much better chance of treating people," he said. Terry will be looking at varying doses of chlorpyrifos, an insecticide used by farmers and the military during the Gulf War, as well as the nerve agent, diisopropylfluorophosphate.

He is the first to look at the agents' impact on the axons, which enable brain cells to communicate.

"We are talking about the highway," he said of the pathway that has information, molecules, growth factors and other things made by the cells moving constantly in both directions. Terry is finding this fundamental brain function may be a particular target of chronic exposure to organophosphates. He's already shown animals with chronic exposure have impared communication in the body.

Now he's looking in the brain at axons as well as the white matter, which surrounds and helps insulate the nerve fibers to ensure clear

communication. Brain studies have documented a shrinkage of white matter in some Gulf War veterans; Terry want to see if chronic exposure has a similar impact: enough to hamper but not destroy communication. He was corresponding author on a paper published earlier this year in the journal *Neurotoxicology and Teratology* that indicates chronic, low-level exposure leads to chronic spatial learning and memory deficits.

Dr. Nathan Yanasak, Director of GHSU's Core Imaging Facility for Small Animals, is collaborating on the new study that will do baseline then follow-up brain images of rats after low-level exposure for 30 days. Then researchers will follow the rats until the agents are no longer detectable in the body. A manganese tracer will gauge activity up and down axons.

"We are looking at real time axonal transport changes in the brains of living animals after organophosphate exposure which has never been done before," Terry said of a perspective that should provide direct evidence of the agents' impact on the brain. "If it's being slowed down, that would tell us the stuff that needs to get down that axon is not getting there fast enough. So how is the traffic moving?" In addition to the images, behavioral testing will measure impact on working memory and the spatial reference memory that helps people navigate.

Like a muscle recovers after overuse, it's possible – but not likely – that once the agents clear the body, any damage they do will resolve. "We don't know unitl we do these studies if it's persistent or not," Terry said.

Organophosphates block an enzyme that breaks down the neurotransmitter acetylcholine so the brain doesn't get overstimulated, Terry said. At large doses, the response includes immediate seizures, spasms and respiratory paralysis or failure. Their use as insecticides during the Gulf War from 1990-91 continues to make headlines with about a quarter of the 697,000 U.S. veterans who served experiencing

ongoing problems with memory, concentration, headaches and widespread pain.

However, the soldiers' exposure to multiple other agents – including depleted uranium, anthrax vaccine, burning fuels and infectious agents – could be causing or at least contributing to the problems, Terry said, which is why direct cause and result studies are needed. Gulf War veterans may have been at additional risk because the nerve agents sarin and cylcosarin likely were released during the 1991 destruction of an Iraqi munitions storage complex.

Terry notes that while the U.S. Environmental Protection Agency strictly regulates organophosphate exposure, many countries do not. Even still, a decade-old survey of 1,000 Americans found 96 percent had detectable levels of a metabolite of a common insecticide in their blood, he said. Pesticide applicators and organophosphate producers are two other groups that may get chronic exposure.

Provided by Georgia Health Sciences University

Citation: Effect of chronic exposure to chemicals used as weapons, pesticides under study (2012, April 18) retrieved 7 May 2024 from https://medicalxpress.com/news/2012-04-effect-chronic-exposure-chemicals-weapons.html