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HEALTH

Is Agent Orange Still Causing Birth Defects?

Vietnam insists that children are suffering today from the lingering effects of the infamous defoliant sprayed by U.S. forces decades ago. Scientists are undecided

By Charles Schmidt on March 16, 2016

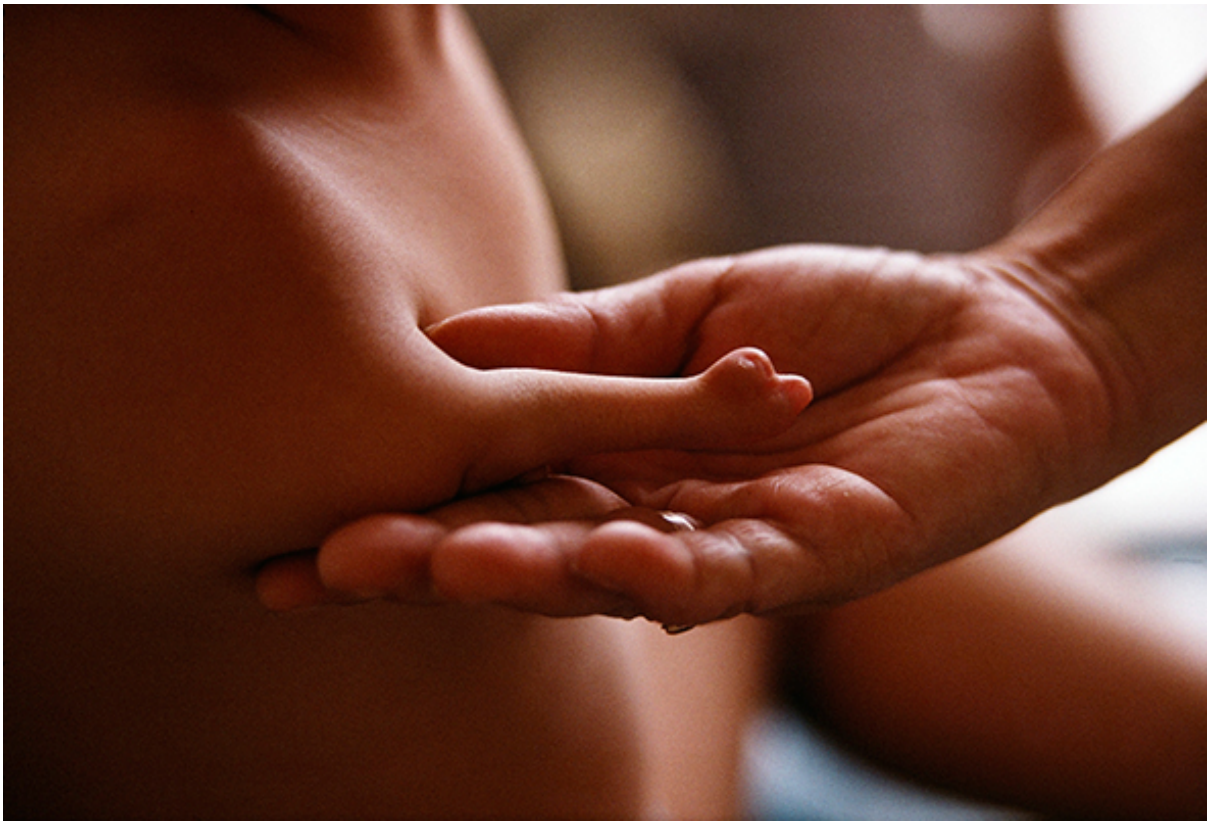
Soldiers at Da Nang airport in Vietnam search for unexploded bombs in 2011, before workers excavated the soil there and heated it to destroy dioxin, a toxic compound in Agent Orange. The U.S. military sprayed the defoliant across areas of Vietnam during the war there in the 1960s.

CREDIT: NGUYEN HUY KHAM Reuters

After he was born with a cleft lip and palate and congenital heart disease, Danh (not his real name) spent his first month in an incubator struggling to breathe. He is now eight years old and thin as a rail. Danh has an endearing smile, but he can't speak, and his mother, Lien (also a pseudonym), says he is mentally disabled. Recently he sat playing with toy cars at home in Da Nang, Vietnam, while Lien talked wearily about her son's many needs.

I had been brought to Lien by a private American aid group called Children of Vietnam that works with poor families in Da Nang. We sat drinking tea in a simple room open to the street, chatting over the din of traffic. Family pictures hung next to a portrait of Ho Chi Minh, Vietnam's communist revolutionary leader. Lien's otherwise soft features hardened when I asked what she thought had caused her son's disabilities. "Agent Orange did this!" she exclaimed through an interpreter, her eyes flashing with anger.

Agent Orange was a defoliant sprayed by the U.S. during the Vietnam War to clear dense vegetation and reveal enemy troops. It was contaminated with dioxin, a potent toxicant that persists for decades in the environment. Danh's grandfather fought in the heavily sprayed Central Highlands, and his father worked at the former U.S. air base in Da Nang, where dioxin was later discovered in the ducks and fish eaten frequently by local villagers. Dioxin has been associated with human cancers, heart disease and other health problems in people who are exposed. But Lien firmly believes her son inherited the toxic legacy of her father and grandfather's exposure. The Vietnamese government, which classifies Danh as a suspected "victim of Agent Orange," claims that hundreds of thousands of its citizens born one and even two generations after the war are battling effects of dioxin they inherited from their parents.



A boy shows his hand and shoulder, with almost no arm in between. The Vietnamese government says hundreds of thousands of children and grandchildren of citizens who were exposed to Agent Orange were born with deformities. The U.S. government notes that there are many causes of birth defects.
CREDIT: KAZUYOSHI NOMACHI Corbis

The U.S. government gives modest compensation to American war veterans for health problems such as leukemia, Hodgkin's disease and Parkinson's disease that are attributed to Agent Orange, based on detailed military records of soldiers who were present during the spray operations. Scientists used those records in studies that later associated Agent Orange with more than a dozen ailments in service men and women. But the government has refused to acknowledge claims that the defoliant also harmed the Vietnamese, in part because it says Vietnam has not provided strong data on who was exposed. Medical records in the country are spotty, and the population was also highly mobile in the chaotic postwar years, making exposures to Agent Orange difficult to prove.

Vietnam claims its data are sound, but the disagreement has sustained tension for years, particularly about effects that might be passed down to subsequent generations. Although U.S. laboratory tests in animals show that genetic damage caused by dioxin can be passed on to offspring, susceptibility varies widely by species, and no studies have been done in humans. Whether animal findings reflect the human experience “would be notoriously difficult to prove,” cautions Robert Moore, a toxicology researcher at the University of Wisconsin–Madison.

Looking to smooth relations, in December 2014 Congress passed a five-year, $21-million humanitarian aid package that, for the first time, provides assistance specifically for severely disabled people living in areas that were sprayed during the war. Charles Bailey, former director of the Agent Orange in Vietnam Program at the Aspen Institute, describes the aid as a breakthrough that “ensures that our humanitarian assistance goes to those with the greatest need.” But the aid package does not explicitly reference Agent Orange as having caused those disabilities. It is more a symbolic gesture meant to assuage the Vietnamese position than an admission of culpability. Forty years have passed since U.S. forces fled Saigon (now Ho Chi Minh City), marking the end of the war. Yet fundamental questions about the multigenerational health legacy of Agent Orange in Vietnam remain hotly contested.

Vietnamese scientists claim the dioxin in Agent Orange damages DNA, which can impair genetic material that is passed from parents to their children and grandchildren. Some U.S. scientists question the Vietnamese studies, but they have not been allowed to conduct their own research in Vietnam, which could involve children such as this boy in a hospital, shown in 2005.
CREDIT: PAULA BRONSTEIN Getty Images

DIOXIN IS THE VILLAIN

With its leafy boulevards, resorts and trendy cafes, today's urban Da Nang is a far cry from the port town that hosted U.S. forces during the war. Scooters and motorcycles fill the main road heading toward the old Da Nang airbase, which is now an international airport. It was from there in 1962 that U.S. and South Vietnamese forces launched Operation Ranch Hand, the herbicidal warfare program.

Produced mainly by Monsanto and Dow Chemical, Agent Orange was a 50–50 mixture of two herbicides—2,4-D and 2,4,5-T—that was sprayed by U.S. troops at the initial request of the South Vietnamese government. Troops also sprayed other mixtures during the war, including agents White, Blue, Pink, Green and Purple, each named for the color of a striped band surrounding the drums it was transported in. The primary goal was to strip away the jungle cover hiding enemy forces, and the spraying took place mainly in South Vietnam and parts of Laos. C-123 aircraft sprayed herbicides from the air, and within two days all the plants touched by the chemicals were dead.

It was not until 1969 that Agent Orange and most of the other mixtures were found to be inadvertently contaminated with the most toxic form of dioxin, known as TCDD. By the time Operation Ranch Hand wrapped up in 1971, two years after the contamination was discovered, at least 20 million gallons of herbicides had been sprayed, exposing 2.1 million to 4.8 million villagers, according to a definitive analysis published in 2003 by Jeanne Stellman, now a professor emeritus of health policy and management at Columbia University.

Animal studies show that TCDD is one of the most poisonous chemicals known. Apart from causing liver damage, cancer and immune problems in directly exposed animals, TCDD is exquisitely toxic to developing babies in the womb. Fed to a pregnant rat, a dose of less than one part per billion—comparable to a single drop in 14,000 gallons of water—will induce female sexual characteristics in a male embryo. Doses on the order of 100 parts per billion in rodents and fish will cause birth defects such as cleft palate, malfunctioning kidneys, heart problems and weak bones.

But TCDD works in mysterious ways: some species succumb to minuscule doses, whereas others are more resistant to its effects. Certain species start out sensitive and then become more resistant with age. There are even differences within species, says Linda Birnbaum, director of the National Institute of

Environmental Health Sciences in Research Triangle Park, N.C. Human susceptibility is unknown because studies cannot be done ethically. That uncertainty drives pitched scientific debates over what constitutes a potentially "safe" level of human exposure.

DNA DAMAGED FOR GENERATIONS?

At the War Remnants Museum in Ho Chi Minh City, a visitor might get the impression that the science is settled. Photographs of grotesquely disfigured people hang on orange walls next to maps showing where the defoliants were sprayed. A sign proclaims that dioxin's effects "can be transmitted to many generations through the damage to DNA molecules and genes." Hospitals in Vietnam have entire wards devoted to the care of purported Agent Orange victims, including the grandchildren of individuals said to have been exposed.

Studies with rats do not prove that generations of Vietnamese are experiencing effects from dioxin, but they suggest that such a scenario is at least plausible. In this situation, initial exposure during the war would have reprogrammed embryonic sperm or egg cells (also known as germ cells) at vulnerable periods during pregnancy, leading to changes being passed from one generation to the next.

Scientists are now making important advances that suggest the chemical has long-lasting and even transgenerational effects. Emerging evidence in rodents at labs around the world shows that TCDD alters the epigenome—the biological system that controls which genes in a cell are turned on or off. It is because of this so-called epigenetic regulation that all the cells in a developing embryo, even though they inherit the same genes from the mother and father, go on to form different tissues. The genes that cause a cell to beat in the heart, for instance, are activated by one epigenetic process, whereas another process turns off genes that would allow that cell to transmit nerve impulses in the

brain.

TCDD can reprogram those epigenetic controls, with consequences that might appear long after the chemical has been cleared from the body. “The effects don’t necessarily occur at the time of TCDD exposure,” explains Michael Skinner, a biologist at Washington State University. “Instead the epigenome can be stuck in an altered state, with effects that can occur at anytime during your life.” Supporting evidence comes from the lab of Alvaro Puga, a molecular biologist at the University of Cincinnati College of Medicine, who gave pregnant mice TCDD and found that the pups were born with nonlethal heart defects that became dangerous only when the animals reached adulthood.

When Skinner gave pregnant rats high doses of TCDD, he found that the second- and third-generation offspring had elevated rates of ovarian and kidney disease and that the fourth generation had lower sperm counts. Asked if those results were relevant to the experience of humans exposed to dioxin in Vietnam, Skinner emphatically answered, “Yes.” Some scientists question that connection as well as the relevance of Skinner’s studies to Vietnam, in part because he subjected his rats to TCCD doses far higher than those that would ever occur in the human population.

The Vietnam case is complicated by the persistence of TCDD in the environment, which might have ongoing effects independent of those passing through the germ line. TCDD’s half-life in the human body ranges from seven to 10 years. Its half-life in soils and sediments can last decades longer, allowing the compound to build up in fish and ducks, both staples of the Vietnamese diet —the very diet of eight-year-old Danh’s father.

Studies conducted between the 1990s and mid-2000s by Vancouver-based Hatfield Consultants revealed seven hotspots—areas where soil and sediment measurements exceed 1,000 parts per trillion (new numbers suggest as many as 28 hotspots). According to Thomas Boivin, Hatfield’s director of

international operations, the top three hotspots were all former South Vietnamese and U.S. air bases in Da Nang, Phu Cat and Bien Hoa. In a 2015 study, scientists at the U.S. Centers for Disease Control and Prevention's Agency for Toxic Substances and Disease Registry found that fish collected from ponds at Bien Hoa were still contaminated at unsafe levels.

Puga thinks TCDD might build up in the fat stores of people who eat contaminated food until it reaches a state in which it accumulates faster than the body can eliminate it. If fat releases the compound into a woman's blood during pregnancy, he says, the "baby could get a whopping dose." Yet without better exposure data and TCDD measurements in blood, that scenario amounts to little more than conjecture. Birth defects already afflict 3 percent of all newborn children worldwide, and the Vietnamese rank among the world's top users of agricultural pesticides, which experiments show can cause birth defects in animals. The population is also chronically deficient in dietary folic acid, a nutrient that protects against nervous system defects during pregnancy.

ELUSIVE DATA

Citing unpublished Vietnamese studies, Le Ke Son, who recently retired as director of Committee 33, a government group responsible for Agent Orange activities in Vietnam, insisted in an e-mail exchange with me that "rates of birth deformities and childbirth incidents in the sprayed areas and the hotspots are definitely higher than in the control areas." Son is a medical doctor and a toxicologist and continues to lead the national research program on dioxin in Vietnam. His views are considered more reasonable than those of government hard-liners.

U.S. scientists typically dismiss the Vietnamese research, however, noting that it rarely appears in high-quality Western journals. Vietnamese authorities have also not allowed American experts to conduct their own studies in Vietnam.

Officials stopped Arnold Schecter, now an adjunct professor at the University of Louisville School of Medicine, as he tried to leave the country with human blood samples for dioxin analysis in 1995.

Hope for cooperation on studies rose in 2000, when David Carpenter, director of the Institute for Health and the Environment at the University at Albany, State University of New York, proposed a five-year, $1-million project. He would take blood samples from women who were about to give birth at hospitals in three cities: Ho Chi Minh, which was near the center of prior Agent Orange exposure; Hanoi, which was far away; and the province of Thua Thien Hue, which was also extensively sprayed. Levels of TCDD in blood would be correlated with three kinds of birth defects: lack of limbs, neural tube defects, and cleft lip and palate.

But the plan unraveled. According to Carpenter, the National Institutes of Health made approval conditional on Vietnam's okay. Hanoi took a year, after which the NIH declared it would only support a $350,000 pilot study. Vietnam balked. After further roadblocks, the NIH and the university ended the project.

"I wasted three years of my life writing those proposals and making multiple trips to Vietnam, and it all came to nothing," Carpenter says. "That was the best chance for a collaborative study, and I'm sure it's not going to happen again." Carpenter says the proposed work made both Hanoi and Washington nervous. "U.S. officials worried that if we associated birth defects with dioxin, then we'd be liable for reparations," he says. "And the Vietnamese worried that if we didn't make that association, they'd lose the propaganda benefits of blaming us for the birth defects."

Carpenter concedes that pulling off the study, or a new one like it, will be difficult. A sizable blood sample, 40 milliliters, is needed for dioxin analysis. And the testing technology is complex and exists in only a few labs around the world, he says.

New results would be prized. A comprehensive review of Vietnamese birth defects data was done 30 years ago. Maureen Hatch, currently a staff scientist at the National Cancer Institute, had reviewed Vietnamese studies, medical records and government statistics and found a litany of problems, including few prewar baseline measures and inadequate controls from unsprayed areas. Still, in a 1985 paper in *Teratogenesis, Carcinogenesis, and Mutagenesis*, she and her co-author, John Constable, wrote that some studies did "seem to show a large number of striking and usually rare anomalies." Some babies were born missing brain and skull parts; others were born without eyes or with shrunken, malformed limbs.

The best association with the TCDD in Agent Orange, she and Constable concluded, was for molar pregnancy. In these cases, sperm fertilizes a nonviable egg, creating a mass of tumorlike tissue that grows in the uterus and occasionally becomes cancerous. A more recent meta-analysis concluded that parental exposure to Agent Orange in Vietnam appears to be associated with an increased risk of birth defects, but the conclusions are limited.

American analysis of U.S. soldiers who were exposed, carried out by the Institute of Medicine since 1991, is more definitive. The institute's 2014 biennial report says there is "sufficient evidence of an association" with soft-tissue sarcoma, non-Hodgkin's and Hodgkin's lymphomas, and chloracne (skin blisters). It also cites "limited or suggestive evidence" for laryngeal, lung and prostate cancers, multiple myeloma, early-onset peripheral neuropathy, Parkinson's, hypertension, ischemic heart disease, stroke and type 2 diabetes. Notably, the report calls evidence for any kind of birth defect "inadequate" except for spina bifida, which falls into the "suggested evidence" category. The U.S. Department of Veterans Affairs provides compensation for these health effects if vets can prove they were exposed to Agent Orange.

A PAYOFF FREE OF GUILT

The Institute of Medicine's classifications seem to be American admissions of direct effects from Agent Orange. Yet questions over whether the defoliant played a role in health problems in Vietnam, especially in subsequent generations, are "trapped in a Sargasso Sea of disputes over causality, liability, compensation and responsibility," Bailey says. The new aid package, he asserts, skirts those disputes and simply prioritizes federal assistance to smaller groups of people with more profound disabilities.

Senator Patrick Leahy of Vermont, who has long worked to tackle the war's lingering environmental threats, coordinated the aid. During the 1980s Leahy was instrumental in the creation of a federal fund that to this day pays to remove unexploded bombs still littering the Vietnamese countryside. Since 2007 he has secured about $100 million for dioxin cleanup in Vietnam. "I think we're past the point of tying compensation to the science," says Timothy Rieser, a legislative aide who works for Leahy on Agent Orange issues. "The U.S. government has by its actions accepted the likelihood that some people were severely affected. And the question now is, How can we best address that?"

Son, formerly of Committee 33, agrees that humanitarian aid should prioritize disabled people in the hotspots, including Da Nang, Bien Hoa and other sprayed areas. "I think $21 million is a good step for the U.S. government," he says. "But it isn't enough."

In an e-mail exchange with me, a spokesperson for Monsanto neither confirmed nor denied any contamination or possible health effects from exposure to the defoliant. It noted that the Monsanto that manufactured Agent Orange was a former company and that the current company only shares the same name. Furthermore, the spokesperson added, "U.S. courts have determined that the contractors who manufactured Agent Orange for the government are not responsible for claims associated with the military use of Agent Orange because the manufacturers were government contractors

carrying out the instructions of government." The spokesperson declined to comment on whether dioxin could have transgenerational effects. Dow Chemical, in an e-mail, said it would not address my questions; a statement on the company's Web site asserts that the U.S. government "specified how Agent Orange would be produced and then subsequently controlled its transportation, storage and use."

In Stellman's view, "chemical companies and a large segment of the U.S. government" would prefer that health problems in Vietnam never be linked conclusively to Agent Orange. On the other hand, she says, "the Vietnamese see just about every birth defect in their country as being caused by Agent Orange exposure. Both sides, however, are off base. Some birth defects in Vietnam are likely attributable to Agent Orange, but the degree to which that's true now is not a question that science can answer. There still hasn't been a definitive study."

ABOUT THE AUTHOR(S)

MORE TO EXPLORE

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Children of Vietnam, a nonprofit aid group: **www.childrenofvietnam.org**

FROM OUR ARCHIVES

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