



AGENT ORANGE:

The 50-Year History & the Newest Chapter of Concerns

Wendi Dick, MD MSPH FACPM, Terra D. Irons, PhD, Terry L. Walters, MD MPH, and Michael R. Peterson, DVM MPH DrPH
 Post-Deployment Health Strategic Healthcare Group, Office of Public Health, Veterans Health Administration,
 Department of Veterans Affairs (VA), Washington, DC, USA

Use in Vietnam

The United States conducted a tactical herbicide program during the Vietnam War to remove foliage that provided enemy cover. Agent Orange [a 1:1 mixture of 2,4 dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T)] was the most widely used "Rainbow Herbicide" in these missions. From 1961-1971, millions of gallons of herbicides were sprayed in Vietnam by the Army (Army Chemical Corp) and the Air Force (Operation Ranch Hand). It was later discovered that many of these herbicides were contaminated with the toxic compound 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD).

Policy Decisions

With concern growing over potential health risks of Agent Orange in Vietnam, Congress passed the "1991 Agent Orange Act" in the absence of exposure data. The Act specified that Vietnam Veterans who served anytime between January 9, 1962 and May 7, 1975 are *presumed* to have been exposed to herbicides. This applies to any Veteran who stepped foot in Vietnam during the war, served on ships that traveled inland waterways (Brown Water Navy), or was on duty in the Korean demilitarized zone between April 1, 1968 and August 31, 1971. An estimated 2.6 million Veterans served in-country during the war and are presumed exposed. Recently, the Institute of Medicine (IOM) concluded that exposure could not be reasonably determined for Veterans whose ships did not enter the inland waterways (Blue Water Navy) (1). As a result, VA policy did not change and Blue Water Veterans seeking compensation are considered on a case-by-case basis.

Recent Concerns: Post-Vietnam C-123 Aircraft

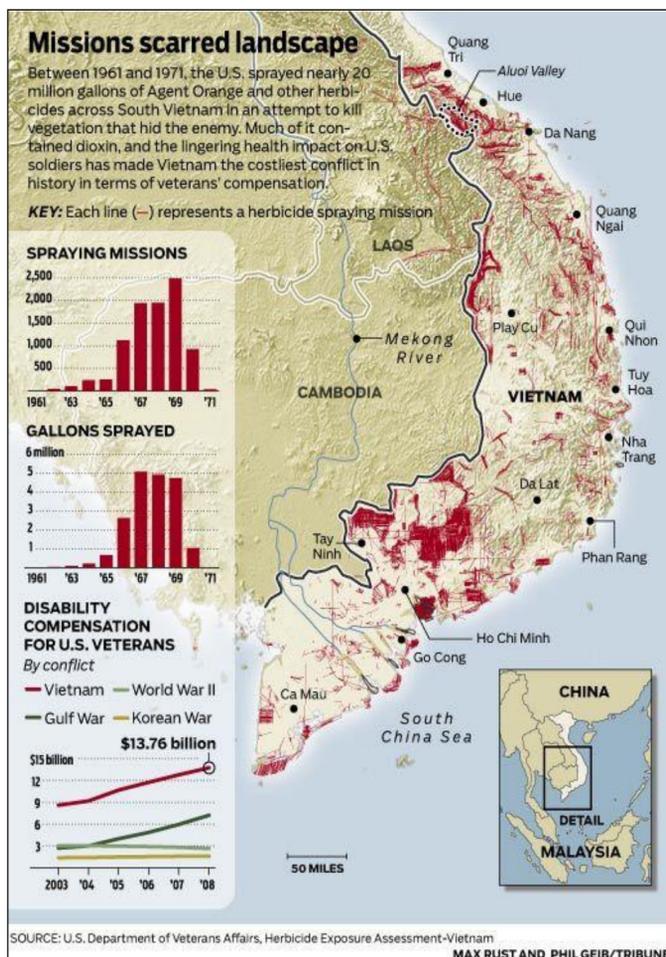
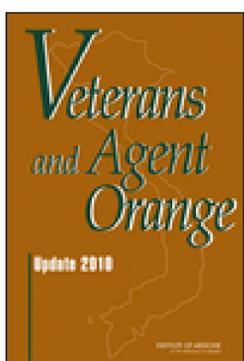
C-123 aircraft were used by the U.S. Air Force and Coast Guard to spray Agent Orange in Vietnam. At the end of the spraying campaign, some planes were reassigned to reserve units for routine cargo and medical evacuation missions spanning the next 10 years. The Air Force sampled a number of these aircraft and detected components of Agent Orange, including TCDD. Some Reservists who flew on these aircraft after their use in Vietnam spray missions have raised concerns about exposure to residual herbicides.

Risk Assessment of Post-Vietnam C-123 Aircraft

- Exposure = concentration present + bioavailability
- Air Force sampling reports – conducted between 1979 and 2009
 - Air contamination – herbicides detected in 1979 (335.5 µg/m³); no dioxins detected in any report
 - Surface contamination – mean herbicide concentration = 589 µg/m² (4 planes); mean dioxin concentration = 116.03 ng/m² (5 planes; 1400 ng/m² on 1 sample from "Patches")
- Routes of Exposure
 - Oral – the most likely route for TCDD to enter the body in this case. This would be due to accidental ingestion from hand-to-mouth contact.
 - Dermal – although residue may be transferred to the skin from the surface of the plane, TCDD does not readily cross human skin (2).
 - Inhalation – the least likely contributing route one year after spraying missions due to rapid drying of Agent Orange droplets, movement via wind, and removal of contaminated dust via decontamination efforts after returning from Vietnam.

Summary and Future Work

VA will continue to monitor the health outcomes of Vietnam Veterans and other Veteran populations who may have been exposed to Agent Orange. Likewise, IOM will conduct biennial Agent Orange literature reviews for VA as mandated by law through 2014. Disability claims from Veterans who are currently ineligible for benefits via presumed exposure will continue to be reviewed on a case-by-case basis, including Reservists who flew C-123 aircraft formerly used to spray herbicides in Vietnam. VA takes the exposure concerns of Veterans very seriously, and will carefully review new sources of information on exposures and health outcomes as they become available.



Properties of TCDD

- Odorless, white crystalline solid
- Melting point > 300°C; very stable
- Highly lipophilic – persistent in soil and the body; insoluble in water (requires an organic solvent carrier)
- Rapidly broken down in the environment when not bound to a biological surface (via photodegradation, microbial degradation, etc.) (3)
 - atmospheric half-life: about 1 hr
- Daily human intake = 50 pg from food, air and water (4)
- Absorption studied in rats 3 days after dosing with TCDD via 3 routes: oral, dermal, and inhalation (5)
 - Major storage depots: liver (33%), adipose tissue (15%), skin (4%), muscle (1%), first-pass elimination (27%)
 - Absorption and body burden: pulmonary (inhalation) > gastrointestinal (oral) >> dermal
- Acts as a tumor promoter by multiple mechanisms; toxicity initiated by binding to the aryl hydrocarbon receptor (AhR)
 - US EPA – Group B2 "probable human carcinogen"
 - IARC – Group 1 "carcinogenic to humans"

Health Outcomes of Exposure

IOM reviews the scientific literature (mainly epidemiology studies) on a biennial basis to assess associations between herbicide exposure and health outcomes (originally mandated by PL 102-4 and extended by PL 107-103). These associations fall into four categories: sufficient evidence of an association, limited or suggestive evidence of an association (chance, bias, and confounding cannot be ruled out), inadequate or insufficient evidence to determine an association, and limited or suggestive evidence of no association. The following outcomes were listed in "Veterans and Agent Orange: Update 2010" (6):

Category	Disease/Condition			
Sufficient evidence of an association	soft-tissue sarcoma	non-Hodgkin's lymphoma	chronic lymphocytic leukemia	
	Hodgkin's lymphoma	chloracne		
Limited/suggestive evidence of an association	laryngeal cancer	cancers of the lung, bronchus, or trachea	prostate cancer	
	multiple myeloma	AL amyloidosis	early-onset peripheral neuropathy	
	Parkinson's disease	porphyria cutanea tarda	hypertension	
	ischemic heart disease	type 2 diabetes (mellitus)	spina bifida in offspring	
Inadequate/insufficient evidence to determine an association	cancers of the oral cavity, pharynx, or nasal cavity	cancers of the pleura, mediastinum, and other sites in the respiratory system and intrathoracic organs	esophageal cancer	
	stomach cancer	colorectal cancer	hepatobiliary cancers	
	pancreatic cancers	bone and joint cancer	melanoma	
	non-melanoma skin cancer	breast cancer	cancers of reproductive organs	
	urinary bladder cancer	renal cancer	cancers of brain and nervous system	
	endocrine cancers	other types of leukemia	cancers at other and unspecified sites	
	infertility	spontaneous abortion	neonatal or infant death and stillbirth in offspring	
	low birth weight in offspring	other birth defects in offspring	childhood cancer in offspring	
	neurobehavioral disorders	other neurodegenerative diseases	chronic peripheral neuropathy	
	hearing loss	respiratory disorders	gastrointestinal, metabolic, and digestive disorders	
	immune system disorders	circulatory disorders	endometriosis	
	effects of thyroid homeostasis	eye problems	bone conditions	
	Limited/suggestive evidence of no association	spontaneous abortion (paternal exposure)		

In 1978, VA created the Agent Orange Registry for Veterans concerned about potential exposure, which includes approximately 500,000 Veterans to date. VA currently offers disability compensation for conditions listed in the "sufficient evidence of an association" and "limited or suggestive evidence of an association" categories designated by the IOM, with the exception of hypertension. A recent study, however, found no elevated adverse health outcomes in Veterans from Operation Ranch Hand (7).

Selected References

1. IOM. Blue Water Navy Vietnam Veterans and Agent Orange Exposure. National Academies Press, 2011.
2. Weber et al. (1991) *Arch Toxicol* 65: 421-428.
3. Young et al. (2004) *Environ Sci Pollut Res Int* 11: 359-370.
4. Travis and Hattemer-Frey. (1982) *Chemosphere* 16:2331-2342.
5. Diliberto et al. (1996) *Toxicol Appl Pharmacol* 138: 158-168.
6. IOM. Veterans and Agent Orange: Update 2010 (Eighth Biennial Update). National Academies Press, 2011.
7. Buffler et al. (2011) *Ann Epidemiol* 21: 673-687.



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For more information on Veterans and Agent Orange exposure, please visit:
www.publichealth.va.gov/exposures/agentorange