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Discussion Articles

Environmental Fate and Bioavailability of Agent Orange and Its Associated Dioxin During the Vietnam War

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Abstract

Background. In 1996, the Committee on the Assessment of Wartime Exposure to Herbicides in Vietnam of the National Academy of Sciences' Institute of Medicine (IOM) issued a report on an exposure model for use in epidemiological studies of Vietnam veterans. This exposure model would consider troop locations based on military records; aerial spray mission data; estimated ground spraying activity; estimated exposure opportunity factors; military indications for herbicide use; and considerations of the composition and environmental fate of herbicides, including changes in the TCDD content of the herbicides over time, the persistence of TCDD and herbicides in the environment, and the degree of likely penetration of the herbicides into the ground. When the final report of the IOM Committee was released in October 2003, several components of the exposure model envisioned by the Committee were not addressed. These components included the environmental fate of the herbicides, including changes in the TCDD content over time, the persistence of TCDD and herbicides in the environment, and the degree of likely penetration of herbicides into the ground. This paper is intended to help investigators understand better the fate and transport of herbicides and TCDD from spray missions, particularly in performing epidemiological studies.

Methods. This paper reviews the published scientific literature related to the environmental fate of Agent Orange and the contaminant, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), and discusses how this affected the potential exposure to TCDD of ground troops in Vietnam. Specifically, the mechanisms of dissipation and degradation as they relate to environmental distribution and bioavailability are addressed.

Results. The evaluation of the spray systems used to disseminate herbicides in Vietnam showed that they were capable of highly precise applications both in terms of concentrations sprayed and area treated. Research on tropical forest canopies with leaf area indices (a measure of foliage density) from 2 to 5 indicated that the amount of herbicide and associated TCDD reaching the forest floor would have been between 1 and 6% of the total aerial spray. Studies of the properties of plant surface waxes of the cuticle layer suggested that Agent Orange, including the TCDD, would have dried (i.e., be absorbed into the wax layer of the plant cuticle) upon spraying within minutes and could not be physically dislodged. Studies of Agent Orange and the associated TCDD on both leaf and soil surface have demonstrated that photolysis by sunlight would have rapidly decreased the concentration of TCDD, and this process continued in shade. Studies of 'dislodgeable foliar residues' (DFR, the fraction of a substance that is available for cutaneous uptake from the plant leaves) showed that only 8% of the DFR was present 1 hr after application. This dropped to 1% of the total 24 hrs after application. Studies with human volunteers confirmed that after 2 hrs of saturated contact with bare skin, only 0.15–0.46% of 2,4,5-T, one of the phenoxy acetic acid compounds that was an active ingredient of Agent Orange, entered the body and was eliminated in the urine.

Conclusions. The prospect of exposure to TCDD from Agent Orange in ground troops in Vietnam seems unlikely in light of the environmental dissipation of TCDD, little bioavailability, and the properties of the herbicides and circumstances of application that occurred. Photochemical degradation of TCDD and limited bioavailability of any residual TCDD present in soil or on vegetation suggest that dioxin concentrations in ground troops who served in Vietnam would have been small and indistinguishable from background levels even if they had been in recently treated areas. Laboratory and field data reported in the literature provide compelling evidence on the fate and dislodgeability of herbicide and TCDD in the environment. This evidence of the environmental fate and poor bioavailability of TCDD from Agent Orange is consistent with the observation of little or no exposure in the veterans who served in Vietnam. Appreciable accumulation of TCDD in veterans would have required repeated long-term direct skin contact of the type experienced by United States (US) Air Force RANCH HAND and US Army Chemical Corps personnel who handled or otherwise had direct contact with liquid herbicide, not from incidental exposure under field conditions where Agent Orange had been sprayed.

Keywords: Agent Orange; dislodgeable foliar residues; forest canopy penetration; herbicide dispersal; Operation RANCH HAND; serum TCDD; TCDD exposure; Vietnam

Introduction

From 1962 to 1971, herbicides were sprayed in Vietnam to defoliate the jungle canopy and destroy crops to deny opposing forces strategic cover and food. Spraying was also done to clear tall grasses and bushes from the perimeters of US and allied base camps and outlying fire-support bases. The most widely used herbicides were the phenoxyacetic acids, 2,4-dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T). The herbicide 2,4,5-T was found in Agents Orange, Purple, Pink, and Green; the latter three being used only during the testing and trial phases in 1962–1964. The herbicide picloram (4-amino-3,5,6-trichloropicolinic acid) was combined with 2,4,-D as the active components of Agent White. Cacodylic acid (hydroxydimethyl arsine oxide) was the active component of Agent Blue. Only the herbicides containing 2,4,5-T were contaminated with 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD).

1 Background

In 1996, the Committee on the Assessment of Wartime Exposure to Herbicides in Vietnam of the National Academy of Sciences' Institute of Medicine (IOM) issued a report entitled, "Characterizing Exposure of Veterans to Agent Orange and Other Herbicides Used in Vietnam: Scientific Considerations Regarding a Request for Proposals for Research" [1]. In that report, the IOM Committee described an exposure model for use in epidemiological studies of Vietnam veterans. This exposure model was to consider: troop locations based on available military records; aerial spray mission data; estimated ground spraying activity; estimated exposure opportunity factors; military indications for herbicide use; and considerations of the composition and environmental fate of herbicides, including changes in the TCDD content of the herbicides over time, the persistence of TCDD and herbicides in the environment, and the degree of likely penetration of the herbicides into the ground.

The final report of the IOM Committee was released in October 2003 [2]. However, several components of the exposure model envisioned by the Committee in its 1996 report were not addressed. These components included the environmental fate of the herbicides, including changes in the TCDD content over time, the persistence of TCDD and herbicides in the environment, and the degree of likely penetration of herbicides into the ground. This paper reviews the scientific literature related to the environmental fate of Agent Orange and the contaminant TCDD and discusses how this affected the potential exposure of combat ground troops in Vietnam to TCDD. Specifically, the mechanisms of dissipation and degradation as they relate to environmental distribution and bioavailability are addressed. This information is critical to a better understanding of how troops and others may have been exposed to herbicides and associated TCDD from spray missions.

2 Herbicide Spraying in Vietnam

2.1 Development of spray equipment

The United States Air Force (USAF) was responsible for training aircrews, developing aerial tactics for herbicide missions, and developing, testing and evaluating the aerial spray equipment used in Vietnam. The development, testing and evaluation of the spray equipment were conducted mainly at Eglin Air Force Base, Florida, and to a lesser degree at the Pran Buri Calibration Grid in Thailand. Responsibility for the selection of the defoliant rested with the US Army at Fort Detrick, Maryland with cooperation of the US Department of Agriculture [3,4].

The spray equipment test and evaluation projects that occurred at Eglin AFB, Florida, have been recently described [4]. The extensive research into the design and testing of herbicide application equipment resulted in highly precise application systems. The aircraft selected by USAF for the RANCH HAND mission was the Fairchild-built C-123B 'Provider.' The aircraft was a high-wing, twin-engine assault transport with excellent maneuverability [3,4]. The aircraft was ideal for the aerial dissemination of herbicides because the high-mounted wings allowed convenient positioning of wing spray booms, and the large cargo compartment and load capacity were ideal to receive a large spray system for internal carriage [3,4]. The layout of the internal spray system and how it interfaced with the aircraft and loading requirements are provided in a schematic (**Fig. 1**).

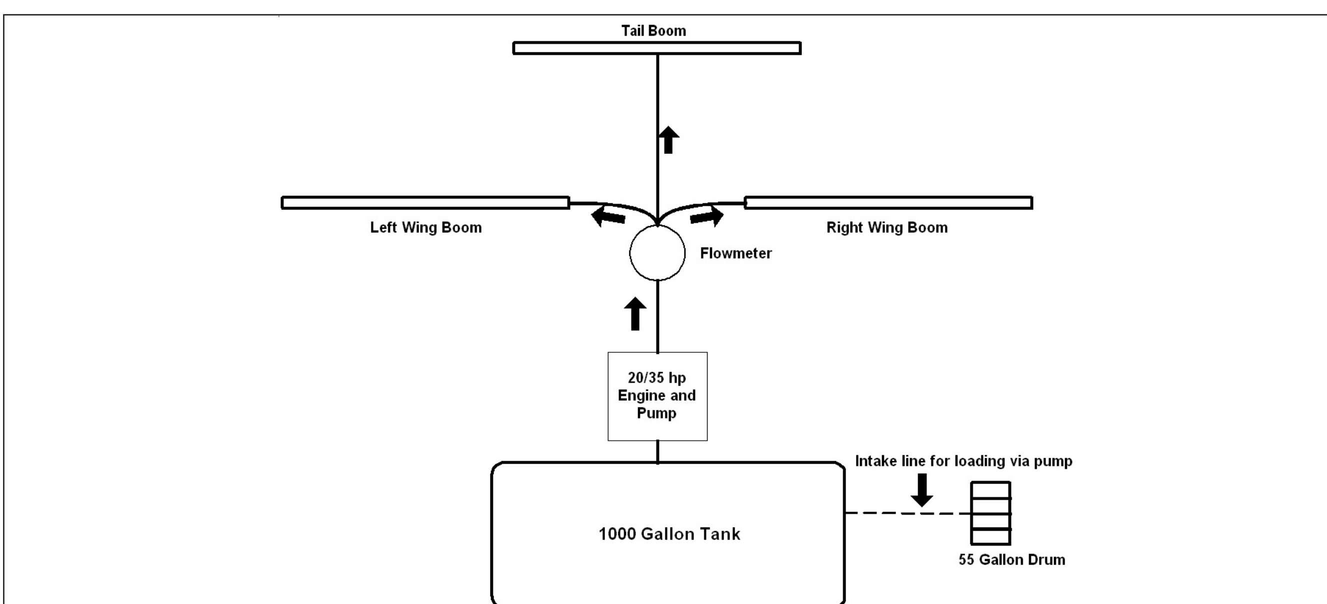

Fig. 1: A schematic of the C-123 'Provider' aircraft with internal spray system

Initially the MC-1 spray tanks, pumps, and spray booms were tested and deployed to Vietnam during the period of 1962–1964 [3,4]. This system was developed in the 1950s for the Korean Conflict but never deployed [3]. Its limitation was that it could only disseminate one-half the desired concentration rate (the minimum biologically effective deposition level), and thus required the aircraft to spray the same area twice to achieve effective defoliation [3]. In 1964, the Air Force developed and tested the AA 45Y-1 Internal Defoliant Dispenser [5]. The added pump and spray booms capacity of the AA 45Y-1 spray system allowed the UC-123 aircraft ('U' designated that the aircraft had been modified to spray herbicides) to make only one spray pass on the mission target in Vietnam [6,7]. Because of intense ground fire in the target area, this modification was critical to the survival of both the aircraft and the aircrews [7,8].

The unwanted dispersal of herbicide droplets by air turbulence was minimized by scheduling RANCH HAND missions only in favorable weather conditions and by controlling droplet size. For actual field application in Vietnam, Agent Orange was most effective in defoliating when applied to target vegetation while the wind was calm (i.e., less than 10 knots), in the absence of precipitation, and at ambient air temperatures near 29°C [7,8]. These operational weather requirements proved critical to mission effectiveness and safety, and were consistently enforced, often resulting in cancellation or retargeting of missions due to unacceptable weather [8].

The responsibility for ensuring that a RANCH HAND mission was either conducted, cancelled, or an alternate target selected rested with the Forward Air Controller (FAC) and the Tactical Air Control Center (TACC) [9]. The procedures implemented by the US Air Force and the US Army, and the role of the FAC to ensure that friendly forces were not in the target area, are described in an accompanying article in this issue [10].

RANCH HAND missions achieved optimum defoliation by flying at 130–140 knots at an altitude of 35–50 meters above ground level (AGL), depending on the vegetation and terrain [7,8]. The UC-123/AA 45Y-1 Spray System was used in more than 90% of the defoliation and crop destruction missions during the Vietnam War. The system consisted of 16 nozzles on each wing boom and eight nozzles on the tail boom. The nozzles were designed to produce a median spray droplet size of 320 to 350 µm. Indeed, 22% of the particles were 500 µm or greater, 76% were between 100 and 500 µm, and only 2% were less than 100 µm [6,11]. Thus, 98% of the droplets produced were greater than 100 µm, resulting in a rapid settling velocity [6,11]. A full tank of herbicide contained 3,600 liters (with 200 liters remaining in the spray system) and was sprayed in approximately 3.5 to 4 min over a spray swath 80 m wide (±6 m) and 14 km in length, for total area coverage of 130 ha [3,7,8]. The total deposition per m^2 was, on average, approximately 2.9 ml.

2.2 Deposition patterns from aerial spray equipment used in Vietnam

As described above, the evaluation of the spray systems used to disseminate herbicides in Vietnam showed that they were capable of highly precise applications both in terms of concentrations sprayed and area treated. The occurrences of grossly excessive deposits could only be attributable to an emergency drop, which rarely occurred [7,8]. A spray swath is depicted schematically (**Fig. 2**, adapted from Flynn) [5]. The line segment between A and F is the effective spray swath, the area that received "the minimum biologically effective ground deposition level" of herbicide. The line segments GA and FG are areas that would receive biologically effective deposition of herbicide if two airplanes, flying in close formation, both treated the areas. The line segment between B and E shows the portion of the spray profile that delivered a biologically effective deposition level. One of the goals of

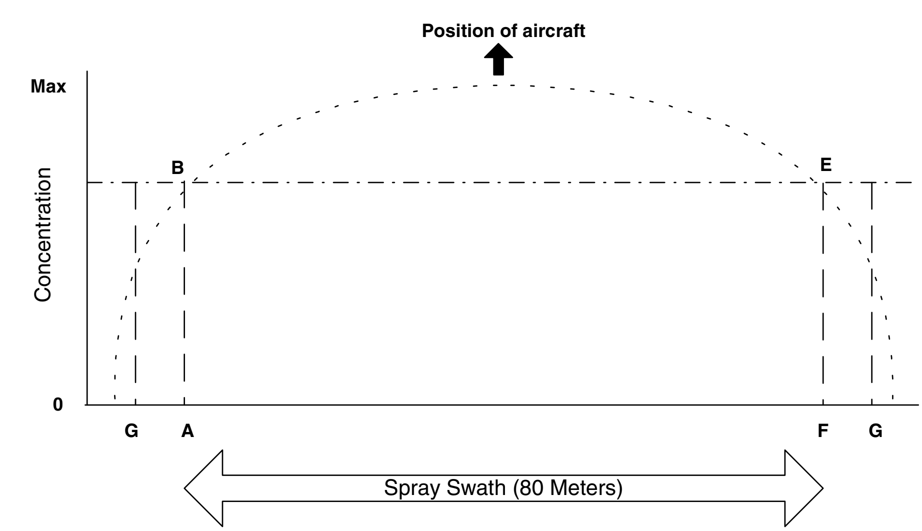

Fig. 2: A schematic cross-section of a deposition concentration profile perpendicular to the direction of flight. The spray system was the A/A45 Y-1 Internal Defoliant Dispenser interfaced with the UC 123 aircraft [adapted from Flynn, 5]. Dashed horizontal line is biologically effective concentration; dotted line is applied concentration

designing the spray systems was to minimize the area of the deposition profile above BE since this represented wasteful excess application of herbicide.

Tests at Eglin AFB, FL showed that 87% of the herbicide would have impacted the vegetation within one minute and within or near to the swath [11]. The remaining 13% of the herbicide took longer to settle due to vortices at the wing tips, drift, or evaporation [11]. Calculations made using Stokes law show that even the <100 µm size droplets, would have a settling velocity of over 30 cm/sec indicating that the droplets would likely have impacted the vegetation less than 3 minutes after spraying. Since spray missions were always undertaken in calm or near-calm wind conditions there was not time for significant lateral movement or 'spray drift.' Any significant lateral movement of spray would require the materials to remain in the air for extended periods of time and they would therefore have been subject to rapid degradation by ultraviolet light (see Section 4.2).

Multiple aircraft were always used to apply herbicide, with the planes flying in close formation to ensure a continuous area of defoliation (**Fig. 3**). The wingmen typically flew so that the pilots could maintain position on the aircraft ahead of them. Forty three percent (43%) of the RANCH HAND spray missions consisted of three aircraft. Just over 70% of the missions consisted of three aircraft or less, although formation of eight and even twelve aircraft occurred beginning in 1967 [8,12]. The total area treated was usually less than one-half km in width and, assuming that the contents of all the tanks were expended, slightly more than 14 km in length.

Review of spray swath information suggested that dissemination of herbicide in Vietnam was very precise and resulted in a pattern of long narrow deposition areas with little herbicide outside the treatment area [13]. This conclusion is supported by biomonitoring data and by drift tests conducted by Taconi and Jones [14]. Application of a variety of products using various technologies that emitted similar drop size spectra provide a comprehensive picture of deposition downward in forested terrain [13,15].

Concentrations of herbicide greater than the biologically effective threshold resulted in defoliation, while concentrations slightly less than the biologically effective threshold resulted in deformed foliage and growing tips by stimulating unequal growth among plant tissues, resulting in slight discoloration [3]. Visual evidence of the precision with which herbicides were applied can be seen in **Fig. 4**.

This aerial photograph displays the very sharp lines of demarcation along the spray swaths in the very sensitive *Avicennia* and *Ceriops* mangroves in Vietnam. Had there been significant drift either way from the swath, traces of

Fig. 4: Aerial photograph taken in 1967 showing the defoliation spray swaths made by three RANCH HAND aircraft in the mangrove region of III Corps. In this instance, the aircraft did not fly in close formation to ensure a continuous area of defoliation. The swaths showed sharp lines of demarcation between treated foliage and untreated foliage. Photo courtesy of the RANCH HAND Collection, Vietnam Archives, Texas Tech University, Lubbock, TX

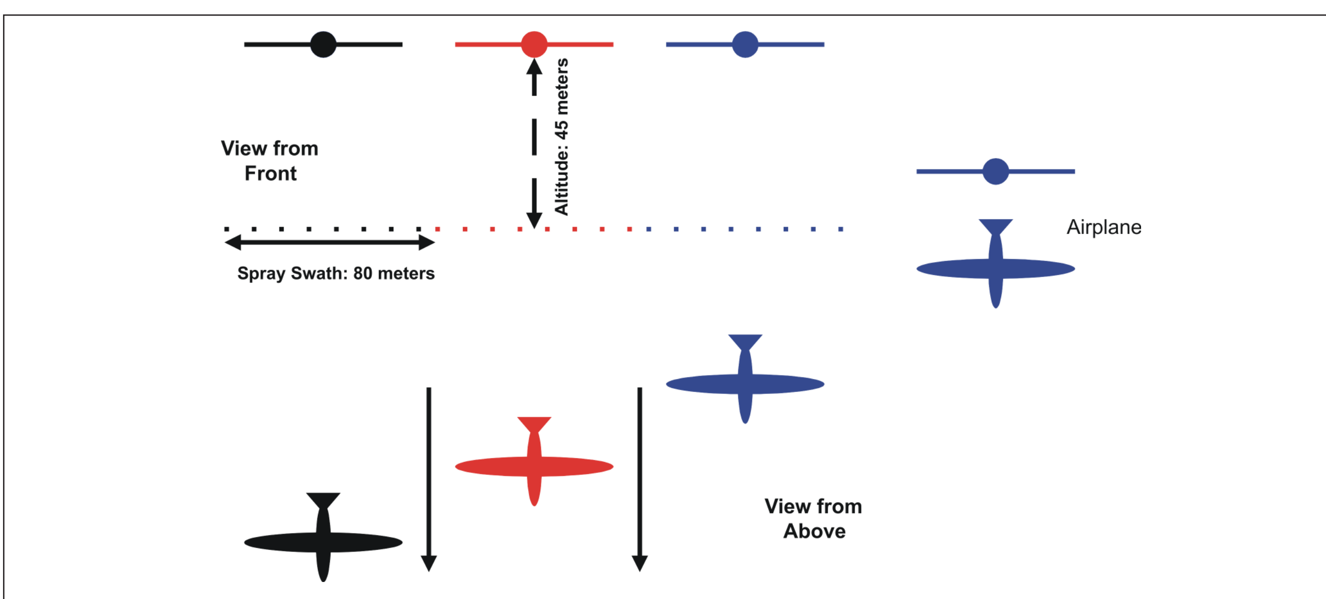

Fig. 3: A schematic of a typical three-airplane spray mission

Fig. 5: Aerial photograph taken in 1968 in III Corps over a mangrove forest sprayed in the Rung Sat Special Zone along the main ship channel to Saigon. Photo courtesy of the RANCH HAND Collection, Vietnam Archives, Texas Tech University, Lubbock, TX

damage would have been visible as streaks of discolored foliage adjacent to the downwind swath margin. Even if wind movement had occurred along the swath, the swaths were long enough that almost any deviation from perfect alignment with the swath would have shown damage away from the swath margin. Other pictures of a spray mission also illustrate the sharp lines of deposited herbicide in a mangrove forest (**Fig. 5**). The second approach in **Fig. 5** is at an angle of 90° to the first.

2.3 Base perimeter spraying

Defoliation by helicopter and ground spraying operations were the responsibility of the US Army Chemical Corps. Helicopter applications were flown at much lower speeds and altitudes and backpack and vehicle-mounted spray systems were effectively used at very low speeds and at ground level [7]. The relatively small proportion of military herbicides applied by these other methods (5% of the total applied [16]) posed less potential for drift than fixed wing applications. These methods did, however, create perhaps the greatest exposure situation for human applicators [17,18,19]. Even such very heavy dermal contact as occurred in these situations still resulted in a large safety factor [17]. Herbicide residues were demonstrated to be difficult to dislodge soon after the spray dried, and workers in sprayed forests were shown to be unlikely to sustain measurable exposure through their clothes [19].

3 The Forest Canopy and the Leaf Area Index

Forests generally have several layers or canopies of foliage structured to receive sunlight and convert it into chemical energy. When gaps occur between leaves, new leaves tend to grow into the spaces where the 'escaped' sunlight can be captured. The amount of sunlight, rain, or herbicide that is intercepted by a forest canopy depends on the density of the vegetation [19]. In a multi-canopy forest, such as in Vietnam, the topmost layer of the canopy receives the largest percentage, and each canopy layer underneath the top layer intercepts a successively smaller portion.

Foliage density can be quantified as a leaf area index (LAI), defined as the total leaf area in proportion to the ground surface below. For example, a value for the LAI of 2.0 means that there are two square meters of leaves per square meter of ground surface. The LAI is used for calculations involving photosynthesis, carbon absorption, and oxygen exchange and to define the amount of canopy penetration by light, rain, or herbicides [19,20,21].

Research has confirmed that the LAI reliably estimates the interception in the forest canopy of aerial herbicide applications such that each unit of LAI intercepts about half of the herbicide that reaches it. Stated mathematically, deposition is equal to deposit reaching the upper canopy times $2^{-(LAI)}$ [19]. A tropical forest with a LAI of 5 is thus likely to intercept about 97% of the total spray. Stems, branches and trunks will generally increase the amount of herbicide intercepted in the forest canopy since they represent lateral deposition surface not accounted for in the leaf area index [19,22]. Total interception by foliage and stems may range up to 99% [22]. In view of the role of ultraviolet light in destruction of TCDD, the interception of light in the same gradient is of considerable importance.

More than half of the Vietnamese jungle subjected to spraying operations was double and triple canopy jungle characterized by dense and diverse tree species [23]. Agent Orange was the herbicide of choice to apply to mature or secondary forests with LAI values ranging from 2 (open secondary) to 5 (mature forest). As the LAI increases, the proportion of applied herbicide intercepted by the foliage increases as well. In relatively undisturbed dense forests, the target canopy with an LAI of 3–5 would nearly always intercept 87–97% of the herbicide sprayed. Vegetation below the canopy receives 3–14% of the spray, with the higher percentage resulting in those areas where the forest was sparse. The underbrush or forest floor received about 1–6% of the total aerial spray [19,22]. These observations, taken together, indicate that little of the Agent Orange and associated TCDD would have penetrated directly to the soil and to any organisms on the ground. Rather, both the Agent Orange and TCDD would have been held on the surfaces of leaves until they fell to the ground. While some Agent Orange might have been washed from the leaves during strong rainfall events, the more lipophilic TCDD would have been less likely to be washed from the waxy surface of the leaves.

The ester formulations of herbicides, such as the n-butyl ester of 2,4-D and 2,4,5-T used in the Agent Orange formulation, exhibited greater herbicidal activity than the parent acids because of improved foliar absorption [24]. The herbicide 2,4,5-T was most effective when applied as the n-butyl ester because of rapid absorption into the leaf surface. Once inside the leaf surface, both the butyl esters of 2,4-D and 2,4,5-T were readily degraded (within hours) through transesterification and β oxidation [24].

3.1 Spray penetration and deposition of particles in forest canopies

Scientists from the US Department of Agriculture studied the penetration and distribution of herbicide sprays through forest canopies in Puerto Rico and Texas [22]. Although the two areas were widely separated geographically, the forests were similar in terms of structure. The test site in Puerto Rico was typical of moist forest formation. The lowest level of vegetation ranged from 2 to 3 m; the intermediate level had a mean height of 9 m; and, the upper canopy had a mean height of >15 m. In Texas, the forest had a dense and relatively unbroken overstory of post and blackjack oak about 12 m in height. The youpon undercanopy also was dense and relatively unbroken (about 5 m in height), but LAI was probably considerably less than that of the Puerto Rico site.

Spray materials were applied from aircraft and from fixed delivery systems. The aircraft were calibrated to deliver 37 L/ha (the UC-123/AA 45Y-1 Spray System used in Vietnam delivered 28 L/ha) at a speed of 65 knots and 5 m above the canopy. The fixed delivery system was mounted on a cableway 5 m above the top canopy, and it was also calibrated to deliver 37 L/ha.

Tests from the fixed cableway and from aircraft provided comparable results. The volume of spray deposited at various levels of the canopy varied with the type of spray material, the type of nozzle, and the nozzle angle. However, variation in volume was not great. The volume of spray reaching lower sampling levels varied proportionately with the amount deposited on the top line above the canopy. On average, about 21% of the spray volume penetrated the upper canopy and about 6% penetrated to the ground level in the experiments conducted in Texas [22].

Similar results were observed in forest brush field ecosystems in the Oregon Coast Range that were aerially treated with glyphosate [20]. Deposits were recorded at various canopy levels to determine interception and residues in foliage, litter, soil, streamwater, sediments and wildlife. The vegetation intercepted nearly all of the applied herbicide with most of the herbicide retained in the tree layers. The authors concluded that most of the herbicide reached its target and then "disappeared rapidly in the moist deciduous forest [20]."

4 Environmental Fate of Agent Orange and TCDD

4.1 Studies of Agent Orange jettisons, storage and disposal sites

From January 1962 to January 1971, RANCH HAND aircraft flew more than 19,000 combat sorties (a sortie is one aircraft mission) in support of defoliation and crop destruction missions [16,25]. In December 1986, the US Army and Joint Services Environmental Support (ESG) [26] released an update of records on helicopter and ground spraying missions, aborts, leaks, and incidents. Included in the category of 'incidents' were instances where RANCH HAND missions ended with emergency jettisons, most of which were considerably less than a full tank. The herbicide was jettisoned in a large diameter stream rather than nozzles in approximately 35 sec (versus 3.5 to 4 min for dissemination during a standard mission) [27]. ESG (now the US Armed Services Center for Research of Unit Records) found records of 48 emergency jettisons/incidents involving Agent Orange/Purple. Eighteen involved the jettison of herbicide at the end of a runway, over jungle or water. Twenty-seven were emergency jettisons that occurred in the target box – three involved aircraft crashes. Therefore although these emergency herbicide dumps may have resulted in increased soil herbicide concentrations, they represented only one quarter of a percent of the total missions flown.

In 1971, a team of scientists from a committee of the National Academy of Sciences (NAS) collected and analyzed five soil samples from an area in Vietnam where 3,700 liters of Agent Orange had been jettisoned in December 1968. No 2,4,5-T herbicide could be detected. However, no analytical methods at the time were sensitive enough to detect small concentrations of TCDD [23, 28]. Additional soil studies conducted in Vietnam and the Philippines by the same NAS team using operational rates of herbicide treatment (i.e., rates similar to those applied by RANCH HAND aircraft, but directly to the soil) found the half-life of 2,4,5-T was short (5 days), and that of 2,4-D was 2 days [28]. Moreover, the team was able to grow several phenoxy-sensitive and locally important vegetables within six weeks of application at rates applied operationally.

These data are consistent with residue studies conducted in 1970 on the spray equipment test site at Eglin AFB, Florida, after receiving repeated aerially applications of Agent Orange (a total of 17,900 liters or approximately 9,500 kg of 2,4,5-T and 9,500 kg of 2,4-D) from January to December 1969 [4,29]. Soil bioassay studies on herbicidal persistence and soil leaching were initiated in April 1970. By considering that all the phytotoxic effects on the bioassay organisms were from 2,4-D and 2,4,5-T, the greatest residue concentration of phenoxy herbicides (in the top 15 cm of soil) was estimated to be 2.8 mg/kg (ppm) (average of 8 soil cores). A follow-up bioassay experiment was conducted eight months later. These bioassays confirmed the rapid disappearance of the herbicides since the phytotoxic effects were less than 0.3 mg of phenoxy herbicides/kg of soil (ppm). Analytical studies of the 14 soil cores collected in December 1970 showed average residues of 8 µg of 2,4-D/kg of soil (ppb) and 4 ppb for 2,4,5-T [4,29].

Recently, the presence was reported of 'high levels' of TCDD in sediment and soil samples in Vietnam [30,31]. Neither reported finding residues of 2,4-D or 2,4,5-T, but did report soil concentrations of TCDD of 0.6 to 1.2 mg TCDD/kg soil (ppm). The source of these samples *was not* from aerial applications of Agent Orange, but rather from highly localized soil on or adjacent to the former Agent Orange storage site at Bien Hoa Air Base north of Ho Chi Minh City. More than 200,000 208-liter drums of Agent Orange were sent to Vietnam and disseminated in spray programs [32]. Sixty-five percent of these drums were sent to Bien Hoa to support RANCH HAND and US Army Chemical Corps Operations from March 1964, when Agent Orange first arrived in Vietnam, to March 1972, when the remaining inventory was re-drummed, removed and sent to Johnston Island in Operation PACER IVY [32]. These data are consistent with studies of Agent Orange storage and disposal operation sites at the Naval Construction Battalion Center, Gulfport, Mississippi, and Johnston Island, Central Pacific Ocean [33,34]. More than 15,000 208-liter drums of Agent Orange were stored at Gulfport, from 1969–1977, and more than 25,000 drums of Agent Orange (the inventory removed from Vietnam) were stored on Johnston Island from 1972–1977. To find such deposits in Vietnam required specific knowledge of location of leaking drums or jettison sites. None of these reflected general distribution of residues available to the general population of soldiers or citizens, and they cannot be used for general exposure indices.

Both inventories of herbicides were destroyed by at-sea incineration in 1977, and a monitoring program was initiated at both locations in January 1978 [33]. Studies of soil residues of 2,4-D and 2,4,5-T confirmed the rapid disappearance (degradation) of the herbicides over a four-year period (1978–1982). In both locations the level of herbicides dramatically decreased from a maximum of 62,000 mg/kg (ppm) (8 samples taken from the top 10 cm of soils from spill sites) to less than 2% of the initial concentration remaining at the end of the 4 years. In the same sampling period and sample sites, the TCDD concentrations decreased from 180 mg/kg (ppm) to less than 100 mg/kg (ppm) (45% loss in 4 yrs). The loss of herbicides and TCDD was attributed to microbial degradation, and volatilization with subsequent photodegradation [33,35]. Both the storage sites were sampled in 1987 (10 yrs after the removal of the drums), and levels of TCDD in composited soil samples ranged from 0.6 to 1.0 mg/kg (ppm) [36].

4.2 The environmental fate of TCDD

Various routes have been proposed for the disappearance of TCDD from the environment. From numerous field and environmental studies conducted on Agent Orange and its associated TCDD in Mississippi, Utah, Kansas, Florida, and Johnston Island, the mechanisms most likely responsible for TCDD disappearance included photodegradation, volatilization, microbial degradation, wind and water movement of contaminated particles, and biomass removal [4,29,33,37]. Of these, the role of sunlight (ultraviolet light), and the subsequent dechlorination of the TCDD molecule, was deemed the most important [4].

Studies of the photodegradation of polychlorinated dibenzo-*p*-dioxins and polychlorinated dibenzofurans associated with herbicide application have featured experiments that consider the variables influencing fate processes. Most notable are the experiments of Crosby and colleagues, 1973–1983 [38–43], Bentson in 1989 [44], Schuler and colleagues in 1998 [45], and Konstantinov and colleagues in 1999 and 2000 [46,47].

The principal processes that control the fate of nonpolar organic substances such as TCDD deposited on foliage include tissue absorption and adsorption or dissipation by evaporation, and photodegradation. These processes are initiated at the leaf-atmosphere interface. At the leaf surface the cuticular waxes represent a physiologically distinct layer where the fate processes are influenced. The properties of waxes of the leaf cuticle vary among plants, and as a result, influence the relative propensities of the different fate processes [48].

The results of the above studies suggest that Agent Orange, and associated TCDD, would have been absorbed into the wax layer of the leaf cuticle within minutes of spraying and could not then be physically dislodged. TCDD adhering to or absorbed in these organic plant surfaces would be destroyed by light within a few hours or longer depending on the level of sunlight. Because the deposit of herbicide and associated TCDD would decrease with leaf area index, and the radiation intensity decreases at the same rate, the absolute dissipation rate should be similar at all levels of the canopy. Should residues have persisted until humans made contact, the presence of a non-polar organic solvent capable of holding TCDD in solution, e.g., an ester of a phenoxy herbicide, would provide an energy barrier in contact with an aqueous medium such as human skin. This would have greatly restricted transfer of TCDD to that person.

A relatively small proportion of the TCDD might be absorbed more deeply into the plant before degradation, where it would become bound and biologically unavailable [19,24]. Some sunlight and ultraviolet radiation may penetrate within the plant. What is not decomposed, however, would not be mobile in the plant or readily dislodged. While a small amount of TCDD might have evaporated from foliage before degradation this TCDD would experience rapid photodegradation, the same fate as the herbicide dispersed in the atmosphere during application [49]. Due to photolysis by sunlight, the atmospheric half-life of TCDD in the vapor phase has been shown to be in the order of 1.0 hr [50,51]. From experimental studies investigating only the OH radical oxidation of TCDD, the atmospheric lifetime of TCDD was about 3 days [52].

When Agent Orange was spread on leaves and exposed to natural sunlight, the half-life of its TCDD content was less than 6 hr [40]. Photodegradation would continue with additional exposure to sunlight, destroying half of any remaining TCDD every 6 hours of full daylight. When Agent Orange was applied to loam soil and exposed to sunlight, degradation of TCDD "was somewhat slower, presumably because of shading of lower layers by soil particles." The requirements for photodegradation of TCDD were: dissolution in a light-transmitting film or material, the presence of a hydrogen-donor (such as herbicide or the waxy cuticle), and ultraviolet light [40,41].

Concentrations of TCDD in rangeland grasses following application of 2,4,5-T herbicides decreased rapidly in outdoor sunlight [53]. Photodegradation of TCDD on a number of surfaces and at a range of light intensities has also been demonstrated [44]. This work showed that the decomposition of TCDD continued in reduced light at a reduced rate (cloudy days and in shade). Generally, the reduced light levels contain the same wavelengths as direct sunlight at roughly equally reduced intensities, including the ultraviolet wavelengths that degrade TCDD. Relatively rapid disappearance of TCDD from leaves was confirmed even under low light conditions [54]. A half-life of 7 to 10 hrs was observed even when ultraviolet light intensities were low. Photodegradation continued even in the absence of a hydrogen-donor, with more than 90% of TCDD degraded after 7 days of exposure to ultraviolet light, showing that water vapor can also serve as a hydrogen donor.

Because herbicide spray missions were scheduled in the early morning on days when there was no precipitation, applications of Agent Orange were typically followed by several hours of sunlight [7,8]. Since liquid Agent Orange itself transmits ultraviolet light and is an excellent hydrogen-donor, photodegradation of TCDD in Agent Orange would have proceeded rapidly and would have occurred even in the relatively shady forest understory, though not as rapidly as in direct sunlight. The resultant defoliation of upper canopy layers would permit penetration of additional sunlight increasing the degradation of TCDD in understory vegetation.

Studies of the effect of waxy cuticle of plants on the degradation of dioxins and furans have shown that photodegradation processes continue at a significant rate even in the absence of herbicide adjuvants or carrier solvent, which may not be available as a result of plant absorption or evaporation over time [45]. When the dioxins and furans were incorporated into the leaf waxes of laurel cherry (*Prunus laurocerasus*), photodegradation was relatively unhindered. This is important since the tropical overstories in wet or dry tropics tend to have thick leaves and waxy cuticles. From these experiments, at least half of the starting amount of each of the dioxins and furans, which included 2,3,7,8-TCDD and 2,3,7,8-tetrachlorodibenzofuran, were degraded within an 8-hr exposure to actual sunlight. During the time that it would take for leaves to die and fall from trees, it would be expected that most of the TCDD would be degraded. For instance, in 4 days with average duration of light of 12 hr, less than 2% of the original TCDD would remain on the leaf surface.

Almost all of the Agent Orange would have been intercepted by the forest canopy or photodegraded on plant and ground surfaces. Only a very small proportion of the TCDD would have penetrated the canopy and reached the ground or understory where personal contact would be made. TCDD is relatively persistent and immobile once bound to soil [4]. If TCDD in soil becomes exposed to sunlight due to soil tilling or other disturbances it will degrade by photolysis [40], but forest soils are seldom tilled. Since a person is most likely to encounter surface soil, it would tend to have negligible TCDD levels because sunlight reaches the surface soil, and subsurface residues would not be readily available for contact. In addition, the principal manner of movement of TCDD in soil is by volatilization and re-adsorption. As TCDD volatilizes at the soil surface and enters the air it degrades by photolysis, if it has not already degraded on the surface [55].

Studies conducted with TCDD deposited on soil using spray equipment on the testing grids at Eglin AFB, Florida, demonstrated that photodegradation during and immediately after application destroyed nearly all of the TCDD in the herbicides applied on the test site. Once below the soil surface, the low residues of TCDD (in the absence of herbicide) remained confined in the top 15 cm for at least 14 yr following application of 32,500 kg of 2,4,5-T [4].

As a result of the very low solubility of TCDD in water and strong binding to soil, including bottom sediments, surface water was not determined to be a major contributing source of exposure to TCDD. Typically, TCDD was not detectable in streams or ditches adjacent to areas in the United States where 2,4,5-T was used repeatedly [54]. However, TCDD can be briefly present in surface water bound to floating particles of soil [33,37,56]. Such TCDD would be exposed to sunlight near the surface of the water and degrade within a few hours or days [38,40,57,58]. TCDD also volatilizes from rivers and ponds, with half-lives of approximately 6 and 32 days, respectively [58]. Once volatilized, TCDD photodegrades very rapidly in the atmosphere, with a half-life of less than 1 hr [58].

The above references to TCDD dissipation rates and influences thereon by environmental factors do not properly reflect on dislodgeability of TCDD from the medium on which residues are held. Research indicates that TCDD has a very strong tendency to adsorb to surfaces [69]. Affinity for surfaces removes TCDD from solution rapidly, and also logically retains very strongly residues held in foliage and litter. Removal of TCDD from bound residues most likely requires either considerable energy or organic solvents, neither of which normally accompany human contact with a TCDD-retaining substrate. In the absence of specific data on transferability of bound residue to animal tissue, logic dictates that physiological dosages from such contact would be below detection limits unless the deposit were still liquid immediately after deposition.

5 Applicable Animal and Human Studies of TCDD

5.1 Animal skin absorption studies

Studies examining the dermal uptake of TCDD by rat skin have demonstrated variability in dermal uptake, depending on the age of the animal. For the oldest animals, more than 80% of an applied dermal dose could be removed either by swabbing the application site, or it was bound to the skin at the application site [59]. In one of the few studies to use dermal application of soil to assess availability, TCDD in various test formulations (including soil) was applied to naked rat skin. Application of TCDD in soil to skin reduced penetration into skin, presumably because of almost instantaneous adsorption to mineral surfaces. Soil treatment reduced penetration of TCDD to the liver from 14% observed for organic solvent applications to less than 0.1% [60].

5.2 Human skin absorption studies

The fraction of a residue that is available for cutaneous uptake from the surface of plant leaves is called the 'dislodgeable foliar residue' (DFR) [61]. For chemicals that are absorbed into plant tissues, this fraction decreases as the chemicals penetrate into the leaves. The DFR is usually determined by a gentle washing of the leaf surfaces to determine the amount of chemical that reasonably could be expected to be adsorbed by human skin [61]. The DFR decreases as chemicals penetrate into the leaf tissue and are no longer 'accessible.' No information is available on DFR values for TCDD or Agent Orange. However, for 2,4-D applied to turf grass, the DFR was 8% of the total plant residue 1 hr after application [62]. This DFR was reduced to 1% of the total 24 hr after application. Only three of five human subjects who exposed bare skin to the 2,4-D treated turf accumulated any uptake of the herbicide. In addition, these three individuals were all exposed only 1 hr after the herbicide application. No residues were detected in any subjects exposing bare skin to the treated turf 24 hr after application.

Given its greater hydrophobicity, we would anticipate that the DFR for TCDD would decrease at least as rapidly as that of 2,4-D. Therefore, these results demonstrate that even 24 hr after application essentially no TCDD residues would be available from herbicide treated leaf surfaces.

The rate of skin absorption of a 2,4,5-T herbicide containing commercially acceptable dioxin levels ($<10^{-7}$) was investigated by applying the herbicide to 900 cm^2 areas of skin on volunteers [17]. The concentrations applied were representative of commercial applications at the time, ranging from 2.4 to 38.4 g/L of acid equivalent 2,4,5-T as an ester emulsified in water. After 2 hr of saturated contact with a large area of bare skin, only 0.15–0.46% of the 2,4,5-T penetrated the skin, entered the body, and was eliminated in the urine. Applications of the greatest concentrations of 2,4,5-T resulted in the highest absolute penetration, but in the least proportion of 2,4,5-T applied. Although TCDD was not measured penetrating the skin directly, other evidence suggests that TCDD penetrates with about the same proportion as observed with 2,4,5-T [63]. The lack of liquid with which the residue would be transferred to the skin in a forest exposure surely reduces transfer even further.

5.3 Contamination of food and potential ingestion

From the previous discussion, it appears that the potential for ingestion of TCDD was very small in Vietnam. However, ingestion needs to be considered as a potential pathway since it has been shown to be a major route of human exposure to dioxins [64]. Although food denial through destruction of crops in enemy-controlled areas was a goal of Operation RANCH HAND, it was unlikely that food crops sprayed with Agent Orange were consumed by ground troops. Food crops were sprayed well in advance of harvest before they matured [7,8]. Susceptible (broadleaf) species wilt quickly and would have been destroyed before consumption. Moreover, the phenolic smell of the butyl esters of 2,4-D and 2,4,5-T was offensive and its presence on food would make it unappealing and unpalatable [37].

5.3.1 Contamination of crops

The most important crop in Vietnam was rice, and the bulk of the crop destruction effort was directed at the rice harvest. Rice growing was concentrated in low-lying coastal 'rice bowls,' many of which were in the eastern coastal areas [7,8]. Agent Blue, which contained no 2,4,5-T or TCDD, was used for destruction of rice crops since rice is not susceptible to Agent Orange [7,8]. Indeed, because 2,4,5-T is so highly species-selective, it has been widely used on maturing rice fields to control weeds without harming the rice crop [28].

Even consumption of crops sprayed by mistake shortly before harvest would be unlikely to result in intake of a significant amount of TCDD. Herbicide and TCDD residues would generally be found on the exterior husk or skin, not the interior edible portion of a crop [65,66]. Any such exterior residues would be reduced by photodegradation in sunlight or would be removed with the outer vegetation layers before consumption. The uptake of TCDD in grass and rice has been studied, and no TCDD residues were found in rice grain from crops heavily treated with 2,4,5-T [53].

Uptake of TCDD through plant roots has been found to be extraordinarily low in the few circumstances where it could be measured, and little or no TCDD residue has been found on plant leaves above ground level or in plant seeds [37, 53,66,67]. Given the restrictions placed on the herbicide spray program to avoid damage to friendly crops, there was little possibility of significant TCDD contamination of agricultural fields in friendly regions and, as discussed above, even less probability of human exposure through consumption of food crops.

5.3.2 Contamination of food animals

Livestock and other animals were generally not significantly exposed to TCDD by application of Agent Orange for the same reasons as humans: the herbicide was largely intercepted in the forest canopy, and TCDD photodegraded rapidly in the environment, dried quickly and became non-dislodgeable, or bound strongly to soil. Animals that grazed naturally or were fed from fields treated with Agent Orange would have been expected to accumulate only minimal residues of TCDD in their tissue based on studies of forest herbivores in a hardwood forest aerially treated with a butyl ester of 2,4-D and 2,4,5-T [68]. The likely source of trace levels of TCDD in some herbivorous animals is the incidental ingestion of contaminated soil. Indeed, examination of the ecological niches of animal species containing TCDD residues in the Eglin AFB studies concluded that each of the species were in close contact with contaminated soil [4].

Accumulation of TCDD by aquatic animals is almost entirely dependent on concentrations in water or sediment [4,30,31,33,69,70]. Any TCDD would typically be found in sediments, and benthic, bottom-dwelling species that ingest substantial amounts of bottom sediment are more likely to have detectable levels of TCDD [4]. Studies at Eglin AFB, Florida, confirmed that bottom-feeding fish in ponds in the contaminated test areas had concentrations of 85 ppt TCDD in their guts and 4 ppt in muscle tissue [4]. Similar results were obtained in Bien Hung Lake, a lake receiving contaminated soil from the former Agent Orange storage site at Bien Hoa Air Base, Vietnam [30].

5.3.3 Assimilation after ingestion

Upon ingestion, organic contaminants such as TCDD must be assimilated from the food items into the human body before they can reach sites of toxic action. Contaminants that are tightly bound to the food matrix or ingested soil can be less efficiently assimilated by the body. For this reason, a significant proportion of an ingested dose does not enter the body. It passes harmlessly through the digestive system. The efficiency with which dioxins are assimilated in animals varies with the chemical, the food or soil type, and the species of animal. For example assimilation efficiency for TCDD for environmentally contaminated soils ranged from a maximum of 63% to a minimum of only 0.5% with an average of 31% [71]. Therefore, in these animals less than one third of the ingested TCDD actually entered the body, with the majority of the dose being excreted in the feces. In contrast, dietary absorption of TCDD from food in humans seems to be nearly complete [64,72] due to the more complete digestion of the foods consumed. Little or no data are available on the assimilation of TCDD from soil in humans.

5.3.4 TCDD in Serum

Testing of serum dioxin levels has been widely regarded as the 'gold standard' for epidemiological studies of Agent Orange and dioxin since its development in the 1980's [73]. Although such testing is expensive, the major industrial studies since the 1980's have employed it to validate various methodologies for estimation of exposure. Many more studies simply relied upon serum TCDD levels to measure exposure to dioxin-containing materials. While the passage of time complicates the use of serum TCDD results, it remains the best possible evidence of an historical absorbed dose of TCDD. Its superior predictive power has been confirmed repeatedly [73].

5.3.5 Studies of Vietnam Veterans

Numerous studies relying on serum dioxin testing have demonstrated that some RANCH HAND and Army Chemical Corps veterans involved in the application of Agent Orange in Vietnam absorbed doses of dioxin that can still be distinguished decades afterwards [74,75]. Similar studies of ground troops have not found elevated levels of dioxin, providing strong evidence that these troops were not significantly exposed to dioxin from Agent Orange [76].

The 1988 serum dioxin study by the Centers for Disease Control and Prevention (CDC) compared levels of serum TCDD in 646 US Army veterans who served as ground troops in the most heavily sprayed regions of Vietnam with those of 97 Vietnam-era veterans who had not served in Vietnam [76]. The distributions of TCDD levels were 'nearly identical' in the two groups, both having means and medians of about 4 ppt TCDD. Neither military and spraying records nor self-reported history of exposure could reliably identify high or low exposure groups, and "most US Army ground troops who served in Vietnam were not heavily exposed to TCDD, except perhaps men whose jobs involved handling herbicides" [76].

These results were consistent with other studies. A planned epidemiological study of ground troops and Agent Orange was discontinued as infeasible. Subsequent CDC investigations of health effects in ground troops focused on whether the overall 'Vietnam experience' increased the risk of cancer or other diseases [77,78,79,80]. These studies identified a number of health effects associated with military service in Vietnam. Other studies examined whether such effects were related to secondary indicators of possible exposure to Agent Orange [81,82]. No such relationships were found.

6 Conclusions

The prospect of significant exposure to TCDD from Agent Orange to ground troops in Vietnam seems unlikely in light of the environmental fate of TCDD, low bioavailability, and the properties of the herbicides and the application circumstances that occurred. Photochemical degradation of TCDD and the limited bioavailability of any residual TCDD present in soil or on vegetation lead to the expectation that dioxin levels in ground troops who served in Vietnam would be low and indistinguishable from background levels even if they had been in recently treated areas. Agent Orange was applied as small droplets that absorb into plant tissue or dried very quickly. It has been reported that after three hours it was not possible to detect any 2,4,5-T rubbed from foliage onto cloth patches while walking through forests aerially sprayed with 2,4,5-T [18].

A very narrow window of time – typically a few minutes – was available after spraying before drying. An individual making contact with treated vegetation while wearing almost any clothing at the point of contact would not be in personal contact. The amount of TCDD actually absorbed due to a single exposure would be extremely small even if contact had occurred. Once Agent Orange and TCDD dried on plant surfaces and the TCDD became bound, it was unlikely for the residue to have become bioavailable thereafter. If it was adsorbed onto woody plant tissue sufficiently that sunlight was blocked, it was not bioavailable.

The Centers for Disease Control and Prevention reported that serum concentration of TCDD in over six hundred veterans judged likely to have been exposed to Agent Orange in Vietnam were the same serum TCDD levels as those veterans who never served in Vietnam [76]. Levels of TCDD did not increase with greater likelihood of exposure based upon military records or upon self-reported exposure. This failure to distinguish serum TCDD levels in ground troops with the highest potential for exposure at a time reasonably close to cessation of exposure highlights that exposure reconstructions based upon analysis of military records are poor predictors of actual absorbed dose.

To absorb dioxin from Agent Orange, direct skin contact with liquid Agent Orange would have been necessary. Those Vietnam veterans who had elevated serum levels of TCDD had direct contact with the liquid herbicide and were involved in part of the RANCH HAND operation or were in the Chemical Corps who also handled Agent Orange in Vietnam [74,75,82].

The experimental laboratory and field data summarized here provide compelling evidence on the fate and dislodgeability of herbicide and TCDD in the environment. This evidence of the environmental fate and low bioavailability of TCDD from Agent Orange is consistent with the observation of little or no exposure in the vast majority of Vietnam veterans. Appreciable accumulation of TCDD would have required repeated long-term direct skin contact of the type experienced by RANCH HAND and Chemical Corps, not incidental exposure under field conditions where Agent Orange had been sprayed.

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