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tion. The longitudinal investigation is continuing under the aegis of the National Institute for Occupational Safety and Health (NIOSH). Recently, another case was diagnosed at a facility in northern Missouri where butter flavoring is manufactured. Suspicion of the causal agent being the flavoring was focused in an animal study performed using rats exposed for 24 hours to the flavorings, which produced severe upper and lower airway changes in the animals.<sup>1</sup>

Diacetyl (2,3-butanedione) is a commonly used food flavoring and also occurs naturally in butter, coffee, and bay oil. It forms the essential oil of butter and butter flavorings and has not previously been described as toxic when inhaled.<sup>2</sup> Diacetyl is not listed in the most commonly used occupational guide to workplace chemical hazards, the *NIOSH Pocket Guide to Chemical Hazards*.<sup>3</sup>

Clearly, these early series of cases are of significance in inferring causality. The relative risk of a few former employees out of a total of approximately 400 is much higher than would be expected for the occurrence of bronchiolitis obliterans in the general population, which has been estimated to be between 1:40,000 and 1:100,000.<sup>4</sup> The effect seems to be seen only in the current and former employees of a popcorn packaging facility and not in the general population of the surrounding county. There was consistency of results of testing by different and independent investigators. Furthermore, a temporal and physical correspondence and a biologic plausibility exist by both analogy of other chemicals and preliminary animal tests. Therefore, the Hill Criteria are fulfilled.<sup>5</sup>

We believe these cases represent a new and potentially lethal occupational pulmonary disease, Popcorn Packers' Workers' Lung. We would encourage all occupational health care providers to monitor employees who work in and around food flavorings by obtaining baseline and periodic values. Any eye, upper respira-

tory, and pulmonary symptoms among these workers require investigation. Unless exposure is stopped and therapy is initiated early on, the changes may be rapidly progressively and irreversible. Good industrial hygiene practices, including engineering projects to improve ventilation, provide personal protective equipment, and reduce exposure to the suspect agents should be urged. If any such cases are identified, the state public health department and NIOSH should be notified immediately.

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#### **A Follow-Up: High Level of Dioxin Contamination in Vietnamese From Agent Orange, Three Decades After the End of Spraying**

*To the Editor:* This is an update of our findings of current dioxin contamination of Vietnamese from Agent Orange phenoxyherbicide, last applied over 30 years ago. Agent

Orange, half 2,4-D and half 2,4,5-T phenoxyherbicides, contaminated with an average of 3 parts per million (ppm) of 2,3,7,8-tetrachlorodibenzo-p-dioxin, or TCDD, was very heavily sprayed in the south of Vietnam between 1962 and 1971 during the US-Vietnam war, with the heaviest spraying between 1967 and 1971.<sup>1,2</sup> The blood from 43 Bien Hoa residents sampled between 1999 and 2001 in the heavily sprayed southern Vietnamese city of Bien Hoa (population 390,000; located 35 km north of Saigon which is now known as Ho Chi Minh City) has now been analyzed for dioxins. These were from a convenience sample of men and women aged 16 to 71 years who were willing to donate over 60 mL of whole blood as part of a Vietnam Red Cross dioxin survey. Comparison blood from Hanoi, where no Agent Orange was used, was also analyzed ( $n = 105$ ). Except for the dioxin contaminant characteristic of Agent Orange, 2,3,7,8-TCDD, no other dioxins or dioxin-like chemicals were elevated. In the case of TCDD, elevated levels were defined as above 5.0 ppt, lipid-normalized. Of the 43 persons, 41 (95%) had elevated TCDD. Comparison blood from Hanoi had an average level of approximately 2 parts per trillion (ppt) TCDD, whereas the range in Bien Hoa varied from 2.4 to a very high 413 parts per trillion (ppt), with a median of 67 ppt, as shown in Table 1. The high value (413 ppt) represents a 206-fold increase above the Hanoi TCDD baseline level. Although Agent Orange was sprayed in Vietnam between 1962 and 1971, an underground spill of Agent Orange also occurred in 1971 at the nearby storage facility at Bien Hoa Air Base. Elevated TCDD was found in children and adults born in this southern region of Vietnam and in northern Vietnamese who recently moved to the area.

Because almost all dioxin body burden comes from ingestion of contaminated animal fat, the findings are almost certainly attributable to the

consumption of dioxin-contaminated fish and other animal products.<sup>3,4</sup> The markedly elevated levels of TCDD from fish samples of the 1970s are presented to support this hypothesis, as seen in Table 2. Very elevated TCDD levels from Agent Orange exposure were found, ranging from 18 to 810 ppt.<sup>5,6</sup> These levels are much higher than current US fish dioxin levels of 0.03 ppt to 1.43 ppt, in our recent findings.<sup>7,8</sup> These Vietnam fish levels represent approximately a 12- to 27,000-fold excess above the recently reported US fish dioxin levels. In the 1970s, human milk levels of TCDD were recorded in the 200 to 1850 ppt range.<sup>2,9</sup> Food from the south of Vietnam sampled in the 1980s had somewhat higher levels of dioxin than did northern food but was not as contaminated with dioxins as the earlier Vietnam fish samples.<sup>10,11</sup> Be-

cause government authorities did not permit food collected between 1999 and 2001 to be taken from Vietnam for dioxin analysis, we have no current food dioxin data from Bien Hoa. Dioxin levels in fish and other Vietnamese food are obviously a very sensitive issue with respect to visitors to Vietnam or to food exportation.

We previously reported very elevated TCDD, in nearby soil where a spill of Agent Orange occurred on the Bien Hoa Air Base (as high as 1 million ppt), and elevated TCDD in sediments in a nearby river.<sup>2</sup> These data suggest certain localized contamination of soil, groundwater, river sediment, and fish from the Agent Orange spill, in addition to contamination from sprayed Agent Orange.

The dioxin analyses for all seventeen 2,3,7,8 chlorine-substituted diox-

ins and dibenzofurans and three coplanar polychlorinated biphenyls were conducted by high-resolution gas chromatography-high resolution mass spectroscopy by a World Health Organization laboratory certified for analysis of dioxin congeners in blood, as previously described.<sup>12,13</sup>

The finding of elevated to very elevated levels of TCDD, the dioxin contaminant of Agent Orange, in almost all Vietnamese living in Bien Hoa city in the south of Vietnam who were sampled between 1999 and 2001 is almost certainly from current and previous dioxin contamination. The most likely route of exposure is from animal fats, especially fish. The proximity of the city to an air base used for Agent Orange storage and as a base for Agent Orange spraying missions strongly suggests the origin of the TCDD to be from the Bien Hoa Air Base. The

**TABLE 1**  
Vietnamese Blood Dioxin Levels Collected at Bien Hoa City, 1999 to 2001

Sample	Year of Birth	TCDD Level (ppt lipid basis)*	Sample	Year of Birth	TCDD Level (ppt lipid basis)
South Vietnam (individual samples)					
1	1962	2.4	23	1942	68.3
2	1950	3.4	24	1962	70.2
3	1952	5.1	25	1935	73.9
4	1962	5.6	26	1960	76
5	1980	5.7	27	1980	87
6	1942	7.1	28	1985	91
7	1950	7.8	29	1962	101
8	1930	20	30	1966	102
9	1947	21	31	1963	103
10	1939	22	32	1963	154
11	1955	23	33	1959	161
12	1955	24	34	1954	162
13	1942	29	35	1955	164
14	1955	30	36	1958	168
15	1982	35	37	1982	174
16	1955	38	38	1985	177
17	1952	39	39	1967	236
18	1979	50	40	1950	238
19	1981	57	41	1954	271
20	1981	62	42	1963	326
21	1983	63	43	1973	413
22	1958	67			
North Vietnam (individual samples)					
1	1930	1.6	4	1930	1.2
2	1924	1.9	5	1932	2.3
3	1939	1.4			
North Vietnam (pooled sample, n = 100)					
Hanoi	1959-79	2.2			

\* TCDD, 2,3,7,8-tetrachlorodibenzo-p-dioxin.

**TABLE 2**  
TCDD\* Levels in Fish and Shrimp From Southern Vietnam, 1970 to 1973

Sample	Location	TCDD Level (ppt wet weight)
Interior		
Carp ( <i>Cyprininae</i> )	Dong Nai River	540
Catfish ( <i>Siluridae</i> )	Dong Nai River	810
Catfish ( <i>Tachysuridae</i> )	Dong Nai River	520
Catfish ( <i>Schilbeidae</i> )	Saigon River	70
River Prawn ( <i>Palaemonidae</i> )	Saigon River	42
Ocean		
Croaker ( <i>Sciaenidae</i> )	Can Gio Village	79
Prawn ( <i>Peneidae</i> )	Can Gio Village	18

\* TCDD, 2,3,7,8-tetrachlorodibenzo-p-dioxin.

previously reported very high soil TCDD levels on small areas of the air base, elevated levels in nearby river sediment, and history of a spill of Agent Orange also point to this conclusion. The very elevated fish TCDD levels (Table 2) found in the past may be associated with very elevated breast milk TCDD (up to 1850 ppt TCDD, an approximately 925-fold elevation above current background levels) found in women in the same region.<sup>9</sup>

The very high percentage of people in the sample from Bien Hoa City (95%) with elevated to very elevated blood TCDD is noteworthy because Agent Orange was last sprayed in Vietnam 30 years before blood collection was done for this study. Because elevated levels were also observed in children born since spraying ended, in new residents formerly from the north where no Agent Orange was sprayed, and in soil and sediment in the southern location, this report documents the persistence of dioxins in the environment leading to uptake of dioxins three decades after the spraying ended.

The data here point out a serious public health issue for which action such as fish consumption advisories may well be indicated. Cleanup of contaminated soil or sediment may be slow and costly, but not eating foods identified as contaminated is an action that, at least in theory, can rapidly be taken with relative ease and at modest cost. Our data has been given to the

Environmental Agency and Ministry of Vietnam and the Health Ministry in Vietnam for their consideration and action.

The findings presented here also raise the issue of dioxin contamination of at least some Vietnamese food, now increasingly exported to other countries. Data such as those presented in this article suggest that some Vietnamese food is currently contaminated with relatively high levels of TCDD. Although we believe such hot spots of contamination in Vietnam are relatively rare because Agent Orange was sprayed in only certain areas in the south of Vietnam, further analysis of food from Vietnam is clearly indicated, whether the food is obtained in Vietnam or in countries to which it has been exported. We hope to work with the Vietnamese government and to do such sampling and analyses in the near future.

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