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CHLORACNE AND THE AGENT ORANGE PROBLEM IN THE U.S.A.
VIETNAM VETERANS

1. INTRODUCTION

In this talk I am giving my personal opinion and assertions and these are not to be construed as official or as reflecting the views of the Veterans Administration (VA).

Dott. B. M. Shepard regrets he was unable to be here. He would have talked about Federal Research Projects in progress at this time: the soft tissue sarcoma studies; the mortality studies; an analysis of suicides among Vietnam Veterans; the U. S. Environmental Protection Agency (EPA) adipose tissue studies for levels of dioxin and Communicable Disease Center (CDC) studies. Instead, I would like to tell you about the area where I work with the Chloracne Task Force, and that is the Agent Orange problem among United States Vietnam veterans.

2. VIETNAM CONFLICT AND THE AGENT ORANGE PROBLEM

During the Vietnam conflict it was decided to defoliate 30 meters on either side of the highways to prevent ambush by the enemy. The phenoxyacetic acid herbicides had been used in the U.S. and around the world in agriculture and forestry work for twenty years with no serious health effects, so it was decided to use a 50:50 mixture of the 2,4,5-Trichlorophenoxyacetic acid (2,4,5-T) and 2,4-dichlorophenoxyacetic acid (2,4-D) in South Vietnam to spray the jungles: leaves died in one or two weeks and fell in about two months. In that thick jungle Tschirley estimated that only 6% of the herbicide actually reached the ground (1). Agent Orange (as it was called because it was transported in 55 gallon drums with a bright orange band) was found later to be contaminated by the highly toxic 2,3,7,8- tetrachlorodibenzo-p-dioxin (TCDD); this is a byproduct of production. From inventory samples it's known that 2,3,7,8-TCDD was present in 47 p.p.m. in early supplies and 2 p.p.m. during the conflict (2). It is estimated that 368 lbs. of TCDD was distributed

in the jungle of South Vietnam between 1965 and 1971. At that time, spraying was discontinued as the South Vietnamese were reporting birth defects and other health effects while U.S. animal researchers were reporting wasting syndromes, birth defects and liver tumors (3).

In 1970, the U.S. veterans became increasingly alarmed that the health effects and birth defects in their children might be due to their exposure to Agent Orange in South Vietnam. So the President created an Agent Orange Policy Group, the Veterans Administration set up an Agent Orange Projects Office and an Agent Orange Registry. Any veteran throughout the country who felt he had a health problem from Agent Orange, could go to his nearest Veterans Administration Hospital and give a history of his exposure and have a complete physical examination. If he had a skin problem he would be referred to dermatology.

3. DIOXIN PROBLEM AND VETERANS ADMINISTRATION

In the meantime, in Europe and in America chemical analyses for dioxin had become more sensitive and 2,3,7,8-TCDD had been found in high levels in fish, and lower levels in contaminated rivers and lakes, in municipal incinerators, in flue gases and fly ash, in beef livers, in cow's milk and in mother's milk. Fat levels in humans in the U.S., Canada and Europe are at about 7-10 nano-grams per Kg. body weight. At the 5th International Symposium on Chlorinated Dioxins in Bayreuth, West Germany, September 16-21, 1985, Dott. Schecter looked at the levels in nine North Vietnamese and found no detectable TCDD, while in people from South Vietnam, the mean was about 22 p.p.t.(4) So what do these levels mean in humans? Most investigators agree that the most sensitive and specific marker of toxic absorption of dioxin in a human is a skin con-

dition: chloracne. Without chloracne no other toxic effects occur (5,6). If therefore the health problems of the U.S. veterans are due to Agent Orange these veterans would have to have chloracne. The Chloracne Task Force appreciated that chloracne is a rare occupational disease and few of the V.A. physicians had ever seen it. Therefore, the first thing that we did was to set up diagnostic criteria which were sent to the 172 Veterans Administration Hospitals in the U.S. The chloracne diagnostic criteria are listed in table I and were divided into four sections:

- | | |
|------------------------------------|-------------------------|
| 1) Essential (to make a diagnosis) | 2) Compatible Histology |
| 3) Acute Toxicity | 4) Chronic Toxicity |

The diagnostic criteria for chloracne following exposure to dioxin are:

(1) exposure to chloracnegens (2) onset or aggravation of acne within a few weeks to two months, rarely later (average one month after exposure) (3) acne with predominance of large open comedones characteristically with straw-colored cysts (no cysts in mild cases) (4) atypical distribution such as the malar crescent of the face, crow's foot area lateral to eyes and in and behind the ears (5) history of 1 thru 4 and scars in distribution of 4 or 4 and 6 (6) severe acne with 3 and 4, plus inflammatory lesions, cysts and abscesses, on the face, ears, behind ears, back, buttocks, scrotum, outer upper arms, chest and thighs (7) compatible histology: comedones with thickened epithelial lining, few P. acnes, squamous metaplasia of outer root sheaths of hairs and sebaceous glands, keratin-filled cysts.

The criteria 1 through 5 are essential to diagnosis and are the most sensitive specific markers for dioxin toxicity.

4. COMMENT ON DIAGNOSTIC CRITERIA

TABLE I
VETERANS ADMINISTRATION CHLORACNE TASK FORCE
CRITERIA FOR DIAGNOSIS OF CHLORACNE
2* to 2,3,7,8-TCDD EXPOSURE

ESSENTIAL

1. Exposure to chloracnogens
2. Onset or aggravation of acne within a few weeks to two months, rarely later (average one month after exposure)
3. Acne with predominance of large open comedones characteristically with straw-colored cysts (no cysts in mild cases)
4. Atypical distribution such as the malar crescent of the face, crow's foot area lateral to eyes and in and behind the ears
5. History of 1 thru 4 and scars in distribution of 4 or 4 and 6 below
6. Severe acne with 3 and 4, plus inflammatory lesions, cysts and abscesses, on the face, ears, behind ears, back, buttocks, scrotum, outer upper arms, chest and thighs. This may occur but is not essential to diagnosis.

COMPATIBLE HISTOLOGY

7. Comedones with thickened epithelial lining, few P.* acnes, squamous metaplasia of outer root sheaths of hairs and sebaceous glands, minimal or absent sebaceous glands, keratin-filled cysts.
8. Onset preceding or coincident with acne of
 - (1) nausea, vomiting, nose bleed, diarrhea, blood in urine
 - (2) headache, fatigue, irritability, insomnia, impotence, loss of libido (delayed onset of these symptoms years later is not an effect of dioxin)
 - (3) lower leg pains, numbness
 - (4) tingling and/or numbness in fingers and toes
 - (5) elevated liver enzymes
 - (6) bursitis, edema arms and legs
 - (7) weight loss
 - (8) triglyceridemia

CHRONIC TOXICITY

- (9) chronic bronchitis, decreased vital capacity
- (10) hypertrichosis on temples, hyperpigmentation of the face, no porphyrins
- (11) porphyria cutanea tarda (PCT) with porphyrins in urine and/or stool
- (12) peripheral neuropathy

* P. = Propionibacterium

1. Exposure to Chloracnegens

The subject must be exposed to a chloracne (aromatic chlorinated hydrocarbon compound) in order to develop chloracne. The substances which cause chloracne are: 1) Polychloronaphthalenes (PCN) 2) Polybromonaphthalenes (PBN) 3) Polychlorobiphenyls (PCBs) 4) Polybromobiphenyls (PBBs) 5) Polychlorodibenzofurans (PCDF) 6) Polybromodibenzofurans (PBDF) 7) 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) 8) others: 1,2,3,4-Tetrachlorobenzene, Dichlobenil (Casoran)-a herbicide, DDT (crude trichlorobenzene). The one in which the Veterans Administration is interested is 2,3,7,8,-TCDD, the contaminant in Agent Orange.

2. Onset of acne usually one month after exposure.

Some of the veterans developed their skin problems three years or more after they came back from Vietnam; these problems cannot be due to Agent Orange Exposure in Vietnam; such a long latent period is never seen.

3. Large open comedones and straw colored cysts are prominent.

(During this session Ms. Fischmann has shown about 20 slides of clinical cases indicating: 1) large open blackheads; 2) small white cysts; 3) dark blue-grey noses; 4) blue fingernails and toenails.

4. Atypical distribution is characteristic.

Such atypical distribution is either not seen or less prominent in acne vulgaris.

5. History of chloracne and scars in atypical distribution.

It had been previously believed that chloracne cleared within a few years of cessation of exposure. However, in 1984 Suskind reported a 30 year follow-up on the industrial accident in Nitro, West Virginia (7). An unexpected finding was persistence of chloracne in 55.7% of the workers initially involved (8). It followed that chloracne, if initiated in Vietnam after exposure to Agent Orange, could be present in 55.7% of those afflicted.

6. Severe acne with acute inflammation.

This may occur but is not essential to diagnosis. This severe form may be confused with cystic acne.

7. Compatible histology

There are very few bacteria because herbicide kills bacteria.

During the conflict, no cases of chloracne had been reported. We have looked very carefully among the veterans using the CTF diagnostic criteria and have found 13 cases of chloracne and the majority of these were in engineering corps.

The first case of chloracne was in a veteran who had been in Vietnam for one year in an engineering corps with no trouble on the skin. He was transferred to a special unit to clear highways. The unit travelled in trucks and camped along the roads without going back to base. One team with bulldozers would put all the dead foliage in a big pile and then another team would come from behind and burn it. So they would get exposed to smoke, which has a much higher concentration of dioxin. They lived very intimately with the soil, they just dug out holes and lived in those, so they must have been breathing in the soil (Fig.1). Dott. Young has said that it takes a few weeks after contam-

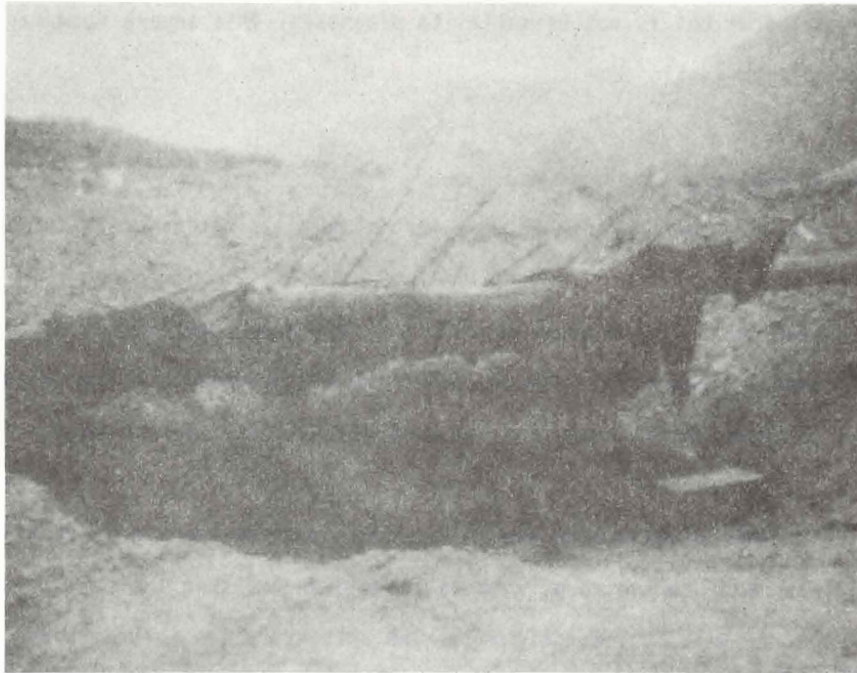


Fig.1 Shelter dug out of Agent Orange sprayed soil. Veterans living in intimate contact with 2,3,7,8-TCDD contaminated soil.

ination for dioxin to be irreversibly bound to the soil so, probably, they had been getting dioxin breathing in smoke and dust and/or eating contaminated food (9).

This veteran, a few weeks after he began his job of clearing roads developed very marked blackheads in the deep creases on the sides of his neck. This is known to occur on skin after chemical exposures. Shortly after he had many pale cysts, blackheads and abscesses on his cheeks, on and behind his ears, back and buttocks. He also had the characteristic clear nose of chloracne (10). In Vietnam his skin problem was diagnosed as cystic acne. In addition, during the acute onset of chloracne, he had headaches, nausea and vomiting, which ceased shortly after removal from exposure.

One veteran, in addition to chloracne, has chronic lesions on his leg. We biopsied that area and noticed that there were some atypical lymphocytes in the infiltrate of a chronic dermatitis. So we are watching it very carefully because there have been some reports in the U. S. and other countries (Report from Sweden not yet confirmed) of soft tissue sarcomas and lymphomas (11,12).

CONCLUSIONS:

It is not known at what blood or tissue level chloracne occurs. The concentration of dioxin in Agent Orange in Vietnam was very low (2 p.p.m.) which explains why chloracne was neither described nor seen in Vietnam during the conflict. Some cases of chloracne were diagnosed in Vietnam as cystic acne and other acnes. Some of the soil in the Missouri horse arenas, where dioxin contaminated salvage oil was sprayed to keep down dust, had concentrations of dioxin as high as 31.8 to 33 ug TCDD per gm. (ppm) (2). So perhaps the con-

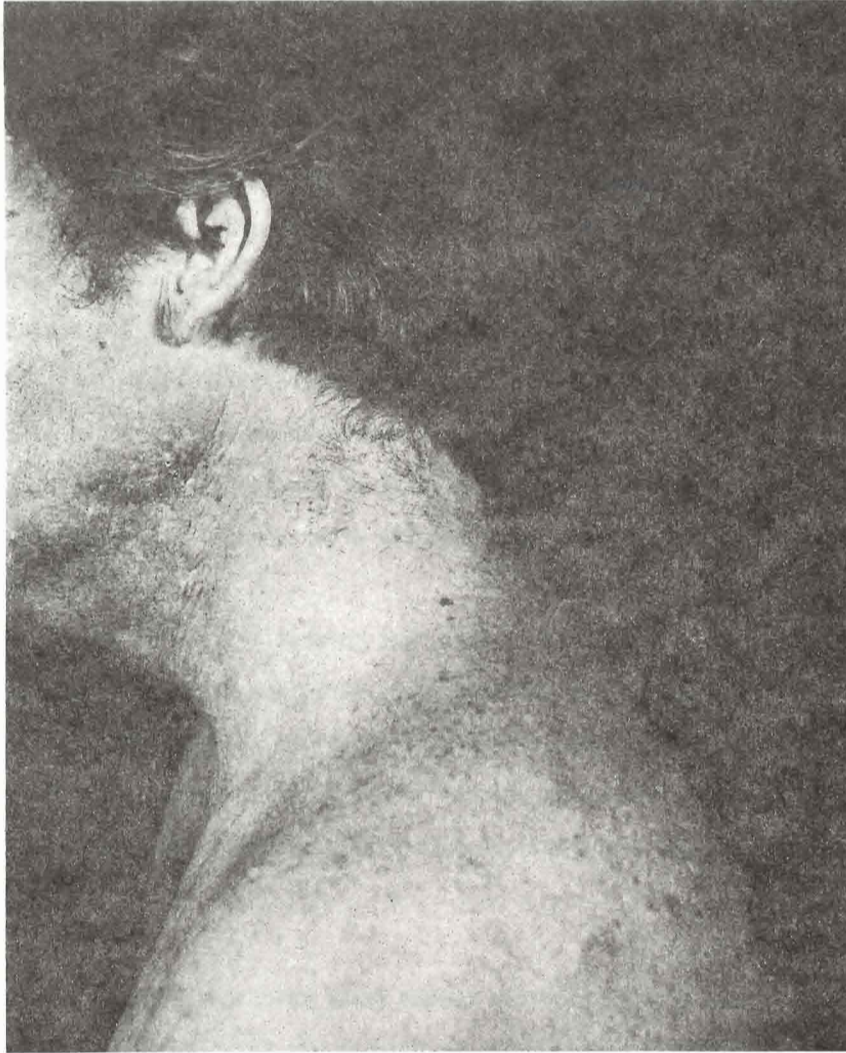


Fig.2 First U.S. Vietnam veteran with chloracne. Seventeen years after exposure to 2,3,7,8-TCDD from Agent Orange sprayed soil, comedones and striking, extensive, 1 to 2 mm pale cysts in neck creases, on and behind ears, shoulders and back are still present. Diagnosis in Vietnam: severe cystic acne vulgaris.

centration in Vietnam was too low to create toxic problems except in a few special instances, where the veterans were contaminated from soil and smoke. The studies on the pilots and technicians who flew on the spraying missions show no major health adverse effects in the veterans (13) and the birth defects study shows no major problems (14). So it would seem that there have been very rare cases of toxicity effects in U.S. veterans, only thirteen veterans with chloracne among the 33,512 studied. It requires further data to know if cancer will be a problem. The significance of the body burden that we all carry today is not known.

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