Uploaded to the VFC Website

June 2014

This Document has been provided to you courtesy of Veterans-For-Change!

Feel free to pass to any veteran who might be able to use this information!

For thousands more files like this and hundreds of links to useful information, and hundreds of "Frequently Asked Questions, please go to:

Veterans-For-Change

Veterans-For-Change is a A 501(c)(3) Non-Profit Organizaton
Tax ID #27-3820181
CA Incorporation ID #3340400
CA Dept. of Charities ID #: CT-0190794

If Veterans don't help Veterans, who will?

We appreciate all donations to continue to provide information and services to Veterans and their families.

https://www.paypal.com/cgi-bin/webscr?cmd=_s-xclick&hosted_button_id=WGT2M5UTB9A78

Note: VFC is not liable for source information in this document, it is merely provided as a courtesy to our members & subscribers.

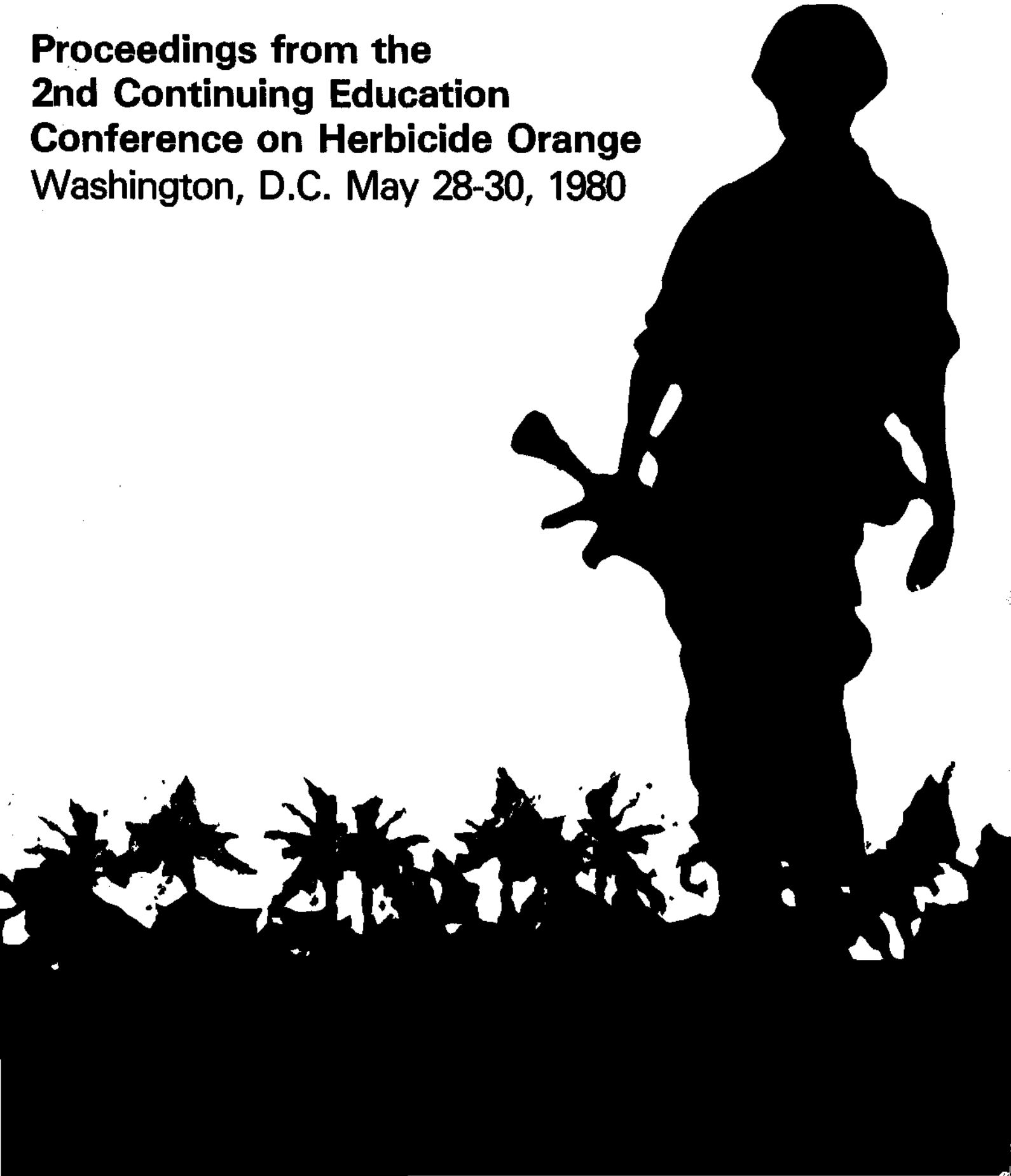
Item ID Number	04937 ☐ **Not Scanned**
Author	
Corporate Author	Office of Special Assistant to Chief Medical Director and
Report/Article Title	Proceedings from the 2nd Continuing Education Conference on Herbicide Orange, Washington, D.C., May 28-30, 1980
Journal/Book Title	
Year	1981
Month/Day	May
Color	☐
Number of Images	82
Descripten Notes	

Veterans Administration

ALVIN L. YOUNG, Major, USAF
Consultant, Environmental Sciences

Proceedings from the 2nd Continuing Education Conference on Herbicide Orange

Washington, D.C. May 28-30, 1980



Office of Special Assistant to Chief Medical Director
Veterans Administration Central Office
Washington, D.C.

And

Office of Academic Affairs
Veterans Administration Central Office
Washington, D.C.

In Cooperation With

South Central Regional Medical Education Center
Veterans Administration Medical Center
St. Louis, Missouri

Presents

2nd Continuing Education Conference on Herbicide Orange
May 28 - 30, 1980

Sheraton Inn - Washington Northwest
8727 Colesville Road
Silver Spring, Maryland

Objectives For Physicians
May 28 - 30, 1980

At the completion of this experience each participant will be able to:

describe the biochemistry, pharmacology and toxicology for animals and humans of Herbicide Orange constituents;

explain how herbicides were used in Vietnam and the possible effects on veterans who were exposed to them;

recognize indicators for possible health effects related to Herbicide Orange exposure;

explain how the VA is responding to the issue of Herbicide Orange;

integrate VACO philosophy of Herbicide Orange into the role of Environmental Health Physicians in local facility;

demonstrate an understanding of unique human needs and problems of Vietnam veterans by showing sensitivity to veterans' concerns relating to health effects of Herbicide Orange;

define and prioritize problems associated with the Herbicide Orange issue that are encountered in their local facility;

develop implementation strategies for overcoming problems associated with Herbicide Orange issues in their local facility.

Objectives For Adjudication Officers' Meeting
May 30, 1980

At the completion of this experience each participant will be able to:

understand the impact on regional office operations of legislative proposals currently before Congress;

insure uniform compliance with adjudicative procedures and guidelines;

carry back workload projections and insights on solutions other regional offices have developed to resolve mutual operations and resource problems.

Program Schedule

Tuesday, May 27, 1980

4:00 - 6:00 p.m.	Registration

Wednesday, May 28, 1980

7:00 - 8:15 a.m.	Registration
8:15 - 9:30 a.m.	General Assembly Welcome Introductions - Mrs. Martha Phillips Miss Dorothy L. Starbuck Dr. William J. Jacoby, Jr. Mr. Rufus H. Wilson Dr. Barclay M. Shepard Overview of Education Program - Dr. David B. Walthall, III
9:30 - 10:30 a.m.	Use of Herbicides in Vietnam and its Environmental Fate - Major Alvin L. Young, USAF
10:30 - 11:00 a.m.	Break
11:00 - 11:45 a.m.	The Pharmacology and Toxicology of Herbicide Orange Constituents in Animals - Dr. Renate Kimbrough
11:45 - 12:30 p.m.	Effects of Dioxin on Human Health - Lt. Col. William H. Wolfe, USAF
12:30 - 1:45 p.m.	Lunch
1:45 - 2:30 p.m.	Diagnostic Indicators for Possible Health Effects Related to Herbicide Orange Exposure - Lt. Col. William H. Wolfe, USAF
2:30 - 3:15 p.m.	Chloracne Recognition and its Significance for Diagnosing Possible Herbicide Orange Toxicity - Dr. Kenneth Halprin
3:15 - 3:45 p.m.	Break
3:45 - 4:30 p.m.	VA's Proposed Epidemiologic Study of Veterans Exposed to Herbicide Orange - Dr. Lawrence B. Hobson
5:00 - 7:00 p.m.	Social Hour - Cocktail Lounge (Cash Bar)

Thursday, May 29, 1980

8:00 - 8:15 a.m.	Opening Remarks - Dr. Barclay M. Shepard
8:15 - 8:45 a.m.	Legal Aspects of the Herbicide Orange Issue - Mr. Guy McMichael, III, Esq. Message from the Administrator
8:45 - 9:30 a.m.	How the VA is Responding to the Herbicide Orange Issue - Dr. Barclay M. Shepard
9:30 - 10:00 a.m.	Break
10:00 - 10:45 a.m.	Public Information Aspects of the Herbicide Orange Issue - Mr. Stratton M. Appleman
10:45 - 11:15 a.m.	"3" Scenarios - Role Playing
11:15 - 11:30 a.m.	Description of Nominal Group Process - Dr. David B. Walthall, III
11:30 - 12:45 p.m.	Lunch
12:45 - 4:30	Group Session a. Defining the Problem b. General Strategies for Problem Resolution

Friday, May 30, 1980

8:00 - 8:30 a.m.	Opening Remarks Feedback from Needs Assessment - Dr. Barclay M. Shepard
8:30 - 9:15 a.m.	Questions & Answers - Panel Discussion
9:15 - 9:45 a.m.	Break
9:45 - 10:15 a.m.	Feedback from Small Groups - Dr. David B. Walthall, III
10:15 - 10:30 a.m.	VACO Expectations of Implementation Plan - Dr. Barclay M. Shepard
10:30 - 12:00 noon	Development of Implementation Plan
12:00 noon	Closing Remarks - Dr. Barclay M. Shepard Post Test

Program Co-Chairman

Barclay M. Shepard, M.D.
Special Assistant to the Chief Medical Director
VA Central Office
Washington, D.C.

David B. Walthall, III, M.D.
Director Continuing Education and
Staff Development Service
VA Central Office
Washington, D.C.

F. A. Zacharewicz, M.D.
Medical Director
South Central Regional Medical Education Center
St. Louis, Missouri

Program Coordinators

Barbara J. Brown, M.S.
Chief, Instructional Design and Educational
Development Division
Continuing Education and Staff Development Service
Department of Medicine and Surgery
VA Central Office
Washington, D.C.

Layne Drash, M.Ed., M.S.
Staff Assistant to the Special Assistant to the
Chief Medical Director
VA Central Office
Washington, D.C.

Program Assistants

Louise Kinder
South Central Regional Medical Education Center
St. Louis, Missouri

Helene T. Mayhew
South Central Regional Medical Education Center
St. Louis, Missouri

Planning Committee

Barbara J. Brown, M.S.
Chief, Instructional Design and Educational
Development Division
Continuing Education and Staff Development Service
Department of Medicine and Surgery
VA Central Office
Washington, D.C.

Richard Colloton
Senior Television Producer
Learning Resources Service
VA Medical Center
St. Louis, Missouri

Layne Drash, M.Ed., M.S.
Staff Assistant to the Special Assistant to the
Chief Medical Director
VA Central Office
Washington, D.C.

Mark C. Gray, M.A.
Chief, Learning Resources Service
VA Medical Center
St. Louis, Missouri

Paul Haber, M.D.
Assistant Chief Medical Director for Professional Services
Department of Medicine and Surgery
VA Central Office
Washington, D.C.

Alexander Kutner
Staff Assistant to Assistant Chief Medical Director for
Professional Services
Department of Medicine and Surgery
VA Central Office
Washington, D.C.

Richard Levinson, M.D.
Deputy Assistant Chief Medical Director for
Clinical Support Services
Department of Medicine and Surgery
VA Central Office
Washington, D.C.

J.C. Peckarsky, Esq.
Director Compensation and Pension Service
Department of Veterans Benefits
VA Central Office
Washington, D.C.

Dean K. Phillips, Esq.
Special Assistant to the Administrator
VA Central Office
Washington, D.C.

Robert Shannon, M.D.
Associate Chief of Staff for Education
VA Medical Center
Baltimore, Maryland

Barclay M. Shepard, M.D.
Special Assistant to the Chief Medical Director
VA Central Office
Washington, D.C.

David B. Walthall, III, M.D.
Director, Continuing Education and
Staff Development Services
Department of Medicine and Surgery
VA Central Office
Washington, D.C.

Lawrence Wheeler, Esq.
Adjudication Officer
Washington Regional Office
Department of Veterans Benefits
Washington, D.C.

John Wisniewski. Esq.
Deputy Director, Compensation
and Pension Service
Department of Veterans Benefits
VA Central Office
Washington, D.C.

F. A. Zacharewicz, M.D.
Medical Director
South Central Regional Medical Education Center
St. Louis, Missouri

Faculty

Stratton M. Appleman
Director for News and Liaison
VA Central Office
Washington, D.C.

Kenneth Halprin M.D.
Chief of Dermatology Service
Professor - University of Miami,
School of Medicine
VA Medical Center
Miami, Florida

Lawrence B. Hobson, M.D.
Deputy ACMD for Research and Development
VA Central Office
Washington, D.C.

William J. Jacoby, Jr., M.D.
Deputy Chief Medical Director
VA Central Office
Washington, D.C.

Renate Kimbrough, M.D.
Toxicology Branch
Center for Disease Control
Atlanta, Georgia

Guy H. McMichael, III, Esq.
The General Counsel
VA Central Office
Washington, D.C.

Martha L. Phillips, M.S.
Acting ACMD for Academic Affairs
VA Central Office
Washington, D.C.

Barclay M. Shepard. M.D.
Special Assistant to the Chief Medical Director
VA Central Office
Washington, D.C.

Dorothy L. Starbuck
Chief Benefits Director
VA Central Office
Washington, D.C.

David B. Walthall, III, M.D.
Director, Continuing Education and
Staff Development Service
VA Central Office
Washington, D.C.

Rufus H. Wilson
Deputy Administrator
VA Central Office
Washington, D.C.

Lt. Col. William H. Wolfe, USAF (MC)
Chief of the Disease Surveillance Branch
Epidemiology Division
School of Aerospace Medicine
Brooks AFB, Texas

Major Alvin L. Young, USAF, BSC
Consultant of Environmental Sciences
Epidemiology Division
Brooks AFB, Texas

Facilitators

Nancy A. Coldeway, Ph.D.
Coordinator, Educational Design
InterWest Regional Medical Education Center
Salt Lake City, Utah

Donald L. Cordes, Ph.D.
Educational Specialist
Continuing Education and
Staff Development Service
VA Central Office
Washington, D.C.

Larry Demarest, Ph.D.
Associate Director for Education
North Central Regional Medical Education Center
Minneapolis, Minnesota

Mark C. Gray, M.A.
Chief, Learning Resources Service
VA Medical Center
St. Louis, Missouri

Steven K. Harmon, Ph.D.
InterWest Regional Medical Education Center
Salt Lake City, Utah

Arthur D. Katser, Ed.D.
Education Specialist
Northeast Regional Medical Education Center
Northport, New York

Rivkah Lindenfield, R.N., Ph.D.
Coordinator of Allied Health and
Administrative Education
Northeast Regional Medical Education Center
Northport, New York

R. L. Matkin, D.M.D.
Co-Director
South West Regional Medical Education Center
Long Beach, California

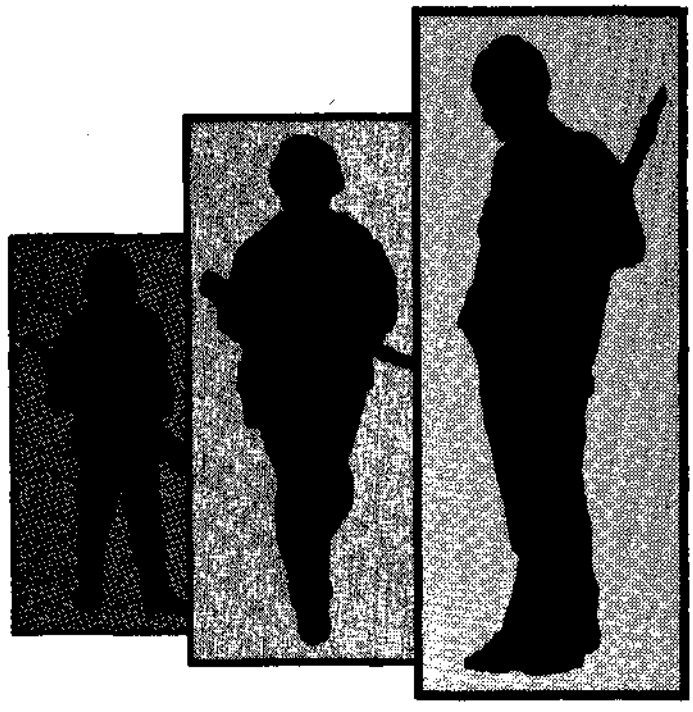
Donald E. Moore, Jr.
Chief of Continuing Education Operations Division
Continuing Education and Staff Development Service
VA Central Office
Washington, D.C.

David B. Walthall, III, M.D.
Director, Continuing Education and
Staff Development Service
VA Central Office
Washington, D.C.

F. A. Zacharewicz, M.D.
Medical Director
South Central Regional Medical Education Center
St. Louis, Missouri

Evaluator

Patrick L. Walsh, Ph.D.
Co-Director InterWest Regional Medical Education Center
Salt Lake City, Utah



Accreditation And Continuing Education Unit Credit

As an organization accredited for continuing medical eduction, the South Central Regional Medical Education Center certifies that this continuing medical education activity meets the criteria for 17 credit hours in Category 1 of the Physician's Recognition Award of the American Medical Association. This program is approved for 2.0 Continuing Education Units (CEU) for Adjudication Officers. Upon completion of the program, a certificate of attendance will be awarded to VA employees and accreditation records will be on file at the South Central Regional Medical Education Center.

General Information

A non-reimbursable fee will be collected from all participants for refreshments served during the meeting. This fee is payable at the time of registration.

Anyone requiring limousine service at the conclusion of the program must make a reservation with the hotel front desk at least one day in advance of departure.

VETERANS ADMINISTRATION

2ND CONTINUING EDUCATION CONFERENCE ON HERBICIDE ORANGE

Sponsored by
the
Veterans Administration
Department of Medicine & Surgery

at
Silver Spring, Maryland
May 28-30, 1980

INTRODUCTION

The 2nd Continuing Education Conference on Herbicide Orange held in Silver Spring, Maryland, from May 28-30, 1980, demonstrated a keen awareness on the part of the Veterans Administration that the education of key medical and adjudication staff is essential to the conduct of a viable Agent Orange program. The transcribed proceedings of this meeting, as contained in this publication, should be viewed as a resource providing an overview describing our perception of current scientific and other evidence relating to Agent Orange.

I cannot stress too strongly my firm conviction, gained from my involvement in Agent Orange activities, that we must consider problems generated by this defoliant in an open minded and forthright manner. We must view our education, in this regard, as a continuing concern and as a professional responsibility which we accept willingly and with genuine enthusiasm. Increasing our knowledge, however, is only one of our goals. Equally important is the need for each of us to demonstrate our sense of respect, compassion and empathy for Vietnam veterans and their families, many of whom are genuinely and understandably worried about the possible adverse health effects of exposure to Agent Orange. We must strive to instill confidence in the minds of Vietnam veterans that we are knowledgeable and that we do indeed share a genuine concern for their mental and physical well-being. This is our responsibility; it is also our privilege.

Please read these proceedings carefully--challenge yourselves to understand and ask questions where answers cannot be found or are unclear. As Special Assistant to the Chief Medical Director for Environmental Medicine, I pledge my continuing support of these endeavors. Let us dedicate our energies and resources to our continuing search for answers.

Barclay M. Shepard

BARCLAY M. SHEPARD, M.D.

CONTENTS

KEYNOTE ADDRESS

RUFUS H. WILSON

DEPUTY ADMINISTRATOR

For some two years now, the Veterans Administration, other Government agencies and many of our publics have been wrestling with a major issue of our times.

The issue is "Agent Orange." It is an issue with sub-issues of health, of national morality, of genes, of public relations, of public concern and public malaise.

Each sub-issue, whether fact or fiction or in-between, raises emotions to a high pitch. Each taxes our intelligence. Each is argumentative in this extreme. And each puts the scientific community of our nation to a great test.

But more than that. Each of the sub-issues have brought the Veterans Administration into a focus of public attention which, to say the least, has brought few plaudits to our agency.

Every person in this room is intricately involved in performing tasks with respect to "Agent Orange." Some examine veterans who think they have disabilities due to it. Some answer telephone questions related to it. Some adjudicate claims. Some write letters. Some interview veterans and their dependents. Some deal with the press.

In most instances, these examinations have been well conducted; those telephone questions well answered; those adjudications correct; those interviews excellent; and those press dealings well performed.

But not always. At least allegedly, some physical examinations have been perfunctory, patient fears have been exacerbated, medical examiners have been accused of not understanding VA Central Office-directed procedures, and the whole idea of "Agent Orange" causing problems such as cancer or birth defects has been "poo-pooed" by a few members of the VA family.

Our lack of real scientific knowledge of this subject has been translated by some into accusations of "not caring." Answers given during telephone and personal interviews have been interpreted as conveying "non-belief" that a problem may exist. Adjudication personnel are accused of being conservance or having a "to hell with it" attitude. Some statements to the press have appeared in print or been quoted on radio or TV in such a way as to indicate that either a problem doesn't exist, is overstated, or is about to go away.

I want to keep our positions in proper perspective. I have deliberately used such words as "allegedly," "some," "on occasion," "accused," "few," "interrupted," or "indicate."

But let me make it as clear as I can where it is that we ought to be.

1. Examinations on "Agent Orange" must never be perfunctory. They must be careful and complete.

2. Physicians must understand that a very real concern--even fear--exists in the minds of many of our claimants that exposure to "Agent Orange" is or will be a forerunner of dread consequences.

3. Procedures as to how to handle "Agent Orange" examinations must be so completely followed as to leave no doubt as to our complete understanding of them.

4. We must never "poo-poo" a claimant's concern -- even if we harbor a suspicion of malingering, trying to get something for nothing, or even if we suspect that he or she is just another disgruntled person.

5. We can well explain that our scientific knowledge is very limited as to "Agent Orange" for that is a solid fact. But we can add that we are searching for the right answers and searching nightly. And we can say that when we get the answers, either positive or negative, that those answers will be quickly and completely shared with everyone concerned.

6. The idea of "non caring" -- limited though it is -- ought to be wiped out in its entirety. We need to always go the extra mile.

7. There is nothing wrong with saying that as of now we have NO scientific proof or medical evidence -- except as to chloracne -- that "Agent Orange" causes other conditions.

8. There is nothing wrong with accepting the idea that a problem does, in fact, exist, because if a problem didn't exist, we in VA wouldn't be spending the over $100,000 it costs to have this Conference.

9. Adjudication of claims must be timely and of quality; explanations need to be factual and compassionate, with emphasis on compassion.

10. And finally, when dealing with the press, we need to be open, candid, concerned, and factual. We nedd to explain again and again what VA is doing as to examining, keeping registers, adjudicating, and researching. We will probably not win the battle of the press on "Agent Orange," but our record needs to be clear that we have made a noble effort. If the fourth estate then distorts or doesn't understand as will sometimes occur our record will be there for all to see.

I have not wanted to overstate our situation in VA and I hope that I have not. I know that the overwhelming majority of VA people have performed exceedingly well as we have tackled the problem of "Agent Orange" and VA is in their debt for that. But I need to tell you that no matter where the Administrator goes, no matter if it is radio, TV, newspapers, magazines, editorial boards, Congressional Committees, Congressional Members, Veterans Groups, or just individual veterans, he is confronted with questions on "Agent Orange." Our biggest problem then is one of perception by our publics.

If you have seen as many newspaper stories and television reports as Mr. Cleland and I have that allege VA callousness about "Agent Orange" you might well reach certain conclusions.

You might become convinced that news media are completely irresponsible, or you might decide that you work for a lousy agency.

Neither of these attitudes is justified.

I'm going to give you some facts about the publicity -- and what's behind the publicity -- then I'm going to give you some numbers that will show you how the veterans have reacted to it. Then I think you'll agree that most of the 9 million Vietnam era veterans are a pretty sophisticated group of people.

My main purpose here this morning is to give you the anatomy of this "Agent Orange" controversy as we see it. We need to cover the special interest groups involved, the media position, and what we can -- as well as what we can't -- do to bring about a better public perspective on this subject.

First I want to emphasize that this is a controversy without adversaries. There are no real villains -- not the news media who criticize us nor the eight or so organizations that manipulate the media. These organizations fall into about 3 basic categories. For most, "Agent Orange" is a spinoff from some more basic objective that most of us would find worthwhile..

Some groups have been in action for as much as 30 to 40 years. Others' movements date from the Vietnam War period. Still others have developed in the past two or three years.

The original objective is one all of us would support. This is the desire to make the world a better place to live -- for people and animals and their natural life-supporting systems.

Those of us who support this overall objective -- and I deliberately include myself -- can be called environmentalists.

Highly organized groups of many kinds of environmentalists have succeeded in drawing attention to the harmful effects of chemicals like DDT and the dangers of misuse of even a natural element like lead. Now they're concerned aobut herbicides, nuclear power and other developments they consider harmful to the environment. When our military forces saw a use of herbicides in Vietnam to uncover Viet Cong hiding places and destroy food crops, a furor developed that caused the military to stop using them.

Agriculture and forestry uses of the herbicides continued. Many environmentalists continued their opposition, but at the time news media paid little attention.

Then in 1978 -- seven years after the last spraying in Vietnam -- a well known environmentalist made a horrifying suggestion. It was only a suggestion, but he raised the spectre that a contaminant in "Agent Orange" might be lying dormant in Vietnam veterans ready to become active at any time and cause health problems.

As you know well, this got immediate public attention.

Vietnam Veterans Against the War in Chicago were among the first veterans to cite this theory as an example of still another horrible consequence of the war.

Another anti-war group, Citizen Soldier, quickly mounted its own media campaign. They damned both the Dept. of Defense for using the herbicides and the VA for cooperating in what they suggested was a government conspiracy. They linked a conspiracy to deny compensation to veteran herbicide victims to denial of universal amnesty to dishonorably discharged veterans.

Others saw the "Agent Orange" issue as an opportunity to build an organization to represent Vietnam veterans.

Other individuals with less clear-cut motives have now joined the debate. Among these are attorneys who are seeking veterans to join them in a class action suit against manufacturers of herbicides.

All of these groups have been quite effective in getting publicity. Five or six TV documentaries have been done. Several network news shows have dealt with the subject and literally hundreds of news stories have covered it from every angle.

We analyzed about 150 of these news stories, selected at random, and here's what we found:

-- 25% discussed the suit against the chemical companies.

-- 85% discussed the herbicide and how easily veterans could have been exposed.

-- 70% described VA as being unresponsive.

-- 10% encouraged veterans to visit VA, but only 5% mentioned the ongoing research toward getting scientific information for resolving veterans' fears.

No wonder some of you feel that news media are irresponsible or that you work for a lousy agency.

Remember, I said that neither conclusion is justified. Why?

It's hard to think your agency is all bad what you consider these points.

It was 6 years after spraying in Vietnam stopped when VA got the first suggestion that a veteran might be suffering from latent effects of "Agent Orange."

That first suggestion came from a VA benefits counselor with little professional background in either medicine or chemistry. She had been a hospital corpsman and an x-ray technician -- in the Navy.

The first news reports were based on a medical theory that still has no support in the scientific community.

But since that very first claim was filed, VA has teken the lead in a government-wide effort to get scientifically valid answers to deal with veterans' fears.

VA has been operating on the principle that if it concerns veterans, it concerns VA. That is why we are giving the information gathering side of this issue more emphasis than any medical subject since VA spearheaded the successful fight against tuberculosis.

The least understood point about this whole thing is that we are not waiting for the long-range scientific results to implement programs for veterans who think they have problems related to "Agent Orange." If they do have a medical problem, it becomes very simple for VA to help them. We can treat those who are eligible, and if there is a disability we can in any way relate to the time period they were in military service we can pay compensation.

Unfortunately, we can't compensate for exposure alone -- even to bullets. There has to be some physical or sychological manifestation of this exposure to qualify under the law for disability. Nor can our doctors assure anyone that they will go through life free of medical problems. No one can do that.

I think you can be proud however, of what VA has done. And I think you can be proud of what you <u>are</u> doing.

There are some numbers that prove we are doing a pretty good job, and at the same time prove that Vietnam veterans are the sophisticated people I described earlier.

For example, VA gets about 1.75 million inquiries per month from veterans. Despite the heavy publicity on herbicides, only 1,217 of these inquiries, in a typical month were related in any way to "Agent Orange."

Yet how many times have you heard that "Agent Orange" is the major issue among veterans?

Only five percent of the 8,130 veterans who have visited our Vet Centers -- which were specifically designed for veterans with readjustment problems -- have expressed concern about this so-called major issue.

Since VA got its first "Agent Orange" claim a little over two years ago, the agency has received two million claims for disabilities unrelated to "Agent Orange." That means we received 1,960 "Agent Orange" claims out of some two million.

Now let's compare that number of claims -- 1,960 -- to the number of veterans who have been examined at VA hospitals and clinics.

At the end of the last quarter it was around 10,000. Let's say about 20 thousand now. This suggests that most of those who are playing it safe by getting an examination are less concerned after being examined and counseled by people like you.

Another interesting statistic is that out of the 1,960 who have been adjudicated have filed claims, 391 have no diagnosis established of any kind and many claimed none.

These expressions of interest or concern about "Agent Orange" -- calls, claims, visits -- vary in their volume in each geographic area in direct proportion to the volume and type of publicity in that area.

The sources for stories to keep this publicitygoing are endless. And the groups I've mentioned are going to keep supplying them to news media. And the media are going to carry them because the people who run newspapers and television stations are going to carry material that causes people to buy newspapers or turn the channel to their station.

Stories about "local man gets cancer from chemicals in Vietnam" will attract a lot more readers and listeners than one saying VA does a good job. That's just the way it is.

The people supplying these stories are good publicists. And they have many other advantages over a government agency in getting their point of view across.

-- They have an attention-getting point of view - the disaster syndrome - coupled with the old theme of the big, untrustworthy government.

-- You are often put on the defensive because you don't often know what their underlying objective is until an interview is well underway.

-- They are not bound by the same rules of debate that we are. Everything we say or do must be carried out with the knowledge that millions of taxpayers are looking over our shoulders - through the eyes of their Congressmen or news media.

We can't exaggerate, we can't misrepresent and we can't cite rumors.

In fact we can't advocate any controversial position which would appear to be self serving.

So what can we do?

In the media contacts we have, we can make VA's role clear. We can say that we are not authorities on the environment, so we can leave the government side of that issue to EPA.

We can say that VA did not use herbicides in Vietnam. We leave that to the Department of Defense.

We can say that our one concern is whether or not veterans -- or their offspring -- have any lasting effects from exposure to herbicides in Vietnam.

We can say that we are exploring every avenue to get the answer to that question. We want to know whatever science can tell us on this subject. The help it might be in adjudicating claims is just one of the reasons, but the main reason is to put us in a position of being able to tell veterans facts about something they fear.

The number of those who feel this fear are a small percentage of the total veterans targeted for this massive publicity.

That's why I again say Vietnam era veterans are usually sophisticated. But even small percentages applied to veteran populations produce large numbers. The fear they feel is real.

Some of the facts we now have will help alleviate some of the fear. But only if the facts are handled with understanding and compassion.

More facts from more credible sources are needed desperately, and there is a government-wide effort now in progress to get those answers.

Depending on what science can tell us, it may be your duty sometime to call back each of the veterans you've seen or talked to about "Agent Orange," and tell him that indeed he might have some health problems in his future that are related to his service in Vietnam.

And I can assure you that VA will conduct the most massive outreach program ever -- <u>if</u> a link is established.

On the other hand -- if science is successful in the almost impossible job of proving a negative -- that there is no link between "Agent Orange" and veterans' present health -- then we have a very sad duty of a different type.

We must then reveal to a generation of veterans which already feels it has been misused by society that they have been used in still another unpopular war. A propaganda war.

If we <u>are</u> caught up in a propaganda war, we have one potent weapon for destroying the credibility of the other side.

Veterans are told that their government sprayed them with deadly chemicals and that VA is callous and uncaring about their problems.

Our challenge when they come to us is to show them that it is not so and that we do care.

For the veteran who is truly concerned, I repeat that an attitude of understanding, caring and concern on your part will do more than words and tests.

Now we come to conference. We meet in a time of stress. We meet with the spectrum of scientific uncertainty all around us. We meet with a feeling that we have done well and yet been unduly maligned. We come long distances. We recall the age old philosophy that says the march of miles must begin with a single step. We are not taking the first single step now or even the first 100 steps. They are far behind us. But there are many steps still ahead. We take them now with a self assurance that we can do better and that we will do better. Let the record of this Conference be clear -- That VA's leaders who are gathered here today -- again faced great challenge and met and conquered it -- for conquer it we must. And conquer it we will.

You who are here today have been asked to be here because of who you are and because of the positions you hold. You have been called upon to do better than you know how to do. That you might be successful is the fervant wish of your government. And the fervant wish of that agency of that government which is your very special concern. I am confident that history will judge you well as you discharge your very difficult responsibilities.

USE OF HERBICIDES IN SOUTH VIETNAM, 1961-1971*

Alvin L. Young
MAJOR, USAF, PHD
Epidemiology Division
USAF School of Aerospace Medicine
Brooks AFB, San Antonio TX 78235

Herbicides used in support of tactical military operations in South Vietnam from 1961 to 1971 are today, ten years after the last herbicide mission, the center of intense scientific debate involving not only medical but also legal, political and ecological issues. This paper reviews the historical and operational concepts and some potential human exposure considerations involving the military use of herbicides in the Southeast Asian Conflict.

Herbicides Used in South Vietnam

Synthesis technology, efficacy data, and field application techniques were developed for the two major phenoxy herbicides, 2,4-dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) during World War II at Fort Detrick, Frederick, Maryland. Following World War II, the commercial use of these two "synthetic" organic herbicides revolutionized American agriculture. In 1950, more than 10 million pounds of these materials were used annually for weed and brush control in the United States. By 1960, in excess of 36 million pounds were used.

In May 1961, the Office of the Secretary of Defense requested the Fort Detrick personnel to determine the technical feasibility of defoliating jungle vegetation in the Republic of Vietnam. By early fall, 1961, 18 different aerial spray tests (defoliation and anticrop) had been conducted with various formulations of commercially-available herbicides. The choice of these herbicides was based upon the chemicals that had had considerable research, proven performance, and practical background at that period in time. Also, such factors as availability in large quantity, costs and known or accepted safety in regard to their toxicity to humans and animals was considered. The results of these tests were that significant defoliation and anticrop effects could be obtained with two different mistures of herbicides. The first was a mixture of the n-butyl esters of 2,4-D and 2,4,5-T and the iso-butyl ester of 2,4,5-T. This mixture was code-named "Purple." The second "military" herbicide was code-named "Blue" and consisted of the acid and sodium salt of cacodylic acid. The colored bands which were painted around the center of the 55-gallon drums served as aid to the identification by support personnel.

The first shipment of Herbicides Purple and Blue was recieved at Tan Son Nhut Air Base, Republic of Vietnam, on 9 January 1962. These were the first military herbicides used in Operation RANCH HAND, the tactical military project for the aerial spraying of herbicides in South Vietnam. Two additional phenoxy herbicide formulations were received in limited quantities in South Vietnam and evaluated during the first two years of Operation RANCH HAND. These were code-named Pink and Green. By January 1965, two additional military herbicides, code-named Orange and White, had been evaluated and brought into the spray program. Herbicide Orange

*A synopsis of Information from Chapters I and III of The Toxicology, Environmental Fate, and Human Risk of Herbicide Orange and Its Associated Dioxin, Air Force Technical Report OEHL-TR-78-92, USAF Occupational and Environmental Health Laboratory, Brooks Air Force Base, Texas. (Authors: A. L. Young, J. A. Calcagni, C. E. Thalken, and J. W. Tremblay.) 1978.

replaced all uses of Purple, Pink, or Green, and eventually became the most widely used military herbicide in South Vietnam. The composition of the three major herbicides used in South Vietnam were as follows:

1. Herbicide Orange

Orange was a reddish-brown to tan colored liquid soluble in diesel fuel and organic solvents, but insoluble in water. One gallon of Orange theoretically contained 4.21 pounds of the active ingredient of 2,4-D and 4.41 pounds of the active ingredient of 2,4,5-T. Orange was formulated to contain a 50:50 misture of the n-butyl esters of 2,4-D and 2,4,5-T. The percentages of the formulation typically were:

n-butyl ester of 2,4-D	49.49
free acid of 2,4-D	0.13
n-butyl ester of 2,4,5-T	48.75
Free acid of 2,4,5-T	1.00
inert ingredients (e.g., butyl alcohol and ester moieties)	0.62

2. Herbicide White

White was a dark brown viscous liquid that was soluble in water but insoluble in organic solvents and diesel fuel. One gallon of White contained 0.54 pounds of the active ingredient of 4-amino-3,5,6-trichloropicolinic acid (picloram) and 2.00 pounds of the active ingredient of 2,4-D. White was formulated to contain a 1:4 mixture of the triisopropanoamine salts of picloram and 2,4-D. The percentages of the formulation were:

triisopropanolamine salt of picloram	10.2
triisopropanolamine salt of 2,4-D	39.6
inert ingredient (primarily the solvent triisopropanolamine)	50.2

3. Herbicide Blue

Blue was a clear yellowish-tan liquid that was soluble in water, but insoluble in organic solvents and diesel fuel. One gallon of Blue contained 3.10 pounds of the active ingredient hydroxydimethyarsine oxide (cacodylic acid). Blue was formulated to contain cacodylic acid (as the free acid) and the sodium salf of cacodylic acid (sodium cacodylate). The percentages of the formulation were:

cacodylic acid	4.7
sodium cacodylate	26.4
surfactant	3.4
sodium chloride	5.5
water	59.5
antifoam agent	0.5

As previously noted, not all of the herbicides used in South Vietnam were used throughout the entire 10 years (1962-1971) encompassed by the Department of Defense defoliation program. In addition, 2,4,5-T formulations used early in the program are believed to have contained higher levels of the toxic contaminant TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin or "dioxin") than did the formulations used in the later years. The three time periods shown in Table 1 can be differentiated on the basis of specific herbicides used and the mean dioxin content.

TABLE 1 THE DIFFERENTIATION OF THREE TIME PERIODS DURING THE US MILITARY DEFOLIATION PROGRAM IN SOUTH VIETNAM AND MEAN DIOXIN CONTENT

PERIOD	HERBICIDES USED (CODE NAMES)	MEAN DIOXIN CONTENT (PARTS PER MILLION)*
January 1962 - June 1965	Purple, Pink, Green	32**
	Blue	0
July 1965 - June 1970	Orange	2+
	White, Blue	0
July 1970 - October 1971	White, Blue	0

*Found only in 2,4,5-T containing formulations.
**Value based on analyses of five samples.
+Value based on the analyses of 488 samples.

Herbicide Orange was the most extensively used herbicide in South Vietnam. Orange accounted for approximately 10.7 million gallons of the total 17.7 million gallons of herbicide used (Table 2). It was used from mid-1965 to June 1970. However, as noted in Table 2, Orange was not the only 2,4,5-T containing herbicide used in the defoliation program. Small quantities of Purple, Pink, and Green, all containing 2,4,5-T were used from 1962 through mid-1965. In subsequent sections of this document, the term "herbicide Orange" will refer to all of the 2,4,5-T containing herbicides used in Vietnam (Purple, Pink, Green, and Orange).

TABLE 2 NUMBER OF GALLONS OF MILITARY HERBICIDE PROCURED BY THE US DEPARTMENT OF DEFENSE AND DISSEMINATED IN SOUTH VIETNAM DURING JANUARY 1962 - OCTOBER 1971

Code Name	Herbicide	Quantity	Period of Use
Orange	2,4-D; 2,4,5-T	10,646,000	1965-1970*
White	2,4-D; Picloram	5,633,000	1965-1971**
Blue	Cacodylic Acid	1,150,000	1962-1971**
Purple	2,4-D; 2,4,5-T	145,000	1962-1965
Pink	2,4,5-T	123,000	1962-1965
Green	2,4,5-T	8,200	1962-1965
	Total	17,705,200	

*Last fixed-wing mission of Orange 16 April 1970; last helicopter mission of Orange 6 June 1970.
**Last fixed-wing mission 9 January 1971; all herbicides under US control stopped 31 October 1971.

Use Patterns of Individual Herbicides

Each of the three major herbicides (Orange, White, and Blue) had specific uses. Ninety-nine percent of Herbicide White was applied in defoliation missions. It was not recommended for use on crops because of the persistence of Picloram in soils. Because the herbicidal action on woody plants was usually slow, full defoliation did not occur for several months after spray application. Thus, it was an ideal herbicide for use in the inland forests in areas where defoliation was not immediately required, but where it did occur it would persist longer than if the area were sprayed with Orange or Blue.

Herbicide Blue was the herbicide of choice for crop destruction missions involving cereal or grain crops. Approximately 50 percent of all Blue was used in crop destruction missions in remote or enemy controlled areas with the remainder being used as a contact herbicide for control of grasses around base perimeters.

Ninety percent of all Herbicide Orange was used for forest defoliation and it was especially effective in defoliating mangrove forests. Eight percent of Herbicide Orange was used in the destruction of broadleaf crops (beans, peanuts, ramie, and root or tuber crops). The remaining 2 percent was used around base perimeters, cache sites, waterways, and communication lines.

Table 3 shows the number of acres sprayed with herbicides in South Vietnam within the three major vegetational categories.

TABLE 3 THE NUMBER OF ACRES TREATED IN SOUTH VIETNAM, 1962-1971, WITH MILITARY HERBICIDES WITHIN THE THREE MAJOR VEGETATIONAL CATEGORIES

Vegetational Category	Areas Treated*
Inland forest	2,670,000
Mangrove forests	318,000
Cultivated crops	260,000
Total	3,248,000

*Areas receiving single or multiple coverage.

Certain portions of South Vietnam were more likely to have been subjected to defoliation. Herbicide expenditures for the four Combat Tactical Zones of South Vietnam are shown in Table 4. These data were obtained from the HERBS tape (a computer listing of all herbicide missions in South Vietnam from 1965 through 1971). Total volume is in close agreement with the actual procurement data shown in Table 2.

TABLE 4 US HERBICIDES EXPENDITURES IN SOUTH VIETNAM, 1962-1971: A BREAKDOWN BY COMBAT TACTICAL ZONE*

Combat Tactical Zones	Herbicide Expenditure (gallons) Orange	White	Blue
CTZ I	2,250,000	363,000	298,000
CTZ II	2,519,000	729,000	473,000
CTZ III (includes Saigon)	5,309,000	3,719,000	294,000
CTZ IV	1,227,000	435,000	62,000
Subtotals	11,305,000	5,246,000	1,127,000
Grand Total			17,678,000

*Source: HERBS tape

In addition to the herbicides, numerous other chemicals were shipped to South Vietnam in 55-gallon drums. These included selected fuel additives, cleaning solvents, cooking oils, and a variety of other pesticides. The insecticide Malathion was widely used for control of mosquitoes and at least 400,000 gallons of it were used from 1966 through 1970. In addition, much smaller quantities of Lindane and DDT were used in ground operations throughout the war in Southeast Asia. The distribution of the herbicides within Vietnam after their arrival did not occur randomly. About 65 percent was shipped to the 20th Ordnance Storage Depot, Saigon, and 35 percent was shipped to the 511th Ordnance Depot, Da Nang.

Military Aircraft and Vehicles Used in the Dissemination of Herbicides

Numerous aircraft were used in the air war in Vietnam, but only a few of these aircraft were used for aerial dissemination of herbicides. The "work horse" of Operation RANCH HAND was the C-123, "Provider." This cargo aircraft was adapted to receive a modular spray system for internal carriage. The module (the A/A 45 Y-1) consisted of a 1,000-gallon tank pump, and engine which were all mounted on a frame pallet. An operator's console was an integral part of the unit, but was not mounted on the pallet. Wing booms (1.5 inches in diameter, 22 feet long) extended from the outboard engine nacelles toward the wing tips. A short tail boom (3 inches in diameter, 20 feet long) was positioned centrally near the aft cargo door. Each aircraft normally had a crew of three men: the pilot, co-pilot (navigator), and flight engineer (console operator). During the peak activity of RANCH HAND operations (1968-1969), approximately 30 U C-123K aircraft were employed. However, many other squadrons of non-RANCH HAND C-123 aircraft were routinely used throughout South Vietnam in transport operations.

The control of malaria and other mosquito-borne diseases in South Vietnam necessitated an extensive aerial insecticide application program in order to control these vector insects. From 1966 through 1972, three C-123 aircraft were used to spray Malathion, an organophosphate insecticide. These aircraft could be distinguished from the Herbicide-spraying aircraft because they were not camouflaged. These aircraft routinely sprayed insecticide adjacent to military and civilian installations, as well as in areas where military operations were in progress, or about to commence.

Approximately 10 to 12 percent of all herbicides used in South Vietnam was disseminated by helicopter or ground application equipment. Generally, helicopter crews were not assigned to herbicide spray duties on a full-time basis and rotated the spraying duties with other mission requirements. The military UH-1 series of helicopters, deployed by the Air Force, the Army, and Navy units, generally sprayed the herbicides. The most common spray system used was the AGRINAUTICS unit. This unit was installed in or removed from the aircraft in a matter of minutes because it was "tied down" to installed cargo shackles and aircraft modifications were not required for its use. The unit consisted of a 200-gallon tank and a collapsible 32-foot spray boom. The unit was operated by manual controls to control the flow valve and a windmill brake. Generally, each helicopter had three crew members.

A summary of the aircraft used in herbicide and insecticide operations is shown in Table 5.

TABLE 5 US MILITARY AIRCRAFT USED IN THE DISSEMINATION OF HERBICIDES AND INSECTICIDES IN SOUTH VIETNAM

Aircraft	Camouflaged	Chemical Disseminated
UC-123/UC-123K	Yes	All Herbicides
UC-123K	No	Malathion
Helicopter		
Air Force UH-1		
Army UH-1B/UH-1D	Yes	Orange, Blue
Navy UH/1E		

Various ground delivery systems were also used in South Vietnam for control of vegetation in limited areas. Most of these units were towed or mounted on vehicles. One unit that was routinely used was the Buffalo turbine. It developed a wind blast with a velocity up to 150 MPH at 10,000 ft^3/minute volume. When the herbicide was injected into the air blast, it was essentially "shot" at the foliage. The buffalo turbine was useful for roadside spraying and applications of perimeter defenses. The herbicides of choise in these operations were Blue and Orange.

Exposure Considerations: Applications and Environmental Parameters

There were relatively few military operations that involved the handling of herbicides by military personnel. A review of operations involving Herbicide Orange in South Vietnam from January 1962 to April 1970 revealed that there were essentially three groups of US military personnel potentially exposed to Herbicide Orange and its associated dioxin contaminant. These three groups were:

1. "Operation RANCH HAND" personnel actively involved in the defoliation program. This group included aircrew members and maintenance and support personnel directly assigned to the RANCH HAND squadrons.

2. Personnel assigned to selected support functions that may have resulted in exposure to Herbicide Orange. This group included, for example, personnel who sprayed herbicides, using helicopters or ground application equipment; personnel who may have delivered the herbicides to the units performing the defoliation missions; aircraft mechanics who were specialized and occasionally provided support to RANCH HAND aircraft; or, personnel who may have flown contaminated C-123 aircraft, but were not assigned to RANCH HAND (e.g., during the Tet Offensive, all RANCH HAND aircraft were reconfigured to transport supplies and equipment, and were assigned to non-RANCH HAND squadrons).

3. Ground personnel who may have been inadvertently sprayed by defoliation aircraft or who, during combat operations, may have entered an area previously sprayed with Herbicide Orange.

The total number of US military personnel exposed to Herbicide Orange is not known. Approximately 1,200 RANCH HAND personnel were exposed in direct support of the defoliation operations; however, there are no data on the number of non-RANCH HAND personnel who may have been exposed. The actual number of people may be in the thousands since at least 100 helicopter spray equipment units were used in South Vietnam, and most military bases had vehicle-mounted and backpack spray units available for use in routine vegetation control programs. The number of military ground personnel who may have inadvertently been sprayed by RANCH HAND aircraft, or who may have entered areas recently sprayed with Herbicide Orange during combat operations is not known. Approximately 10 percent of South Vietnam was sprayed with herbicides, and most of this area was contested and/or controlled by enemy forces. Most areas sprayed were remote, unpopulated and forested. Because of the dense canopy cover, the target of the defoliation operation, the amount of herbicide penetrating to the forest floor would have been small. The exposure of personnel could have occurred by essentially three routes:

1. Percutaneous absorption and inhalation of vapors/aerosols by direct exposure to sprays.

2. Percutaneous absorption and inhalation of vapors by exposure to treated areas following spray application, and

3. Ingestion of foods contaminated with the material.

The chemical and physical characteristics of Herbicide Orange and the spray, as it would have occurred following dissemination from a C-123, are important factors in assessing relative exposure to the Herbicides and TCDD.

Table 6 reviews the pertinent chemical and physical characteristics of Herbicide Orange. Table 7 reviews both the application parameters of the spray system used in the UC-123K aircraft and the characteristics of the spray itself. Generally, herbicides were sprayed in the early morning or late afternoon, so as to minimize the effects of air movement on particle dispersion.

TABLE 6 PERTINENT CHEMICAL AND PHYSICAL CHARACTERISTICS OF HERBICIDE ORANGE

Formulation Concentrated	(8.6 lb ai/gal)*
Water Insoluble	Density = 1.28
Vapor Pressure	3.6×10^{-4} mm Hg at 30°C
NBE** 2,4-D :	1.2×10^{-4}
NBE 2,4,5-T :	0.4×10^{-4}
TCDD :	1×10^{-9}
Viscous	40 centipoises at 20°C
Noncorrosive to metal Deleterious to paints, rubber, neoprene Long Shelf life	

*Pounds active ingredient (2,4-D and 2,4,5-T) per gallon.
**NBE - Normal Butyl ester.

TABLE 7. APPLICATION PARAMETERS AND SPRAY CHARACTERISTICS OF THE C-123 MODULAR INTERNAL SPRAY SYSTEM

Aircraft speed	130 KIAS*
Aircraft altitude	150 feet
Tank volume	1,000 gallons
Spray time	3.5-4 minutes
Particle size:	
100 microns: 1.9%	
100-500 microns: 76.2%	
500 microns: 21.9%	
87% impacted within 1 min	
13% drifted or volatilized	
Mean particle volume	0.61 microliters
Spray swath	260 $\pm$ 20 feet
Mean deposition	3 gallons/acre
Total area/tank	340 acres

*Knots indicated air speed

Ground combat forces normally would not have been expected to have entered a previously treated area for several weeks after treatment, during which time numerous environmental factors would have reduced the potential for exposure to military personnel. An indepth review of the environmental fate of Herbicide Orange and TCDD concluded that the vast majority of the phenoxy herbicides would have impacted forest canopy, the intended target.

Rapid uptake (e.g., within a few hours) of the ester formulations of 2,4-D and 2,4,5-T would have occurred. Most of the herbicide probably would have undergone rapid degradation (weeks) within the cellular matrix of the vegetation. However, some of the herbicide may have remained unmetabolized and would have been deposited on the forest floor at the time of leaf fall. Soil microbial and/or chemical action would likely have completed the degradation process. Herbicide droplets that impacted directly on soil or water would have probably hydrolyzed rapidly (within hours). Biological and nonbiological degradative processes would have further occurred to significantly reduce these residues. Some volatilization of the esters of 2,4-D and 2,4,5-T would have occurred during and immediately after application. The volatile material most likely would have dissipated within the foliage of the target area. Photodecomposition of TCDD would have minimized the amount of biologically active volatile residues moving downwind of the target area.

Accumulation of phenoxy herbicides in animals may have occurred following ingestion of treated vegetation. The magnitude of this accumulation would have likely been at nontoxic levels. Herbicide residues in animals would have rapidly declined after withdrawal from treated feed.

Most TCDD sprayed into the environment during defoliation operations would have probably photodegraded within 24 hours of application. Moreover, recent studies suggest that even within the shaded forest canopy, volatilization and subsequent photodecomposition of TCDD can occur. Since translocation into vegetation would be minimal, most TCDD that escaped photodegradation would probably have entered the soil-organic complex on the forest floor following leaf fall. Soil chemical and microbial processes would have further reduced TCDD residues. Bioconcentration of the remaining minute levels of TCDD may have occurred in liver and fat of animals ingesting contaminated vegetation or soil. However, there are no field data available that indicate that the levels of TCDD likely to have accumulated in these animals would have had a biological effect.

The environmental generation of TCDD from 2,4,5-T residues, through thermal or photolytic processes, would have been highly unlikely and of no consequence.

SUMMARY

The choice of herbicides used in South Vietnam in Operation RANCH HAND, 1962-1971, was based upon those herbicides that had been widely used in world agriculture, shown to be effective in controlling a broad spectrum of vegetation, and proven safe to humans and animals. The major herbicides used in South Vietnam were by phenoxy herbicides 2,4-D and 2,4,5-T. These two herbicides were formulated as the water insoluble esters and code-named by the military as Purple, Orange, Pink and Green. A water soluble amine formulation of 2,4-D was used in Herbicide White. Two other herbicides were extensively used by the military, picloram (in White) and cacodylic acid (in Blue).

An estimated 107 million pounds of herbicides were aerially disseminated on 3 million acres in South Vietnam from January 1962 through October 1971. Approximately 94 percent of all herbicides sprayed in Vietnam were 2,4-D (56 million pounds or 53 percent of total) or 2,4,5-T (44 million pounds or 41 percent of total). The 44 million pounds of 2,4,5-T contained an estimated 368 pounds of the toxic contaminant 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD or dioxin). Ninety-six percent of all 2,4,5-T was contained in Herbicide Orange; the remaining 4 percent in Herbicides Green, Pink and Purple. However, Herbicides Green, Pink and Purple contained approximately 40 percent of the estimated amount of TCDD disseminated in South Vietnam. Green, Pink and Purple were sprayed as defoliants on less than 90,000 acres from 1962 trhough 1964, a period when only a small force of US military personnel were in South Vietnam. Ninety percent of all the Herbicide Orange (containing 38.3 million pounds of 2,4,5-T and 203 pounds of TCDD) were used in defoliation operations on 2.9 million acres of inland forests and mangrove forests of South Vietnam.

The handling, transport and storage procedures employed for the herbicide generally precluded physical contact with the herbicides by most military personnel. However, personnel assigned to the RANCH HAND squadron and to individual helicopters responsible for the dissemination of herbicides were the most likely military personnel exposed to the herbicides.

The methods employed in spraying the herbicides, the geographical areas designated for dissemination of the herbicides, and the action of the environment on the herbicides generally precluded direct physical contact with the herbicide by military personnel assigned to other military programs.

2,3,7,8-tetrachlorodibenzodioxin (TCDD) - Toxicity in Animals Releyance to Human Health, With Notes on 2,4,5-T, Picloram, Cacodylic Acid, and 2,4-D.

Renate D. Kimbrough, M.D.
Center for Disease Control
Bureau of Laboratories
Public Health Service
Department of Health and Human Services
Atlanta, Georgia 30333

TCDD (2,3,7,8 tetrachlorodibenzodioxin), a chlorinated aromatic lipid soluble hydrocarbon (Fig. 1) is the most toxic representative of a group of chlorinated dibenzodioxins. Aside from the 2,3,7,8-tetrachlorodibenzodioxin, other tetrachlorodibenzodioxins also exist, such as the 1,3,6,8-techrachlorodibenzodioxin or the 1,2,3,4-tetrachlorodibenzodioxin. These other isomers are not nearly as toxic, or, in fact, as far as we know, have very little toxicity (Poland and Glover 1973). Present analytical methods utilizing gas chromatography and mass spectrometry do not definitely distinguish between these different isomers, but report all of them as TCDD. In addition to the TCDD isomers, other chlorinated congeners of dibenzop-dioxin occur, such as octochlorodibenzodioxin, heptachlorodibenzodioxin, and hexachlorodibenzodioxin. Depending on where the chlorines are positioned on the ring, they are orders of magnitude less toxic than TCDD. None of these compounds were ever made for commercial purposes. They occur as trace contaminants when chlorinated phenols are made from chlorinated benzenes. Since chlorinated phenols are utilized to make such herbicides as 1,4,5-T (trichlorophenoxy acetic acid), Silvex (2,4,5-trichlorophenoxy propionic acid), and hexachlorophene, these produces are also contaminated. During the distillation process (Fig. 2), much of the TCDD, together with some other chemicals, such as chlorinated xanthines, is removed from the commercial produce and collected as the still bottom residue. This residue contains concentrations of TCDD that may be as high as 1,000 ppm (mg/kg). These waste materials in the past were often not properly disposed of and have, on occasions, resulted in illness (Kimbrough, et al. 1977). During the 1950's and early 1960's, commercial products in some instances contained levels of TCDD which ranged from 1 ppm to 30 ppm or more. Presently manufactured 2,4,5-T contains less than 0.1 ppm TCDD.

Recently, it has been demonstrated that chlorinated dibenzodioxins, including TCDD, are formed on combustion in municipal incinerators and by heating chlorophenols (Chlorinated Dibenzodioxin Task Force 1978, Eichman, et, al. 1979; Jansson and Sundstrom 1978; Kimble and Gross, 1980; Langer, et al. 1973; Rappe and Buser 1979). TCDD can also be released into the environment when an uncontrolled exothermic reaction occurs during the production of 2,4,5-trichlorophenol, resulting in an explosion. A list of companies where such explosions have occurred was published by Hay (1979).

One way of measuring acute toxicity is by determining which dose given orally to animals will kill 50% of the, the so-called oral LD50. The oral LD50 for different species is given in Table 1. Although in some species such as the guinea pig, the amount killing 50% of the animals is much smaller than in the mouse, for instance, these results show that TCDD is extremely toxic for all species. According to the toxicity ratings by Gleason, et al (1969), TCDD would have to be classified as a supertoxic compound and a taste, or less than 7 drops of the material, could be lethal in humans.

The symptoms and signs observed in animals and humans are summarized in Table 2. The time to death may be delayed as long as 40 days after a single dose. This is very unusual. With most other compounds, animals receiving a toxic dose will die within 2 weeks.

Numerous experiments have been conducted to elucidate the mechanism of action of TCDD. Thus far, these experiments have not been very rewarding (Neal, et al. f979). The extreme wasting of animals for instance with almost total loss of body fat is not caused by decreased food consumption or poor absorption of nutrients. In some animal species (rat, rabbit, horses, and to some extent, mice) severe liver damage occurs, while this is not the case for guinea pigs or subhuman primates. In guinea pigs, the thymus and the lymphatic system are primarily affected, although the immune response is also impaired in other species, such as rats and mice. The effect on the immune response is particularly noticeable in the neonatal and suckling period (Vos, 1977). Atrophy of the thymus is observed and peripheral lymphocytopenia

has been reported. Guinea pigs exposed to as little as 40 ng TCDD per kg b.w. weekly for 8 weeks had depressed delayed hypersensitivity reactions to tuberculin (Vos, et al. 1973) and in mice, graft vs. host reactivity was suppressed following doses of 0.5 ug/kg body weight weekly for 4 weeks (Vos, et al. 1973).

Recently, it has been found that a good correlation exists between the toxicity of TCDD and the ease with which aryl hydrocarbon hydroxylase (AHH) can be induced in different species of animals. AHH is one enzyme of the hepatic mixed function oxidases. This enzyme metabolizes the precarcinogen benzpyrene. It seems unlikely that induction of this particular enzyme could be involved in toxicity; however, this correlation does suggest the possibility that the "recognition site" for TCDD which triggers the "de novo" synthesis of AHH also triggers the toxic response. A cytosolic protein which specifically binds TCDD has been identified (Poland, et al. 1976). Binding of TCDD to this protein is apparently the initial event in the cell which results in coordinate induction of a number of proteins and eventually causes toxicity. Sweeney and Jones (1977) treated genetically responsive (DBA/2J) and nonresponsive (DBA/2J) mice to the induction of arylhydrocarbon hydroxylase. The uroporphyrinogen decarboxylase activity was decreased in the liver of mice in the responsive mice, but not in those where arylhydrocarbon hydroxylase could not be included. Urinary uroporphyrin excretion was increased in the responsive, but not in the nonresponsive mice.

It has recently also been demonstrated that after the cytosol receptor binds TCDD, the complex translocates to the nucleus (Greenlee and Poland, 1979).

In addition to the marked acute toxicity of TCDD, its chronic or cumulative toxicity is even greater. For instance, daily consumption of 0.1 ug TCDD per kg b.w. in the diet lead to weight loss, hepatic porphyria and abnormal liver function tests within one year in rats. These rats also had lower hemoglobin levels white blood cell counts (Kociba, et al., 1977).

Similarly, 5 of 8 adult female rhesus monkeys that were fed an approximate total dose of 3 ug TCDD per kg body weight over a 9-month period died within 7-12 months after onset of exposure (Allen, et al., 1977).

Part of the reason for the cumulative toxicity is that TCDD has a relatively long half life of 17 to 31 days, depending on the circumstances of the studies and the species used, and is preferentially stored in the liver and in adipose tissue. Proportionally, the rat stores more TCDD in the liver than primates. Apparently TCDD is slowly excreted in bile and 90% of the TCDD derived material in bile does not cochromatograph with the parent compound. This material may represent one or more metabolites (Matthews and Kato, 1979). TCDD is fairly well absorbed from the gastrointestinal tract and is also absorbed through the skin. In rabbits, for instance, liver necrosis can be produced when the material is painted on the ear (Kimbrough, 1974, Kimbrough, et al., 1977). In addition to these more general toxic effects, TCDD also causes very characteristic diseases in different species, such as chick edema disease, chlorance and hepatic porphria cutanea tarda as it is called in humans. It, furthermore, has biochemical effects which can be measured in serum (Fig. 3) and affects reproduction. TCDD is not the only chemical that can produce these changes. Chick edema, chloracne and hepatic porphyria have also been reported following the exposure to some congeners of chlorinated dibenzofurans and polychlorinated biphenyls. Chloracne also occurs following exposure to chlorinated naphtalenes, 3,3',4,4'-tetrachloroazobenzene, and 3,3'4,4'-tetrachloroazoxybenzene which are contaminants of 3,4-dichloroaniline and herbicides made from 3,4-dichloroaniline (Morse, et al., 1979).

The signs and symptoms of chick edema disease are listed in Table 3. Several outbreaks of chick edema disease have occurred in the United States (Kimbrough, 1974) since about 1957.

Hepatic porphyria in man is a disorder of porphyrin metabolism which can either be inherited as a congenital anomaly or be caused by exposure to certain chemical compounds.

Among these so-called porphyrinogenic chemicals are the halogenated hydrocarbons, hexachlorobenzene, certain brominated and chlorinated biphenyls and TCDD.

In man, hepatic porphyria is usually associated with a considerable increase in total porphyrins, especially urinary uroporphyrin. In recent years, it has been discovered that qualitative changes in the pattern of porphyrins in the urine provide a far more sensitive indicator for disturbances in the pathway of heme synthesis than the quantitative changes. For instance, at a total porphyrin excretion which falls within the normal range, the proportion of porphyrin metabolites containing eight and seven carboxylic groups may be increased relative to those containing six, five and four carboxylic groups. There is evidence that one of the key processes involved at the molecular level is the inhibition of the enzyme uroporphyrinogen decarboxylase.

In the most severe form of porphyria, porphyria cutanea tarda (PCT), a diagnostic indicator is the simultaneous appreciable increase of both uro- and heptacarboxylic porphyrin in urine. PCT is present when 45 to 70% of the total porphyrins is uroporphyrin and 25 to 35% is heptacarboxylic porphyrin. This relative distribution pattern of the urinary porphyrins is so characteristic that a diagnosis can be made from a single examination of a small urine sample, even without knowledge of the 24-hour urine volume (Doss, 1974).

In studies of the porphyrins in liver biopsies and urine, it has been found that chronic hepatic porphyria (CHP) without clinical symptoms begins with the accumulation of uro- and heptacarboxylic prophyrin in the liver, followed by a gradually increasing excretion of porphyrins in the uring (200-1400 ug/l).

The increase in the excretion of uro- and heptacarboxylic porphyrin in the urine and the accumulation of both of these prophyrins in the liver result from a decrease of the activity of uroporphyrinogen decarboxylase (Doss, et al., 1976).

Chronic exposure to polyhalogenated aromatic compounds, including TCDD, causes porphyria in man, rat, rabbit, Japanese quail, chicken and mouse, but not in young rats, guinea pig, mink, minipig (Strik, 1973). Japanese quail an chicken develop porphyria from polyhalogenated aromatic compounds more readily than rat, rabbit, or man (Strik, 1973).

Following dermal exposure to TCDD or after ingestion, humans develop a skin disease called chloracne. Most instances of chloracne have been due to occupational exposure.

Depending on the severity of the exposure and the susceptibility of the individual workers, some will develop an occupational disease commonly referred to as chloracne after having had exposure to the hologenated cyclic compounds mentioned above for several weeks or months. Following exposure to high concentrations of TCDD, the onset may be more rapid. Even after a single exposure to TCDD, the onset of chloracne may be delayed for several weeks, but if the exposure is severe, it may appear in as little as 2-3 days.

The clinical features of chloracne, regardless of the type of chemical that caused it, have been most consistent. The most distinctive cutaneous lesion is the chloracne cyst (Crow 1970). This lesion is skin colored, measuring from 1-10 mm in diameter with a central opening. The other dominant lesion is the comedo (Fig. 4). Usually these lesions start over the maxillary bone, then involve the entire face, the neck, ears. Often thenose and nasolabial folds are not as extensively involved. In males, the genitalia may be involved. Furthermore, lesions may be present on the back, arms and legs, and other areas of the body, particularly where garments are in close contact with the skin.

The comedones and cysts can become secondarily infected and large pustules may form. Cysts may rupture and cause foreign body granulomata.

Once chloracne has developed, it may remain active for many years, and particularly when secondary infections occur, deep-pitted scars may remain as a residual effect. These scars can be quite disfiguring (Fig. 5). No specific treatment is available and most palliative means have not been very effective. Treatment in the past has included Vitamin A acid, UV light, X-ray, lancing and expressing of pustules. However, the best treatment is prevention, although dermabrasion has also been effective (Crow, et al., 1970).

A skin lesion exactly like chloracne can be produced on rabbit ears or hairless mice and the muzzle of rhesus monkeys. In cattle and horses, a microscopically slightly different skin lesion which is also called hyperkeratosis or x-disease develops following exposure to compounds that produce chloracne in humans. In cattle and horses, the skin lesion is usually accompanied by hair loss in the affected areas and the epidermis is covered by a thick layer of keratin (Kimbrough et al., 1974 and 1977). Prior to the ability to detect chloracnegenic compounds by chemical analysis, the rabbit ear test was utilized to screen technical products for their presence (Adams et al., 1941).

In rabbits, monkeys and men, the microscopic appearance of the skin lesion varies, depending on the interval between last exposure and the time the biopsy was obtained. Microscopic examination of human skin biopsies from chloracne cases or tissue sections from rabbit ears with hyperkeratosis show markedly dilated hair follicles that are filled with keratin. Eventually the entire follicular appendage becomes transformed into a sac of keratin (Fig. 6). The sebaceous glands involute and the epithelial cells lining the follicles and adjacent to them proliferate.

In rodents, TCDD has also been found to be carcinogenic. In female rats, an increase of hapatocellular carcinomas and carcinomas of the hard palate, the nasal turbinates and the lungs was observed at a daily dietary does of 0.1 ug TCDD/kg body weight (Kociba, et al., 1978) (Table 4). At this dietary level, tissue levels reached in he liver were 24 ppb (ug/kg) and in fat, 8.1 ppb (ug/kg) of these rats.

The teratogenic and fetotoxic effects of TCDD have received much publicity. In mice, cleft palates have been induced at a dose of 1.0 ug/kg b.w. It was also found that 2,4,5-T (trichlorophenoxy acetic acid), if combined with TCDD, results in cleft palates when a dose of 0.2 ug/kg of TCDD is given and 60 mg/kg 2,4,5-T. The other findings in mice are enlarged renal pelvis and atrophic thymus at a dose of 1 ug/kg b.w. In rats, a does of 0.125 ug/kg causes hemorrhage, subcutaneous edema, and dilated renal pelvises in the fetus. In addition, abortions have been observed in horses (Kimbrough, et al., 1977) and subhuman primates (Allen and Barsotti, 1979). In female subhuman primates, an increase in 17 betaestratiol and progesterone was also noted. Anomalous development of the soft palate in rhesus macaques (Macaca mulatte) prenatally exposed to TCDD has also recently been reported (Zingeser, 1979) as a preliminary finding.

The effect of TCDD on male fertility has not been as extensively studied. Usually higher doses of TCDD are required to produce morphologic changes in the testes (Allen, et al., 1979; McConnell and Moore, 1979) of monkeys and rodents.

2,4,5-T and Picloram

2,4,5-T (2,4,5-trichlorophenoxyacetic acid) is an herbicide which was introduced commercially in 1944 (Fig. 7).

The acute oral LD50 in rats is 500 mg/kg and in dogs 100 mg/kg (Martin, and Worthing, 1974). Accordingly, 2,4,5-T would have to be considered as very toxic according to the toxicity rating of Gleason, et al. (1969). 2,4,5-T is not very persistent in mammals and most of it is excreted within 24-48 hours in rats. In dogs, half life values for clearance from the body are 86.6 hours (Piper, et al., 1973). Excretion occurs primarily through the kidneys. In rats, about 68.3% is excreted as free 2,4,5-T. Small amounts of conjugates and 2,4,5-trichlorophenol are also excreted in the urine. In mice, the percentage of free 2,4,5-T is only about 30% (Grunow and Bohme, 1974). These findings show that there are some species differences in the metabolism of 2,4,5-T. Studies on fetal uptake of 2,4,5-T in mice showed that it is low until gestation day 10. On day 12 and 13, the fetal concentration was higher. Concentration of 2,4,5-T in the yolk sac also occurs (Denker, L., 1976). 2,4,5-T per se in high doses is also teratogenic in mice (Neubert and Dillmann, 1972).

Rats fed daily doses of 3,10, or 30 mg 2,4,5-T/kg body weight for 2 years showed some adverse effects at the two higher doses levels, namely, a decrease in body weight gain and increases in urinary excretion of coproporphyrin and uroporphyrin. The kidneys showed mineralized deposits in the renal pelvis and an increased content of iron positive staining pigment in the tubular epithelium in female rats. An increased incidence of tumors was not noted in the exposed groups (Kociba, et al, 1979).

Hardell and Sandstrom conducted a case control study in humans in Sweden using 52 patients with mesenchymal tumors and 208 controls. The controls were matched for age, sex, year of death and place of residence for those that were alive. Deaths from malignant tumors or suicide were excluded. A total of 29 controls were actually from other municipalities than the cases to which they were matched. Another prerequisite was that the controls were to have been working until 2 years before retirement or death. It was found that the relative risk for solf tissue sarcomas after exposure to phenoxyacetic acids of chlorophenols was 6.2 over the controls (Hardell and Sandstrom, 1979). It is not clear from the report whether a bias may have been introduced because some controls with malignant tumors were excluded from the study. Further studies in exposed populations may elucidate this problem.

Investigations of chromosome aberrations induced by phenoxyacetic acids in animals are inconclusive. Dominant lethal tests with 2,4,5-T in mice were negative. The induction of chromosome aberrations with 2,4,5-T butylester and acid has however been reported from cytological investigations on rats and Mongolian gerbils.

In cytological studies of oogenesis in Drosophila, various chromosomal disturbances were recorded after treatment with a 2,4,5-T butylester formulation. However, no chromosome aberrations were indicated in genetic analyses after treatment of male Drosophila with the same preparate. An increase of recessive lethals has been reported in Drosophila after treatment with high doses of 2,4,5-T and 2,4-D (Ramel, 1978).

The mutagenic potential of TCDD has recently been reviewed (Wassom, et al., 1977/1978). Experimental results thus far are ambiguous in that some studies did show a mutagenic effect, while other experiments suggest the opposite.

Picloram

Picloram (4-amino-3,5,6-trichloropyridine-2-carboxylic acid) - a white powder with a chlorine-like odor - is a systemic herbicide. On an acute basis, it is not very toxic. The acute oral LD50 values range from more than 750 mg/kg in cattle to 8200 mg/kg in rats (Martin and Worthing, 1974). A study in chickens showed no effects on reproduction (Somers, et al., 1978), nor have mutagenic effects been demonstrated. A bioassay study conducted by the National Cancer Institute (1977) in rats and in mice was interpreted as negative. However, neoplastic nodules were noted in rat livers. A high incidence of c-cell hyperplasia and c-cell adenemas of the thyroid was also noted in the exposed rats. Time weighted average dosage levels were 7,437 - 14,875 ppm (mg/kg).

No systemic effects have been reported in workers exposed to picloram. However, irritation of the skin and mucous membranes can occur.

Cacodylic Acid

Cacodylic acid is the trivial name for dimethylarsinic acid which was introduced in 1958 for herbicidal use. The acute oral LD50 of the technical grade powder in rats is 1,350 mg/kg body weight which makes this a moderately toxic product and for a 70 kg man, an ounce to a pound (450 grams) would be fatal (Gleason, et al., 1969). In rabbits, the acute dermal LD50 is greater than 3,000 mg/kg. (Industrial Biotest Laboratories, 1975). Cacodylic acid neither causes eye nor skin irritation in animals. In general, trivalent arsenic compounds are more toxic than the pentavalent arsenic compounds. Sodium cacodylate has been used therapeutically in the same conditions as inorganic arsenic at a dosage of 25-150 mg per day.

The effects of cacodylic acid are essentially those of inorganic arsenic to which it is partially reduced in the body.

Arsenic inhibits the activity of many enzymes by reacting with sulfhydryl groups. There are very few data on kinetics and metabolism of arsenic and its compounds. Arsenic is distributed primarily to the liver, kidneys, intestinal wall, spleen and lungs.

When arsenite was given intravenously to human volunteers, it was excreted in urine primarily as arsenite and arsenate with the latter predominating. These findings suggest in vivo oxidation and preferential excretion of arsenic in urine (Nealey, et al., 1959). No such studies have been conducted with cacodylic acid.

A number of epidemiological studies have been conducted in people who are exposed to high concentrations of arsenic in drinking water and in workers exposed occupationally to arsenic compounds. The health effects that have been associated with such exposures are Raynaud's phenomenon, acrocyanosis, abnormal skin pigmentation, hyperkeratosis, involvement of the nervous system involving sensory nerves first, chronic coryza, and cardiovascular manifestations. Arsenic may also suppress the immune response selectively.

Arsenic is considered a human carcinogen. An increased incidence in cancer of the lungs, liver and skin has been observed in humans following exposure to high concentrations of arsenic. So far, it has not been possible to produce cancer in animals with aresenic. Arsenic also causes fetal death at high doses and malformations at lower exposure in hamsters, mice and rats.

Bacterial systems have revealed that arsenic interferes with DNA repair (NRC 1977, USDHEW 1975). In a naturally occurring disease in humans, xeroderma pigmentosum, DNA repair is also deficient. In such patients, a higher incidence, particularly of skin cancer, is observed. It is possible that arsenic by impairing DNA repair prevents cells from effectively dealing with initiators of cancer at low concentrations. This, then may result in an increased incidence of cancer in people who have been exposed to high concentrations of arsenic while such exposure would not result in an increased incidence of cancer in the general population. A review of the toxicity of cacodylic acid was recently prepared by the United States Environmental Protection Agency.

2,4-D

The acute oral LD50 for ,24-D in different animal species ranges from 375 mg/kg body weight to 1000 mg/kg body weight. In dogs, the acute oral LD50 is 100 mg/kg body weight. (Hill and Carlisle, 1957, Rowe and Hymas, 1954; Drill and Hiratzka, 1953). The oral LD50 for the 2,4-D esters and salts are also within the same range. Symptoms of acute toxicity in different animal species include stiffness of the extremities, incoordination, lethargy, stupor, coma, and it is assumed that this in some animals is due to ventricular fibrillation. Symptoms of myotonia have also been reported.

Apparently, 2,4-D uncouples oxidative phosphorylation (Browdy, 1952). 2,4-D is readily absorbed, metabolized and primarily eliminated in the urine, with plasma half lives varying from 3 to 12 hours (Erne, 1966 a & b). Most of the 2,4-D is excreted as such in the urine of rats. A minor portion is conjugated with glycine, taurine and glucuronic acid (Grunow and Boehme, 1974). The 2,4-D also passes through the placenta and can be detected in the fetus and in amniotic fluid (Federova and Belova, 1974).

Feeding studies in rodents and dogs show that the material is not particularly toxic when given repeatedly. Dogs fed dietary levels of 500 mg/kg 2,4-D for a period of two years showed no adverse effects (Hansen, et al., 1971). In a three-generation reproduction study with Osborne Mendel rats, dietary levels of 500 mg/kg did not cause any adverse effects. However, diets containing 1,500 mg/kg 2,4-D did reduce the percentage of pups surviving to weaning and the weights of the weanlings (Hansen, et al., 1971). The administration of 2,4-D as isopropylbutyl or isooctyl ester orally or subcutaneously during days 6 to 14 of pregnancy increased the incidence of fetal abnormalities among BL 6 AKR and/or C_3H strains of mice. (NTIS 1968 a and b). The carcinogenic potential of 2,4-D was reviewed in 1977 by the International Agency for Research on Cancer (IARC). It was concluded that all studies which have been conducted so far to determine whether 2,4,-D is carcinogenic, had limitations due either to inadequate reporting or to the small number of animals used and no evaluation of the carcinogenicity of this compound could be made. The report also cites the results of a single cohort study of a small number of workers exposed to various herbicides, including 2,4-D; 2,4,5-T and 3-amino-1,2,4 triazole (amitrole). It was determined that the results of this study were not sufficient to evaluate the carcinogenicity of 2,4-D in men (IARC, 1977).

Acute human toxicity following exposure to 2,4-D has also been observed. A single oral dose of about 3 to 4 grams (43-70 mg/kg of 2,4-D causes symptoms of poisoning in men, while daily doses of 500 mg/day/person or 7 mg/kg were tolerated without ill effects for 21 days. Intravenous doses of 800 mg/day/person or more, the last dose being 200 mg or about 37 mg/kg, did not produce side effects in a patient who received 2,4-D for the treatment of disseminated coccidiomyosis. When the same patient was given 3,600 mg of 2,4-D intravenously, about 51 mg/kg, he became comatose, suffered fibrillary muscle twitching, hyperreflexia and urinary incontinence (Hayes, 1963). Ingestion of at least 80 mg/kg body weight of 2,4-D was fatal with severe degenerative changes of the ganglion cells of the central nervous system (nielsen, et al., 1965). In another episode, a farmer accidentally swallowed 110 mg/kg body weight of 2,4-D and 230 mg/kg body weight of S-ethyldipropylthiocarbamate and 2.3 mg/kg body weight of epichlorohydrin. He developed twitching and paralysis of intercostal muscles. In addition, abnormal liver function tests, hemoglobinuria and myoglobinuria were observed (Berwick, 1970). Since this patient was also exposed to other chemicals, the toxic effects observed were not solely caused by 2,4-D. An additional fatality following exposure to 2,4-D was reported by Dudley, et al. (1972). Several cases of peripheral neuropathy following percutaneous absorption of 2,4-D have been reported in humans (Goldstein, et al., 1959; Todd 1962; and Berkley and Magee, 1963). EEG changes were noted in seventeen farm workers involved with the transport of 2,4-D derivatives (Knotek, 1973). Inhalation of 44% 2,4-D caused unconsciousness 2 to 3 hours later, followed by vomiting, myalgia, muscular hypertonia and nodal tachycardia (Paggiaro, 1974). Similarly, ataxia and reflex disorders which persisted for two months were reported in individuals who had inhaled large amounts of 2,4-D (Monarca and DeVito 1961). This effect on the neuromuscular apparatus observed following poisoning with 2,4-D in humans can also be demonstrated in animals (Eyzaguirre, 1948). The phenomena observed in these animals are indistinguishable from those occurring in spontaneous myotonia of men. Additional studies on the myopathy produced by 2,4-D have been done by Henee (1968 a and b). Apparently the myopathies observed following the exposure to 2,4-D are closely related to those induced by corticosteroids. The basis of the lesion is mytochondrial proliferation which may either return to normal or proceed to irreverisble degeneration of mytochondria with consecutive loss of myofibrils. To produce these muscular lesions, toxic doses were used. No reports are in the literature to indicate whether doses which are not generally toxic would also have neuromuscular eff-cts. The human case reports must be taken with some reservation since no base line data was available.

Apparently humans excrete 2,4-D as rapidly as do animals. When 5 human volunteers ingested a single dose of 5 mg/kg 2,4-D, the elimination from plasma occurred by first order kinetics with an average half life of 11.7 hours. Essentially, all 2,4-D was absorbed from the gastrointestinal tract and no clinical effects were noted. (Sauerhoff, et al., 1976).

REFERENCES

1. Poland, A. and Glover, E. (1973) Chlorinated dibenzo-p-dioxins: potent inducers of aminolevulinic acid synthetase and aryl hydrocarbon hydroxylase II. A study of the structure - activity relationship. Mol. Pharmacol. 9 736-747.

2. Kimbrough, R.D., Carter, C.D., Liddle, J.A., Cline, R.E., and Phillips, P.E. Epidemiology and pathology of a tetrachlorodibenzodioxin poisoning episode. Arch. Environ. Health 32, 77-86, 1977.

3. Chlorinated Dioxim Task Force. 1978. The trace chemistries of fire - A source of and routes for the entry of chlorinated dioxims into the environment. The Michigan Division, Dow Chemical USA, Midland, Michigan, 46 pg.

4. Dobbs, A.J., and C. Grant. 1979. Photolysis of highly chlorinated dibenzo-p-dioxins by sunlight. Nature 278: 163-165.

5. Eichman, G.A., R.E. Clement, and F.W. Karsek. 1979. Analysis of fly ash from municipal incinerators for trace organic compounds Anal. Chem. 51(14): 2343-2350.

6. Jansson, B., and G. Sundstrom. 1978. Formation of polychlorinated dibenzo-p-dioxins during combustion of chlorophenol formulations. Sci. Total Environment (The Netherlands) 10: 209-217.

7. Kimble, B.J., and Gross, M.L. 1980. Tetrachlorodibenzo-p-dioxin quantitation in stack - collected cool fly ash. Science 207: 59-61.

8. Kimbrough, R.D. 1974. The toxicity of polychlorinated polycyclic compounds and related chemicals. Crit. Rev. Toxicology. 2: 445-498.

9. Langer, H.G., Brady, T.P., and Briggs, P.R. 1973. Formation of dibenzodioxins and other condensation products from chlorinated phenols and derivatives. Environ. Health Perspect. 5: 3-7.

10. Rappe, C. and Buser, H.R. 1979. Formation and degradation of polychlorinated dibenzo-p-dioxins (PCDDs) and dibenzo-furans (PCFDs) by thermal processes. Presentation to the Division of Pesticide Chemistry, American Chemical Society Washington, DC, Mimo..21p.

11. Hay, A. (1979) Accidents in trichlorophenol plants: A need for realistic surveys of a certain risk to health. NY Acad. Science 320, 321-324.

12. Gleason, N.N., Gosselin, R.E., Hodge, H.C. and Smith, R.P. Clinical Toxicology of commerical products. The Williams and Wilkins Co., Baltimore 1969.

13. Vos, J.G. Immune suppression as related to toxicology. CRC Crit Rev. Toxicol. 5, 67-101, 1977.

14. Vos, J.G., Morre, J.A. and Zinkl, J.G. Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin on the immune system of laboratory animals. Environ. Health Persp. 5, 149-162 (1973).

15. Neal, R.A., Beatty, P. and Gasiewicz, T.A. Studies of the mechanisms of toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Ann. N.Y. Acad. Sci. 320, 204-214. (1979).

16. Poland, A., Grenlee, W.F. and Kende, A.S. Studies on the mechanism of action of the chlorinated dibenzo-p-dioxins and related compounds. Ann. NY Acad. Sc. 320, 214-230, 1979.

17. Poland, A., Glover, E., and Kende, A.S. Stereospecific high affinity binding of 2,3,7,8-tetrachlorodibenzo-p-dioxin by hepatic cytosol. J. Biol. Chem. 251, 4926-4946, 1976.

18. Grenlee, W.F., and Poland, A. Nuclear uptake of 2,3,7,8-tetrachlorodibenzo-p-dioxin in C57BL/6J and DBA/2J mice. J. Biol. Chem. 254, 9814-9821, 1979.

19. Kociba, R.J., Keyes, D.G., Beyer, J.E., Carreon, R.M., Wade, C.E., Dittenber, D.A., Kalnins, R.P., Frauson, L.E., Park, C.N., Bernard, D.S., Hummel, R.A. and Humiston, C.G. (1978) Results of a two-year chronic toxicity and oncogenicity study of e,3,7,8-tetrachlorodibenzo-p-dioxin in rats. Toxicol. Appl. Pharmacol. 46, 279-303, 1978.

20. Allen, J.R., Barsotti, D.A., Van Miller, J.P., Abrahamson, L.J., and Lalich, J.J. Morphological changes in monkeys consuming a diet containing low lwvels of 2,3,7,8-tetrachlorodibenzo-p-dioxin. Fd. Cosmet. Toxicol. 15, 401-410 (1977).

21. Matthews, H.B., and Kato, S. The metabolism and disposition of halogenated aromatics. Ann. N.Y. Acad. Science 320, 131-137, 1979.

22. Kimbrough, R.D. (1974). The toxicity of polychlorinated, polycyclic compounds and related chemicals, CRC Crit. Rev. Toxicol. 2, 445-498.

23. Morse, D.L., Baker, E.L., Kimbrough, R.D., and Wisseman, C.L. Propanilchloracne and methomyl toxicity in workers of a pesticide manufacturing plant. Clin. Toxicol. 15, 13-21 (1979).

24. Doss, M. Porphyrins and porphyrin precursors. In: M.C. Curtius and M. Roth (Eds.) Clin. Biochem. Principles and Methods, Vol. II. Degruyter, Berlin pp. 1339 (1974).

25. Doss, M., Schermuly, E., Look, D., and Henning, H. Enzymatic effects in chronic hepatic porphyria. In: M. Doss (Ed.) Porphyrins in human diseases. Karger, Basel pp. 286-298 (1976).

26. Strik, J.J. T.W.A. Species differences in experimental porphyria caused by polyhalogenated aromatic compounds. Enzyme 16, 224-228 (1973).

27. Crow, K.D., Chloracne. A critical review including a comparison of two series of cases of acne from chlornaphthalene and pitch fumes. Trans. St. Johns Hosp. Dermatol. Soc. 56, 79-99, 1970.

28. Adams, E.M., Irish, D.D., Spencer, H.C., and Rowe, V.K. The response of rabbit skin to compounds reported to have caused acneform dermatitis. Ind. Med. 2, 1-4, 1941.

29. Zingeser, M.R. (1979). Anomalous development of the soft palate in rhesus macaques (Macaca Mulatta) prenatally exposed to 2,e,7,8-tetrachlorodibenzo-p-dioxin. Teratol. 19, 54A-55A.

30. Allen J.R., Barsotti, D.A., Lambrecht, L.K., and Van Miller, J.P. Reproductive effects of halogenated aromatic hydrocarbons on nonhuman primates. Ann. NY Acad. Sci. 320. 419-425, 1979.

31. McConnell, E.E. and Moore, J.A. Toxicopathology characteristics of the halogenated aromatics. Ann. NY Acad. Science 320, 138-150 (1979).

32. Martin, H., and Worthing, C.R. Pesticide Manual. Brit. Crop Protection Council. Mr. A. W. Billitt, Clacks Farm Barcley Worchester, England (1974).

33. Grunow, W. and Bohme. Chr. Uber den Stoffwechsel von 2,4,5-T and 2,4-D bei Ratten and Mausen. Arch. Toxicol. 32, 217-225 (1974).

34. Denker, L. Chapter IV, The herbicide 2,4,5-T: early placental barrier and accelerated fetal uptake with advancing gestation. Acta Pharmacol. et Toxical. 39, 59-72, 1976.

35. Piter, W.N., Rose, J.W., Leng, M.L. and Gehring, P.J. The fate of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) following oral administration to rats and dogs. Toxicol. Appl. Pharmacol. 26, 339-351, 1973.

36. Neubert, D. and Dillman, I. Embryotoxic effects in mice treated with 2,4,5-trichlorophenoxy-acetic acid and 2,3,7,8-tetrachlorodibenzo-p-dioxin. Naunyn Schmiedebergs Arch. Pharmacol. 272, 243-264, 1972.

37. Kociba, R.J., Keyes, D.G., Lesowe, R.W., Kalnins, D., Dittenber, D., Wade, C.E., Gorzinski, S.J., Mahle, N.H., and Schwetz, B.A. Results of a two year chronic toxicity and oncogenic study of rats ingesting diets containing 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) Fd. Cosmet. Toxicol. 17, 205-221, 1979.

38. Hardell, I. and Sandstrom, A. Case control study: soft-tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols. Brit. J. Cancer 39, 711-717, 1979.

39. Ramel, C. Chlorinated Phenoxy Acids and Their Dioxins. Ecol. Bull. (Stockholm) 27: 182-185(1978).

40. Wassom, J.S., Huff, J.E., and Loprieno, N. A review of the genetic toxicology of chlorinated dibenzo-p-dioxins. Mutation Res. 47, 141-160 (1977/1978).

41. Carcinog. Program, Div. Cancer Cause & Prev., NCI, Bethesda, MD 20014. Bioassay of picloram for possible carcinogenicity, Natl. Tech. Inform. Serv. PB-276, 471: 94p; 1977.

42. Somers, J.D., Moran, E.T., Reinhart, B.S. (Dep. Anim. & Poultry Sci., Univ. Guelph, Ont. NIG 2W1, Canada) Reproductive success of hens and cockerels originating from eggs sprayed with 2,4-D, 2,4,5-T and picloram followed by early performance of their porgency after a comparable in ovo exposure. Bull. Environ. Contam. Toxicol. 20(1): 111-119, (1978).

43. Industrial BiotestLaboratories "Acute Toxicity Studies with Bolls Eyes" JBT No. 601-05911 submitted to the Ansul Company, Marinette, Wisconsin EPA Pesticide Petition No. R0058981 (Jan. 13, 1975).

44. Mealey, J., Jr., Brownell, G.L., and Sweet, W.H. Radioarsenic in plasma, urine, normal tissues and intracranial neoplasms. AMA Arch. Neurol. Psychiat. 81, 310-320 (1959).

45. National Research Council. Drinking Water and Health, pp. 316-344, National Acad. Sci., Washington, DC 1977.

46. US DHEW (NIOSH) Criteria for a recommended standard, occupational exposure to inorganic arsenic. HEW Publ. No. 75 - 149 Supt. Doc., US Govt. Printing Office, Washington, DC 20402.

47. United States EPA Initial Scientific Review of Cacodylic Acid #EPA 540/1 - 75 - 021 (1975). Available from NTIS Springfield, VA. 22151.

48. Hill, E.V. & Carlisle, H. Toxicity of 2,4-dichlorophenoxyacetic acid for experimental animals. J. Indust, Hyg. Toxicol., 29, 85-98 (1947).

49. Rowe, V.K & Hymas, T.A. Summary of toxicological information on 2,4-D and 2,4,5-T type herbicides and an evaluation of the hazards to livestock associated with their use. Amer. J. Vet. Res., 15, 622-629 (1954).

50. Drill, V.A. & Hiratzka, T. Toxicity of 2,4-dichlorophenoxyacetic acid and 2,4, 5-trichlorophenoxyacetic acid: a report on their acute and chronic toxicity in dogs. Arch. Industr. Hyg. Occup. Med. 7, 61-67 (1953).

51. Brody, T.M. Effect of certain plant growth substances on oxidative phosphorylation in rat liver m-tochondria. Proc. Soc. Exp. Biol. 80, 533-536, (1952).

52. Erne, K. Distribution and elimination of chlorinated phenoxyacetic acids in animals. Acta Vet. Scand. 7, 240-256 (1966a).

53. Erne, K. Studies on the animal metabolism of phenoxyacetic herbicides. Acta Vet. Scand. 7, 264-271 (1966b).

54. Grunow, W. & Bohme, C. Uber den Stoffwechsel von 2.4.5-T und 2.4-D bei Ratten und Mausen. Arch. Toxicol. 32, 217-225 (1974).

55. Fedorova, L.M. and Belova, R.S. Incorporation of 2,4-dichlorophenoxyacetic acid into the organs of animals: paths and dynamics of its excretion. Gig. i Sanit. 2, 105-107 (1974).

56. Hansen, W.H., Quaife, M.L., Habermann, R.T. & Fitzhugh, O.G. Chronic toxicity of 2,4-dichlorophenoxyacetic acid in rats and dogs. Toxicol. Appl. Pharmacol. 20, 122-129 (1971).

57. NTIS (National Technical Information Service) Evaluation of Carcinogenic, Teratogenic and Mutagenic Activities of Selected Pesticides and Industrial Chemicals, Vol. 1, Carcinogenic Study, Washington, DC, US Department of Commerce (1968a).

58. NTIS (National Technical Information Service) Evaluation of Carcinogenic, Teratogenic and Mutagenic Activities of Selected Pesticides and Industrial Chemicals, Vol. 2, Teratogenic Study in Mice and Rats, Washington, DC, US Department of Commerce (1968a).

59. LARC. Monographs on the evaluation of carcinogenic risk of chemicals to man. Some Fumigants, the herbicides 2,4-D and 2,4,5-T, chlorinated dibenzodioxins and miscellaneous industrial chemicals. 15, 111-138 (1977).

60. Hayes, W.J. Clinical Handbook on economic poisons. Public Health Service Publ. 476. U.S. Govt. Printing Office, Washington, DC (1963). Reprinted Oct. 1971.

61. Nielsen, K., Kaempe, B. and Jensen-Holm, J. Fatal poisoning in man by 2,4 dichlorophenoxyacetic acid (2,4-D), determination of the agent in forensic materials. Acta Pharmacol. et Toxicol. 22: 224-234, (1965).

62. Berwick, P. 2,4 Dichlorophenoxyacetic acid poisoning in man. JAMA 214: 1114-1117 (1970).

63. Dudley, Jr., and Thapar, N.T. Fatal human ingestion of 2,4-D, a common herbicide. Arch. Pathol. 94: 270-275 (1972).

64. Goldstein, N.P., Jones, P.H. and Brown, J.R. Peripheral neuropathy after exposure to an ester of dichlorophenoxyacetic acid. JAMA 171: 1306-1309 (1959).

65. Berkley, M.C. and Magee, K.R. Neuropathy following exposure to a dimethylamine salt of 1,4-D. Arch. Intern. Med. 111: 351-352 (1963).

66. Todd, R.L. A case of 2,4-D intoxication. J. Iowa Med. Soc. 52: 663-664, (1965).

67. Knotek, M., Marcinkowska, B. and Pietraszek, Z. Elecrtoencephalographic investigations in farm workers exposed to derivatives of arlalcanocarboscy acids. Pol. Tyg. Lek. 28 (27): 937-939 (1973).

68. Paggiaro, P.L., Martino, E., and Mariotti, S. Su Un Caso di intossicazione de acido 2,4-dichlorofenossiacetico. Med. Lav. 65 (3-4): 128-135 (1974).

69. Monarca, G. and DeVito, G. Acute poisoning through 2,4 dichlorophenoxyacetic acid. Folia Med. 44: 480-485 (1961).

70. Eyzaguirre, C., Folk, B.P., Zierler, K.L. and Lilienthal, Jr., J.L. Experimental myotonia and repetitive phenomena, the veratrinic effects of 2,4-dichlorphenacetate (2,4-D) in the art. Am. J. Physiol. 155, 69-77 (1948).

71. Heene, R. Elektronenmikroskopische Befunde bei experimenteller Myopathie durch 2,4-dichlorophenoxyacetat (2,4-D) beim Warmbluter. Deutsch Ztschr. fur Nervenheilkunde 193, 265-278 (1968a).

72. Heene, R. Histochemische und morphologische Befunde bei experimenteller Myopathie durch 2,4 Dichlorphenoxyacetat (2,4-D) beim Warmbluter. Acta Neuropathologica 10, 166-169 (1968b).

73. Sauerhoff, M.W., Braun, W.H., Blau, G.E. and LeBeau, J.E. The fate of 2,4 dichlorophenoxyacetic acid (2,4-D) following oral administration to man. Toxicol. Appl. Pharmacol. 37 (1): 136-137, (1967).

LEGEND FOR FIGURES

Fig. 1 Chemical structure of TCDD.
Fig. 2 Production process of 2,4,5-trichlorophenol.
Fig. 3 Effect of TCDD on blood and serum enzymes.
Fig. 4 Active chloracne in a worker.
Fig. 5 Permanent scars left as a residual in a worker who had severe chloracne.
Fig. 6 Dilated hair follicle showing morphological changes consistent with chloracne (H + E x 100).
Fig. 7 Chemical structure of 2,4,5-T.
Fig. 8 Chemical structure of picloram.
Fig. 9 Chemical structure of cacodylic acid.

Table 1. Acute Oral LD50

female rats	45 ug/kg
male rats	22.4 ug/kg
male guinea pigs	0.6 ug/kg
rabbits	115 ug/kg
dogs	30-300 ug/kg
mice	114 ug/kg

Table 2. The effects of TCDD in animals and humans

A. Animals

1. severe weight loss
2. delayed death (up to 40 days)
3. repeated dosing - toxic at much lower dosage levels than with single dose - thus cumulative
4. teratogenic - fetotoxic
5. hemorrhages in different parts of the body
6. necrosis, ulceration mucosa of the stomach
7. atrophy of the lympathic system
8. liver damage
9. chick edema disease
10. hyperkeratosis, x-disease in cattle?
11. hyperkeratosis rabbit skin
12. hepatic prophria

B. Humans

1. occupational skin disease on contact

    a. chloracne, halogen acne, perna diseases (melanosis, hyperkeratosis)

    b. cable rash

2. porphyria cutanea tarda (hepatic porphyria)
3. systemic disease - mainly liver and GI tract
4. peripheral sensory neuropathy

Table 3. Chickedema Disease

Grossly

1. Fluid accumulation, pericardial sac, peritoneal cavity and subcutaneous tissue.
2. Pale liver.
3. Eechymolic hemorrhage.
4. Pale swollen kidneys.

Microscopic lesions

1. Endotheliosis of arteriole and small arteries.
2. Proliferative changes in glomeruli.
3. Necrosis of hepatocytes in liver.
4. Decrease of albumin.
5. Pulmonary edema.
6. Perivascular lymphocytic infiltration.
7. Edema of the cardiac muscle and lymphocylic infiltration of the cardiac muscle.

Table 4. Incidence of TCDD Induced Tumors in Female Rats (Kociba, et. al. 1978)

	Incidence per dosage level (ug/kg/day)			
Type of tumor	0	0.1	0.01	0.001
Hepatocellular carcinoma	2/86	11/48	2/50	0/50
Squamous cell carcinoma of the lungs	0/86	7/49	0/50	0/50
Squamous cell carcinoma of hard palate of nasal turbinate	0/86	4/49	1/50	0/50

DIAGNOSTIC INDICATORS OF PHENOXY HERBICIDE/DIOXIN TOXICITY

WILLIAM H. WOLFE*
LT COLONEL, USAF, MC
Epidemiology Division
USAF School of Aerospace Medicine
Brooks AFT, San Antonio, TX 78235

*Address Inquiry: Lt Colonel William H. Wolfe, USAF, MC
Chief, Disease Surveillance Branch
Epidemiology Division
USAF School of Aerospace Medicine
Brooks AFB, San Antonio, TX 78235

Phone: (512) 536-3471/2715

Ideally, one would like to have a sensitive and specific examination or laboratory procedure to detect herbicide and/or TCDD or their effects. Unfortunately: 1) There is a lack of clearly defined end points in the scientific literature, 2) There is no distinct clinical syndrome or unique effect other than chloracne, 3) The signs and symptoms currently attributed to exposure are confounded by age, and other causes, 4) The herbicide effect, if present, may be lost in common symptoms from other causes of disease (unlike vaginal Adeno-Carcinoma from diethyl stilbesterol, and 5) Confusion between acute, sub-acute and chronic effects.

Currently, research efforts are being directed toward the development of methods to identify specific herbicide/TCDD signs or symptoms and differentiate them from background effects normally seen in any similar population. Improvements in biochemical technology and the conduction of epidemiologic studies with a sufficient number of study subjects and statistical power may clarify this issue. Until then, we must be content to base the design of any diagnostic program on information obtained from assessments of the animal data, epidemiologic studies, case reports, Veterans Administration claims experience, and areas of concern to the veterans themselves. From these sources, the following target organ systems/areas can be identified: 1) Dermatologic, 2) Hepatic, 3) Neoplastic, 4) Neuropsychiatric, 5) Endocrine/reproductive, 6) Renal, 7) Immunologic, 8) Hemopoietic.

Any examination to detect effects of Herbicide/TCDD must be comprehensive in order to evaluate the wide range of possible or suggested effects of herbicide/Dioxin explosure, but should also be practical. Tests and procedures should be of a accepted technology and should be subjected to rigorous quality control standards to enhance their validity. Some procedures are primarily of research interest, and should be subjected to more detailed evaluation before inclusion in a reasonable screening program.

Biopsy for Dioxin - With current technology, this procedure is quite sensitive (parts per trillion) but not very specific. It is generally unable to differentiate between the 22 isomeric forms of TCDD. Dioxins from sources such as automobile exhaust, cigarettes, and commercial or industrial incinerators can be mistaken for the TCDD from 2, 4, 5-T herbicide sources. The test is quite difficult to do on human tissue, and TCDD is very similar to DDE and the PCB's, thus requiring an extensive amount of specimen purification.

If a fat biopsy was positive for TCDD, there is no assurance that exposure to herbicide had indeed occurred or that adverse health effects would follow. Conversely, if a biopsy was negative, it would not rule out previous exposure and subsequent health effects. We do know that the body can accumulate TCDD and selectively store it in adepose tissue, but the dynamics of this process are unclear, and the duration of TCDD storage is unknown. Other tests such as the pattern of porphyin metabolites fall into this category of intriguing but currently unwarranted tests in a screening examination.

Examples of specific tests and procedures that might be considered in an evaluation for herbicide effects can be compiled. However, since many of the signs and symptoms attributed to herbicide and dioxin exposure are somewhat common, similar evaluation of a suitable comparison group should be carried out to determine the prevalence of the symptom of interest in both groups. In this way, variations in symptom occurrence can be correlated with exposure.

A comprehensive medical history should of course be obtained. It should be directed toward those target organ systems or diseases of concern and should attempt to elicit information concerning the likelihood of exposure to Dioxin and other potentially confounding chemical and physical agents. Potential confounding exposures are listed in Table 1.

A general, comprehensive examination should follow, with emphasis on the areas of prime interest. The clinical laboratory evaluation can range from the simple to the complex, but the individual tests should be carefully selected to cover as many of the suggested signs and symptoms as possible. Evaluation of hepatic, renal, and endoctrine function, red and white blood cell production and cholesterol/triglyceride metabolism should definitely be included. A dermatologic examination coupled with urine-porphyrin and/or porphobilonogen testing will help evaluate the suggested effects of TCDD on the skin. Since so many of the symptoms attributed to Dioxin exposure are subjective in nature, a careful psychological evaluation should be carried out in conjunction with the clinical neurological examination and psychological reaction to the media presentations on this issue must be considered as well. Nerve conduction velocities should also be a part of the evaluation.

An evaluation of reproductive function should be conducted and should include as a minimum: semen analysis and a careful fertility history of the patient and his wife or wives. The presence of birth defects in offspring should also be determined.

Immunological status can best be evaluated by careful history-taking with emphasis on susceptibility to infections. Various skin sensitivity tests can also be used, but frequently will not demonstrate abnormalities until well after a history of frequent infectious disease is evident.

Other tests such as testicular biopsies, mitogenic responses of lymphocytes, and T and B cell lymphocyte determinations have been suggested by some investigators. At this time, these procedures may be desirable on a case by case basis, but are not suitable for large scale screening efforts. In any attempt to evaluate the potential adverse effects of herbicide/Dioxin exposure, substantial effort must be put forth to enhance the quality of the collected data. In the ideal setting, a single group of examiners should carry out the evaluation. This is often logistically impossible, especially with a problem as large as the herbicide/TCDD issue and compromises must be made. Therefore, trained and highly motivated personnel, both medical and paramedical, should be used in any effort to examine veterans alleging health effects from herbicide exposures. Examinations and history-taking protocols should be prepared and followed precisely. These efforts will insure that all veterans receive the medical care they deserve and valuable medical and scientific data will be collected. It must be remembered that a specific determination of cause and effect between abnormal health status and herbicide/Dioxin exposure cannot be made purely on a clinical evaluation. Cause and effect determinations must await the results of detailed epidemiologic and statistical evaluations in conjunction with clinical studies.

We must keep in mind that the purpose of a diagnostic program such as the one planned by the VA is not to condemn or defend the use of herbicides in the Vietnam War, but rather it is to identify any adverse health effects in personnel who were exposed to those chemicals and contaminants.

TABLE 1

POTENTIALLY CONFOUNDING EXPOSURES

Toxic chemical and physical agents in the modern environment:

- Pesticides
- Cleaning agents
- Industrial chemicals
- Alcohol
- Tobacco
- Therapeutic drugs
- "Recreational" drugs
- DDT, PCB, other Dioxins
- Radiation

Other diseases:

- Viral
- Bacterial
- Parasitic

HUMAN HEALTH EFFECTS FOLLOWING EXPOSURE TO THE PHENOXY HERBICIDES AND TCDD

WILLIAM H. WOLFE*
LT COLONEL, USAF, MC
Epidemiology Division
USAF School of Aerospace Medicine
Brooks AFB, San Antonio, TX 78235

Address Inquiry: Lt Colonel Williams H. Wolfe, USAF, MC
Chief, Disease Surveillance Branch
Epidemiology Division
USAF School of Aerospace Medicine
Brooks AFB, San Antonio, TX 78235
Phone: (512) 536-3471/2715

HUMAN HEALTH EFFECTS FOLLOWING EXPOSURE TO THE PHENOXY HERBICIDES AND TCDD

Introduction:

While the phenoxy herbicides and TCDD have been studied extensively, clear-cut definitive information concerning the adverse effects of these chemical compounds in humans is extremely difficult to find. Acute and sub-acute effects are fairly uniformly reported in reports of inadvertant exposures, suicidal gestures, and industrial accidents and epidemiologic studies. Yet there is a great deal of confusion concerning the presence or absence of truly long-term effects. In order to develop an understanding of the potential adverse effects of these exposures, we must carefully evaluate clinical case reports and epidemiologic studies, assess the disability claims experience of the Veterans Administration, and attempt to make reasonable extrapolations from the results of animal studies.

Leterature Review:

Many problems are encountered in reviewing the herbicide/dioxin literature:

1) Statistical limitations of sample size and study power
2) Multiple confounding factors such as age and other chemical exposures
3) Impure compounds - 2,4,5-T/TCDD
4) Confusion between acute, sub-acute, and chronic effects
5) The predominance of subjective clinical signs and symptoms
6) The absence of a clearly defined syndrome

Case Reports:

Much of the medical knowledge concerning the effects of 2,4-D, 2,4,5-T, and TCDD exposures in humans is derived from individual case reports. Since most of the patients described in these reports were exposed to multiple chemical agents, it is difficult to determine which specific symptoms were caused by which chemical. Nevertheless, dermatologic and neuropsychiatric diseases have been reported in many of these cases and have been recognized as major signs and symptoms for study in subsequent epidemiologic investigations of herbicide/TCDD exposures. Since the neuropsychiatric symptoms of herbicide exposure are numerous and largely subjective in nature, they have been extremely difficult to assess or measure clinically. In addition, hepatic dysfunction, and various renal, gastrointestinal and cardiac disturbances are "linked" to exposures to these chlorophenolic compounds. Since 2,4-D, 2,4,5-T and TCDD were all involved in Vietnam exposures, we must try to evaluate each chemical compound separately.

1) 2,4-D

A vast array of signs and symptoms have been attributed to 2,4-D and the ones reported most consistently are listed in Table 1. The components of the asthenic syndrome, peripheral neuropathy and hepatic dysfunction are of particular interest. Other symptoms of acute systemic toxicity occur, but usually resolve within four to six weeks. The peripheral neuropathy often associated with 2,4-D exposure has an early onset, causes prolonged disability of variable degree, and recovery usually occurs in most cases within three years following exposure. Electromyography in some patients has demonstrated denervation, and some clinical investigations have detected decreases in nerve conduction velocities. One autopsy study demonstrated a demyelination process within the brain of a 76 year old male who committed suicide by ingesting 2,4-D in kerosene.

TABLE 1

SIGNS AND SYMPTOMS OF 2, 4-D TOXICITY IN HUMANS

Asthenia
Peripheral Neuropathy
Sweating/Fever
Cardiac Disturbance
Renal Dysfunction
Liver Dysfunction
GI Disturbance
Headache
Pneumonitis
CSF Protein Abnormalities
Convulsions

2) 2,4,5-T/TCDD

Since 2,4,5-T is contaminated with TCDD in the manufacturing process, its effects on humans are extremely difficult to evaluate. In all studies of 2,4,5-T exposures, its effects could not clearly be distinguished from the possible effects of TCDD. The present knowledge of the effects of TCDD have been derived from studies of trichlorophenol workers and laboratory personnel using TCDD. Symptom/sign complexes attributable to exposure to 2,4,5-T and TCDD are listed in Table 2. Chloracne generally begins in the zygomatic/temporal region and is often found on, in, and behind the pinna of the ear. This is an oily acne-like skin condition characterized by comedones and inclusion cysts around the eyes and ears. It may result in scarring and has been associated with premature aging of involved skin areas. In severe acute cases, lesions have spread to the throat, neck, axillary, and inguinal areas.

The skin condition is frequently preceded by erythema and blepharoconjunctivitis. Acute lesions usually disappear within two years, but have been found to occur intermittently up to 30 years after heavy exposures in industrial groups. Porphyria cutanea tarda and hypothyroidism have also been suggested as acute or sub-acute effects following 2,4,5-T/TCDD exposure. Other symptoms such as asthenia, liver and renal dysfunction, neuropathy, and gastrointestinal and cardiac disturbances are probably due to known mechanisms, similar to those seen in 2,4,D exposure.

TABLE 2

SIGNS AND SYMPTOMS OF 2, 4, 5-T/TCDD TOXICITY IN HUMANS

2, 4, 5-T/TDD	TCDD
Porphyria	Chloracne
Hyperpigmentation	Porphyria
Asthenia	Hyperpigmentation
Peripheral Neuropathy	Asthenia
Cardiac Disturbance	Peripheral Neuropathy
Liver Dysfunction	Cardiac Disturbance
GI Dusturbance	Live Dysfunction
	Hypothyroidism
	Hearing/Small Disturbances

Numerous news media presentation concerning the effects of 2,4,5-T/TCDD exposure have been produced and distributed in the last 2 1/2 years. Two of the most frequently cited exposure episodes in the United States are: (1) the inadvertant spraying of farm areas in Globe, Arizona, in 1969; and (2) the accidental exposure of six children, two adults, and numerous animals to TCDD contaminated oil used for dust control in a Missouri horse arena in 1971. An extensive scientific review and analysis of the Globe, Arizona, incident concluded that adverse effects on the health of humans and animals were not produced by the spraying. In the Missouri incident, many of the animals died, and the exposed humans developed chloracne and other acute toxic effects; however, all of the humans were healthy after five years of the follow-up study. Of course, an assessment of fertility, teratogenesis and carcinogenesis in these people should be made in the future.

Epidemiologic Studies:

Numerous epidemiologic studies of industrial populations have strengthened the link between exposure to TCDD and the environment of chloracne. Associations between TCDD and psychological abnormalities have also been suggested. In 1978, Hardell and Sandstrom in Sweden investigated the occupational exposures experienced by soft tissue sarcoma patients using a case-control study design. They did find an association between cancer and exposure; however, many of their patients had been exposed to multiple chemicals, and exposure histories were often inexact or were obtained from relatives rather than the workers themselves. Also, these exposures could not be quantified or measured.

Tung (1973) reported an abnormal increase in the occurence of primary carcinoma of the liver in Vietnam (26 cases per year during 1955-1961 versus 144 cases per year during 1962-1969), and attributed the increase to a suspected carcinogenic effect of TCDD. However, his study compared the number of diagnosed cases during each time period and did not adjust the data for changes in medical care delivery system. If hospital medical care were available, more cases of any disease would be diagnosed and reported. Also, the role of aflatoxin as an alternative cause of liver cancer was not addressed by Dr. Tung. A study sponsored by the Environmental Protection Agency (EPA) in 1979 in Alsea, Oregon, found a statistically significant increase in spontaneous abortions in areas where 2,4,5-T herbicide was routinely used in reforestation programs. However, differences in the availability of specialty obstetrical care and in the patterns of health care delivery existed between the exposed an ‹control areas, and these differences were not taken into consideration

by the researchers. Variations of the ascertainment of spontaneous abortions in each of the areas severely limited the validity of the data, and of the conclusions derived from them. Recent studies conducted in Australia and New Zealand (1978) were unable to document an association between neural tube birth defects and the use of 2,4,5-T herbicide.

After an industrial accident in Seveso, Italy, in July 1976, a population of 220,000 people was exposed to TCDD, and extensive ongoing clinical and epidemiologic studies of these people are underway. These studies have involved more than 30,000 children as well as 1,024 severely exposed children and adults. Recent data indicate that most cases of chloracne arising from this incident have resolved. The growth and development of newborn infants and children, immunological response, chromosomal diseases, and the morbidity and mortality patterns of the study population have not been found to be significantly altered by the exposure. Although 38 cases of birth defects were reported in early 1977, approximately six to eight months after the industrial accident, this increase is thought to represent surveillance artifact. The social pressures operating in the Severo population prior to the accident fostered underreporting of birth defects and the social atmosphere after the accident made the occurrence of a birth defect much more culturally acceptable. This post-accident congenital malformation rate is not significantly different than the rate in similar but unexposed areas of Central Europe, and chromosomal studies of aborted exposed fetuses were no different than similar studies in unexposed fetuses.

Progress reports following the initial studies of the Seveso accident by Reggiani and others have revealed: (1) a continued decrease in the prevalence and severity of chloracne in the exposed population; (2) an increase in idiopathic clinical and subclinical neurologic disease as demonstrated by delayed peripheral nerve conduction velocities; and (3) increases in the prevalence of idiopathic hepatomegaly (8%) and alternations in liver function tests which returned to normal over an 18-month period of follow-up. Thus far, immunologic, cytogenetic, and embryomorphologic analyses have been unable to detect significant differences between exposed and nonexposed individuals. At this time, there is no good scientific evidence linking fetotoxicity, teratongenicity or carcinogenicity in humans to 2,4,5-T/TCDD exposures. Currently, there are no epidemiologic data associating TCDD with any long-term health effects in humans other than intermittent chloracne; however, while there is no evidence validating serious long-term health effects, neither is there strong evidence for lack of effect. Most previous epidemiologic studies have not had suffucient sample size or statistical power to detect increased risks of low incidence/prevalence conditions, and the period of observation in many follow-up studies has been inadequate to detect conditions with long lag times between exposure and illness.

Several valuable epidemiologic studies are currently in progress. Two comprehensive studies of workers exposed to TCDD at Monsanto manufacturing plant in Nitro, West Virginia, are currently being conducted (Mt. Sinai Medical Center, New York, and the Kettering Laboratory, University of Cincinnati, Ohio). Chemical industry employees had been exposed over long periods of time and were previously evaluated in 1953 and 1956, following an industrial accident in 1949. Dr. Raymond Suskind of the Kettering Laboratory has reported a follow-up study of 122 workers 28 years after heavy exposures to TCDD in the accident. There were 32 deaths in the group, but the relative risks of death were 0.69 for all causes and 1.0 for malignancy; however, no firm conclusions can be drawn due to the small numbers of subjects involved in the study. A mortality study of Dow Chemical Company workers revealed similar results. Dow is currently conducting a reproductive survey of the spouses of 2,4,5-T/TCDD exposed workers, but results of this study are not yet available. In Czechoslovakia, a study involving a ten-year follow-up of TCDD exposed workers is underway. Thus far, this study has found subtle but distinct variations in porphyrin metabolism three to four years after heavy exposure, but the reproducibility, significance, and duration

of these abnormalities is presently unknown. Preliminary reports of a larger study of long-term morbidity by Suskind at the Nitro site have failed to reveal significant abnormalities other than persistent mild chloracne and decreased nerve conduction velocities, possibly associated with alcohol intake. These new studies, and the continuing evaluations of the Seveso, Italy, population, should provide valuable data to clarify the issue of 2,4,5-T/TCDD and human health effects. The large study group involved in the Seveso effort should provide good statistical power, and the Nitro, West Virginia, and Czechoslivakian efforts will help to evaluate the effects of exposure after prolonged periods of time (10-30 years). The results of these studies should fill major gaps in the knowledge of 2,4,5-T/TCDD epidemiology and shoudl prove to be useful in evaluating the long-term effects of these compounds on health and reproductive outcomes.

Veteran Complaints:

Numerous media presentations emphasizing both military and civilian herbicide exposures have described a remarkably wide spectrum of health effects being claimed by the veterans. Based on current guidelines established by the Veterans Administration (VA), the only chronic residual effect of defoliant exposure is chloracne, and none of the symptoms cited in the claims have been demonstrated to be secondary to Herbicide Orange exposure. Based on the scientific literature, chloracne has been associated with prolonged high level exposure. All other toxic effects are viewed to be rapid in onset and to run abrief course followed by recovery with little or no residual disease. In fact, the vast majority of the claims alleging exposure to Herbicide Orange have not been for chloracne. Table 3 summarizes the descriptive characteristics of the first 361 claimants, while Table 4 presents the distribution of these complaints by symptom category.

TABLE 3

SUMMARY OF DESCRIPTIVE CHARACTERISTICS OF HERBICIDE-RELATED CLAIMS SUBMITTED TO THE VETERANS ADMINISTRATION AS OF 30 APRIL 1979

Total Number of Claims: 361
Sex: 100% Male
Mean Age: 34 years
Mean Number of Alleged Symptoms per Veteran: 2.3
Branch of Service: (Service history identified in 66.8% of claims)

US Army	66.4%
US Marine Corp	17.4%
US Air Force	11.2%
US Navy	5.0%

Overall, the group of claimants exhibited a high frequency of readily identifiable disorders (e.g., dermatologic, psychiatric, and cancer). Further evaluation of the early claims revealed that of the total number of claimants (361), 16.3% had previous diagnoses of psychiatric disorders (20% of these diagnosed with schizophrenia). However, conclusions from these data are limited because the normal incidence/ prevalence of these conditions in a similar but unexposed population is presently unknown.

Summary:

Thus far, the only universally recognized long-term health effect from 2,4,5-T/TCDD exposure is chloracne. Other effects have been alleged by numerous people and/or suggested by animal studies; however, there is a lack of good human scientific evidence to support them as other than acute or sub-acute effects in humans or as effects in laboratory animals. While these other effects are unproven in a cause and effect manner, they all should be considered in evaluating individual veterans or groups of veterans since the statistical power of the available negative studies has usually been suboptimal. Only through the completion and analysis of carefully planned and conducted scientific studies can the Herbicide Orange/Dioxin question be answered. Epidemiologically sound studies with good statistical power coupled with thorough physical examination procedures will provide the best data to determine whether or not persistent adverse health effects occur in humans subsequent to phenoxy herbicide and dioxin exposures.

TABLE 4

PERCENT OF VETERANS SUBMITTING CLAIMS BY SIGN/SYMPTON CATEGORY AS OF 15 SEP 1979

CATEGORY	PERCENT
Dermatologic	50
Nervousness/Headache/Fatigue	23
Peripheral Neuritis	15
GI/GU	13
Malignancy	11
Decreased Libido	6
Respiratory	5
Ear/Nose/Throat	5
Cardiovascular	4

N = 417 Claims

NOTE: 190 Other Claims Alleged "Exposure" Without Illness

CHLORACNE RECOGNITION AND ITS SIGNIFICANCE — Dr. Kenneth M. Halprin

Our next speaker is Dr. Kenneth M. Halprin, who is Professor of Medicine at the University of Miami and Chief of Dermatology at our Miami VA Hospital. He is a graduate of the University of Chicago, undergraduate and Medical School where he did his internship and his residency in Dermatology and was on the faculty there starting in 1963. Dr. Halprin will talk to us today on the Chloracne Recognition and its Significance for Diagnosing Possible Herbicide Orange Toxicity. In addition, Dr. Halprin has very kindly agreed to chair our Chloracne Task Force, which is looking at the diagnostic criteria for this skin condition and he'll tell us a little bit about the work of that Task Force. Thank you - Dr. Halprin -

DR. HALPRIN:

The Committee consists of four people: Dr. Ronald Reisner in Los Angeles, Dr. Ed Gomez in New York, Dr. Sidney Klaus in New Haven, and myself. We're trying to put together a simple pamphlet for the Environmental Health Physician and a more detailed one for dermatologists who will be examining the patients referred by the

Environmental Health Physician. We're hoping that patients will not be sent by the Environmental Health Physician to residents to be examined for the skin lesions. It is not appropriate for them to be trying to make this kind of determination. These patients should besent to the staff dermatologist if there is a suggestion of an acneiform dermatosis. We will develop a network of dermatologists in every region, who will see these patients, so that we'll have trained dermatologists filling out the same forms all through the system.

I should say that the remarks I make today are my own - they are not the result of a committee discussion and I do not know whether the other members of the committee would agree with them.

One would expect that this should be a simple presentation. I should be able to stand here and show you some pictures of chloracne due to exposure to the dioxin in Agent Orange and you could then proceed to pick them out during your examinations. Unfortunately, it is not so simple.

First, there are no documented cases of chloracne from Agent Orange, so I cannot show any pictures of them - all of the documented occurrences of chloracne are from industrial accidents or industrial exposures.

Dioxin is one of a variety of halogenated organic compounds which are known from industrial exposures to produce blackheads, pustules, cysts, and eventually scars. That is acneiform lesions. The individual lesions cannot be told from acne due to a variety of other chemicals such as tars and oils and fuels, nor can they be told from ordinary hormonally induced adolescent acne. All are due to insults to the pilosebaceous unit.

Chloracne, which by definition is an acneiform eruption which follows exposure to a halogenated organic compound, has been known for at least fifty years. The original outbreaks were due to the chlorinated naphthalenes. Although chloracne is the hallmark of exposure to these agents, it is only a hallmark when you know they have been exposed. When you have an explosion in a plant, an industrial accident, or an industrial exposure, and all of the workers develop lesions within one to several months later, which are of a particular keratotic and cystic type involving almost every pilosebaceous opening on their face or arms - then you know that this is chloracne induced by the halogen. The individual lesions themselves are not specific. It is just the profusion of them coming up all at once in a time sequence related to the preceding accident. All documented cases of chloracne are in relation to industrial exposure. They have occurred within plants making these chemicals or in relation to an accidental release of these compounds. By looking at a few lesions or even many lesions on somebody's face, back or chest, now, there is absolutely no way to say that a particular case of acne is chloracne. The diagnosis requires known exposure to a halogenated organic compound known to induce acne and cannot be made without such knowledge. On the other hand, you can't rule chloracne out and you can't rule out that he's been exposed either during Vietnam or after Vietnam.

The second problem concerns how long would chloracne be expected to last if it did occur? The evidence would indicate that somebody exposed over ten years ago would not have it now, even if he had had it then. I think in the industrial exposures you've heard about, for example, in the Missouri arena episode, those patients who had chloracne with a well-known documented exposure, lost their lesions over the next four years - they were gone. In the Seveso episode, where 32,000 children were examined after the 1976 explosion, the several hundred children who had chloracne, when they followed them up two years later, all of the ones that were severe or very severe were gone or had retreated to a mild category. This was within a space as short as two years. In the Nitro, West Virginia case, which was followed

up by Dr. Susskind, within 4 to 5 years when he went back to see those people, the original acneiform lesions, cysts, pustules and acute acne lesions were gone. There is some question about the persistence of lesions only in one area and that is on the cheek, on the malar eminence of the face. This is a very peculiar area and blackheads and scars in this area may be due to other causes (e.g., sun exposure). It is very common in the older age group to have blackheads in these areas. We therefore have the problem that even if a veteran did develop an acneiform lesion due specifically to dioxin in Vietnam, the likelihood of his having it now, ten years later, is very small. What we would see are scars, the remains of the preceding inflammatory process in hair follicles which would wipe them out and leave scars. The scars cannot be told from scars from acne lesions caused by other agents or formed as the result of the natural course of intrinsic acne.

What exactly is the Environmental Health Physician going to see in the way of skin lesions in the Vietnam veterans who come for examination. The great majority of these lesions are not going to be acne at all. 30% of the general population has a significant skin condition at any one time. Skin disease, per se, is the most common finding in our population, and therefore, the veterans are going to have a number of skin diseases. Most of these will be fungus infections of the feet, psoriasis, dermatitis of various sorts, moles, warts; a whole variety of skin lesions.

Some, a minority, will present with acneiform lesions - and these are the ones that we would like the Environmental Health Physicians to send to the dermatologist for further evaluation. The reason I say the minority, is that the age group affected by teenage acne is from approximately age 15 to the early 20's. These veterans are well over that age and they therefore will not have much acne. "Adolescent" or hormonal acne is the most common skin disease. It affects almost 100% of the population. If you are looking at people who are in their 30's, most of them will have gotten over their adolescent acne, but there will still be a number of cases which will go on indefinitely, into the 30's, 40's, even 50's. Their lesions will be like their preceding teenage acne, only more severe in terms of cysts and it will involve the chest and back more than the face. This is intrinsic or hormonal acne - we're not talking about chloracne - regular acne - and these are the patients who are going to give the examining physician the most difficulty. The Environmental Health Physician should recognize that they do have an acneiform eruption and send them to the dermatologist.

What I'm going to try to do is to give you some feeling for acne, because that's what you're going to be looking at, and we will look at various types of acne and, in addition, some diseases which affect the face, which are not acne. Then we will look at some of the true industrial chloracne.

Now these slides will all be of acne - not chloracne. You cannot tell the difference looking at individual lesions - chloracne is just like intrinsic acne and it is just like the acne caused by tars, pitches, and cutting oils. These materials get into or are secreted by the sebaceous gland and affect the duct of the sebaceous gland to cause it to hyperkeratinize. Many of the slides are by kind permission of Springer-Verlag Company, who were the publishers of a book in 1975, put out by Gerd Plevig and Al Kligman, which is a superb treatise on acne.

The hallmark of acne is the "blackhead" - an open pore filled with keratotic melanized material (a comedone). This occurs with chloracne or any other kind of acne. In addition, there are "whiteheads." In the whitehead the keratinous material distends the follicle but has not reached the surface.

Acne is a disease of the pilo-sebaceous apparatus, a hair follicle with its attached sebaceous gland. At puberty, testosterone, and other androgenic compounds make the sebaceous gland grow enormously and without this development of the sebaceous gland, you cannot get true intrinsic or hormonal acne. The sebaceous gland contributes the oil which is then acted upon by bacteria to give the irritant which causes the follicle wall to keratinize. External material like tar, pitch and dioxin, can cause the follicle wall to start to proliferate and give rise to a hyperkeratinized follicle. On the face, there are actually three different kinds of pilo-sebaceous follicles. There are some with very small fine hairs and small sebaceous glands, which are called vellus hair follicles and they are very numerous but do not contribute to the acne. Those of the beard have an enormous hair shaft with a very strong hair and good sized oil gland, but the rapid growth and strength of the hair shaft pushes the oil out, doesn't allow it to accumulate. Acne tends to involve the non-beard areas more than the beard because this hair is so good at sweeping the canal clean. The "sebaceous follicle" has a large sebaceous gland and an inadequate hair. The sebaceous follicles are most frequent on the face, chest and back. These are the glands and the areas that are prone to intrinsic or hormonal acne.

The whitehead is formed in the sebaceous follicle by hyperkeratinization of the follicular canal just above where the sebum enters it. This will fill the canal and plug it - this is called a microcomedone. At this stage, there is nothing you can see on the surface - it's only by histology that you can find these lesions. In normal acne, the agent which irritates the wall and makes it hyperkeratinize is sebum, the oil made by the sebaceous glands. This oil is attacked by bacteria, proprioniobacterium acnes, which splits the triglycerides and makes free fatty acids out of the triglycerides. These bacterial products stimulate the follicle wall and make the cells hyperproliferative and they start to accumulate keratin in the canal. When the keratin mass distends the follicle wall you have a "whitehead." If you are looking from the surface, you would see a small pore - but it wouldn't be black, the pore is so small that all you would see is a tiny dot and underneath it, a whitish mound (whitehead) of the distended follicular canal. The sebaceous glands arqund the whitehead are very small. In normal acne, when the gland gets choked off, these glands atrophy. In acne due to external agents such as dioxin, these glands also atrophy. This whitehead is the culprit leading to the more severe types of acne, because it can rupture. The follicle wall cells continue to make more keratin, the pressure on the wall increases enough to rupture the wall and when keratin gets into the tissues, the tissues develop an enormous inflammatory response to the foreign debris. If, on the other hand, the keratin mass forces the port to open then the lesion appears as a blackhead and the material can be expressed out. Blackheads or comedones are less likely to cause the deep inflammatory problems as compared to the whiteheads. Blackheads are most easily seen, but is is the whitehead that we worry most about, in terms of scars and inflammatory disease. Again, the sebaceous glands are almost non-existant after these lesions have formed.

Comedones or blackheads occur in intrinsic acne, they occur in oil-induced acne, the occur in tar and pitch-induced acne, they occur in industrial chloracne from halogenated organic compounds such as dioxin. You cannot tell these apart, nor do I believe you can tell the histology apart. In both cases, the duct of the pilosebaceous canal has keratinized and the sebaceous gland has disappeared.

In the pustular lesion essentailly what has happened is that an enormous number of white blood cells have come to the ruptured wall of a whitehead and the contents are seentially floating on a sea of pus and will be extruded through the surface.

In nodular acne an intesne inflammatory reaction surrounds a deeper more solid lesion without obvious pus in it. Again, it's due to a whitehead having ruptured through the wall.

Cystic lesions are like whiteheads with only a minute surface opening and are filled with keratinous debris but deeper, so that when you look at them, they appear to be not so superficially located, you cannot see a white color. They look flesh colored rather than white and are obviously located deeper in the skin. They rupture also and produce deep nodular lesions and abscesses.

In summary, the sebaceous follicle develops into a microcomedone with a keratinized canal. This forms a whitehead with its keratinous mass filling and spreading the canal and very small atrophied sebaceous glands. Pustules, inflammatory nodules, cysts and abscesses develop when these break out into the dermis. If the microcomedone with further keratin formation is able to open the surface pore, a blackhead is formed and keratinous material can be expressed through the opening. These usually remain as dilated pores. It takes from two to four weeks for this irritant reaction on the duct to produce enough heratin to block the duct, so that acne, induced by external agents, will not show up from from two to four weeks. It is not simply something external that plugs the opening, which would be apparent right away. This is an actual chemical irritation of the cells lining the duct and they have to make new cells to fill up the duct, which takes from 2-4 weeks.

Acne lesions will heal with scarring because the dermis has been damaged. The epithelium grows down into the inflammatory lesion trying to heal it and it will encapsulate all of the debris and eventually extrude it to the surface, but a hole will be left - an "icepick" type of scar. This occurs with intrinsic acne, as well as with other kinds. I don't see how they can be told apart.

Dr. Kimbrough mentioned the rabbit ear, which is a very nice system for showing the ability of agents to keratinize a pilosebaceous duct. They form black plugs in the hair follicles. Sebum taken from the back of a normal individual and rubbed on the rabbit ear will produce comedones. Sebut as made normally by the sebaceous gland is acnegenic. If sebum which has been acted upon by the bacteria - Proprionobacterium acnes is rubbed on the rabbit ear, it is even more acnegenic. The free fatty acids, around 12 carbon chain length, are highly acnegenic. The rabbit ear can be used to demonstrate the comedogenic activity of normal sebum as well as the comedogenic activity of all other agents (tar, pitch, cutting oils, dioxin, etc.) which cause an acneiform eruption in humans.

Intrinsic acne doesn't have to occur just on the face. In some patients with severe acne, they don't outgrow it at age 21 to 25 and especially on the trunk it may continue indefinitely with enormous comedones, cysts, and periodic inflammatory abscesses. This is called nodulo-cystic or conglobate acne. These people are terribly scarred and psychologically devastated by this deases. You will be seeing these people - they are a significant number in the population and some will have been in Vietnam, just on the basis of chance. It can also occur in areas which acne does not usually affect, like the buttocks, and the arms, and ears. Tropical acne was well-known in World War II in the South Pacific. People who had normal acne and were drafted to serve in a hot, moist, tropical climate tended to develop extremely severe acne of the chest and back, especially when they had a back pack on and regulation uniforms. Troops with tropical acne were sent back to a temperate climate and their tropical acne went right away. It was thought that in Vietnam, tropical acne would be a severe problem, but it turned out not to be.

The body is also the area that gets exposed to cutting oils and various solvents, tars, and industrial chemicals. So industrial acne is often also a cystic and pustular type on the chest and back when their clothes become saturated with the acnegenic agent. These industrial agents are usually not halogenated phenolic compounds like dioxin, but if you had dioxin on your clothes, the same clinical picture would result.

Acne involving the nape of the neck is called pomade acne and used to be due to things like Brilliantine. These are agents in oils and greases which are irritating to the walls of the pilo-sebaceous duct. Many cosmetics will cause acne lesions on this same basis.

A true dioxin exposure can produce almost pure blackheads, which cover the forehead, around the malar areas and onto the cheeks.

In Favre-Racouchot Disease - a very common degenerative disease on the malar areas, the pilo-sebaceous ducts become filled with the same blackhead material that you see in the industrial exposures to halogenated organic chemicals. I don't know how, histologically or clinically, you can tell the two apart.

There are some causes of acne which are not local or topical. This is an iodide acne, from iodides taken internally. Iodides and bromides, for reasons we really don't understand, will go to the sebaceous duct and irritate the follicle and produce an acneiform eruption.

Another eruption which can be confused with acne is a folliculitis of the beard area. You don't see blackheads, what you do see are pustules. Unlike acne, the cheek is spared. Especially in blacks, these bacterial infections of the hair follicles can form papular granulomas and cause an enormous amount of destruction and trouble. Again there are no blackheads - this is not a true acne - this is a folliculitis.

Rosacea of the face is fairly common with pustules, but not blackheads. Telangiectatic blood vessels are common as is involvement of the nose.

Here we're going to see some cases of true chloracne caused by industrial exposures. These slides are from Dr. James Taylor, who is the Dermatological Environmental Health Physician at Western Reserve in Cleveland, and I would like to thank him for their use.

This is a case of 2,4,5-T containing dioxin induced skin lesions, and in addition to the blackheads on the malar area, this brings out the other finding in the skin, which is hirsutism and hyperpigmentation of this sun-exposed malar area. These are very similar to what you see with porphyria, so the two kinds of skin conditions you can see with chloracne are chloracne itself and hirsutism and hyperpigmentation of the malar area.

These are some children from the Seveso accident. This was two weeks after the accident and you can see an acute burn. This was probably due to the caustics released in the accident - not to the dioxin. It looks like a scald. One month later, they're starting to develop acneiform lesions and I think you can appreciate that these are becoming whiteheads and blackheads. It takes over a month for this to happen because these follicles have to produce keratin and it takes that amount of time for enough material to be produced to plug the opening. This was four months after the accident and you can see some mild blackheads left on the cheek of one of these patients.

Here is a Yusho victim - one of the Japanese who ate rice contaminated with PCB's and dibenzofurans. The people who ate this rice developed the same signs and symptoms as with dioxin. The skin lesions were blackheads, papules and scars, a true chloracne. In addition, they developed nerve problems and muscle problems and hepatic problems. Now, almost all of these people did develop chloracne. In two-thirds of them, it was gone in approximately six years. This condition in these particular patients is the best proof that dioxins and dibenzofurans do not have to be put on the skin to cause chloracne. These people ate the material. Now, the skin lesions in most of these patients have disappeared, despite the fact that their other symptomatology, such as their nerve problems, have continued.

Where does this bring us to in regard to the patient who is going to walk into the Environmental Health Physician's office? Did he or did he not have chloracne at the time he was in service? That's the crucial question. If he didn't have it within one to six months of having been exposed, he would never have it. It had to develop at the time of exposure or shortly thereafter to have been due to the herbicide. Did veterans in Vietnam develop chloracne? What evidence there is suggests that they probably did not. I have three reasons for saying that: (1) The ranchhands, who were the most heavily exposed of all, have no evidence of having complained of chloracne, and they had yearly physical examinations. Certainly something as striking and dramatic as all of these hair follicles, all at once, being turned into cysts and comedones all over their exposed areas, would have been obvious to any physician. I don't believe they would have missed it. (2) By chance, during 1968, 1969, and 1970, there was an Armed Forces Epidemiological Board Survey of skin conditions in Vietnam, unrealted to Agent Orange. Col. Allen of the Army was in charge of that effort. It was an effort to assess the skin problems that were occurring in Vietnam veterans - not just at the hospital and aid station level, but to go out to the battalions and see what was there in the field, because most skin problems were not severe enough for troops to present themselves at an infirmary. They published their findings in 1977. It was the first volume of what was to be a continuing history - a medical history of the Vietnam War. They did not see chloracne. I called Col. Allen and spoke to David Taplin and Dr. Harvey Blank who had gone there. They did not see chloracne. Tropical acne they did see, but it provided less than 10% of the disability. Up to 75% of some units were out of action due to skin diseases from fungal and bacterial infections of the skin - but they do not remember seeing chloracne. I do not think they would have missed it. These are highly qualified people, who would recognize as strange something affecting a large proportion of troops of one batallion at any one time and appearing on the exposed areas as a keratotic follicular disease. They didn't see it. (3) In the populations which are analogous to the Herbicide Orange exposed troops, which would be those who spray the forests, the rights-of-way, the railroad rights-of-way, the telephone lines - these are the people who are using exactly the same material that was used in Vietnam, and to my knowledge, there has not been an chloracne in that group of people. The only chloracne is in the industrial accidents and in the industries manufacturing the material amongst the workers, but not in the normal use of the herbicide. For these reasons, I suspect that the troops in Vietnam probably did not get chloracne at that time.

The other question is if they did get it, would we expect to see it now? I've already expressed to you my feeling that almost all of the studies I know of indicate that chloracne after it occurs disappears within a period of one to five years, and for us to find active chloracne ten years later is unlikely. I think one might find scars as a result of it but that is all.

QUESTIONS:

Please stand at the microphone and identify yourself so everybody can hear.

I'm Doctor Evans from Des Moines. If i understand, it appears to me this is a complete reversal of what we were told at the meeting last Fall. Then we were told that chloracne was the only ailment definitely linked to Agent Orange. Second, I would like to inquire if the doctors here have seen chloracne in the last year.

DR. HALPRIN: Chloracne would be the only skin lesion definitely linked to Herbicide Orange, since it is the only skin condition known to follow exposure to these halogenated organic compounds, but to make the diagnosis of chloracne, you must prove - it's a Catch 22 - a preceding halogenated exposure. You can't say any particular group of skin lesions in chloracne - because by definition, the chloracne has to

follow the halogen exposure. A group of lesions cannot be told apart from regular acne or acne induced by cutting oils, tars, solvents, from chloracne - they're identical. Chloracne is only unique in that it follows in this very characteristic time sequence the exposure to the halogenated compound. So that although it is true that chloracne would be the only indication of a true exposure to dioxin, there is no way of making that judgment now.

Also, I think in the past there was more emphasis on the fact that some of the industrial cases of chloracne, tended to drag on, and as I said, the widespread active lesions over the extremities and face disappear within one to five years. In most studies, those lesions are not that persistent. In our time frame of ten years, I would expect that 90% would be gone on the basis of the known industrial exposures that I am aware of.

QUESTION: Klineman from Los Angeles. I wonder, first of all, if the use of antibiotics, such as were used during the Vietnam War, or at any time thereafter, would affect the clinical course of the disease or its subsequent recognition, and secondly, whether these different forms of acne that you describe are equally responsive to the new treatments now with retinoic acid.

DR. HALPRIN: The antibiotics would not affect the course of chloracne since a bacteria is not primarily responsible. They do respond some to retinoic acid - they do not respond to antibiotics.

QUESTION: Dunne from Nashville. Can you tell us a little bit more about the tropical acne that was reported in Vietnam and how that was able to be distinguished from chloracne?

DR. HALPRIN: It was distinguished by the fact that most of those people had mild acne before they went in the service, and it occurs on the areas covered by their uniforms - on the trunk, back and chest, whereas exposure to Agent Orange, coming from the air would give facial involvement, behind the ears and on the arms, which are exposed. It's an inverse of what you'd expect from chloracne. They did find that up to 10% of disability was due to this tropical acne in Vietnam. It wasn't the major problem that they expected it would.

Are there any other questions? I think it might be interesting - I think you, sir, asked for a show of hands of those of you who believe that you may have seen chloracne. Let's try to get an order of magnitude impression as to how many of you think you may have seen chloracne among those veterans either who came in complaining of possible exposure or Vietnam veterans who you may have been treating for other reasons or be aware of. Could we have a show of hands?

DR. HALPRIN: Don't let me frighten you. If you think you've seen it, say so.

CHAIRMAN: We have <u>one</u> - very good. O.K.

DR. HALPRIN: In regard to the chloracne which is in the VA diagnostic roster and the disability cases, there are charts which have the diagnosis of chloracne in relation to an acneiform eruption in many veterans. There are at least 80 charts that I know of in the VA system, which have that discharge diagnosis. How those diagnoses were arrived at, we don't know. We intend to take a very close look at them. I suspect chloracne used to be used rather loosely, as a synonym for a severe recalcitrant, persistent acne. It should not be used that way. It has a very specific definition coming up after exposure to these halogenated organic compounds. Since in the past it didn't really matter what it was called - cystic acne or chloracne or recalcitrant cystic acne, or acne conglobata - nobody bothered to check the accuracy of these diagnoses. I do think we have to look at all of these charts to see just what is being called chloracne.

EPIDEMIOLOGICAL STUDY MANDATED BY PL 96-151

Dr. Lawrence B. Hobson

An epidemiological study by the Veterans Administration was mandated by Congress at the end of the last calendar year in Public Law 96-151. This legislation required the Veterans Administration to conduct a study of those people who had been exposed while in service in Vietnam to defoliant agents, namely, I am sure, Herbicide Orange since that was by all odds the most common one. There was no stipulation as how the epidemiological study is to be conducted but there was a requirement that the protocol or design of the study would have to be approved by the Office of Technology Assessment, the OTA, which is an arm of Congress.

This provoked a rash of discussion particularly in the General Counsel's office because it seemed to challenge the division of powers in the Federal Government. The requirement for OTA approval brought congress into an executive or administrative decision. In due time the legislation wended its way through the General Counsel's office and through Department of Justice, I understand. The Department of Justice said that, in fact, the requirement is unconstitutional, if an arm of Congress has the power to approve, it also has the power to disapprove the implementation of the legislation.

President Carter felt that the Bill had to be signed because it contained elements essential to the operation of the Veterans Administration and signed it into law. At the same time he announced that he was instructing the Veterans Administration that "approval" portion of the legislation was unconstitutional and that we were not to seek approval of the OTA.

There promptly followed a letter from a Congressman saying that regardless of what we had been instructed to do we should proceed as though we are required to get approval from the OTA which, of course, put us in an unenviable position.

We still have been told by the administration not to seek the approval of the OTA. On the other hand, the OTA is staffed by professionals. We have and will cooperate with them in the development of the protocol and in its implementation. We are not trying to shut them out but we will not seek their approval.

Since the integrity, honesty, and sincerity of the Veterans Administration has been challenged so many times, we decided - and I think the decision was a wise one - that we would not undertake to design the study. To be honest, our only desire in performing this study is to get what factual information we can. We want to find out whether exposure to Herbicide Orange produces ill effects that either persist or appear ten or twenty years after exposure. We want to know the frequency of such effects and, therefore, the likelihood that an individual will get them.

Our intent in the design and conduct of any study is precisely that and nothing else. We are trying to divorce it so far as we are able from political considerations but, having decided that the Veterans Administration would not design the study, we faced the question of whether it should be designed by another Federal agency or by someone outside the Federal government. We decided on the latter and issued a Request for Proposal, a request for bidders to propose how they would go about designing such a study under contract.

The Request for Proposals has been published and answered. I am not at liberty to tell you how many people bid. A selection panel has met once but was unable to find that anybidders were qualified or gave enough information to decide whether they were qualified. So we are going back to the bidders to ask for additional information after which we will decide who will be given the task of designing the study.

Now, who is going to conduct the study? In large part, this depends on practicalities. It may be that we can go outside the VA for the conduct of the study. We were afraid from the start - and I am still worried - about the availability of someone who can conduct a study so large as this one may turn out to be.

I have dupplied under pressure an estimate of cost per year to do the work. The estimate is foolish, as I am only too well aware, because we do not know what the design is yet. I do not know how to calculate costs at this time but there certainly is an upper limit beyond which Congress is not willing to go. If the study proves so large that a non-VA group cannot perform it, either for financial reasons or for lack of facilities, we will probably have to turn to the VA hospitals. At least some of your facilities may be asked to do the actual examinations required by the protocol. If so, the work will be done under a rigid design which stipulates precisely what is to be done.

The data from the examinations will not be interpreted by the VA alone. I am sure that practically everyone who reads our reports will have an idea of their meaning but the formal interpretation will be by an outside group that has not yet been selected.

The agreement with Congress is that when the design is completed it will be submitted - not for approval but for comments - to the Office of Technology Assessment as well as to the National Academy of Sciences, the Joint Presidential Committee on Herbicides and the VA's own Advisory Committee. Today I had a phone call from the Office of Management and Budget reminding me that we must submit to them too because we will ask questions of the public and they must review and approve the questionnaire.

If more groups have to review the protocol, heaven knows when we will be able to start the study. No one has been able to get a fast review from some of these organizations as the Air Force can certify. In short, I cannot give you realistic dates because much of the work lies outside our control. I am sure, however, that some people are going to be very restive and accusatory of the VA for being dilatory in getting the study started. I can assure you that we have been as expdeitious as possible.

That briefly is the state of affairs, where we expect to go, and as good a projection as I can give you at the present. I cannot discuss the design because we do not have it yet and I cannot estimate the duration until we have the design.

You may be interested to know that last week I received a letter from the equivalent of the Veterans Administration in Australia saying that they too were willing to undertake an epidemiological study of the Australian veterans who were exposed to herbicides in Vietnam. They number about 40,000 Vietnam veterans in contrast to about 2.4 or so million American veterans of that conflict.

The Australians feel that they can do this study more quickly than we could - and I think they are right - in part because of their limited population and in part because of their medical and beneficiary setup. It will be very interesting to see what they develop as a design and whether in fact they are able to implement it. So far as I can tell they do not intend to have as extensive a study of each individual as we have envisaged. They will certainly look for genetic defects; that is a commitment on their part as well as on ours.

LEGAL ASPECTS OF AGENT ORANGE

Mr. Guy McMichael

Dealing with the legal aspects of Agent Orange is somewhat like dealing with the public relation aspects of surgery; there may be public relation aspects to it but it does not seem to be central to the whole idea of surgery and indeed trying to find out the answers to the many questions posed by Agent Orange does not seem at first blush to be principally a legal question but a scientific question. Fortunately or unfortunately, however, we are a litigious society. Increasingly, our response to problems, when faced with problems is simply to sue the bastards. That is physically satisfying if you are doing the suing; not so satisfying if you are the bastard. Unfortunately, we find ourselves in the illegitimate category on a number of aspects, and I do want to try to place some of this in context. I think we have to recognize that the law constantly impinges on how we approach the task of finding answers to Agent Orange. We have a law that mandates a study; that law outlines when certain things are to be accomplished, outlines what it expects us to find, whether or not we are capable of finding those things, much in the way in which Congress enacts laws and appropriates money demanding that we find a cure for cancer with the best of all possible intentions, but it does not necessarily foreordain the result. We are doing an epidemiological study. The law provides that the Office of Technology Assessment will have a role in approving the protocol. Lawyers conferred on this and came to the conclusion that as a constitutional matter, a branch of Congress could not have a formal role in actually approving or disapproving the study. At the same time, having come to the conclusion that as a constitutional matter the Office of Technology Assessment (OTA) would not have a final veto, we have--understanding the intent behind the law--clearly indicated that we plan to consult most closely with the OTA and that we find it inconceivable that we would proceed with our study and with our protocol if there were any serious objections by the OTA. Hopefully, the law and the scientific process are alike in that we attempt to order those facts in a logical way from which rational conclusions can be drawn. At least that is the objective we were all taught. I know I was taught that in law school and have been trying with varying degrees of success to apply that. Let me just talk a little about some of the concerns that exist and how some people are responding to those concerns.

First, I would like to refer to a case known as White v. Cleland. One of the advantages of becoming Administrator is that you go down in history as a named defendant in many suits so that you are assured at least a footnote in history. This suit challenges our issuance of an Agent Orange program guide. Mr. White argued that a program guide which set forth rules concerning the handling of Agent Orange compensation claims did not adhere to the requirements of the Administrative Procedure Act (APA) regarding rulemaking; particularly with respect to the opportunity for public comment. That is--the opportunity for people to come in and comment on a proposed rule. Normally, the VA is not subject to the requirements of the APA because of the way in which it is written (although as a practical matter we have by our own regulations voluntarily subjected ourselves to that Act.) Our defense to the suit, however, has been that the program guide was informational and instructional in nature. It was not regulatory and it did not set down inflexible rules that must be followed, and, therefore, was not subject to the APA rulemaking procedures. We both have filed motions for summary judgment. We have had arguments before the judge and are awaiting a decision on that.

We have a similar suit, you might be interested in knowing, on a program guide dealing with those veterans exposed during radiation atomic testing in the fifties. I noticed with some interest an article in U.S. Medicine the other day in which attorneys for the plaintiff are quoted as saying, "Well, we do not really disagree

with anything that is in the program guide; we just do not like the way they went about it." That is sometimes, I think, difficult for some people to understand; if there is no fundamental disagreement as to the material that is contained in a program guide, then why are they objecting to it? I think, in part, because lawyers believe strongly that if there are procedures by which you do things, then those procedures ought to be followed; that there is a value in public participation in the development of rules thataffect them; and that even though there may be nothing wrong with this guide, if we are not called on it, who knows what will happen the next time. Again, I want to emphasize that we do not think that the program guide, which was informational in nature, was subject to the rulemaking procedure. But this does indicate the kind of concern that, I think, signals to our office that any step we take with respect to Agent Orange is likely to be challenged whether or not there seems to be substantive disagreement with what we are doing. There is a great deal of concern about this and one way in which some people may very well express that concern is by "suing the bastards."

Perhaps the most important case, and the one that receives the most media attention, is a case dealing with Agent Orange product liability. In this suit, the plaintiffs are seeking, first, the establishment of a tax exempt reserve fund to meet the health and welfare needs of Agent Orange victims including compensation for lost income, medical care, and vocational rehabilitation. Second, they are seeking a ban on the sale of 2,4,5-T. One might wonder why, if they are concerned about providing medical care and compensation for veterans, they didn't directly sue the VA, and instead, sued the chemical companies. Well, the answer, in part, may be that it is very difficult to sue the VA in a situation like this on individual claims primarily because of a section that is contained in Title 38, known as Section 211(a), which bars a suit by veterans on individual claims for compensation or medical care. The law establishes procedures under which, if an individual is turned down in a claim for compensation, he or she may appeal to the Board of Veterans Appeals here in Washington, D.C., and their decision is final. There is no further judicial review allowed. That provision has come under increasing scrutiny in recent years. A number of people feel that as a matter of principle, regardless of how well the VA adjudicates claims, it ought to be subject to judicial review, to review by an independent judicial branch, and there have been a number of hearings and suggestions for legislation. The Senate, in fact, has passed legislation which would permit judicial review of veterans whose claims have been turned down. To date, the House has not had hearings on it. Our prognosis is that the House will not act on the legislation this year, but probably will seriously consider it next year. We have further indications that veterans groups which have long been opposed to judicial review will probably change their positions at their national conventions this summer. There may also have been another reason for suing the chemical companies, that being that if indeed there is a villan worse than the VA, it is probably the chemical companies in the eyes of those who are doing the suing.

In response to the suit, the defendant chemical manufacturers have denied that Agent Orange has posed a health hazard but they have said if it did pose a health hazard, then the U.S. should beheld liable and not them, because Agent Orange was made according to U.S. specifications. That is a typical response in law suits where someone will say, "I didn't do it, I am not responsible, but if there is something wrong here it is not my fault, it is the other guy's fault." They will then bring in the other party as what is known as the third party defendant. That is what they have done to the United States. So, we have now been brought into the suit sort of sideways and they are arguing, first, that we have failed to test Agent Orange properly before its use; second, that the United States in spraying Agent Orange in Vietnam failed to use it properly; third, that the United States failed to instruct personnel in the proper use, and failed to supervise its use; fourth, that the United States failed to afford adequate protection to the users; and fifth, that the Government

failed to warn adequately veterans of health consequences of exposure, and failed to provide appropriate medical care and treatment early on, thereby aggravating the veteran's disabilities. The chemical companies are not asserting that the Government did all this, they are only saying that if, in fact, there is a danger posed by Agent Orange, we want you to know that we have plenty of theories by which we think we are not liable but the Government is liable.

The tendency in this case has been for the attorneys for the plaintiffs to go around to several cities, locate veterans who believe that they were adversely affected by Agent Orange and to have them bring suit. So suit has been brought in a number of District Courts. Under the rules of procedure of Federal District Courts, these have all been consolidated in New York under what are known as multi-district litigation rules; so there is only one court handling what essentially are similar suits all over the United States, and that court will hear and define the rules for various pretrial motions and discovery.

There are a number of other things we have to do in connection with this suit. Every time we examine someone who believes that he was adversely affected by Agent Orange, you prepare a medical record on him. That medical record has to be forwarded to us, we have to make two copies. We make a copy for the Justice Department. We make a copy for the plaintiffs in the suits so that they will be able to obtain this information as the suit progresses. This, I think, is taxing work to all of us. Good news perhaps only to Xerox. But it is the nature of the suit and there is going to be a great deal of paper generated before its all over.

A third suit I would like briefly to discuss concerns a suit brought just recently by the National Veterans' Law Center against the VA, attempting to seek a temporary restraining order and a preliminary injunction against our proceeding with contracting for the protocol in the epidemiological study. A temporary restraining order is one where you go into court right away and say, "Listen, something really horrible is happening, and I know you have not heard from the other side but stop them from doing whatever they are doing, hold a hearing right away. Meanwhile, we would like you to set a hearing for a preliminary injunction which may not be permanent but at least will prevent them from proceeding." We had, I think, a day's notice, less than a day's notice, on the hearing on the temporary restraining order. We had to hustle to get our information, but we did appear in court the next day. Plaintiff proceeded with documents, averrments, attachments, affidavits of several hundred pages in length; at the very least, from a legal point of view, I think we did an excellent job in defending how we have been proceeding. The action brought by the National Veterans' Law Center alleged that the study as described in the RFP, the request for proposal,would not meet the intent of Congress, which is to have an unbiased, scientifically valid study. We had a hearing that, I think, lasted almost two hours. It was obvious that the judge had read all of the plaintiff's pleadings the night before. We had excellent cooperation from the Justice Department.

Based on the hearing, Judge Harold Greene denied the request for the temporary restraining order. He held that their action was premature and that the ultimate study design selected by the VA may, in fact, be unbiased and fully consistent with congressional intent. That does not get us out of the woods yet. He urged that we consult with the plaintiffs to find out what their objections were to see if they had merit so we might accommodate them in those areas where they had concern, and we have had meetings with attorneys for the plaintiffs in that respect. I do not anticipate that this action is over or completed. Again, it is, I think, simply another indication that we will, in addition to all of the difficulties in getting at the scientific truth of this, be plagued with legal actions along the way too, and I am taking lessons in learning serenity on that and have at least attempted to view this with some degree of equanimity.

Let me just speak about a couple of other things going on. The Environmental Protection Agency (EPA) has an administrative action going. Following reports of a variety of health problems and a study purporting to show an increased incidence of miscarriage in Alsea, Oregon, following exposure to 2,4,5-T, EPA issued an emergency suspension of most domestic uses of 2,4,5-T. Hearings to determine the risk of exposure are now ongoing and, if necessary, hearings to determine benefits of continued use will be held. Thereafter, a decision will be made. But obviously, these sorts of proceedings by another Federal agency and the information or evidence that is adduced at that hearing will have a great deal of influence and impact on us. I might say that what a court or an administrative tribunal finds may not be consistent with what scientists find. A court could, indeed, find the Copernicus' theories were incorrect, that the sun revolves about the earth, and make such a judicial determination. That does not necessarily settle the scientific questions involved. I bring up this point to indicate that we are dealing on two different tracks. Determinations by the court, while having a tremendous effect on us by determining our actions, are not necessarily coincident with what the ultimate scientific judgment is, if indeed, we can agree whatever the ultimate scientific judgment is.

Finally, I would like to speak briefly about a case entitled the United States v. Vertack and Hercules. This was an action brought against manufacturers, I believe, in Arkansas for various violations of the toxic chemical disposal statutes. In that case, plaintiffs sought civil penalties and injunctive relief to abate the continuing discharge of toxic and hazardous waste and pollutant--principally dioxin--into navigable waters, soil, atmosphere, and groundwater. The court, which just rendered a decision this month, made a number of interesting findings. First, in findings of fact, it found that dioxin is a highly toxic chemical which, given sufficient dosage and sufficient exposure, causes various health problems in laboratory animals and in human beings. Second, the court found that dioxin is shown to be carcinogenic in animals in concentrations in the parts per trillion range, and, that it is suspected, but not proven, to be a carcinogen and teratogen in humans. That was the extent of the findings of fact. The test that the court applied is whether there was an imminent and substantial endangerment exposed to the public at large by the discharge of these dioxins. Relying on some previous cases of determining what the basic term "endangerment" meant, and indeed this is the love and the life of the law of defining words, the court found that while there is a low probability of harm from dioxins, there is a serious and dire risk from exposure to dioxin should the hypothesis advanced by the plaintiff prove to be valid. Like the old argument by Pascal about God, he may or may not exist but the consequences are enormous if he does exist and you act as if he did not. The court found that endangerment means less than actual harm and includes the risk of harm, and I think that is important for us that the risk may be assessed from suspected but not completely substantiated dangers. The holding in the case was that the escape of dioxin constituted an imminent and substantial endangerment to the health of persons and was subject to abatement.

In addition to everything the Federal Government is doing with respect to Agent Orange, there is an active interest on the part of a number of States. The State of New Jersey, certainly no stranger to chemicals, has established a commission to examine the health effects of veterans exposed to dioxin. The State of Minnesota, which has been very concerned about this, has actively supported an outreach program to encourage veterans to get Agent Orange examinations from the VA. Those of you from hospitals in Minnesota know that the response has been fairly heavy. New York has held hearings on the health effects of exposure and actions taken by the VA. If we get many more states involved, I am afraid we may have Dr. Shepard involved in a permanent road show. Also, there is a California measure which, if enacted, would require the State Veterans' Affairs Department to help veterans to file claims with the VA for herbicide-related disabilities.

I would like to conclude my remarks by talking a bit about VA disability compensation law. We pay disability compensation for conditions that can be related to service. The disability need not be caused by military service, but if it is coincident in time of development with the period of active military service or if an existing disability is aggravated during service then disability benefits are paid to the extent that earning power is decreased as a result of that disability. The law mandates that we give the benefit of the doubt to those filing claims. It does not necessarily require that a casual relationship be established. Thus, if we can trace a case of chloracne, for example, back to the time of the veteran's service we can pay disability compensation for that chloracne without having to make a determination that Agent Orange caused the condition. Similarly, if we can trace a cancer which may develop at a later point in time, if we can trace its genesis to a point in time in which the veteran was serving in the military, we can pay disability compensation without having to determine what caused that cancer, or indeed, if Agent Orange was the agent responsible for the development of that cancer. There may be a number of diseases whichare directly related to Agent Orange which manifest themselves in veterans that we cannot relate back to the service without some new evidence suggesting that these diseases develop as a result of exposure to a particular substance or combination of substances. We have a number of proposed laws introduced in Congress, one by Congressman Daschle, and one by Congressman Downey, which when examined seem ineffective at best or deceptively inarticulate at worst. These bills say the VA should find out what Agent Orange causes in the way of illness and pay benefits for them. If that is what it really means, that is doing nothing more than restating the obvious because that is what we do now. We are paying benefits for anything we can connect to a veteran's experience in service. On the other hand, if it is saying that they know, theyare convinced, that there are certain things that are, in fact, caused by exposure to Agent Orange, they have not spelled those out in the legislation.

What implications for compensation payments will our study on Agent Orange have, and what might happen? No one knows until we get some of the evidence in. It does seem to me, however, that if our studies show a higher incidence of certain disorders among Vietnam veterans than among non-Vietnam veterans, then we are at lease faced with the question of raising a presumption that those disorders are peculiar to their service in Vietnam. At least, that is one consistent experience all of them could have. Absent a finding of some other rational explanation, it would seem to me that if we do find a significantly higher incidence of particular disorders among Vietnam veterans, then we may very well want to examine the possibility of implementing new legal presumptions for service-connection. Again, we cannot at this point venture a guess as to whether we will find significantly higher incidences.

Barclay Shepard, M.D.

I would like for the next half hour or so to make some comments concerning some of the efforts that are going on both inside and outside our agency and give you some of my thoughts as to where we should be going.

First of all, we have a very small staff in Central Office and obviously we can't do the whole job alone. We need the help and cooperation many people in Central Office and many people in our various field activities. It is hoped that in the next three or four weeks we will have a small suite of offices in Central Office so that we will be co-located. Right now we are scattered around various places, but hopefully we will have a more efficient office structure in the near future.

I would like to take some time to talk about the registry. It is an important issue and I think it is one in which there has been a lot of misinterpretation. Like so many things that have been established in a desire to meet a crisis and get something started, it may be now that looking at it in retrospect, it is not all that some people intended it to be and this is no criticism of the way it was put together in the context of the atmosphere that existed at that time. So please don't interpret any of my remarks as being critical of what has been done other than as being constructively critical.

First of all, I would like to mention a few things that the registry is not. The registry, by no stretch of the imagination, is an epidemiological study. It is not intended to be that and it never was intended to be that and should not be construed as being that either now or in the future. Now that isn't to say that some of the information that will be gathered in the registry will not be useful to us. It would be a sad waste of a lot of your time if that were not the case. Bear in mind that the information gathered in the registry comes from a self-selected group of individuals, therefore, it can't be considered a study group or a cohort group. It will however, provide us with some information in terms of patterns of symptoms and maybe, patters of physical findings. We just don't know that yet, and the reason we don't know that, is that we haven't analyzed the data from the registry. We are now developing a technology for accomplishing just that. We've been working very closely with some very dedicated people in our Data Management and Biostatistics Division in Central Office and we are now putting together and have actually put together a computer program which will retrieve the data which has been put into the data bank from these data sheets that you all have been providing to VA Central Office. Some of you may say, "Why is it that after all these months we haven't gotten further along than what we have?" Without getting defensive on that issue, let me just say that it probably is a lot more complex than appears on the surface. Some of those complexities are the result of some of the things that Mr. McMichael referred to regarding litigation which is impacting on this process. Hopefully, we are overcoming that. Some of it is as simple as staffing. It is going to take a fair number of man hours to work through this material, but we are working on it. In regard to improving the process, perhaps streamlining it, making it easier to use in the field and therefore, making data more readily accessible, very shortly we will be revising the questionnaire. In this regard I would like to put together an Advisory group dealing directly with this issue and if any of you have some ideas about how to proceed long these lines, I would very much welcome your letting me know. Obviously, we can't do this alone and you people are much more experienced at dealing with it at the local level than I am or any of my staff. So again, we sincerely solicit your input on ways in which we can improve the questionnaire. Some of the things that are fairly obvious

to me that I have already alluded to is the fact that most veterans don't know with any degree of certainty the level of exposure. Some of them do, of course. The Ranch Hand folk have a pretty clear idea, but the average marine or soldier doesn't have a good idea of exposure, I am sure that they were aware of the fact that herbicides were used. They could see the effects of the herbicides, but that doesn't necessarily correlate very well with how much herbicide was actually in the atmosphere at the time they were in defoliated areas. We are also going to revise the circular and perhaps clarify some of the instructions that have come out from Central Office. Again, if you have any suggestions in that regard, please communicate them to us.

We've been saying ever since Mr. Cleland testified before the House and Senate Veterans' Affairs Committees in February that we have about 10,000 veterans in the registry. We haven't been keeping an accurate count of just who or how many there are in the registry, so we're sort of going on saying well there are about 10,000. It has become obvious that that's not adequate. One of the reasons that we don't have an accurate count is that we've changed some of the methodology. You used to send all the information into Central Office and Central Office coded it. That became an overwhelming task so that we have asked you in the field to do the coding and send the code sheets and back up information to us. In that process, the monitoring in terms of the volume of numbers has been less than accurate. What I probably would be asking each facility to provide us with is a very brief monthly report as to how many, what your total count is; what your count is as of the end of the reporting month; and what is your backlog. These are three questions that seem to be recurring and unless we tighten up our reporting system, there is no convenient way in which we can have that information on short notice. That question did come up a short time ago and I was asked how many we really did have on the registry. I was not able to give anywhere near an accurate count. The regions were queried and they put together probably a fairly accurate count, but it was done very rapidly and there was no good process in place to accomplish that. I think that is something we need to do. It should not be very complicated. I don't want to add any heavy burdens on any of you, but I think that should not be too difficult to process.

If you have any questions about the registry we can certainly handle those at the question and answer panel, or if we have a little time left over maybe we can address it. I consider the registry right now as a very important thing because it is one of the things that is ongoing. It's also one of the efforts that is generating information. An effort in which we have to play some catch-up in terms of how we are going to retrieve and analyze the data obtained. Another area that we're involved in is the Literature Search. I'm sure some of you have heard that Congress, in addition to the Epidemiological Study, has mandated the Veterans Administration to do a careful review of the world literature on the subject of agent orange. That obviously is a very large task and obviously also, to be useful, its got to be more than a bibliography. I think many people have generated bibliographies. Major Al Young, U.S. Air Force has a very complete bibliography. Other, I notice in your packets, I think the Palo Alto VA Medical Center has put together what looks like a very nice bibliography. Obviously, that's the first step in this job. But a more important step is an analysis of the content of that bibliography and we have now advertised for a contract for preparation of a complete bibliography of the world's literature on Agent Orange. This will include a complete analysis of that bibliography and a critical review and ranking by scientific merit. In many instances where there may be differing conclusions based on similar kinds of data, an evaluation as to why those differences exist with an explanation of those differences will assist those people who are not particularly expert in these matters, will have an interpretation by an expert as to why these differences exist. I think that when we get through with this, hopefully by the middle to the end of December, we will probably have a substantial compendium of information on this subject. We will, of course, circulate that broadly.

Dr. Halperin has given you an update of the Chloracne Task Group and I am very encouraged as to how that is proceeding. As he has indicated to you, you will probably have in the next two months some pretty solid material on which you can make some of these sticky judgments. I think he alluded to the fact that it is hoped that there will be a group of dermatologists, a consultant group, within the VA who will serve in the capacity making judgments in questionable cases relative to symptoms of chloracne and maybe even one or two super duper consultants, other consultants outside the VA, may be asked to comment on the problem if it gets to the point where we do need outside assistance. Another area of effort is the Interagency Work Group on Phenoxy Herbicides and Contaminants, sometimes referred to as the White House Task Force. This is a very interesting group of people, chaired by Mrs. Bernstein, who is the General Counsel for the Department of Health and Human Services, formerly HEW and now designated as HHS. She is a very able person, who has a keen interest and dedication to this problem. She chairs these meetings with a great deal of aplomb and I think the work of the committee, the strength of the committee, is that it brings together all federal agencies which have an interest in this matter. Represented on that committee among others are the Department of Defense, Environmental Protection Agency, HHS, and the Department of Agriculture. Two subcommittees of that working group, (1) a scientific panel which is headed by Dr. John Moore, and (2) an information and public relations panel chaired by Mr. McMichael. The scientific panel committee meets on a monthly basis. It has taken on such tasks as reviewing the whole problem that exists around the Air Force's Ranch Hand study. The scientific panel is meeting on that issue now and will report to the whole committee their recommendations on such matters as: should the Air Force proceed with the study in-house and to what extent should it adjust or modify the protocol based on the criticism and suggestions of NAS. The IWG will then consider those recommendations and will make its own recommendation to DOD and the Air Force as to how that should best be handled.

Making a news release criticizing the Air Force's study from a non-scientific point of view, that is, attacking the credibility or suggesting that the study should be done outside the Department of Defense because of the credibility issue is not an appropriate thing for NAS to do. They may think that they can communicate that in all kinds of ways, but to make a news release and publish it across the country was inappropriate and I have so stated to the members of the IWG.

You've heard of our Epidemiological Study and our status of that. I don't think I need to say any more except that perhaps you are hoping to hear more from Dr. Lawrence D. Hobson than you did yesterday. It was hoped that the day before yesterday the selection of the contractor would have been made and he could have announced that to this group. Unfortunately in the process of reviewing the proposals it became evident that they needed some more information. They determined that they could not simply go out and ask that information of the contractor who had not provided that information in the first place. Instead they had to go back and query all the proposals in order to keep the whole matter legal. Therefore, it's going to take a little more time, but I hope not too much more time. We should have an announcement, I think, forthcoming within the next two to three weeks. The issue of which veterans were exposed to herbicides and which were not remains a sticky one. Sticky because it is very difficult even though the Air Force kept very accurate records of where the spraying was conducted. The Army and Marine Corps have very accurate and readily retrievable information. All the information on the spraying missions is on tape and can be rapidly retrieved. That isn't quite the case with troop movements in Vietnam. There is a considerable amount of difficulty identifying those units in which there was a greater possibility of exposure versus those with minimal or no exposure. However, DOD is working hard on this. I met with a group the other day and they are going to do a test run of some data they have on troop movements to see if they can identify one battalion of Marine Corps and one Army

battalion each of which had a high likelihood of exposure. The only way they can really do that is by studying movements that were in close proximity geographically and timewise of the areas that were sprayed. They are now putting together a test run to test their ability to retrieve this data. We should have some of those results pretty soon. I am hopeful that we may have come up with fairly credible information in this regard and certainly, if that is the case, that will make the task of the epidemiological study easier and again, more credible. We don't have that firmed up yet, but we are working on it. We've been engaged in some other activities. Much of our work in Central Office is kind of a "brush fire" crisis operation. We are constantly being approached by members of the news media. I think we probably collectively get 10-15 calls a day. We try to respond to these in a timely fashion. Obviously, some of them want to have TV interviews, radio interviews, or come and tape our remarks. I might say that by and large these requests are very reasonable. I've done a few myself. Some of them are done in the form of telephone interviews. Sometimes they will actually come to Central Office and do tape recordings, occasionally a video. The media, in general, are really quite reasonable. If you find yourselves in a position where you're being asked to do that kind of thing, I think it's appropriate that you respond to media requests in a level-headed and dispassionate way. After all, it's only through this kind of effort that we'll ultimately convince the media and concerned veterans groups that we have an open mind on the subject and that we are willing to share information. We need to guard against being defensive even in the face of some rather inflammatory or adverse comments. I think that we need to thicken our skins a little bit and not take too personally allegations of insensitivity on our part. As Mr. McMichael indicated, there is of course, a high level of interest on the part of congressional committees. We deal closely with them and hopefully working in a harmonious manner with the staffs of those committees in order to share information as it becomes available. A number of veterans organizations have approached us in one way or another. We are working with the National Veterans Law Center to try to come to some logical and reasonable method of exchanging information so that they can proceed with the task that has been laid before them of representing their constituency in an enlightened fashion.

That about concludes my remarks in terms of what we're doing. Obviously, it is a big job and together I hope we can come to some kind of resolution on this. I don't think it's the kind of thing that's going to go away. I would like to close my address. I will answer your questions in just a minute. I think that it's safe to say that one of the reasons why we are in the position we're in, that is, a sort of catch-up position, is that there was not a well structured department of environmental and preventive medicine in VA Central Office. I think all of us practice preventive medicine, or try to practice preventive medicine and try to be aware of environmental issues and how they affect present or potential patients. However, there really hasn't been such a structure in Central Office. I think that, in part, is part of the problem. It is my hope that during the next year or so we can structure such a department and recommend it to the CMD and the Administrator so that when the next environmental or occupational crisis comes up that we perhaps will have an organizational structure that will be able to effectively deal with such problems.

I can now take questions if you like.

Bernard Bach, M.D., Cincinnati: I have one suggestion and one question, not to you, but to the group. My suggestion is that the questionnaire follow the new armed forces questionnaire for radiation exposure. It's excellent and saves the physician time. Did you see that yet? My question to the group is, since generally there are feelings in the field that we who see the patients are asked to do more and more with less and less, do those of you who see the patients have any help? Do you have any nurse assistants to help you see the patients, or are you doing it alone, like I've done for years now? How many of you have help in the form of nurses assistants? How

many do it alone? I think with a personnel shortage that what we need are more doctors and literally, more money. Do we get it?

Dr. Shepard: Good question. I would hope that I would see as one of my jobs the making of that evaluation. To determine if we are, in fact, being overtaxed. I'm sure there are many areas in which the volume of work is higher than the level of staff that has been provided. I think we need to make a determination on that subject and help solve problems that exist. I hope that that will be one of the subjects of your group discussions, because it's very germane and I think it needs to be discussed.

Donald Belcher, M.D., Seattle: I was interested in your comments about attempting to match the troop movement information with Air Force spraying data. Recently, we had a situation where the person who was thought to have won the women's race in the Boston Marathon was observed to be taking a different track than most of the contestants had taken. I, from my own military experience, think it's very difficult to really pin my movements to a specific day and circumstance, particularly 15 years ago. We often went off on reconoiter patrol activities. No one knew where we were. We really didn't know where we were and it seems to me actually unlikely that we're going to be able to pinpoint individual movements. We may be able to do this for a few people, but for the majority it's going to be very difficult. I'd like to ask the question, if we're unable to document a candidate's actual location on a given date, are we simply going to have to go on his stated exposure data, because I'm not certain we will be able to use anything else.

Dr. Shepard: That depends on whether you're talking about the epidemiological study or the adjudication process. Let me assume that you're talking about the epidemiological study. I have talked to Dr. Hobson on this very issue. We agreed that if, in the best judgment of people from DOD and statisticians, that we cannot identify with some reasonable assurance a cohort group that was exposed and another group that were not exposed, then we may have to go back to Congress and ask them to scrub the law. It may be that this cannot be done. We don't want to start out with that presumption until we test our data and see what we can come up with. That is why it's so important that DOD tests the system, so to speak, to find out what we can determine. I think it may be that this study cannot be done in any kind of incredible scientific fashion simply because the data base isn't there. I hope that is not the case, because I think it will just prolong and continue the agony, but it's a possibility.

Dr. Edmund D. Benedek, Pittsburgh: If you are going to include ranking of scientific merit in a literature survey, do you really believe that the lawyers are not going to get into the act to determine or to second guess this point? The way contracts are let, and this apparently has not been done yet, do you really believe that this is possible to complete a study in six months even if the lawyers would not interfere?

Dr. Shepard: I don't have any anticipation that the lawyers won't interfere. Well I say interfere, that may be a bit strong, I am sure the lawyers would be concerned. I'm not sure exactly what methods they would take to interfere with the process I don't see what would be gained by that. I'm hopeful that they won't interfere, in any detrimental fashion. I don't know. It's quite possible that it can't be accomplished in six months. I would hope that it could be and we will hope to aim at that time frame, but I'm not an epidemiologist and I'm certainly not conversant with the world literature on herbicide orange. So, I really don't have a sense of the order of magnitude of the job. For those of you who are interested in administration of contracts, this will be on a cost-reimbursable basis, not a closed-bid basis that may color the process a little bit.

I think we ought to go on with the program and then if you would save your questions for the question and answer panel you will have a good deal of time to discuss these issues further.

Remarks of Stratton M. Appleman

on the

Public Information Aspects of Agent Orange

I have some good news for you. You're going to get to sit back in these confortable chairs for about the next 35 minutes and do nothing but watch TV. There's bad news too -- it's not the Wide, Wide World of Sports. And for you local people, it's not the Kempre Open.

But we do have a film that you should see. This film dates from March 1978 -- it first appeared in Chicago on station WBBM. And it has since been used in ways that make it very important to you. I'll cover that in about five minutes after you've seen it.

Many of you have seen it. But I would suggest you might want to take a second look at it because this is the link that established the veteran connection with the herbicide debate. This film brought the veteran into the environmental debate. It all started in Chicago in 1978, in March, and immediately produced about 350 claims.

For those of you who've seen it, I want to just point out that I looked at it again yesterday - I think for about the fifth time - and I saw some things in it in a new perspective. And I'd suggest that you might want to look at it that way too.

(FILM)

The reason we felt that was important to you is because we think this covers just about every point you heard yesterday, though it was covered in a completely different way. This isn't all the film, by the way. It runs on - it's a full hour.

They have Dr. Commoner on once more a little later. Strictly on a theoretical basis, Commoner states that if dioxin can be stored in fat -- and he stresses the "if" -- then dioxin can be in the fat for an indefinite lenght of time without causing harm. Then, theoretically the veteran could go through a period of weight loss and release the dioxin to do its harm. Now that's the way he sets up the theory for long-range effects.

We felt you should see this presentation because this is not only where the veteran who comes to you is coming from, but this is where the newsman, who comes to you and asks questions, is coming from.

This film has been updated three times since Bill Curtiss first aired it in 1978. Every time - on the anniversary date - March of '79 and March of '80, he has updated it. The last one he did after going to Vietnam and interviewing Dr. Tung and looking at some of Dr. Tung's research methods.

Incidentally, he does, again in this last film as he did in the one you just saw, indicate that he has some reservations about Dr. Tung's research methods.

To update you on some of the people you saw in the film -- I mentioned Bill Curtiss. Then there's Maude DeVictor whom you saw. She is still with VA. She's a loan guaranty specialist out at the Chicago office now. She's been promoted.

Dr. Tung who was mentioned has visited the U.S. since then. During his visit, he talked with VA people at three locations. Each time he stressed the point - after being asked about deformities and abortions - he stressed the point - that his observations dealt only with females. I understand that since then, seeing the interest in this subject in the U.S., he has started some experience to prove that dioxin also affects males.

Barry Commoner, who was prominent in this film, is running for President on the environmental ticket. One of his main platform planks is solar versus nuclear power.

The thing you might want to note about this preparation - I'm sure most of you noticed - is the emphasis on deformities. While everything they said appears to have a basis in fact, even in this film they talked about these deformities occurring among females who were exposed. All the way through, as I saw it, it was the female who were exposed. All the way through, as I saw it, it was the female, even among horses and other animals. Dr. Commoner mentioned it in reference to the Missouri accident. Yet after each mention of deformities there was a quick transition to showing the deformities among the children of male veterans allegedly exposed in Vietnam. The technique is to establish a scientific base, or the factual base, for technique is to establish a scientific base, or the factual base, for deformities that occurred among the people who were known to be exposed to dioxin. Then you switch to show we have deformities among offspring of veterans who were exposed to Agent Orange.

There was also a strong tendency in this, and I've seen it work among many people with whom I've watched it, to use or cause you to use Agent Orange and dioxin interchangeably. Your media people will invariably, innocently, make that mistake. They know dioxin is poison, but they extrapolate that that means Agent Orange is poison. After all, Agent Orange contained as much as 50 parts of dioxin per million.

Now, another propaganda technique, or information technique you might notice is the way they use this business of the Dow Chemical Company saying, "Yes, there is a better chance that they could have been harmed in Vietnam than in the United States." That was introduced by showing harm that clearly came from dioxin. Then, they said very dramatically, "The herbicide used in Vietnam was a hundred thousand times greater than was being used here in the States."

"Even Dow Chemical Company says there's a greater chance that those exposed in Vietnam would be harmed," Curtiss says. Then when you see the Dow Chemical Company spokesman, he answers, "Yes, there is a greater chance of problems from the way it was used over there than the way it is used here."

Remember that this film was not <u>just</u> shown on TV. It not only has been updated. This film is being used constantly by at least three organizations we know of in local press conferences. The press conference is called, this film is shown; the technique then is to bring out a local person, a local veteran with a problem. And, as you know, that's not hard to do. That problem, whatever it is, is linked to Agent Orange, and this immediately localizes every bit of information in the film because there's a local person involved. This is why this information has been in small newspapers throughout the country.

I know some of you have seen this kind of press conference and the effects of it in your local area. The Boston area has really been swamped with it, as well as Buffalo and Syracuse. But let me show you one that took place just last week.

Here's the <u>Fayetteville Observer</u>, Fayetteville, N.W. -- "Agent Orange Peril Cited." Typical -- "A man dying of cancer, a man who suffers from skin rashes and warts, and a widow stood before the press here today and told of misery they claim

was caused by Agent Orange, a herbicide used in Vietnam." Then they run through everything that was in this film because the reporter had seen the film just before these people were brought out.

That press conference also produced this story -- "Lawyers to File Suit for Herbicide Victims. Two Fayetteville attorneys say they will file suit on behalf of several Vietnam veterans in North Carolina who contend they are suffering from a variety of ailments caused by repeated exposure to defoliants in Vietnam."

Very big story, and I'm sure many of you have seen this same story in your area. It's those of you who haven't seen it that need to be aware because many of you will see these same stories, with different characters, cropping up in your area.

Here's a story of the same date. This is in the News and Observer from Raleigh which tells who's behind this.

"Vietnam veterans who feel there health was damaged by herbicides in Vietnam announced Tuesday that they would open an office in Fayetteville to help veterans who have been affected by the chemical. Agent Orange Outreach, Inc., a non-profit volunteer organization, will try to inform N. Carolina's 180,000 Vietnam veterans about the dangers of the defoliant used widely in Vietnam by the U.S. Tod Ensign, co-chairman of Citizen Soldier" (that's the parent organization for this one -- in this drive they use the "Agent Orange Outreach, Inc."; they've used other names in other areas). But, "Tod Ensign, a co-chairman of this Citizen Soldier, a national veterans advocacy group, said at a news conference in Raleigh, 'Their attitude now is a passive one.'" Here he's speaking of the government -- you.

I deliberately read down to get Tod Ensign's name because he's just produced a book, "GI Guinea Pigs," which is written with another member of Citizen Soldier, Michael Uhl. Many of you will be asked to get on a radio program and discuss this book with Ensign. I've been asked. In my case I turned it down. I'm attacked in the book, incidentally. I've gained new stature here. Attacked also are Harry Truman, Jack Kennedy, Max Cleland and many, many other people that I'm proud to be associated with.

Now, this is what you're facing, but what can you do about it? What can you, when you get these inquiries, do about it? Possibly the best thing is the type of thing outlined to you during this conference. Try tc give the veteran with whom you're coming in contact face-to-face, a better perspective on his problem, now that you know where he's coming from. But I would not back away from dealing with news media. Somebody asked me this morning if that was against VA policy to deal with news media on this. Certainly not. We obviously do not want, on any issue, to get in a posture of fighting veterans, debating with veterans, in the media, or on any public forum. But when you have an opportunity to help veterans gain a better perspective on something that they are concerned about, I would say that's your obligation.

There are some things to avoid. I think in any kind of situation it's always better to choose your own forum. You should choose carefully, because there's a possibility that you may inadvertently be drawn into debating in a forum where you're at a disadvantage. I would suggest to you there might be techniques for avoiding that.

There is one way of avoiding getting trapped, where you might be set up so you can't win -- and I recognize a few individuals here today who have been trapped in situations like that. But one way is when you get a call from a medium respond as you always would, courteously and forthrightly.

But I think I would follow a technique that I invariably use. I arrange a call-back. I don't try to have all the answers in my first conversation with a man, because obviously I don't have all the answers. I promise to get the answers and get back. This gives me several advantages.

One is that I can get the answers. But second, it gives me a chance to think it out. It gives me a chance to consult with my superiors, to consult with all the authorities on the subject, and decide just what are the facts. What's significant in this particular case?

But the third thing it gives you, it gives you an opportunity to make sure you're dealing with the person this phone voice represents himself to be. The guy who calls you and tells you he's from NBC isn't always from NBC. He isn't even always from the local radio station. That call-back will give you many, many advantages. The other thing, the other step I would offer to you, would be as you seek guidance from your own hospital or regional office staff, don't forget the man who has been designated as your public relations liaison. Each of your organizations should have one. He's been through a training course in the past year. He knows where to get information from other sources. He knows whom to contact in the information from other sources. He knows whom to contact in the information setup. In each area you have a regional information officer that reports directly to our office. Each of those people is well oriented on the issue of Agent Orange, well oriented on media attitudes and the people who have pre-set positions on these things. Their guidance can be invaluable to you when you're dealing, especially when you're dealing with a national medium.

My office, that's Frank Hood's office, the Assistant Administrator for Information Services - Frank or I or any member of our staff - Larry Moen, who's here today - would be glad to talk with you personally if you can't reach one of your local people.

*U S GOVERNMENT PRINTING OFFICE: 1981 341-407/3444