

## Chapter IV

### PHYSICAL EXAMINATION METHODOLOGY

Subsequent to the administration of the questionnaire, a voluntary comprehensive physical examination was offered to all individuals in both the exposed and comparison groups. The primary prerequisite for entry into the examination phase of the study was the completion of the baseline questionnaire. In the event that the initially selected comparison chose not to participate in both the questionnaire and the physical examination, a replacement was selected from among the other comparisons in the matched set, as depicted in Chapter II, Figure II-1. The two and one-half day examination was conducted in Houston, Texas by the Kelsey-Seybold Clinic, P.A. At the time of evaluation, an extensive physical examination, medical history with a review of systems, and in-depth laboratory analyses were conducted. A concise Examiner's Handbook in the Air Force Health Study Protocol placed strong emphasis on quality assurance and was used to minimize variability and insure comparability of data over the 12-month duration of the physical examination contract. Strict compliance with this document was required. Physical examinations were performed at the earliest practical time following the completion of the questionnaire, since close sequencing would limit the development of major symptoms or diseases in the interval between the questionnaire and the examination.

Physical examinations were performed at a single location and all contractor personnel evaluated the participants without knowledge of their exposure status. The number of examiners and the turnover of staff members was kept to a minimum to limit between-examiner variability. A more detailed discussion of the physical examination quality control program is contained in Chapter VI.

All laboratory tests were subjected to rigid quality control, and laboratory and physical examination data were measured on a continuous scale whenever possible to improve statistical power in the analysis. An Air Force physician was present at the examination site throughout the duration of the contract to act as a liaison between the subjects, the contractor and the Air Force, and to insure that the examination protocol was scrupulously followed. Although the on-site monitors closely observed each examiner and technician, the monitors remained unobtrusive during the examinations, and were not permitted to confirm, criticize or otherwise influence the examiners' findings.

The components of the physical examination were specifically selected to address those medical end points known or suspected to be caused by phenoxy herbicides and dioxin (Crow, 1970; Kimbrough, 1980). The question of whether significant chronic effects are produced in humans is a controversial issue (Homburger et al, 1979; Reggiani, 1980; Wolfe and Lathrop, 1983). Reviews of physical chemistry data, animal toxicity data, human exposure case reports, and epidemiologic studies have been relatively unsuccessful in identifying specific and objective medical end points for the chronic effects of exposure (Jirasek et al, 1973; Jirasek et al, 1974; Poland, 1979; Young, 1978). The list of known

or suspected acute and subacute effects following TCDD exposure is extensive, and many of the end points are highly subjective and extremely difficult to evaluate (Oliver, 1975; Poland et al, 1979). While chloracne appears to be a consistent, chronic effect of moderate to heavy exposure, the implication of this condition on long-term health is unknown (Young et al, 1978). At best, a list of potential organ systems which should be carefully evaluated can be developed.

Ideally, one would like to have a sensitive and specific examination or laboratory procedure to detect the effects of these chemicals in human tissues. Unfortunately, there is a lack of clearly defined end points in the scientific literature, and, other than chloracne, distinct clinical syndromes or unique effects indicative of chronic illness have not been identified. The signs and symptoms currently attributed to exposure are confounded by age and other causes, and the effect, if present, may be lost in common symptoms from other causes of disease (in contrast to conditions such as diethyl-stilbestrol-induced vaginal adeno-carcinoma and angiosarcoma of the liver caused by vinyl chloride exposure). In the absence of sensitive and specific indicators of exposure, a comprehensive examination format was developed around these target organ systems listed in Table IV-1. The complexity and the length of the evaluation and the invasiveness of each examination procedure were all key factors in the final choice of the examination components since all of these factors have a significant impact on the compliance behavior of the individuals considering participation in the study.

Table IV-1

TARGET ORGAN SYSTEMS/CONDITIONS

Dermatologic

Hepatic

Neoplastic

Neurological/Psychiatric

Endocrine/Reproductive

Immunologic

Hemopoietic

A general summary of the major components of the examination is presented in Table IV-2, and examples of the examination forms are included in Appendix VI. The laboratory procedures conducted on each subject are listed in Table IV-3. For each participant 20 cc of serum, 100 cc of urine, and all remaining semen were aliquoted and stored at -70°C for future analyses. When technology developments identify additional analytic procedures which will

assess the health effects of phenoxy herbicides and dioxin, these specimens will then be tested. The slides used in the 10,000 white blood cell differential and the semen analysis were also preserved.

Table IV-2

RANCH HAND II  
PHYSICAL EXAMINATION

General Physical Examination	(Internist)
Neurological Examination	(Neurologist)
Dermatological Examination	(Dermatologist)
Electrocardiogram	(Resting, 4-Hour Fasting)
Pulmonary Function Study	(1 Second Forced Expiratory Volume, Vital Capacity)
Chest X-ray	
Nerve Conduction Velocities	(Ulnar, Peroneal, Sural)
Psychological Evaluation	
Minnesota Multiphasic Personality Inventory (MMPI)	
Cornell Wechsler Memory Scale I	
Wechsler Adult Intelligence Scale (WAIS)	
Wide Range Achievement Test (WRAT)	
Halstead-Reitan Neuropsychological Battery	
Patient Outbriefing and Discussion of Individual Results	(Internist) (PhD Psychologist)

Table IV-3

LABORATORY PROCEDURES

Chemistry Panel:	
Blood Urea Nitrogen (BUN)	Serum Glutamic Oxaloacetic Transaminase (SGOT)
Creatinine	Serum Glutamic Pyruvic Transaminase (SGPT)
Cholesterol	Gamma Glutaryl Transpeptidase (GGTP)
High-Density Lipoprotein Triglyceride	Lactic Dehydrogenase (LDH)
	Creatine Phosphokinase (CPK)
	Blood Alcohol
Total Bilirubin	
Direct Bilirubin	
Alkaline Phosphatase	
Glucose	} Fasting and 2 Hour
Cortisol	
Hormone Assay:	
Leutenizing Hormone (LH)	Triiodothyronine (T3)
Follicle Stimulating Hormone (FSH)	Total Thyroxine (T4)
Testosterone	Free Thyroxine Index (FTI)
Hematology Panel:	
Erythrocyte Sedimentation Rate	
Prothrombin Time	
Serological Test for Syphilis (RPR)	
White Blood Cell Count (with 10,000 cell differential)	
Red Blood Cell Count	
Hemoglobin	
Hematocrit	
Red Cell Indices	
Platelet Count	
Urinalysis	
24-Hour Urine:	
Volume	
Delta Amino Levulinic Acid	
Coproporphyrins	
Uroporphyrins	
Porphobilinogen	
Creatinine	
Semen Analysis:	
Volume	
Count	
Abnormal Forms	
Hepatitis B Testing:	
Surface Antigen	
Antibody to Surface Antigen	
Core Antibody	

Under special circumstances, additional laboratory procedures were carried out on selected participants. Those individuals with a history of having fathered children with birth defects had blood drawn for a determination of karyotype. The serum of participants with a medical history or review of systems indicating the possibility of an immune system deficiency was evaluated by immunoelectrophoresis. Antinuclear antibody determinations were performed on individuals with a history suggestive of connective tissue disorders. In addition, all individuals with a past history of hepatitis were tested for antibody to hepatitis A virus.

After 20 April 1982, all participants whose study identification number ended in either 1, 3, 6 or 9 were selected for special immunologic testing. Blood from these individuals was drawn and sent to a subcontractor for the evaluation of B and T cell counts, enumeration of T cell subpopulations, and studies of B and T cell function following mitogen stimulation. In all, 592 randomly selected subjects took part in this portion of the evaluation.

Since human sensitivity and compassion could seriously enhance participation in the follow-up phases of the study, every opportunity was taken by the contractor and the Air Force to make the experience enjoyable, relaxing and rapport building. Study participants were housed in a comfortable motel, and transportation, meals and a modest stipend were provided. Family members were encouraged to accompany the participants, but at no expense to the government. Any emergency medical care required by the participants during their stay in Houston was provided by the contractor and paid for by USAF. Additionally, any diagnostic procedures necessary to clarify potentially life-threatening conditions were also performed (computerized tomography, cardiology consultation, etc.). Detailed in-briefings were provided to all participants (and optionally to accompanying family members), in order to explain the background and nature of the study as well as the routine medical requirements for the fasting status laboratory procedures. During waiting periods between examination phases, participants were encouraged to become acquainted with other participants and ask any questions they had about the examination, its rationale or the Air Force Health Study. The normal tension associated with psychological testing was relieved by frequent breaks. Any individual problems were quietly and diplomatically managed by the contracting staff and the site monitor. Over 95% of the participants expressed praise for the quality and thoroughness of the examination and pledged to return to the next examination.

Subjects arrived in Houston on either a Sunday or a Tuesday afternoon. A 1-hour briefing was given to each group of participants by the Air Force monitor and a Kelsey-Seybold physician. During this briefing, the purpose of the study and a detailed explanation of the examination content and schedule were discussed. The next 2 days (Monday/Tuesday or Wednesday/Thursday) were spent in the examination. Upon arrival at the clinic on the first morning, all participants were met by two Kelsey-Seybold staff members: the Patient Coordinator and the Program Director. After the day's events were explained, medical history and other forms were completed and blood specimens were drawn. All participants on active flying status with the Department of Defense or FAA had their blood drawn while reclining. Others had the option of sitting or lying.

All fasting blood specimens were obtained following a minimum of seven hours without alcohol, food or cigarettes. Participants were requested to consume a 250-gram carbohydrate diet for the 3 days prior to their arrival to prepare for the fasting and 2-hour postprandial glucose testing. All alcoholic beverages were to be avoided as well. Compliance with these requirements and the 24 hour urine collection was determined. Breakfast followed the blood draw and postprandial specimens were then obtained at appropriate times. One-half of each group underwent physical examination on the first day while the other half were in psychological testing. On the second day, the schedule was reversed. During the final half-day, each participant received detailed briefings from a PhD psychologist and one of two Internal Medicine specialists. During these briefings, the results of all portions of the physical examination performed at the Kelsey-Seybold Clinic were discussed with the subject, any questions he had were answered, and suggestions for medical treatment or follow-up were made when indicated. If immediate follow-up was indicated, direct contact with the participant's personal physician was made, and appropriate treatment was arranged. The results of those laboratory procedures performed at subcontracting laboratories and the results of the MMPI were not discussed. Payment of expense vouchers and the provision stipend checks were delayed until after the completion of the debriefing to encourage attendance at these sessions.