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# Selected Pesticide Residues or Metabolites in Blood and Urine Specimens from a General Population Survey

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**The National Center for Health Statistics collaborated with the National Human Monitoring Program of the U.S. Environmental Protection Agency (EPA) in a four-year study to assess the exposure of the general population to selected pesticides through analysis of blood serum and urine specimens. Specimens were collected on a national probability half sample of persons 12-74 years of age from 64 locations across the United States comprising the sample areas in the Second Health and Nutrition Examination Survey (NHANES II) and analyzed for selected organochlorine, carbamate, chlorophenoxy and organophosphorus pesticides. Medical, nutritional and pesticide usage data are also available for each sample person. Preliminary results of the blood serum and urine analyses indicate that the general population is being exposed to some of these types of pesticides. Since 1970, EPA has conducted a national probability sampling of human adipose tissue. Specimens obtained on a survey design representative of the general population were analyzed for selected organochlorine pesticides and toxic chemicals. Findings from the 1978 survey also indicate exposure of the general population to some of these chemicals. Medical data collected from both surveys have yielded no overt correlations between health effects and residue levels. More intensive statistical analyses are underway to investigate the possible existence of more subtle relationships.**

## Introduction

Residues of pesticides and their metabolites in various human tissues and fluids collected from the general population are indicative of the total body burden of these pesticides and of past and present exposure to them. Most members of the general population are not occupationally exposed to pesticides; their contact comes from other more covert sources. Pesticides may gain entrance to the human body through the intestine subsequent to ingestion; through the lungs as a result of airborne pesticide-laden dusts, vapors and aerosols; by penetration through the intact skin; and (rarely) by absorption directly into the bloodstream through broken skin.

Once within the human body, the residue is subjected to numerous metabolic processes. In the case of certain lipophilic organochlorine pesticides, residues of the parent compound or metabolites are assimilated and stored in the lipid portion of adipose tissues. Residues of these chemicals also may be detected in the lipid portion of such fluids as milk and blood serum. On the other extreme are the pesticides which are rapidly metabolized and excreted. Certain of the organophosphorus and carbamate pesticides undergo these dynamic changes. Other chemicals such as certain organochlorine and chlorophenoxy herbicides are capable of passing directly through the human body virtually intact

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and are then excreted. Residues are demonstrative of the extent of the environmental distribution of the particular pesticide and, when coupled with laboratory animal or other data showing adverse biological effects, signal a potential public health hazard. Population exposure data could be an element in determining priorities for research on health effects of particular pesticides.

The National Human Adipose Tissue Monitoring Survey is operated by the U.S. Environmental Protection Agency to determine on a national scale the incidence and level of exposure to pesticides experienced by the general population and to identify trends in these factors when they occur. Two of the major sources of information on pesticide exposure are the Second National Health and Nutrition Examination Survey (NHANES II) and the National Human Adipose Tissue Monitoring Survey. In NHANES II, the National Center for Health Statistics (NCHS) and the National Human Monitoring Program for Pesticides (EPA) cooperatively collected and analyzed blood and urine specimens for selected pesticide residues and their metabolites. In the National Human Adipose Tissue Monitoring Survey samples collected by cooperating pathologists are analyzed.

This paper briefly describes the collaborative NHANES II study and presents some preliminary, statistically unweighted results to describe the general levels of positive findings based on blood and urine sample analyses. Selected results only are shown for the National Human Adipose Tissue Monitoring Survey in 1978 to further illustrate the general exposure in our population to some chemicals. Although no analyses of medical data and levels observed have been done, no health effects associated with pesticide poisoning were noted by the physician during the examination phase of the study.

# NHANES II Study

## Background

The NHANES programs are designed to obtain health and nutritional status information that can best or only be obtained by direct physical examinations, tests and measurements performed on representative samples of the civilian, noninstitutionalized population of the United States. The programs have provided health professionals with estimates of the total prevalence of selected illness, impairments and other indicators of health and nutritional status and the distribution of many conditions or characteristics in the target population by sex, age, income levels, race and region. For the medical community to know what is uncommon, it must know what is common. Repeated NHANES studies can provide data to monitor changes in these prevalence levels and distributions over time. When analyzed for associations, the data collected can often also be used to identify special groups and/or conditions which should be further studied for better understanding or treatment.

The methodologies employed in NHANES I and II have various strengths and weaknesses and present logistical and conceptual challenges that must be dealt with in successfully collecting, analyzing and interpreting the data. Detailed descriptions of the surveys are available in the *Vital and Health Statistics* series publications (*1-4*).

## Content

The general procedures and content of NHANES II included a general medical examination and screening by a physician, including a medical history, body measurements, a dietary interview covering food consumption during the 24 hr prior to examination, and numerous laboratory tests on whole blood, serum and urine specimens. Depending on age, additional tests and procedures were also included that provide data on diabetes, kidney disease, heart disease, hypertension, certain allergies, disc degeneration, pulmonary function, hearing, speech and nutritional problems. From a national probability sample of persons 6 months to 74 years of age, survey personnel collected blood and urine samples for pesticide residue and metabolite determinations from a subsample of individuals 12-74 years old. The results of this effort could establish baseline data on the exposure of the general population to organophosphate, carbamate, chlorophenoxy and certain organochlorine pesticides; correlate residue and metabolite data with various medical and nutritional parameters; and collect some information on the pesticide use patterns of the general population.

## Sample Design, Selection and Interviewing Procedures

Approximately 28,000 persons representing a national probability sample of the civilian noninstitutionalized population 6 months to 74 years of age were selected in 64 communities throughout the four broad Census regions of the United States shown on the map (Fig. 1). Approximately 21,000 people were examined between February 1976 and February 1980.

Each community in the United States was grouped into one of 64 strata on the basis of similar charac-

FIGURE 1. NHANES II sample areas.

teristics such as region, population density, urbanization, and type of industry. One community was selected from each stratum. Some communities such as New York and Los Angeles were populous enough to define a unique stratum and, hence, were selected into the sample with a probability of one. Within a community, a systematic sample of clusters of 16 households were selected; NHANES sample units are a random selection of 8 of the 16 households of each cluster with "poverty" segments oversampled at a rate of 2 to 1. A Census Bureau interviewer conducted a household interview and selected the NHANES sample persons from the household roster according to the following rules: 3/4 of those persons <6 yr and 60-74 yr; 1/4 of those persons 6-59 yr.

Upon completing the household interview and the required medical histories, the census interviewer arranged an appointment for examination in the NHANES mobile examination centers. Included in the medical history were several questions relating to pesticide usage practices.

## Specimen Handling and Analysis

All collection and handling equipment in contact with serum and urine specimens were tested as possible sources of contamination. No contaminating materials were identified. A 5-mL aliquot of each sample person's serum was placed into "clean" glass vials, frozen and shipped packed in dry ice to EPA for subsequent analysis at a contract laboratory. All pesticide residue analyses were conducted by contract laboratories using only methodologies specified by the program. These laboratories were equipped with gas-liquid chromatographs with electron capture and flame photometric detectors. All laboratories were required to maintain acceptable performance levels in the interlaboratory quality assurance program, established and moderated by the EPA Environmental Toxicology Division, Research Triangle Park, North Carolina. This laboratory also served as a source of technical consultation for the analytical portion of the program.

An interfering serum separation substance present in Vacutainers used in 10 of the 64 sample locations caused serum samples from these areas to be discarded from laboratory analyses. The effect of this loss on the final interpretation of the data is unknown at this time.

The multiresidue approaches used to analyze the samples permit characterization of some 38 pesticides and toxic compounds. Thin-layer chromatography, electrolytic conductivity detectors and, in some cases, combined gas chromatography–mass spectrometry were employed as confirmatory analytical techniques. In addition, organochlorine residues in pooled extracts of the human adipose tissue and blood serum specimens were confirmed by combined gas chromatography–mass spectrometry.

**Table 1. Occurrence of selected pesticide residues in human blood serum.[a]**

| Residue[b] | Possible origin | Frequency of detection, % |
|---|---|---|
| Total DDT | DDT and its analogs | 99 |
| β-Benzene hexachloride | BHC | 14 |
| Dieldrin | Aldrin/dieldrin | 9 |
| *trans*-Nonachlor | Chlordane/heptachlor | 6 |
| Hexachlorobenzene | Chlorinated benzene manufacture | 4 |
| Heptachlor epoxide | Chlordane/heptachlor | 4 |
| Oxychlordane | Chlordane/heptachlor | 4 |
| Other BHC isomers | BHC | < 1 |
| Mirex | Mirex | < 1 |
| Heptachlor | Chlordane/heptachlor | < 1 |

[a]Based on the analysis of approximately 4200 specimens from persons in 54 locations of NHANES II, 1976–1980.
[b]Limits of detection: 1–2 ppb 1–2 μg/L).

A mechanism was established between EPA and NCHS so that laboratory findings indicative of acute effects were reported to the volunteer's primary health care provider.

## Results

The statistics presented in Tables 1-6 are not national estimates, but instead show the percentage of positive test results among a subsample of participants in NHANES II aged 12-74 yr who resided in various types of communities across the United States with characteristics representing cross-sections of socioeconomic and demographic strata. The oversampling of poverty segments at a rate of 2 to 1 is not accounted for in this presentation, but will be in the final weighting processing.

In blood samples (Table 1), nearly all tested in NHANES II had detectable DDT and its analogs. Significant proportions of the serum samples tested also had detectable levels of residues possibly originating from BHC, aldrin, dieldrin, chlordane, heptachlor and chlorinated benzene manufacture. More detailed analyses of the data have not been undertaken, but each percentage point could represent about 1.5 million persons when the final weighting of the data has been completed.

In urine samples, about 79% of these tested had detectable levels of pentachlorophenol. Significant proportions of the samples had detectable levels of pesticide-related phenolic residues (Table 2): 3,5,6-trichloro-2-pyridinol, 2,4,5-trichlorophenol and *p*-nitrophenol. Detectable levels of dicamba and 2,4-D were less common. Residues of malathion-related metabolites in urine specimens occurred, but quite infrequently (Table 3). Residues of carbamate pesticide metabolites in urine occurred in 2-4% of the tested samples (Table 4).

The frequency of detection of some dialkyl phosphate residues ranged from 6 to 12% of those tested

**Table 2. Occurrence of pesticide-related phenolic residues in human urine.[a]**

| Residue[b] | Frequency of detection, % |
|---|---|
| Pentachlorophenol | 79 |
| 3,5,6-Trichloro-2-pyridinol[c] | 7 |
| 2,4,5-Trichlorophenol | 4 |
| *p*-Nitrophenol[d] | 3 |
| Dicamba | 1 |
| 2,4,-D | 1 |
| 2,4,5-T | 0 |
| Silvex | 0 |

[a]Based on analysis of approximately 6000 specimens from persons in all 64 locations of NHANES II, 1976-1980.
[b]*Limits of detection:* 5-30 ppb (5-30 μg/L).
[c]Metabolite of chloropyrifos.
[d]Metabolite of methyl and ethyl parathion.

**Table 3. Residues of malathion metabolites in human urine.[a]**

| Metabolite[b] | Frequency of detection, % |
|---|---|
| α-Monocarboxylic acid | 1.4 |
| Dicarboxylic acid | < 1 |

[a]Based on analysis of 5973 specimens from persons in all 64 locations of NHANES II, 1976-1980.
[b]Limits of detection: 30 ppb (30 μg/L).

**Table 4. Residues of carbamate pesticide metabolites in human urine.[a]**

| Chemical[b] | Frequency of detection, % | Possible pesticide origin |
|---|---|---|
| Carbofuranphenol | 4 | Carbofuran |
| 3-Ketocarbofuran | 3 | |
| Isopropoxyphenol | 4 | Propaxur |
| α-Naphthol | 2 | Carbaryl |

[a]Based on the analysis of 6000 specimens from persons in all 64 locations of NHANES II, 1976-1980.
[b]Limits of detection: 10-40 ppb (10-40 μg/L).

**Table 5. Occurrence of dialkyl phosphate residues in human urine.[a]**

| Dialkyl phosphate residue[b,c] | Frequency of detection, % |
|---|---|
| Dimethyl phosphate (DMP) | 12 |
| Diethyl phosphate (DEP) | 7 |
| Dimethyl phosphorothionate (DMTP) | 6 |
| Diethyl phosphorothionate (DETP) | 6 |
| Dimethyl phosphorodithioate (DMDTP) | < 1 |
| Diethyl phosphorodithioate (DEDTP) | < 1 |

[a]Based on analysis of 5976 specimens from persons in all 64 locations of NHANES II, 1976-1980.
[b]Probable metabolites of some organophosphate insecticides.
[c]Limits of detection: 20 ppb (20 μg/L).

(Table 5); dimethyl phosphorodithioate (DMDTP) and diethyl phosphorodithioate (DEDTP) residues were detected less frequently.

As another source of data the human monitoring program's testing of adipose tissues (*5*) provides some information suggesting that there is general exposure of the population to some of these organochlorine pesticides. (Table 6).

## Conclusions

The preliminary unweighted data from NHANES II suggest rather widespread exposure of the general population aged 12-74 yr to certain pesticides. The data also suggest that most people are not occupationally exposed; they come in contact with these substances through other sources. Due to selective sampling by poverty segments and age group, the final weighted results could change significantly from the results presented. Weighting will not significantly affect such results as those shown for DDT and its analogs (99% positive) and pentachlorophenol (79% positive).

What, if any, adverse health effects are associated with the exposure to these chemicals is not clear. No overt health sequelae attributable to these residues were apparent during the medical examinations of these persons. Additional statistical analyses of the data will be performed to investigate the possible existence of more subtle relationships.

The data are being properly weighted and added to other examination, socioeconomic and demographic information available from NHANES II study and will be collaboratively analyzed by NCHS and EPA staff over the next year. Since NHANES II was a cross-sectional study, the analyses will only demonstrate statistical association of exposure results and health status measures. Causal relationships between exposure and health effects will depend on carefully controlled research studies of a longitudinal nature.

The results will be documented and released in a variety of forms: microdata tapes, *Vital and Health Statistics* reports, journal articles and presentations at professional meetings. For those using the microdata tapes, a limited amount of technical assistance is available as resources permit, but complete documentation covering data collection, specimen analyses and other aspects of the study will be provided.

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**Table 6. Occurrence of selected organochlorine residues in human adipose tissue.[a]**

| Residue[b] | Possible origin | Frequency of detection, % |
|---|---|---|
| Total DDT | DDT and its analogs | 100 |
| *trans*-Nonachlor | Chlordane/heptachlor | 97 |
| Heptachlor epoxide | Chlordane/heptachlor | 96 |
| Oxychlordane | Chlordane/heptachlor | 95 |
| Dieldrin | Aldrin/dieldrin | 95 |
| β-Benzene hexachloride | BHC | 94 |
| Hexachlorobenzene | Chlorinated benzene manufacture | 93 |
| Polychlorinated biphenyls | PCB's | 23 |
| γ-Benzene hexachloride | Lindane | 2 |
| Other BHC isomers | BHC | < 1 |
| Mirex | Mirex | < 1 |

[a]Based on the analysis of 785 specimens from the National Human Adipose Tissue Monitoring Program Fiscal Year 1978 survey.
[b]Limits of detection: 10-20 ppb (10-20 μg/L).

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