

Residues and Metabolites of Selected Persistent Halogenated Hydrocarbons in Blood Specimens from a General Population Survey

by Robert Murphy* and Clair Harvey*

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 National Health and 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. Results of the blood serum analyses indicate that the general population is being exposed to some of these types of pesticides. For selected pesticide residues, the percent quantifiable positives and median serum levels by age group are presented for three regions of the United States. 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 1979 survey also indicate exposure of the general population to some of these chemicals.

Residues of pesticides and their metabolites in various human tissues and fluids are indicative of the total body burden of these pesticides and of past and present exposure to them. Once within the human body, the residues are 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. The scope of this paper is restricted to pesticides of this nature, even though some information was gathered on pesticides which are rapidly metabolized and excreted or which are capable of passing directly through the human body virtually intact and are then excreted. Body residue information collected on the general population is 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 Monitoring Program 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 of the general population are the Second National Health and Nutrition Examination Survey (NHANES II), 1976-80, and the continuing National Human Adipose Tissue 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 Survey samples collected by cooperating pathologists in geographically dispersed sites across the United States are analyzed.

First, the collaborative NHANES II study is described and, then, results are presented to describe the general levels of positive findings based on blood sample analyses. Selected results from the National Human Adipose Tissue Survey (1) in 1979 are mentioned 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

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associated with pesticide poisoning were noted by the physician during the examination phase of the NHANES II 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. 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 programs 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 (2-5).

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 through 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 and correlate residue and metabolite data with various medical and nutritional parameters.

Sample Design, Selection and Interviewing Procedures

Approximately 28,000 persons representing a national probability sample of the civilian, noninstitutionalized population 6 months through 74 years of age were selected in 64 communities throughout the four broad Census regions of the United States shown in the map



FIGURE 1. NHANES II sample areas.

(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 characteristics such as region, population density, urbanization, and type of industry. One community was selected from each stratum. Some communities such as New York or 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 were a random selection of 8 of the 16 households of each cluster with "poverty" segments oversampled at a rate of 2 to 1. Census Bureau interviewers contacted persons at the selected housing units, conducted household interviews, and selected the NHANES sample persons from the household rosters according to the following rules: 3/4 of those persons less than 6 years and 60-74 years; 1/4 of those persons 6-59 years.

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.

The response rate for the household interview and medical history portion of NHANES II was about 91%; about 73% were examined. Although analysis of the potential nonresponse bias has not been done with respect to exposure to pesticides, it was assumed in this report that examined and nonexamined sample persons were similar. NHANES II blood lead, carboxyhemoglobin level, and other analyses have suggested this assumption is reasonable. This assumption will be examined in detail during the next few months.

Specimens 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 a "clean" glass vial, 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, NC. This laboratory also served as a source of technical consultation for the analytical portion of the program.

The multiresidue approaches used to analyze the samples permit characterization of some 38 pesticides and toxic compounds. Thin-layer chromatography, elec-

trolytic 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.

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. Unfortunately these losses concentrated in the western region's sample sites. Hence, the weighted estimates presented in this paper refer only to the Northeast, Midwest, and South regions.

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 statistically weighted NHANES II results indicate that the general population has been broadly exposed to selected persistent halogenated hydrocarbons. Estimates presented in Figures 2-9 are subject to sampling errors which are shown in Table 1. These sampling errors take into account the complex survey design. Table 2 presents the number of serum specimens used in developing estimates of the percent quantifiable positives. Differences observed in median blood levels by age group have not been tested for statistical significance but are commented on to suggest general levels.

Table 1. Standard errors of the percent quantifiable positives by age groups for each residue discussed: NHANES II, 1976-80.

Residue	Standard error, %			
	12-74 years	12-24 years	25-44 years	45-74 years
<i>p,p'</i> -DDT	2.9	2.2	3.3	3.8
<i>p,p'</i> -DDE	0.2	0.3	0.3	0.2
Dieldrin	1.2	0.5	1.1	2.6
β -Benzene hexachloride	2.3	0.6	2.5	3.9
Hexachlorobenzene	0.9	0.8	0.9	1.5
<i>trans</i> -Nonachlor	0.9	0.8	0.8	1.5
Heptachlor epoxide	0.7	0.4	0.7	1.1
Oxychlorodane	1.0	0.8	0.6	1.6

Table 2. Number of serum specimens used to estimate percent quantifiable positives by age group for each residue discussed: NHANES II, 1976-80.

Residue	No. of serum specimens			
	12-74 years	12-24 years	25-44 years	45-74 years
<i>p,p'</i> -DDT	3261	992	920	1349
<i>p,p'</i> -DDE	3366	1021	949	1396
Dieldrin	3039	928	855	1256
β -Benzene hexachloride	3126	955	876	1295
Hexachlorobenzene	2269	685	627	957
<i>trans</i> -Nonachlor	3218	987	902	1329
Heptachlor epoxide	3235	991	907	1337
Oxychlorodane	3208	993	899	1316

***p,p'*-DDT**

Based on NHANES II, 1976–1980 results, 31% of the population 12–74 years of age in the Northeast, Midwest, and South was exposed to *p,p'*-DDT (Fig. 2).

The percent of population exposed increased from youngest to oldest age group from about 14 to 51%. The median level for quantifiable positive results over all age groups was 3.3 ppb; the median level increased from youngest to oldest age groups from 2.7 to 3.5 ppb. The range of quantifiable positive levels was 2 to 58 ppb.

From the National Human Adipose Tissue Survey, FY 1979 the percent of quantifiable positives based on 795 specimens was 98.6%. The difference in percent exposed is not unexpected, since the body materials tested were different.

***p,p'*-DDE**

NHANES II results estimated are about 99% of the population 12–74 years of age during the period of the survey and in the Northeast, Midwest, or South regions was exposed to *p,p'*-DDE (Fig. 3).

The median level for quantifiable positive results was 11.8 ppb; the median level increased from youngest to oldest age group 5.9 to 18.3 ppb. The range of quantifiable positive levels was 1 to 378 ppb.

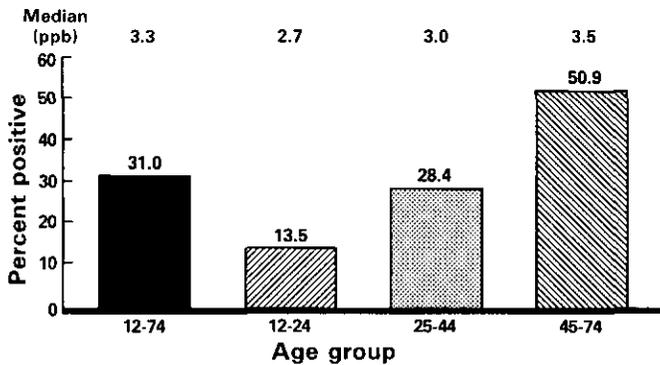


FIGURE 2. Percent positive and median *p,p'*-DDT level for positives by age. Limit of detectability, 2 ppb. Data for Northeast, Midwest and South only.

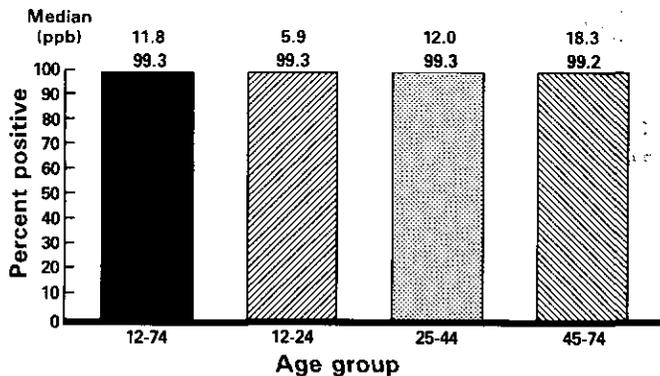


FIGURE 3. Percent positive and median *p,p'*-DDE level for positives by age. Limit of detectability, 1 ppb. Data for Northeast, Midwest and South only.

The corresponding estimate of percent quantifiable positives from the National Human Adipose Tissue Survey, FY 1979 was 99.1%.

β -Benzene Hexachloride

NHANES II estimated that 13.9% of the population 12–74 years of age in the Northeast, Midwest, and South regions was exposed to β -benzene hexachloride (Fig. 4).

The percent of the population exposed increased from youngest to oldest age group from 3.2 to 26.8%. The median level for quantifiable positive results was 1.7 ppb. The median level from youngest to oldest age group increased but the increase may not be statistically different. The range of positive levels was 1 to 28 ppb.

The National Human Adipose Tissue Survey, FY 1979 estimated almost 92% quantifiable positives.

Dieldrin

From NHANES II results, an estimated 8.6% of the population 12–74 years of age in the Northeast, Midwest, and South regions were exposed to dieldrin (Fig. 5).

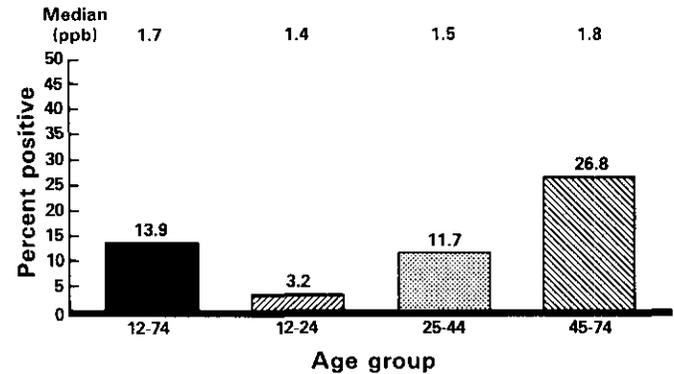


FIGURE 4. Percent positive and median β -benzene hexachloride level for positives by age. Limit of detectability, 1 ppb. Data for Northeast, Midwest and South only.

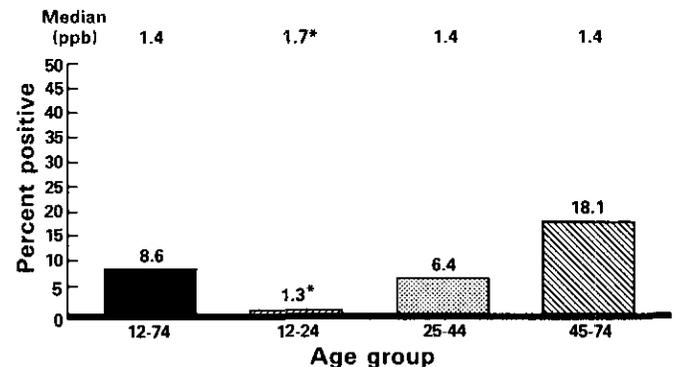


FIGURE 5. Percent positive and median dieldrin level for positives by age. Limit of detectability, 1 ppb. Data for Northeast, Midwest and South only. The data for the 12–24 age group reflects a sample size less than 30 or relative standard error of 25% or more.

The percent of the population exposed rose from youngest to oldest age group from about 1.3 to 18.1%. The median level for quantifiable positive results, 1.4 ppb, did not vary much by age group. The estimated median for the 12–24 group is unreliable due to small numbers of positives. The range of quantifiable positive results was from 1 to 16 ppb.

The National Human Adipose Tissue Survey, FY 1979 estimated quantifiable positives at about 96%.

trans-Nonachlor

NHANES II, data indicated that 4.4% of the population 12–74 years of age in the Northeast, Midwest and South regions was exposed to *trans*-nonachlor (Fig. 6).

The portion of the population exposed increased from about 1.4 to 8.9% from youngest to oldest age group. The median level for quantifiable positive results was 1.4 ppb, and it did not vary much by age group. The range of quantifiable positive results was 1 to 17 ppb.

In the National Human Adipose Tissue Survey, FY 1979, the estimated percent quantifiable positives was about 97%.

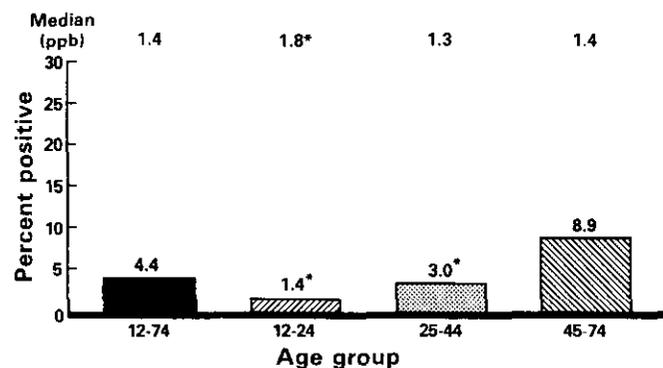


FIGURE 6. Percent positive and median *trans*-nonachlor level for positives by age. Limit of detectability, 1 ppb. Data for Northeast, Midwest and South only. The data for the 12–24 age group reflects a sample size less than 30 or relative standard error of 25% or more.

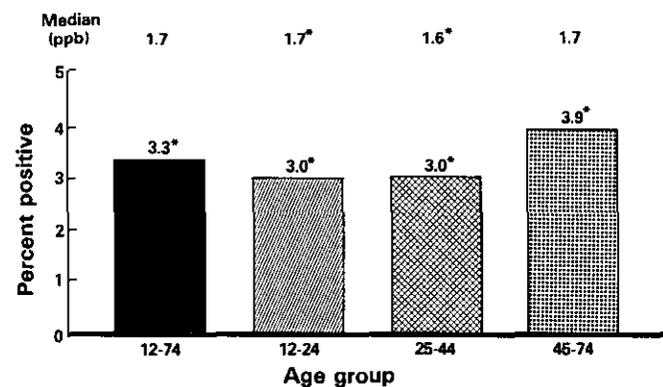


FIGURE 7. Percent positive and median hexachlorobenzene level for positives by age. Limit of detectability, 1 ppb. Data for Northeast, Midwest and South only. The values marked with an asterisk (*) reflect a sample size less than 30 or relative standard error of 25% or more.

Hexachlorobenzene

From NHANES II results, about 3.3% of the population 12–74 years of age in the Northeast, Midwest, and South regions was exposed to hexachlorobenzene (Fig. 7).

The percent of the population exposed was about the same over all the age groups. The median level for quantifiable positive results was 1–7 ppb, and it did not vary much by age group. The range for quantifiable positive results was 1 to 17 ppb.

In the National Human Adipose Tissue Survey, FY 1979, the estimated percent quantifiable positives was about 91%.

Heptachlor Epoxide and Oxychlordane

From NHANES II results, about 2.5% of the population 12–74 years of age in the Northeast, Midwest, and South regions was exposed to heptachlor epoxide or oxy chlordane (Figs. 8 and 9).

The percent quantifiable positives by age group was generally based on too few sample persons to be reliable

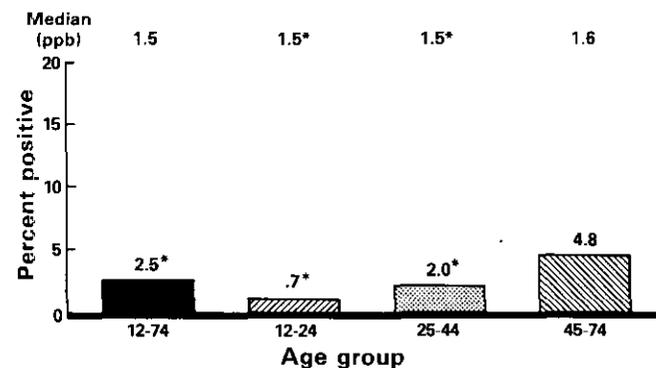


FIGURE 8. Percent positive and median heptachlor epoxide level for positives by age. Limit of detectability, 1 ppb. Data for Northeast, Midwest and South only. The values marked with an asterisk (*) reflect a sample size less than 30 or relative standard error of 25% or more.

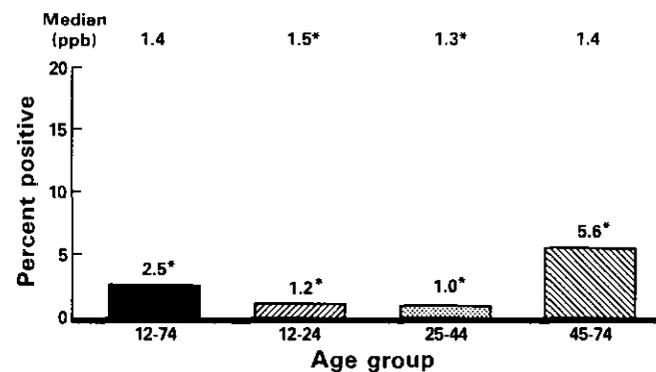


FIGURE 9. Percent positive and median oxychlordane level for positives by age. Limit of detectability, 1 ppb. Data for Northeast, Midwest and South only. The values marked with an asterisk (*) reflect a sample size less than 30 or relative standard error of 25% or more.

for comparative purposes. The median level for quantifiable positive results for heptachlor epoxide was 1.5 ppb over all age groups; for oxychlorane, the median level was 1.4 ppb. The medians did not vary significantly by age group. The range of quantifiable positive values for both heptachlor epoxide and oxychlorane was 1 to 23 ppb.

In the National Human Adipose Tissue Survey, FY 1979, the estimated percent of quantifiable positives for heptachlor epoxide and oxychlorane was 95 and 94%, respectively.

Conclusions

The data from NHANES II from the Northeast, Midwest, and South regions indicate widespread exposure of the general population aged 12-74 years to certain pesticides. The data also suggest that most people are not occupationally exposed; they come in contact with these substances through other sources.

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 have been properly weighted and are being added to other examination, socioeconomic and demographic information available from the NHANES II study. They will be collaboratively analyzed by NCHS and EPA staff over the next year. Among the analyses planned are the determination of potential bias associated with nonresponse and identification of population subgroups with highest body burdens of these residues. Since NHANES II was a cross-sectional study, the analyses will only reveal 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. The microdata tapes should be available through the National Technical Information Service in April 1985.

Research needs to further utilize data collection mechanisms such as NHANES include:

- Developing methods for specimen testing that are cheaper and more reliable
- Developing standard reference materials for use in laboratories so that quality control can be improved and between laboratory comparisons can be made and interpreted
- Developing acceptable protocols for linking exposure measures to health effects or risk factors. The less invasive the measurements developed are, the more likely a mechanism such as NHANES can be employed to obtain general population data.

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