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PCDDs AND PCDFs IN HUMANS

by

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ABSTRACT

Numerous instances of human exposure to polychlorinated dibenzo-*p*-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) have been documented. Following the development of sufficiently specific and sensitive analytical methods during the past few years, many reports have appeared on PCDD and PCDF levels in human blood and adipose tissues. Studies have examined the PCDD and PCDF levels resulting from accidental and occupational exposures of various groups, including chemical plant workers, forestry and tannery workers, and Viet Nam veterans who had handled Agent Orange. The general background levels in the U.S., Federal Republic of Germany, Japan, and Sweden were also determined. The results of these studies indicate that a background level of PCDDs and PCDFs is present in the overall population. In some cases, individuals exposed to specific PCDDs or PCDFs exhibit higher levels than the general population. Isomer distribution patterns are relatively consistent and indicative of sources and metabolism. This paper reviews the available data on human PCDD and PCDF levels in exposed and general populations.

INTRODUCTION

Humans are exposed to polychlorinated dibenzo-*p*-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) from a variety of sources. These PCDDs and PCDFs are absorbed via the skin, lungs, or gastrointestinal tract and are deposited, because of their non-polar, lipophilic properties, in the fatty tissues. PCDDs and PCDFs tend to have a half-life of several years in the human body. Because of their high toxicity, in animals, measurement of human body concentrations and correlation of these measurements to exposure are important.

Occupation, general background, and a number of special circumstances have all led to human PCDD and PCDF exposure. People working in plants that manufacture chlorinated organics, such as aromatics, phenolics, herbicides, and disinfectants have been exposed. Herbicide applicators such as forestry workers and the Air Force Agent Orange sprayers known as Ranch Hands[1], have also been exposed. Several special PCDD and PCDF exposures have occurred, namely the Yusho incident;[2] the

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Seveso, Italy, industrial accident;[3] various PCB fires,[4] and the waste oil from a hexachlorophene plant in Verona, MO, which was spread over horse arenas and roads throughout Missouri, most prominently in Times Beach.[5]

The general population is exposed to background concentrations of PCDDs and PCDFs that arise from effluents from the normal use of products containing trace levels of PCDDs and PCDFs as well as the industrial processes cited. Moreover, a variety of combustion processes make PCDDs and PCDFs that are released into the environment and then enter the human body either directly via ambient air or indirectly via the food chain. These combustion sources are thought to include incineration of chlorinated organics in industrial processes and in municipal solid waste incinerators. In addition, the "trace chemistries of fire" theory[6] proposes that most sources of carbon and chlorine can, under the right conditions, generate trace quantities of PCDDs and PCDFs. This expands the potential sources of PCDDs and PCDFs to essentially all combustion sources, including fossil-fuel power plants, and automobiles.[7]

Throughout this paper, individuals with specific known sources of occupational or special exposure are termed "exposed," while those whose only known source of PCDDs or PCDFs would be from general background sources are termed "nonexposed."

Measurement of PCDD or PCDF concentrations in human tissues can be used to indicate and study exposure. Monitoring these concentrations over time yields information about their residence time in the human body. Finally, it is important to remember that PCDDs and PCDFs are complex families of 75 and 135 compounds, respectively. The relative concentrations of the individual congeners yield important information about the source of the compounds and also the selectivity of the human uptake and retention of these compounds which can be extremely important in toxicological studies. Unfortunately, much of the published information, especially in the U.S. and with earlier work when methods were less developed, addresses only 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (2,3,7,8-TCDD; commonly called "dioxin"). This emphasis on measurement of 2,3,7,8-TCDD has occurred because it is the most toxic member of the family.

This paper reviews the human levels of PCDDs and PCDFs and discusses some of the implications of the current knowledge. Although levels of PCDDs and PCDFs had been reported in milk and a number of internal organs, e.g., the liver and pancreas, this paper focuses on levels in blood and adipose tissue, for which substantially more data are available.

Adipose Concentrations

Figure 1 presents the concentrations of 2,3,7,8-TCDD in adipose tissue from exposed and nonexposed individuals from several studies as summarized by Patterson.[8] It can be seen from Fig. 1 that there are generally, but not exclusively, higher levels of 2,3,7,8-TCDD in exposed individuals relative to nonexposed individuals, both in the controlled studies and across studies. For nonexposed individuals normal background levels appear to be around 10 ppt. (parts per trillion).

The ranges of reported levels of several key 2,3,7,8-substituted PCDDs and PCDFs in congeners in nonexposed individuals are presented in Fig. 2.[8] These ranges illustrate a general upward trend in concentration with number of chlorines for the PCDDs; i.e., OCDD levels are typically about two orders of magnitude higher than 2,3,7,8-TCDD levels. The trend is not as pronounced with the PCDFs, especially considering that the upper end of the OCDF range is based on five very high values from an early study by Stanley.[9] These values have not been reproduced and may have been reported in error.[10]

PCDDs and PCDFs were shown to be absent (detection limits of 0.3-5 ppt) from muscle tissue taken from nine 2800-year old Chilean mummies.[11] In life, the mummies were heavily exposed to wood smoke. These data indicate that PCDDs and PCDFs are products of the modern chlorinated organic production/use/disposal cycle, not generic combustion ("trace chemistries of fire").

Blood Concentrations

Figure 3 presents concentrations of 2,3,7,8-TCDD in blood from exposed and non-exposed individuals from five studies, as summarized by Patterson.[8] For nonexposed individuals, based on the limited data available, normal background levels appear to be around 5 ppt.

Figure 4 gives preliminary data from some blood samples collected within months of the 1976 explosion of a chemical plant producing 2,4,5-trichlorophenol dispersed 2,3,7,8-TCDD in Seveso, Italy.[5] These samples, only recently made available for analysis, illustrate the difference between exposed and nonexposed populations on a limited basis. The observed overlap of 2,3,7,8-TCDD concentration between individuals with and without chloracne is not explained. Further work on samples from this incident is in progress.[12]

Correlation of Adipose Blood Concentration

Comparisons by Patterson[13] and Kahn[14] have shown fairly good correlation of PCDD and PCDF concentrations in blood and adipose tissue. In both studies, the blood concentration was expressed on a lipid-weight, or blood-fat, basis rather than whole-blood basis. Because of the ease and acceptability of obtaining blood samples relative to adipose biopsy, it is desirable to statistically establish this relationship so that blood levels can be used as indicators of body burden.

Isomer Distribution

The 2,3,7,8-substituted congeners, notably those listed in Fig. 2, are preferentially retained by humans. Chromatograms published by Miyata et al.[15] from a Yusho victim's tissue, as compared to chromatograms of Yusho oil, are particularly illustrative of this retention. This phenomenon is especially important, since the 2,3,7,8-substitution pattern corresponds to the toxicity of the PCDDs and PCDFs. The significance of this retention with respect to the action of the dioxin receptor sites in the body is unknown.

Retention in the Body

The length of retention in the body is generally expressed in terms of half-life, the time required to reduce the concentration to half of that originally present. Half-lives for 2,3,7,8-TCDD of 7.1 years

(ranch hands) and 5.8 years (self ingestion of radio-labeled compound by H. Poiger) have been reported and reviewed.[3]

The half-lives of other PCDDs and PCDFs are not known. It may be conjectured that the non-2,3,7,8-substituted congeners would have relatively short half-lives. Among the 2,3,7,8-substituted congeners, it is reasonable to speculate that, based on solubility properties, higher homologs would have longer half-lives than those with fewer chlorines.

SUMMARY

PCDDs and PCDFs appear to be widespread and possibly ubiquitous, environmental pollutants that are found at the part per trillion level in all modern humans studied. 2,3,7,8-TCDD appears to have a normal background concentration of about 10 ppt in adipose and about 5 ppt in blood lipids. Other 2,3,7,8-substituted PCDDs and PCDFs are also generally present in humans, many at much higher concentrations than the 2,3,7,8-TCDD. In exposed individuals, 2,3,7,8-TCDD concentrations are above background level, occasionally into the thousands of parts per trillion.

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DISCLAIMER

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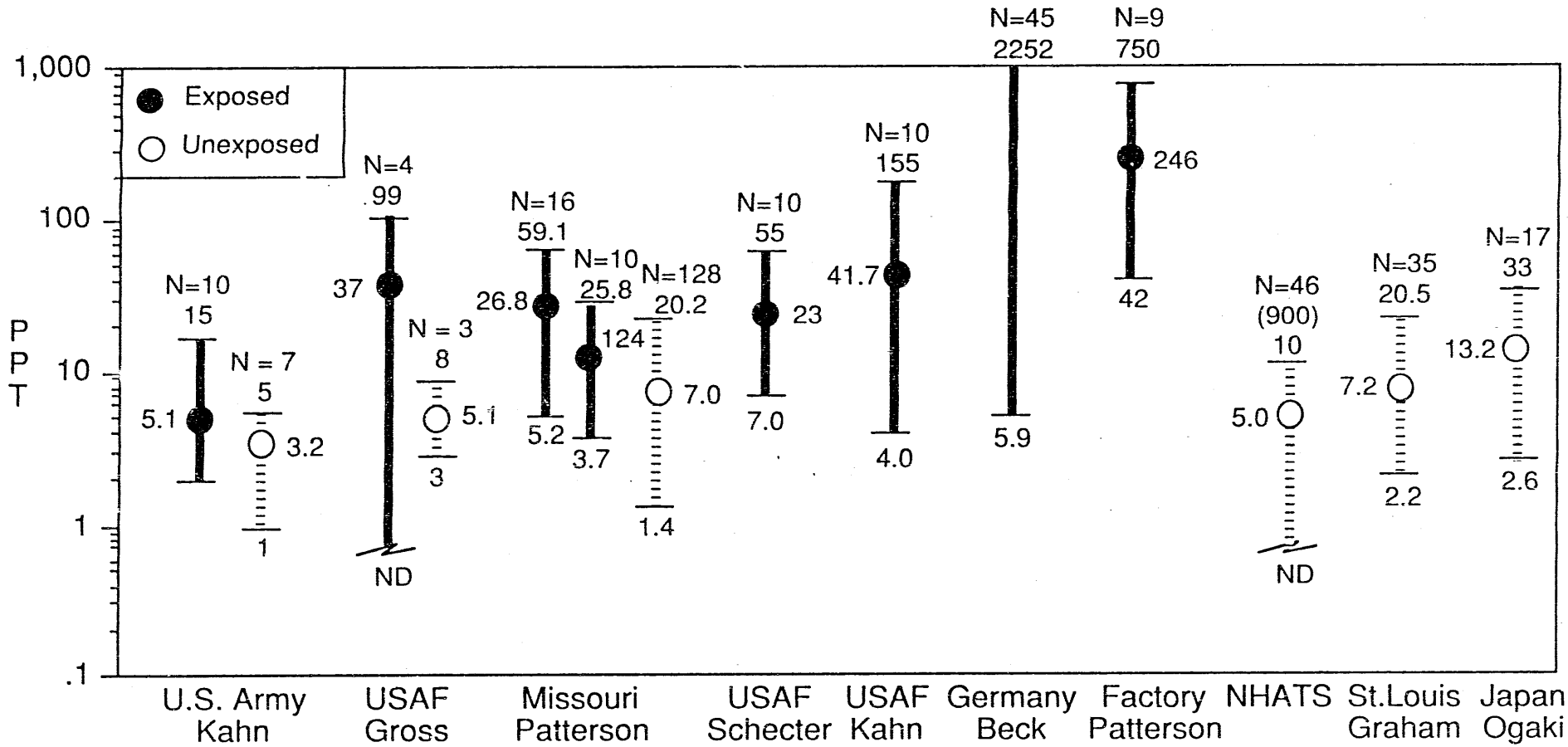
FIGURE CAPTIONS

Fig. 1: 2,3,7,8 - TCDD Adipose Levels in Exposed and Nonexposed Individuals. For each study, a one-word population description and the lead author are given; see Ref. 8 for full references. The number of individual specimens (N=x) is given above the bar representing the range. The mean is given between the upper and lower range values. ND = "not detected". For the NHATS study, data from the analysis of composite specimens representing 900 individuals were reported. Source: Ref. 8.

Fig. 2: Ranges for Non-TCDD Congeners in Nonexposed Adipose Tissue. Highest and lowest reported values from 10 studies are presented. ND = "not detected". Source: Ref. 8.

Fig. 3: 2,3,7,8 - TCDD Serum Levels in Exposed and Nonexposed individuals. See Fig. 1 for explanation. Source: Ref. 8.

Fig. 4: Serum TCDD Levels in Individuals from Seveso, Italy. Zone S = control individuals. Zone A = individuals in area of highest exposure. Source: Ref. 5. Reproduced with permission of U.S. Department of Health and Human Services/Public Health Service.



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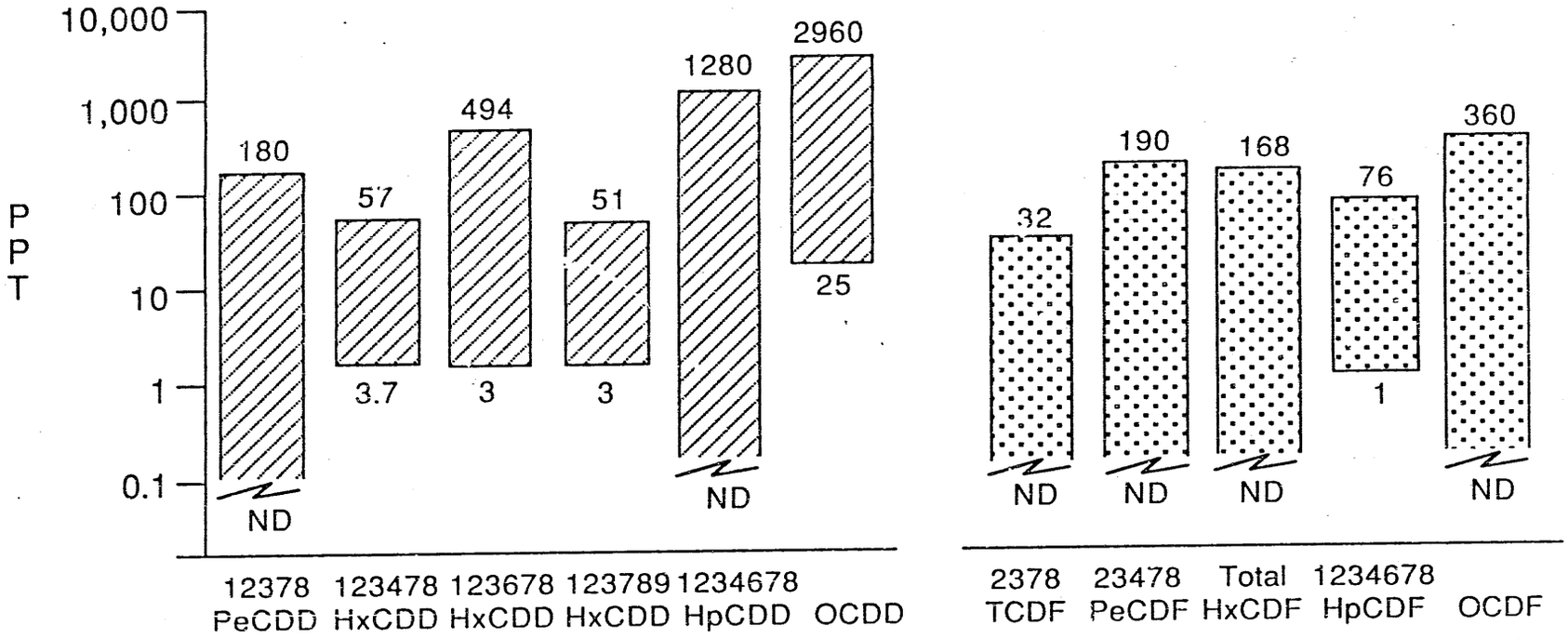

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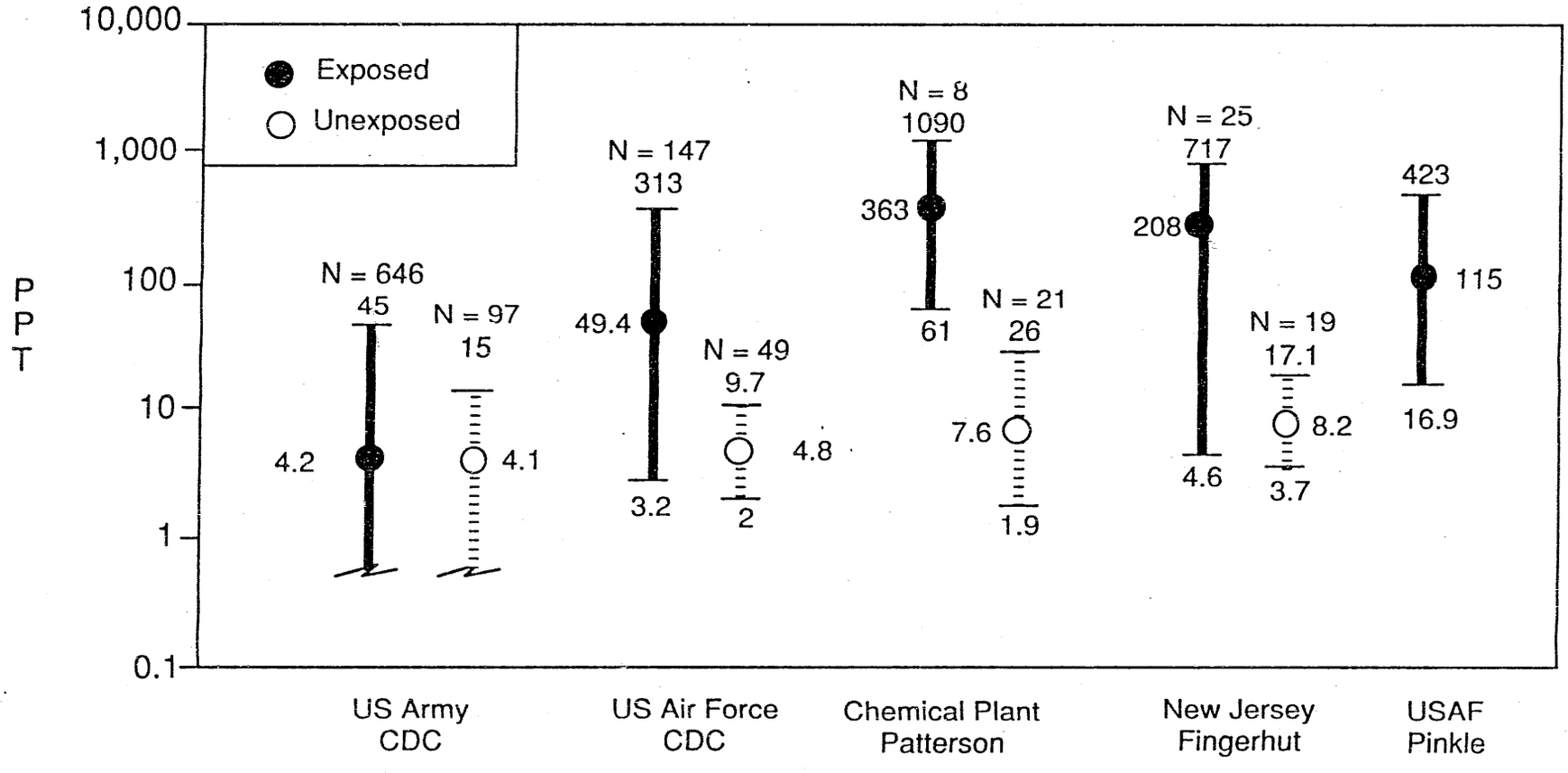

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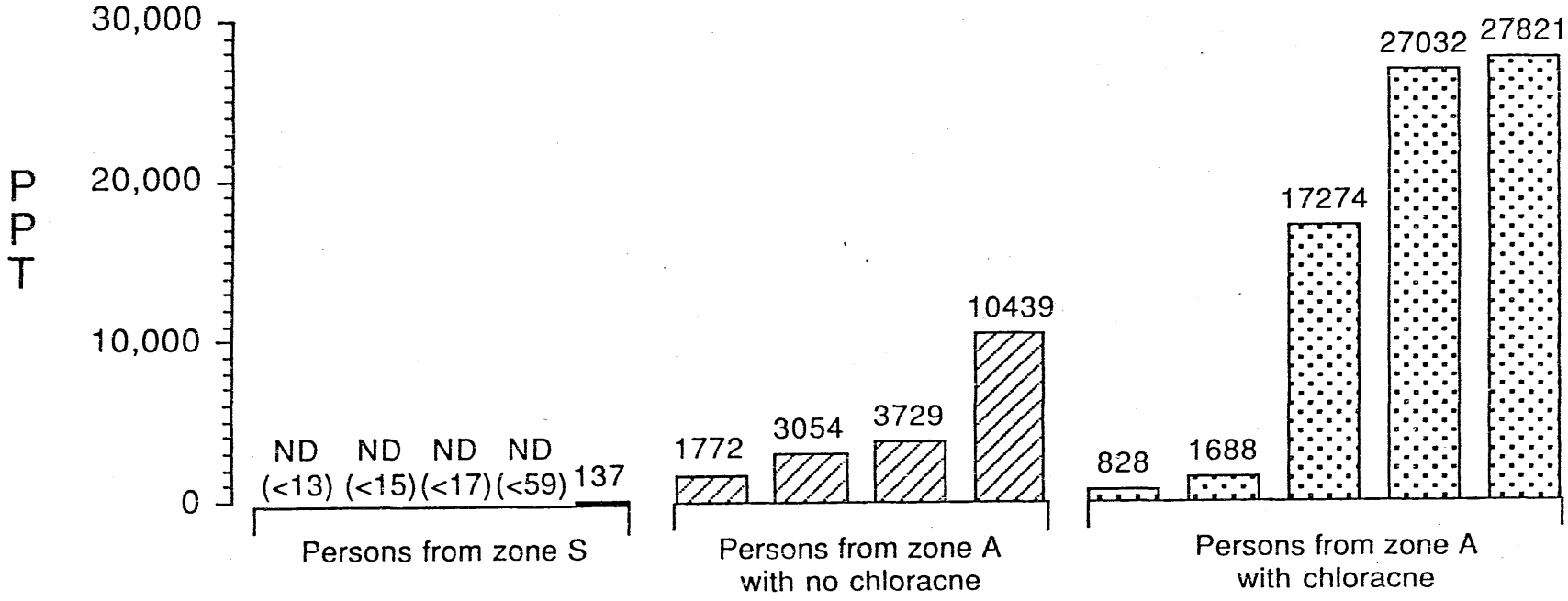

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