

## **Chloracne, goiter, and anemia 13 years after PCB/PCDF poisoning: Follow-up of the Taiwan Yucheng cohort**

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### **1. Introduction**

Polychlorinated biphenyls (PCBs) and related compounds are among the most widespread environmental pollutants;<sup>1)</sup> they have been routinely detected in human tissue samples since the 1960s. In 1979, a mass poisoning occurred in central Taiwan from cooking oil contaminated by heat-degraded PCBs.<sup>2)</sup> Symptoms included chloracne, hyperpigmentation, and peripheral neuropathy, and the illness was referred to as "Yucheng" (oil disease). By 1983, a registry set up and maintained by the Taiwan Provincial Department of Health included 2061 subjects.<sup>3)</sup>

To evaluate morbidity in the surviving members of the cohort, we contacted them and interviewed them in 1992-1993, 13 to 14 years after the exposure had taken place. The Yucheng cohort is quite young; the median age in 1979 was about 20 years. For this investigation, we focused on those older than age 30 in 1992, in whom we expected there would be greater morbidity.

### **2. Subjects and Methods**

From 1979 to 1983, the Taiwan Provincial Department of Health registered 2061 cases based on signs and symptoms of the illness or a history of consumption of the contaminated oil.<sup>2)</sup> We acquired the registry from Department of Health in 1991. Taiwan has local household registration offices in every village, town, and city precinct, which keep records of deaths, changes of residence, and maintain forwarding addresses. Using the address listed in the Yucheng registry, we located each subject's record at their registration office, and traced them through December 31, 1991. We identified as controls the persons who lived nearby the Yucheng subjects in 1979 from the archives of the registration offices. Controls had to be of the same sex, within three years of age of the index registry member, and not themselves in the registry.

There were 2061 subjects included in the Yucheng registry. Of them, 70 were offspring of the exposed subjects who were born after June 30, 1978, during or after the incident, and thus had only or mostly transplacental exposure; we excluded them from the study. Of the remaining 1991 Yucheng subjects, 154 (7%) did not appear in the registration offices' records at the 1979 addresses given by the Yucheng registry, or had no address, and thus could not be traced further; therefore a total of 1837 Yucheng subjects were traced. We selected the 912 Yucheng subjects who were alive and were 30 years of age or older on Jan. 1, 1992 for morbidity study. We attempted to contact these Yucheng subjects and one control living near to the index address in 1979. Home interview were done by trained personnel who held at least a bachelor's degree. The following question was

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asked: "Have you ever been diagnosed as having the following disorder by a western-style medical doctor?" Disorders of the following systems were asked by our interviewers: eye, oral, ear, nose, and throat, lung, cardiovascular, musculoskeletal, gastrointestinal, genitourological, hematological, neurological, endocrine, and skin. Interviewers were unaware of the subjects' exposure status.

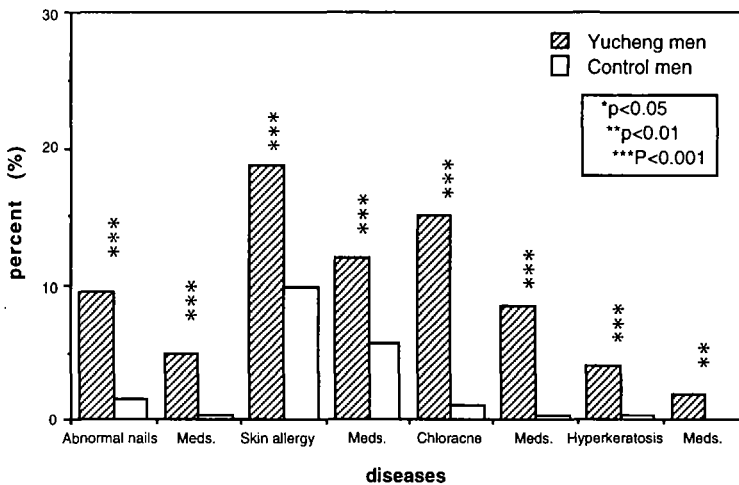
Although we selected matched controls, subjects receiving interview were not always in pairs, and so we broke the match and used chi-square techniques, analyzing the disorders by sex.

### 3. Results

Eight hundred and eight of the Yucheng subjects and 739 of the controls responded to the interview. The participating Yucheng men averaged 49.8 year of age; and control men 50.4 ( $p=0.54$ ). Yucheng women averaged 46.7 year of age; and control women 47.1 ( $p=0.67$ ). The original findings from 1979 persist in many of the patients; 17% have chloracne, compared to 2% of the controls. Similarly, abnormal nails and hyperkeratosis were all much higher in the exposed. Skin allergy, not noted to be part of the syndrome originally, became the most frequent reported disease among the exposed (Figures 1 and 2). Liver disease was not reported more frequently in Yucheng subjects, as was the absence of elevated reports of cancer.

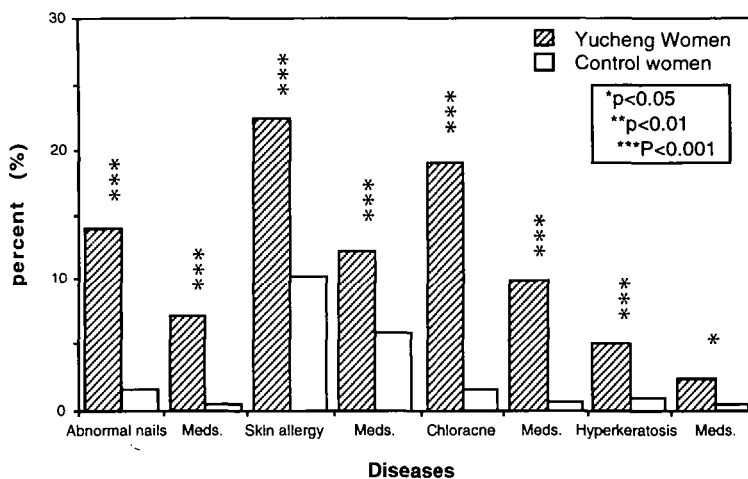
Both Yucheng men and women reported higher rates of goiter and headache (Figures 3 and 4), but neither group reported the diagnoses of hyper- or hypothyroidism more frequently. The exposed women reported having anemia and requiring medication for anemia 2.5 times more frequently. The exposed men reported arthritis 4 times more frequently than the controls, and required medication 3 times more frequently (Figure 5). They also reported herniated disk 2.5 times more frequently, and required medication 5 times more frequently.

**Figure 1. Percent (%) of reported diseases in Yucheng men (N=344) and their controls (N=327)**



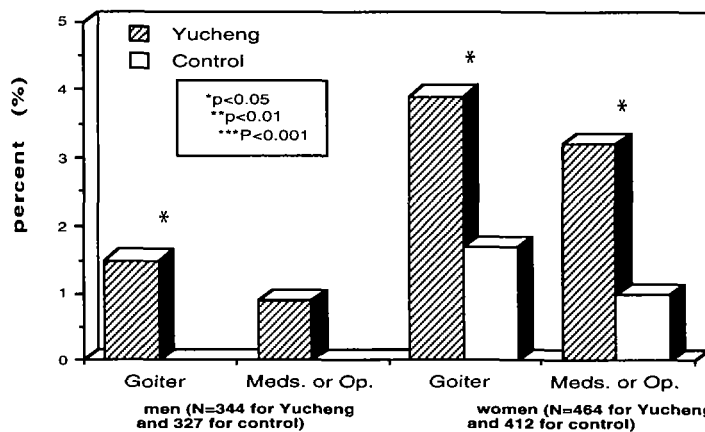
\*Meds: reported % of taking medication for the medical conditions on the left.

**Figure 2. Percent (%) of reported diseases in Yucheng women (N=464) and their controls (N=412)**



\*Meds: reported % of taking medication for the medical conditions on the left.

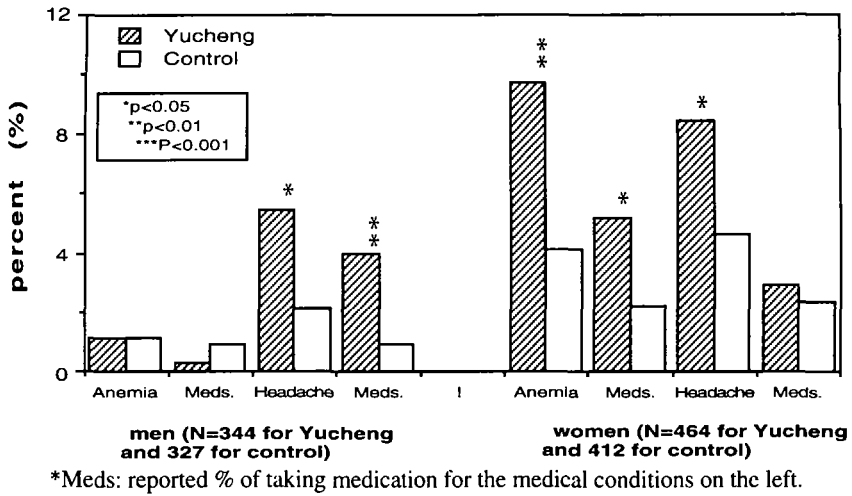
**Figure 3. Percent (%) of reported diseases in Yucheng subjects and their controls**



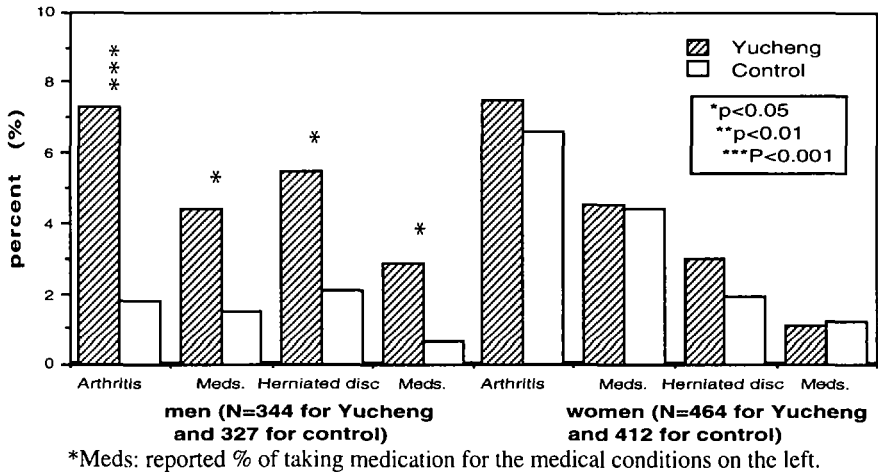
\*Meds or Ops: reported % of taking medication or operation for the medical conditions on the left.

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**Figure 4. Percent (%) of reported diseases in Yucheng subjects and their controls**



**Figure 5. Percent (%) of reported diseases in Yucheng subjects and their controls**



## 4. Discussion

This study provides information on the current clinical status of the Yucheng cohort members. Further clinical evaluation of those conditions found in excess will be necessary, but it is clear that many of these individuals are still affected 13 years after the exposure. Chloracne is known to be

an extremely chronic condition when it results from internal rather than dermal exposure. Cases of Yusho, which was a similar poisoning in Japan 11 years earlier, had acneform rash and pigment abnormalities years later. PCBs do affect the thyroid, causing vacuolization of the gland after prenatal exposure and perhaps by occupying receptor. The fact that the patients reported euthyroid goiter implies that PCBs/PCDFs interference with gland structure or perhaps iodine metabolism rather than with receptor function. Since some PCBs are weak estrogens, the anemia limited to women plausibly implicates some relation to menstrual blood loss. We need data on the young women to evaluate this finding further, and have begun locating and interviewing them.

There is not yet excess cancer mortality or incidence in this cohort, as there was in Yusho as early as 9 years after exposure and which continues. This difference may be because the Yucheng cohort was so young at exposure. There do not appear to be higher rates of infection, which was seen in the transplacentally exposed children, despite the well known immunosuppressive potential of these chemicals. There also does not appear to be continuing symptomatic conjunctivitis, which was quite severe soon after the outbreak, nor peripheral neuropathy, which was also seen earlier.

This study was limited in scope. It depends on the accuracy of recall and the veracity, conscious or not, of those interviewed. There does not appear to be a tendency of the exposed persons to report global increases in illness, however. Medical record verification is very difficult logistically at this point in follow-up, since the cohort is now spread throughout Taiwan and gets care from many different physicians. Control selection was difficult, and we know that there was some selection against those who died. Although we would have required live controls anyway, there may be other biases in the household registration office records that do not affect their use for administrative purposes but cause problems in research. We are not aware of such problems, and believe that these controls, who would have lived nearby the exposed at the time of exposure, are the best that can be found at this point.

This episode, while a public health disaster, has also been an opportunity to examine the long term consequences of exposure to high doses of these very widely dispersed chemicals to the community at large. Most other information comes from mortality studies of PCB workers, but they are adults when exposed, commonly mostly male, and exposed to uncontaminated PCBs. This study provides a preliminary picture of the Yucheng cohort, who had high exposures to PCBs/PCDFs in 1979, and continued internal exposure, since these compounds are so poorly excreted.

## 5. Acknowledgment

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## 6. References

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