## 1. Overview Across Studies: Summary of Results on Reported Water Use and Pregnancy Outcomes

### BACKGROUND

On N vember 17, 1981, a leak of toxic chemicals was discovered near an underground waste solvent storage tank at the Fairchild Camera and Instrument Company in San Jose, California. This tank was located about 2,000 feet from a well (Well #13) which supplied drinking water to nearby industrial and residential areas. On Dec mber 7, this well was removed from service. At that time 1,1,1-trichloroethane (TCA) was found in this well at 1,700 ppb. Following notification of the contamination, the affected community expressed concern about the possible health effects of this exposure. Adverse reproductive outcomes were of particular c ncern.

T address this problem, the Epidemiological Studies and Surveillance Section f the California Department of Health Services (CDHS), in collaboration with the Santa Clara County Health Department, conducted two epidemiological studies to look at the possible relationship between adverse pregnancy outcomes and the water contamination. One of these was an interview study of all pregnancy outcomes in two census tracts; the other was a county-wide hospital-based study of major cardiac def cts. These studies, which have been referred to as the "Fairchild studies", were completed and results released to the public in January 1985 (1). Associations were found between residence in areas thought likely to have been served by contaminated water and increased rates of spontaneous abortions and birth defects. Congenital cardiac defects, which were studied among 1981-1982 births, were associated with residence at birth in the area that probably received the contaminated water in one of the two study years (1981). CDHS could not identify any sources of confounding or bias which could account for these findings. However, the relationship between the water contamination and these adverse outcomes remained uncertain because of the distribution of cases in time and space.

Several follow-up studies were undertaken in order to pursue these results and much of the data contained in this report is derived from them. However, this report is not directed to an analysis of the "Fairchild problem". That issue is addressed in a separate report being released concurrently (2). This report is conc rned with another issue which arose during analysis f the original Fairchild studies: the question f water exp sure and its p ssible relationship t adverse pregnancy outcom s, independent of the Fairchild contamination episode.

In the original community-based interview study (Fairchild I), we noted that women who abstained from drinking tap water had no spontaneous abortions, and that the rate of spontaneous abortion increased with the number of cups of cold tap water consum d by women during their pregnancy. This association was seen in the exposed area and, to a lesser extent, in the control area. Therefore, this effect could not be attributed solely to the Fairchild contamination. A similar association was seen for birth defects, although numbers were very small. We have examined the relationship between water exposure variables and pregnancy outcomes in a number of data sets. In addition, further testing of well and tap water have been conducted to l k for possible chemical or bacteriological agents. This report summarizes these investigations.

## METHODS

### Study Designs

The possible relationship between reported tap water use and adverse pregnancy outc mes was examined in several studies. Table 1.1 includes a brief summary f the designs of the studies which will be discussed in this report. A map showing th study areas is included (Figure 1.1).

In addition to data sets collected in response to the Fairchild incident, a study of pregnancy outcomes, conducted to examine the possible reproductive effects f aerial malathion spraying, was analyzed with respect to water exposure. The results pertaining to malathion will be presented separately; the water analysis of this data s t is referred to in this report as the Malathion study (although the water analysis is unrelated to malathion exposure). This is a case-control study imbedded in an HMO-based cohort. It is the only one of the studies presented here which contains data on women who lived outside Santa Clara County. Study subjects receiv d prenatal care at one of three Kaiser facilities (Santa Clara, Redwood City or Hayward) and resided in Santa Clara, San Mateo or Alameda counties.

The recently c mpleted Fairchild follow-up study (Fairchild II) was analyzed with resp ct to water exposure. This study examined pregnancies in the census tract considered exposed in Fairchild I, as well as a second census tract thought equally likely to have been exposed to the Fairchild leak. A matched control area was selected for each "exposed" tract. While Fairchild I included pregnancies occurring in 1980-81, before the contaminated well was shut down in December 1981, Fairchild II also included pregnancies after that time (1982-85).

After the interviewing phase for Fairchild II was under way, we learned of a recent unpublished report suggesting that lengthy showering and bathing might deliver as much xposure to volatile contaminants as water consumption. Since it was too late to ask questions on showering and bathing of all subjects in Fairchild II, we r int rviewed a sample of cases (spontaneous abortion and birth defects) and contr ls (normal live births) about their patterns of showering and bathing. This case-control study is called Fairchild IIA. We also pursued the showering question in th county-wide case-control studies described below.

To btain showering and bathing data on additional cases, and to obtain detailed inf rmation on the use of water filters (e.g., type, location) as well as on additional potential confounders, the remaining Fairchild cases and a sample of normal controls were reinterviewed. In this report, data from this second substudy (Fairchild IIB) are combined with those from Fairchild IIA when looking at show ring and bathing, and data from Fairchild II are used when looking at water consumption and other variables common to all three data sets.

One f the two original Fairchild studies had looked at the prevalence of major cardiac anomalies in the area served by the water company which operated Well #13 compared to the prevalence in the remainder of the county. All data for this study w re abstracted from hospital medical records. No analysis by tap water consumption could be carried out since no interviews had been conducted. In a follow-up study, referred to as the Cardiac study in this report, detailed water us information was obtained via interview for cases of major cardiac anomalies born in 1981-83 and matched controls selected from birth certificates. Since this study was county-wide, data for ground, surface, and mixed water users could be xamined separately.

A county-wide study of spontaneous abortions ascertain d through hospital pathology lab ratories is currently being completed. These cases, along with matched controls selected from birth certificates, are being interviewed after the birth of the contr l. In this study, designed primarily to look at solvent exposure and spontaneous abortion, detailed information on water consumption, showering and bathing has been obtained. In this report we include results from the first 817 completed interviews, representing approximately 50% of the total study population and a completion rate of at least 80% in each of the first four "waves" of interviewing. This study is referred to as the Spontaneous Abortion Case-Control Study, or SACCS.

## Conventions and Definitions

Th re are certain conventions and methods which are used throughout the report. Thes are summarized in this section. General guidelines and definitions are given here and any deviations from these are noted in the discussion of the separate studies. To insure consistency of presentation, a standard set of abbreviations and notations are used throughout the report. These are summarized in Appendix A. Since a large number of variables were considered in multivariate analyses, we attempted to define these uniformly across studies. These variables, the definition of categorical variables and the choice of the base line category for dummy variables are contained in Appendix B.

### Study pregnancy

Except for the Malathion study, which included a few women with more than one study pregnancy, only one pregnancy per woman is included in these analyses. This was accomplished in the Fairchild studies by selecting one pregnancy at random for each subject. The use of one randomly selected pregnancy per woman is necessary to avoid the bias introduced by including multiple pregnancies. This bias arises because women who have had a spontaneous abortion are more likely to try to become pregnant again and carry a greater risk of spontaneous abortion in subsequent pregnancies. Choosing a random pregnancy avoids this bias. (The associations between reported tap water use or bottled water use and spontaneous abortion were similar when using all pregnancies or a random sample of pregnancies). For Fairchild IIA and IIB, a stratified sample was



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drawn from all Fairchild II resp ndents; subsequently the w men selected were interviewed about only one pregnancy.

## Outcome variables

Spontaneous abortions (SABs) and birth defects were the principal outcomes analyzed in these studies. Low birth weight was also analyzed in relation to water exposure in Fairchild II and Malathion. A spontaneous abortion was defined as an involuntary termination of pregnancy before 20 weeks gestation, calculated from the last menstrual period. The exception is the Malathion study in which an involuntary fetal loss of up to 28 weeks was categorized as an SAB unless a fetal death certificate had been filed. All spontaneous abortions included in these analyses were validated by medical record review, physician interview or pathology report. All birth defects were validated by physician confirmation or medical records. Therapeutic abortions, ectopic and molar pregnancies were excluded from all analyses. Stillbirths were excluded from all but the Malathion study. Birth weights were obtained from birth certificates; low birth weight was defined as birth weight under 2500 grams.

## Rates of spontaneous abortion and birth defects

The rate of spontaneous abortion is the ratio of all spontaneous abortions t all pregnancies. In these studies the numerator has been approximated by the number of recognized spontaneous abortions since the number of unrecognized spontaneous abortions is unknown. This approximation results in an underestimate of the true SAB rate. The denominator has been approximated by the sum of live births (including reportable anomalies) and spontaneous abortions. The exclusion from the denominator of ectopic and molar pregnancies and stillbirths as well as some fraction the number of therapeutic abortions, results in an overestimate of the true spontaneous abortion rate. It is necessary to use these approximations since data were n t collected on therapeutic abortions, subclinical loss or other forms of pregnancy loss. In what follows, "rate of SAB" refers to the ratio of recognized SABs to SABs plus live births. The prevalence of a birth defect refers to the ratio of number of live births with the defect to the total number of live births, so defects in stillbirths are not included, which may underestimate the prevalence of particular anomalies.

For the case-control studies, rates wer estimat d using Bayes' Theorem (3) and confidence intervals for these estimated using the normal approximation to the binomial distribution.

Wording of contact letters

Potential respondents were contacted by letter whenever possible. In all studies but the Malathion study these contacts were followed by a phone interview. In the Malathion study respondents were sent a mailed questionnaire followed up by phone interviews when necessary. The wording of these initial contact letters differed from one study to another. They are contained in Appendix C. Fairchild I and II were the only studies in which water was mentioned as the exposure of concern in the c ntact letter.

Exposures under study

Tap water consumption was an exposure under study in all of these analyses. There are a number of dimensions by which tap water consumption was categorized. These include: place of consumption (home, work, elsewhere), temperature (cold, hot), water type (ground, surface, mixed) and use of filters in the home (none, softener, filter). Unless otherwise stated, "tap water" refers to cold tap water (or drinks made from cold tap water) consumed at home. Where tap water consumption was quantified (glasses/day), it represents the usual consumption during the first trimester except in Fairchild I, in which consumption was reported throughout pregnancy. A comparison of the water consumption questions is contained in Table 1.2. The wording of these questions, as contained in each study questionnaire, is contained in Appendix D.

Data were also available on bottled water consumption. No distinction was made betw en hot and cold bottled water use. Brand of bottled water was obtained in Fairchild I and IIB. Bottled water use was quantified in glasses per day and represents consumption during the first trimester. In all studies but Cardiac, women were asked about bottled water use at home and at work. In the Cardiac study only home bottled water use was ascertained. Home and work use of bottled water were combined for purposes of analyses.

Th third factor under study was the exposure to water through inhalation and dermal contact. These exposures were not studied in Fairchild I and II or in th

Malathion study. F r Cardiac, SACCS and Fairchild IIA, only duration and frequ ncy of showering and bathing were available. Total minutes of showering and bathing was computed by adding frequency multiplied by duration of showering and bathing, except for SACCS in which only duration of showering was asked. (In SACCS the average duration of bathing was estimated from Fairchild IIA.) In Fairchild IIB data were also collected on other activities which may convey similar exposure (e.g. bathing others, washing dishes, use of jacuzzi and hot tub). Data on swimming pool use are available from Fairchild I.

## Analytic methods

### Univariate analyses

Crude rates, as defined above, were examined first for each outcome by each exposure variable. Crude relative risk estimates were calculated, together with 95% confidence intervals and significance probabilities. Significance probabilities were calculated using Fischer's exact test when required becaus of small numbers. Odds ratios were estimated using the method of Gart when cell sizes were small (4) except in the Malathion study which used the method f Jewell (5). For consistency, odds ratios were used to approximate the relative risk in both the cohort and case-control studies. In these estimates, the control group contained live births but excluded reportable anomalies. Confidence intervals for crude odds ratios were calculated using SAS, Version 5, which is based on the Taylor's Series method (6). Descriptive statistics were calculated for all demographic variables and for potential confounders and effect modifiers.

### Stratified analyses

Stratified analyses were carried out on the variables defined in Appendix B. In each case a test for homogeneity was performed and summary odds ratios (Mantel-Haenszel) were calculated when appropriate.

### Multivariate analyses

Before regression analyses were carried out, the shapes of the functional relationships between the study variables and the outcomes of interest wer examined. In particular, because of the nonlinear relationship between tap water consumption and SAB, a quadratic t rm was c nsider d. Similarly, becaus of nonline rity betw en age and SAB, maternal ag was trichotomized. Subsequently, multiple logistic regressions were carried out using SAS and BMDP (6,7). In addition, discriminant analyses were performed to identify factors which distinguish tap water drinkers from nondrinkers.

Survival analysis could only be conducted in the Malathion study, which was the only study with fairly precise entry times (i.e. when women sought prenatal care or had a positive pregnancy test). Cox regression was also attempted for Fairchild II, but because of the imprecise nature of the entry times, this analysis did not appear to provide better information than logistic regression and is not included here.

## Water Testing

In addition to the epidemiological studies discussed above, considerable testing f well and tap water was conducted. The details of the testing protocol and results are contained in Section 9. Since 1984, public water systems that use groundwater are required to monitor their sources for unregulated organic chemical contaminants. This monitoring is in addition to testing for specific organic and in rganic chemicals which has been required in California since 1977. Because f the concern that existing monitoring would not detect nonvolatile organic chemicals, radon and bacterial organisms, additional testing was conducted both at the source and the tap. Water samples were taken from the highest producing wells in the three water districts serving the four Fairchild study areas. These areas received unchlorinated ground water during the study period. Samples from some surface water sources were also tested, as was bottled water. Water samples were analyzed for Total Organic Carbon (TOC), Total Organic Halides (TOX), radon and bacteria, using a broad bacterial screen. Subsequently, tap water samples were collected at the homes of 48 subjects from Fairchild IIB. Homes were selected s that an equal number of spontaneous abortions and live births would be tested and an equal number of each would be sampled from the four census tracts.

## Reproductive Toxicology

In addition to conducting additional testing of source and tap water, the reproductive toxicology literature was reviewed for known or suspected reproductiv toxins which might be waterborne. This review is contained in Section 8. The epidemiological data and results of water testing have sugg sted the desirability f conducting a repr ductive toxicology study in rats. The pr toc l for this study is contained in Appendix A to Section 8. In this study, rats will drink water from several sources before and during pregnancy. Several reproductive endpoints will be examined, including resorptions and structural malformations.

## RESULTS

### Demographics

Demographics for all studies are compared in Table 1.3. Maternal age was c mparable in all studies. As expected, women with SABs were slightly older than m thers of live born infants. The mean educational level of women in the tw county-wide studies (Cardiac and SACCS) was lower than in the Fairchild and Malathion studies, reflecting the fact that the latter two study populations are drawn from distinct populations and are not representative of the county as a wh le. There was considerable variation in ethnicity across studies. The county-wide studies contained 20%-25% Hispanics compared to about 15% in the Malathi n study and 3%-10% in the Fairchild studies. An unexplained finding is the relatively low proportion of SABs in the non-White, non-Hispanic population in Fairchild II, but not in any other study. Wide variation in the percentage f bottled water drinkers was seen, largely due to a temporal increase in the use of bottled water during the 1980's. The relatively low rate of bottled water use se n in the Cardiac study also reflects the fact that only home use of bottled water was ascertained in that study while the others included use at work. Length of pregnancy among SABs was compared. Despite the varying methods of SAB ascertainment, the mean age at pregnancy termination was similar across studies. The highest mean age at pregnancy termination was seen in the Malathion study. This is consistent with the lower SAB rate in this study (8%) compared to Fairchild II (10%).

### Reported tap water consumption and spontaneous abortion

Odds ratios for spontaneous abortion by water consumption are summarized in Table 1.4 and rates (or their estimates) are contained in Table 1.6 and shown graphically in Figure 1.2. Similar results are seen when these odds ratios are adjusted f r confounding by multivariate analysis. Rates of SAB for nontap water drinkers are consistently lower than rates usually reported in the literature and range from 0.0% to 7.7%, while rates in tap water drinkers are n t unusually high (8.4% -

13.1%). However, overall r tes in all studies wer similar to those usually reported (Figure 1.3).

A positive, nonlinear relationship is seen between tap water consumption and spontaneous abortion in both Fairchild I and II (Figure 2.2 and 3.1). In particular, the rates of spontaneous abortion in women who drank no cold tap water at home were 0.0% and 3.3% in Fairchild I and II, respectively. Rates increase in women drinking 2-3 glasses/day, after which the curve exhibits a "plateau". Thes results were similar in the full data set and among random eligible pregnancies.

In the Malathion study, amount of tap water was not quantified, nor were cold and hot tap water consumption determined separately. Instead, women were asked t compare their tap water consumption to bottled water consumption, which was quantified. Women who drank more tap than bottled water had a crude SAB rate 1.7 times that for women who drank only bottled (or mostly bottled) water.

In SACCS the association between cold tap water consumption and SAB was similar to that seen in the Malathion study (OR=1.5). In addition a significant dose-response, with amount of cold tap water consumed, was seen.

A number of water-related variables were examined, including water source (i.e.,surface or ground), water company, geographic area, and use of water filters. All women in the Fairchild studies lived in areas served by ground water. In the Malathion study, most women received mixed water, although an appreciable fracti n (39%) drank surface water. Only 2.6% drank ground water unmixed with surface water. Study subjects in Malathion resided in three counties. In this study, the association between tap water and SAB was stronger in water sources which contained groundwater (ground or mixed) than in surface water only (1.9 vs. 1.4) (Table 1.8). However, the association between reported tap water consumption and spontaneous abortion was seen in all water sources. This is shown in Figure 1.4. In the Malathion study rates of SAB among tap water drinkers are similar across counti s; when controlling for water type there was no significant difference between residents of Santa Clara County and those living in other counties. Therefore, this phenomenon is not restricted to a single county or water source.

Limited information n water filter us was availabl from Fairchild II, and more detailed information from Fairchild IIB. In Fairchild II women were asked whether they used filters connected at the sink or tap (which are those most likely to be filters and not water softeners). For the 11% responding positively to this question, the SAB rate among tap water drinkers was similar to that for women who drank no tap water (4.0%). Results from Fairchild IIB, which asked about type, l cation and frequency of service of filters, are similar.

Data on hot water consumption are available only from Fairchild IIB. This study suggests that the associations between SAB and tap water are similar for h t and cold water; the OR for drinking any cold or hot water was 7.5 compared to 3.8 and 2.8 for cold and hot water respectively (Table 1.9).

Bottled water and spontaneous abortion

Tap water consumption and bottled water consumption are negatively correlated. Therefore, it is not surprising, given the positive association between tap water and SAB, that each of these studies finds a negative association between b ttled water consumption and SAB. As can be seen in Table 1.4, the relative risk estimat s f r bottled water use and SAB are fairly consistent across studies (0.3-0.7). No d se-response is seen in the Fairchild studies for the two categories of bottled water consumption (usually and not usually). However, in SACCS the OR decreased from 0.9 for 1-2 glasses of bottled water to 0.5 for 6+ glasses per day. In that study, bottled water use also modifies the tap water association; an elevated OR f r tap water is seen only for non-bottled water drinkers, in whom it is 2.0.

In Fairchild I we asked the brand of bottled water used most often and found that a single brand (Alhambra) was used predominantly both at home (43%) and at w rk (90%). Stratifying on brand did not identify any within-brand differences, although numbers for most brands were small.

Showering, bathing and spontaneous abortion

Questions on showering and bathing were included in the Fairchild reinterviews (Fairchild IIA and IIB) as well as in SACCS. In the Fairchild studies, longer showers were positively associated with SAB (OR= 2.8, 95% CI 1.5,5.3). However, in SACCS a reverse trend was seen. Thus, no clear pattern emerges for the relationship betw en SAB and show ring and bathing. Data n showering and bathing are summarized in Table 1.4. Exp sures thr ugh bathing others, washing dishes and using hot tubs were asked only in Fairchild IIB and did not appear to contribute any additional risk.

Tap water consumption and birth defects

In both Fairchild I and II the prevalence of reportable birth defects in women reporting no tap water consumption was unusually low (0.0% and 0.4% respectively). The prevalence of birth defects among tap water drinkers varied around a mean of 4.2%, with no dose-response relationship seen. The prevalence of reportable birth defects in tap water drinkers is somewhat higher than that seen by the California Birth Defects Monitoring Program in the five Bay Area counties (2.5%). In the Malathion study, an OR of 1.6 was seen for cold tap water consumption and birth defects (0.6, 4.0). In this study, prevalence of birth defects varied by facility, but controlling for facility did not alter the odds ratio appreciably. In the Cardiac study, a modest association with tap water was seen (OR=1.5, 95% CI 0.8, 2.9). Crude odds ratios and their confidence limits are contained in Table 1.5. Prevalence estimates are shown in Table 1.7 and Figure 1.5. It can be seen that the associations are similar across studies, although only one (Fairchild II) achieves statistical significance at the 5% level. Although the prevalence in tap water drinkers was somewhat elevated in the Fairchild studies, reportable defects overall were similar to expected (Figure 1.6).

Bottled water consumption and birth defects

Data on birth defects and bottled water use are fairly consistent across studies. In all studies, odds ratios of less than 1.0 were found for women who consum d any bottled water but all 95% confidence intervals included 1.0. Cardiac anomalies were about twice as prevalent in nondrinkers as in drinkers of bottled water. Estimated prevalence was 1.7 per 1,000 in drinkers and 3.3 per 1,000 in nondrinkers. However, numbers were small and the difference did not approach statistical significance (Figure 1.7).

Duration of showering and bathing in relation to birth defects

N significant associations were seen between duration of showering and bathing and birth defects in either Fairchild IIA and IIB. In the Cardiac study, the observed association throughout the county was in the opposite direction from that in the Fairchild data. H wever, in a separate report (2), this study f und a positive ass ciation with l ng sh wers and baths for r sidents of the area receiving water contaminated by the Fairchild spill compared to residents outside that area.

Low birth weight and water consumption

Low birth weight was analyzed in relation to water consumption in Fairchild II and Malathion. No relationship was seen between low birth weight and either t p or b ttled water consumption. Low birthweight analyses for Fairchild II are c ntained in Section 3. This analysis for the Malathion study is not included.

Water Testing

Results of well water testing in Section 9 indicate that levels of TOC, TOX and radon in the public water systems and bottled water were low. In the Fairchild study areas TOC from wells supplying water for public use ranged from 0.3-0.8 ppm. The highest TOC and TOX levels were in the EBMUD treated water which was sampled as a control. Radon levels were below the median for well waters that have been sampled in California. Each of the public water systems and bottled waters met the requirements for coliform bacteria. Other bacterial counts were elevated in s me bottled water but not well water. These low levels of TOC and TOX at the well are in contrast to elevated TOC levels found at the tap in all homes sampled in the four Fairchild study areas. TOC levels in the homes ranged from 1.6 ppm t 8.9 ppm and averaged 4.8 ppm (Figure 1.8). The levels were similar in the four census tracts comprising the Fairchild II study area and in homes of SABs and live births (4.7 ppm vs.4.8 ppm). Elevation in TOC from source to tap was not seen in chlorinated sources (Figure 1.9). The chemical or bacteriological agent(s) responsible for this increased TOC is not known. However, certain chemical contaminants, including TCA and DCE, have been ruled out. In addition, high lev ls of a non-specific bacterial screen (heterotrophic plate count) were seen in the first water drawn in the morning in many homes sampled in the Fairchild study areas. Bacterial counts for later samples were much lower (Figure 1.10). Attempts to identify the source(s) of these elevated levels are continuing.

Discussion

The data presented in this report are perplexing. The cohort studies docum nt an unusually low rate of spontaneous abortion among women who reported drinking no tap water (and/or drinking bottled water) while pregnant. The cas -c ntrol studies provide relative risk estimates consistent with thes findings. These studies also suggest a reduced prevalence of birth defects in tap water abstainers, although this does not reach statistical significance in most studies. These associations are seen independently for hot and cold water consumption in the single study that had data on hot water use. The negative associations with bottled water consumption are difficult to separate from the positive associations with tap water. The associations with tap water may be modified by the use of water filters. The role of dermal and inhalation exposures conveyed by showering and bathing is uncertain. These findings are fairly consistent across several large studies and carry significant public health implications. We now consider alternative explanations for these results.

We see the alternative explanations in three categories. First, the epidemiological results could be due to chance. Chance is an unlikely explanation f r these findings, given the number of studies in which we see these results and the sample sizes of these studies.

Second, these results may be due to bias or confounding. A number of potential sources of bias and confounding are discussed in detail in Section 10. We consider a wide range of scenarios, and conclude that biased recall of exposure is th most likely candidate among these possible explanations. This seems plausible because the number of unexposed cases who must be reclassified to explain the associations between tap water abstention and spontaneous abortion is small. Furthermore, the associations are strongest in the two studies in which women were alerted to the water hypothesis by the initial contact letter. Finally, these Fairchild studies were conducted in areas most likely to be concerned about their water due to the publicity surrounding the Fairchild contamination episode.

Finally, the reduced risks of adverse pregnancy outcomes observed in these studies may have been caused by decreased consumption of tap water or by consumption of bottled water. We have considered various potentially harmful agents which might be found in tap water and the possibility that bottled water may contain minerals or other constituents which could improve pregnancy outcome. In Section 9 we pr sent results of water testing to date. This section documents an increase in Total Organic Carbon (TOC) and bacterial counts somewhere in the water distribution system. While levels f TOC at the w ll (or other source) are l w (ab ut 0.5 ppm) and bacterial counts are n gligible, TOC l vels ar ab ut an order f magnitude higher in water taken at the tap (5-8 ppm) and high bacterial counts are als seen in tap water. These elevations are seen in homes of SAB cases and live births equally. They are also seen equally in the "exposed" and "control" areas of the Fairchild study. While the increases in TOC and bacterial counts between well and tap seen in unchlorinated ground water may be irrelevant to the epidemiological findings, it is conceivable that these two sets of findings are related.

In conclusion, we feel that these epidemiological and laboratory findings hav sufficient public health importance to warrant further study. While we have g ne t great lengths to identify sources of bias in the epidemiological studies and specific contaminants in the laboratory studies, it will not be possible t res lv these issues without further investigation. These studies will take several years t complete. Therefore, we are presenting these results now, although they must be c nsidered preliminary, and in the nature of a "progress report", because f the public's right to be informed about findings which may have a large public health impact.

## References


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Table 1.1

Comparison of Study Populations and Designs

| Name | Areas Studied | Years | Study Design | Number[a] |
|---|---|---|---|---|
| Fairchild I | 1 Great Oaks census tract<br>1 Control tract in SCC[e] | 1980-81 | Cross-sectional | 349 Pregnancies<br>(39 SAB[b], 16 BD[c]) |
| Fairchild II | 2 Great Oaks census tracts<br>2 Control tracts in SCC[e] | 1980-85 | Cross-sectional | 1016 Pregnancies<br>(100 SAB, 36 BD) |
| Fairchild IIA and IIB | Random sample of Fairchild II | 1980-85 | Case/control in cohort defined cross-sectionally | 123 SAB, 31 BD, 260 LB[d] |
| Malathion | Catchment areas for Kaisers: Santa Clara, Hayward, Redwood City | 1981-82 | Case/control in retrospective cohort | 474 SAB, 144 BD, 1249 LB |
| Cardiac | SCC[e] | 1981-83 | Case/control | 147 BD, 176 LB |
| SACCS | SCC[e] | 1986-87 | Case/control | 251 SAB, 566 LB |

[a] Number actually used in analysis after exclusions; except SACCS.
[b] Spontaneous abortion
[c] Birth defect
[d] Live birth
[e] Santa Clara County

Table 1.2
Water Consumption Information Requested in Six Studies

| Consumption Information Requested | 1. Fairchild I | 2. Fairchild II | 3. Fairchild IIB | 4. Cardiac | 5. Malathion | 6. SACCS |
|---|---|---|---|---|---|---|
| Cold tap water @ home | yes | yes | yes | yes | no | yes |
| Cold tap water @ work | yes | yes | yes | yes | no | yes |
| C ld tap water lsewhere | no | no | yes(3) | yes | no | no |
| Cold tap water (place unspecified) | no | no | no | no | yes(5) | no |
| C ld tap water quantified | yes | yes | yes | yes | (5) | y s |
| Hot tap water @ home | yes | no | yes | no | no | no |
| H t tap water @ work | yes | no | yes | no | no | no |
| Hot tap wat r elsewhere | no | no | yes(3) | no | no | no |
| Hot tap water (place unspecified) | no | no(2) | no | no | yes(5) | no |
| Hot tap wat r quantified | yes | no | yes | no | (5) | (6) |
| Bottled water @ home | yes | yes | yes | yes | yes | y s |
| Bottled wat r @ work | yes | yes | yes | no | yes | yes |
| Bottled water (place unspecified) | no | no | no | no | yes | no |
| Bottled wat r quantified | no(1) | no(2) | yes | no(4) | yes | y s |
| Tap water before pregnancy | no(1) | yes(2) | no | no | no | yes |
| Tap water first trimester | no | yes | yes | yes | yes | yes(6) |
| Tap water total pregnancy | yes(1) | yes(2) | no | no | no | no |
| Change in tap water during pregnancy | no | no | no | no | no | yes |
| Bottled wat r b fore pregnancy | no(1) | no(2) | no | no | no | no |
| Bottled water first trimester | no | no | yes | yes | yes | yes(6) |
| Bottled wat r t tal pregnancy | yes(1) | yes | no | no | no | no |
| Change in b ttled water during pregnancy | no | no | no | no | no | no |

1 Use in the three months before pregnancy and during the pregnancy not distinguished. Any use and usual us of bottled water distinguished. Tap water use not asked if women usually drank bottled water.

2 Use of tap and bottled in the three months before pregnancy and during the total pregnancy asked. Use in the first trimester asked separately for tap but not bottled water. Hot water use not asked but total liquid consumption quantifi d. Any use and usual use of bottled water distinguished.

Table 1.2 (Continued)

3 Tap water consumption elsewhere asked but use of hot and cold water not separated other than at home or w rk.

4 Bottl d water quantified as "sometimes" or "usually". Tap water use at home and work not distinguished. Hot water use not asked although use of caffeinated coffee and tea in first trimester was quantified.

5 Hot and cold water use not distinguished. Tap water use was qualitatively compared to bottled water use. Only bottled water use was questioned.

6 Hot water use not asked although use of caffeinated coffee and tea were quantified. Asked amount of tap water us d the month bef re pregnancy, change in use during pregnancy, week of change and amount after change. Water consumption asked for 20 weeks r length of pregnancy if SAB occurred earlier. Did not ask change in bottled water, only t tal c nsumed at work and home for same time period.

## Table 1.3

## Across-Study Comparison of Demographics

| Variable | Fairchild I SAB | Fairchild I LB[a] | Fairchild II SAB | Fairchild II LB[a] | Fairchild IIA & IIB SAB | Fairchild IIA & IIB LB[a] | Malathion SAB | Malathion LB[a] | Cardiac BD | Cardiac LB | SACCS SAB | SACCS LB |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Maternal age (mean) | 27.7 | 27.3 | 28.6 | 28.2 | 28.6 | 28.8 | 28.7 | 26.7 | 26.9 | 26.7 | 29.7 | 27.8 |
| % HS graduate or greater | 94.9 | 98.0 | 93.1 | 94.4 | 93.4 | 95.8 | 91.9 | 92.5 | 81.8 | 83.0 | 82.9 | 82.0 |
| % Hispanic | 2.6 | 5.1 | 10.7 | 10.0 | 8.9 | 8.1 | 15.0 | 15.5 | 22.3 | 25.0 | 20.7 | 25.5 |
| % Non-White, Non-Hispanic | 12.8 | 14.3 | 4.9 | 16.2 | 5.7 | 16.5 | 19.4 | 20.4 | 18.2 | 21.6 | 24.3 | 22.0 |
| % (Some r all) B ttled water drinkers (home r work) | 17.9 | 29.3 | 26.2 | 50.5 | 23.6 | 49.2 | 20.0 | 26.0 | 10.2[b] | 17.6[b] | 55.0 | 63.1 |
| Approximat weeks pregnant (mean) | 10.6[c] | --- | 11.1 | --- | 11.4 | --- | 12.8 | --- | --- | --- | 10.9 | --- |

[a]Excludes reportable birth defects

[b]At home only

[c]Mean months pregnant = 2.5

sum.tb2

Table 1.4

Across-Study Summary of Crude Odds Ratios for Spontaneous Abortion and Water Exposure

| | OR (Any vs. no tap) | 95% CI | OR (Any vs. no bottled) | 95% CI | OR (Long[b] vs. short showers) | 95% CI |
|---|---|---|---|---|---|---|
| Fairchild I | 14.4[a] | (0.9, 238.4) | 0.6 | (0.2, 1.3) | NA | --- |
| Fairchild II | 4.0 | (1.8, 9.1) | 0.3 | (0.2, 0.6) | 2.8[c] | (1.5, 5.3) |
| Malathion | 2.0 | (1.1, 3.7) | 0.7 | (0.5, 0.9) | NA | --- |
| SACCS | 1.5 | (1.1, 2.1) | 0.7 | (0.5, 1.0) | 0.8 | (0.5, 1.2) |

[a] Small sample estimate (Gart)

[b] More than 50 minutes per week

[c] Fairchild IIA and IIB

Table 1.5

Across-Study Summary of Crude Odds Ratios for Reportable Birth Defects and Water Exposure

| | OR (Any vs. no tap) | 95% CI | OR (Any vs. no bottled) | 95% CI | OR (Long[b] vs. short showers) | 95% CI |
|---|---|---|---|---|---|---|
| Fairchild I | 6.4[a] | (0.4, 108.7) | 0.3 | (0.1, 1.4) | NA | --- |
| Fairchild II | 22.0[a] | (1.3, 360.4) | 0.8 | (0.4, 1.5) | 1.6[c] | (0.6, 4.4) |
| Malathion | 1.6 | (0.6, 4.0) | 0.8 | (0.6, 1.3) | NA | --- |
| Cardiac | 1.5 | (0.8, 2.9) | 0.5 | (0.3, 1.0) | 0.8 | (0.4, 1.2) |

[a] Small sample estimate (Gart)

[b] More than 50 minutes per week

[c] Fairchild IIA and IIB

Table 1.6

Rates[a] of Spontaneous Abortion by Water Use

| Study | Any Cold Tap Water | No Cold Tap Water | Any Bottled Water | No Bottled Water |
|---|---|---|---|---|
| Fairchild I[b] | 13.1 | 0.0 | 7.5 | 12.4 |
| Fairchild II[b] | 11.6 | 3.3 | 5.5 | 14.6 |
| Malathion[c] | 8.4 | 4.1 | 6.6 | 8.7 |
| SACCS[d] | 11.1 | 7.7 | 8.8 | 11.9 |

[a]Cases per 100 pregnancies.

[b]One randomly selected pregnancy per woman.

[c]Rates estimated by Bayes' Theorem using overall SAB rate of 8%.

[d]Rates estimated by Bayes' Theorem using overall SAB rate of 10%.

Table 1.7

Prevalence of Reportable Birth Defects[a] by Water Use

| Study | Any Cold Tap Water | No Cold Tap Water | Any Bottled Water | No Bottled Water |
|---|---|---|---|---|
| Fairchild I | 6.2 | 0.0 | 2.3 | 6.4 |
| Fairchlid II | 3.9 | 0.4 | 2.7 | 3.5 |
| Malathion[b] | 2.6 | 1.6 | 2.3 | 2.6 |
| Cardiac[b, c] | 0.3 | 0.2 | 0.2 | 0.3 |

[a]Cases per 100 live births.

[b]Estimated using Bayes' Theorem.

[c]Major cardiac defects only.

Table 1.8

Odds Ratios for Spontaneous Abortion
by Water Type Among Tap Water Consumers

| Study | Water types | OR | 95% CI |
|---|---|---|---|
| SACCS | Surface vs. ground | 1.04 | (0.37, 2.9) |
| SACCS | Surface vs. mixed | 0.81 | (0.37, 1.8) |
| Malathion | Surface vs. ground or mixed | 0.81 | (0.66, 0.99) |

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Table 1.9

Odds Ratios for Spontaneous Abortions and
Birth Defects by Type of Home Tap Water Consumption
(Fairchild IIB)

| | Type of Tap Water | | |
|---|---|---|---|
| | Hot or Cold | Hot | Cold |
| Spontaneous Abortions | 7.5 (2.2, 25.4) | 2.8 (1.5, 5.3) | 3.8 (1.7, 8.3) |
| Birth Defects | 3.2 (0.7, 14.5) | 1.9 (0.7, 4.8) | 2.5 (0.8, 7.7) |

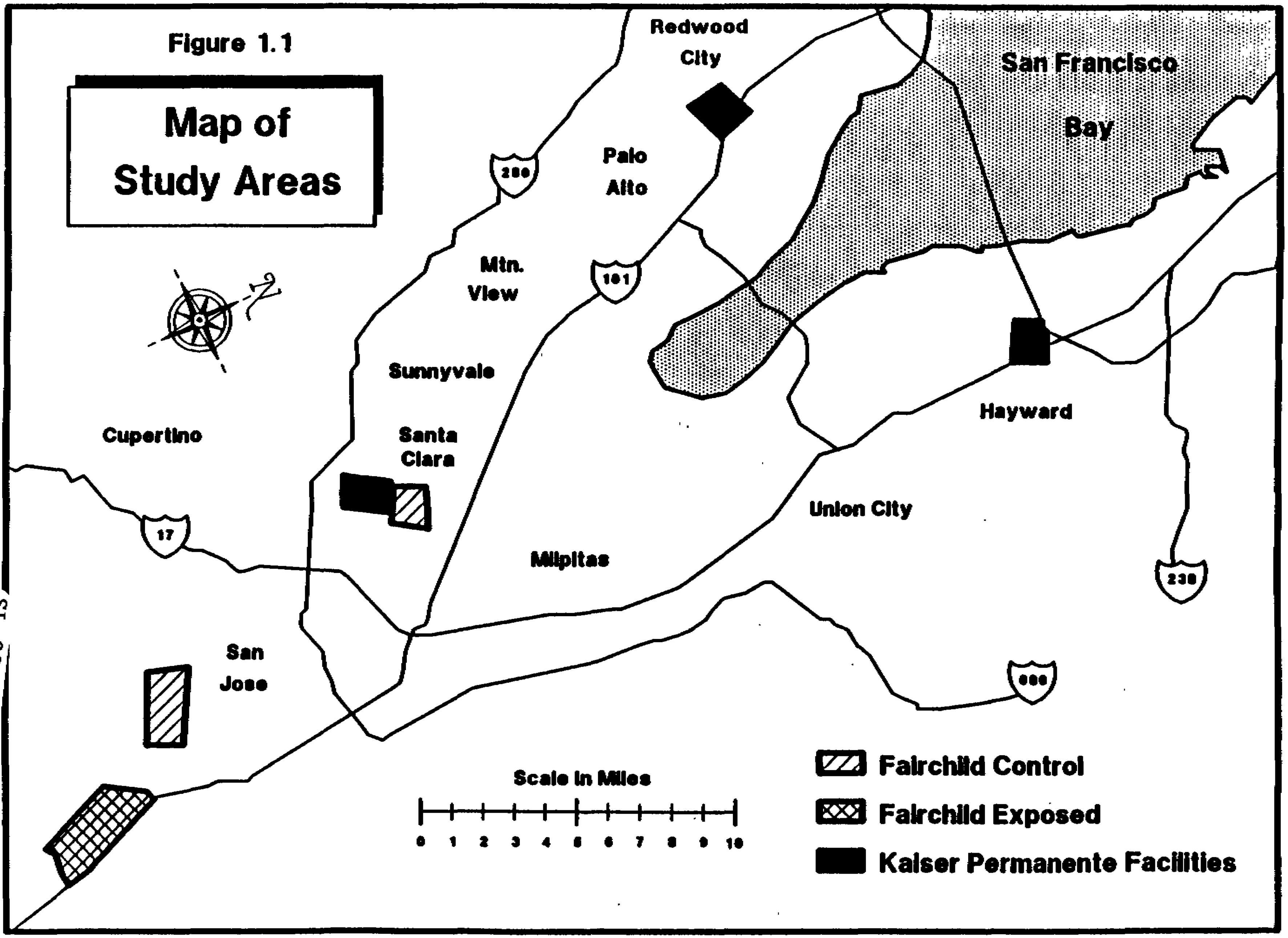
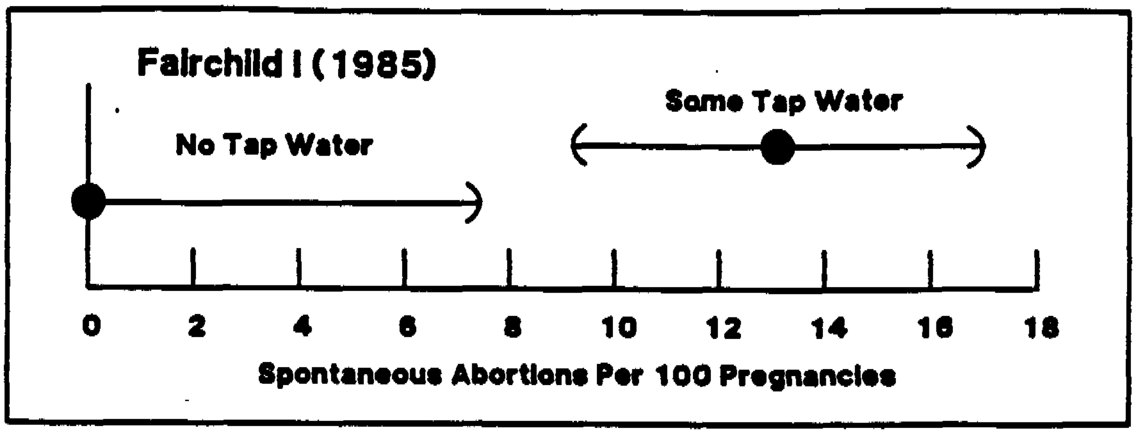
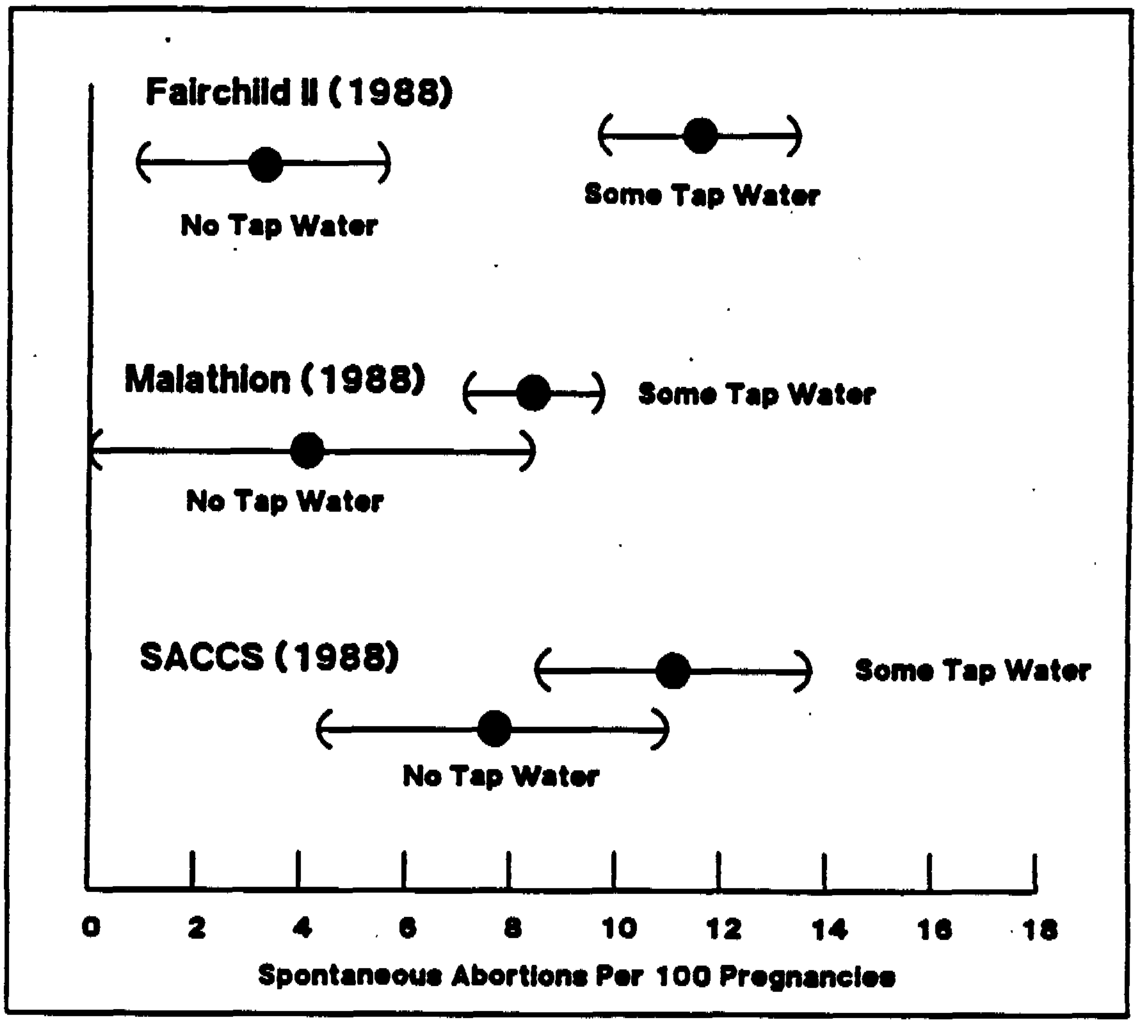


Figure 1.1
Map of Study Areas
Redwood City
San Francisco Bay
Palo Alto
280
Mtn. View
101
Sunnyvale
Cupertino
Santa Clara
Hayward
Union City
17
Milpitas
238
San Jose
880
Scale in Miles
0 1 2 3 4 5 6 7 8 9 10
Fairchild Control
Fairchild Exposed
Kaiser Permanente Facilities

**Figure 1.2 Spontaneous Aborti n Rat s and 95% Confidence Intervals By Reported Tap Water Use in Four Studies**




= Spontaneous Abortion Rat ( ) = 95% C nfid nc int rval

**Figure 1.3 Overall Rates of Spontaneous Abortion and 95% Confidence Intervals vs. Expected**

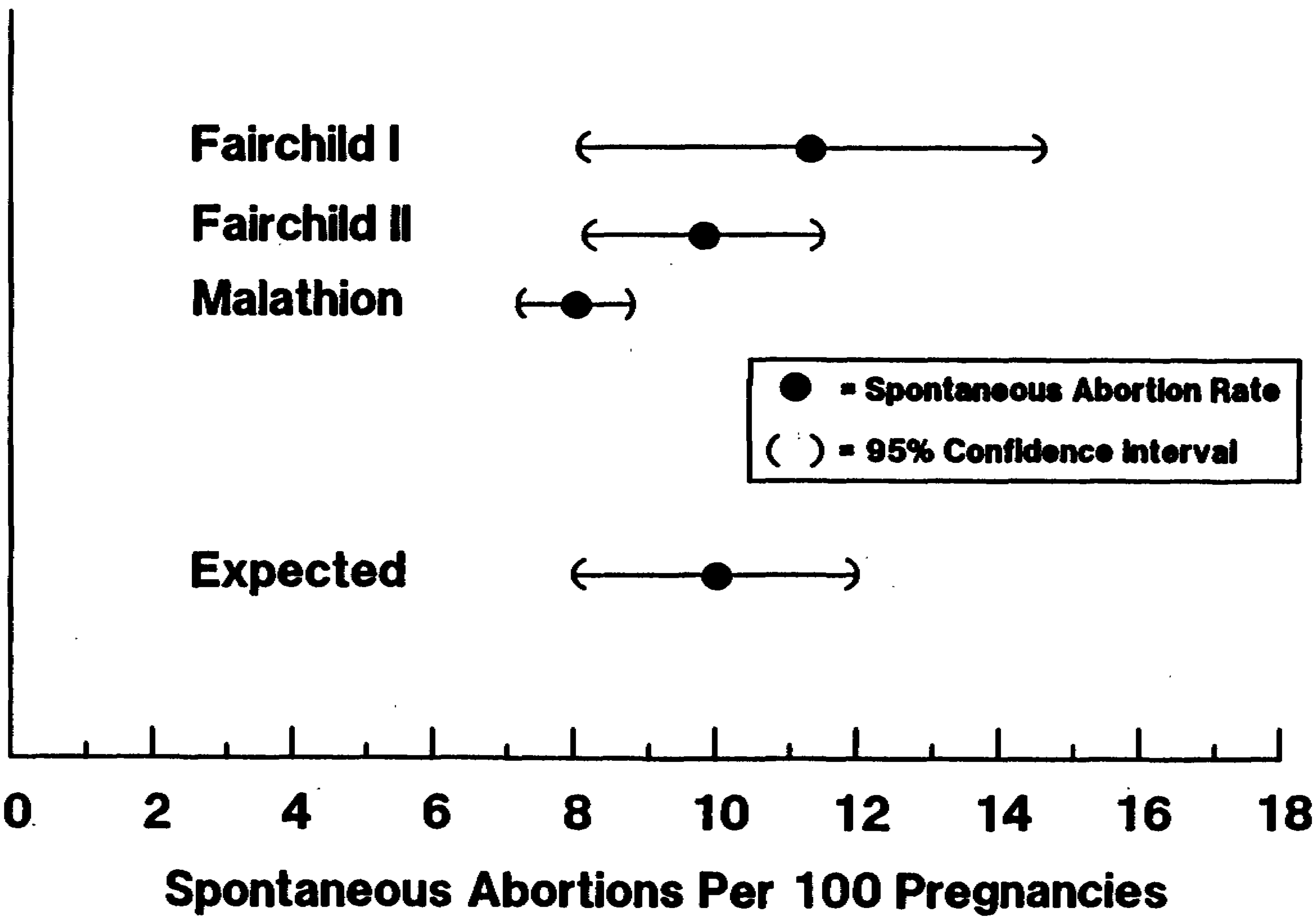


**Figure 1.4 Odds Ratios and 95% Confidence Intervals For Spontaneous Abortion and Tap Water Use By Water Type**

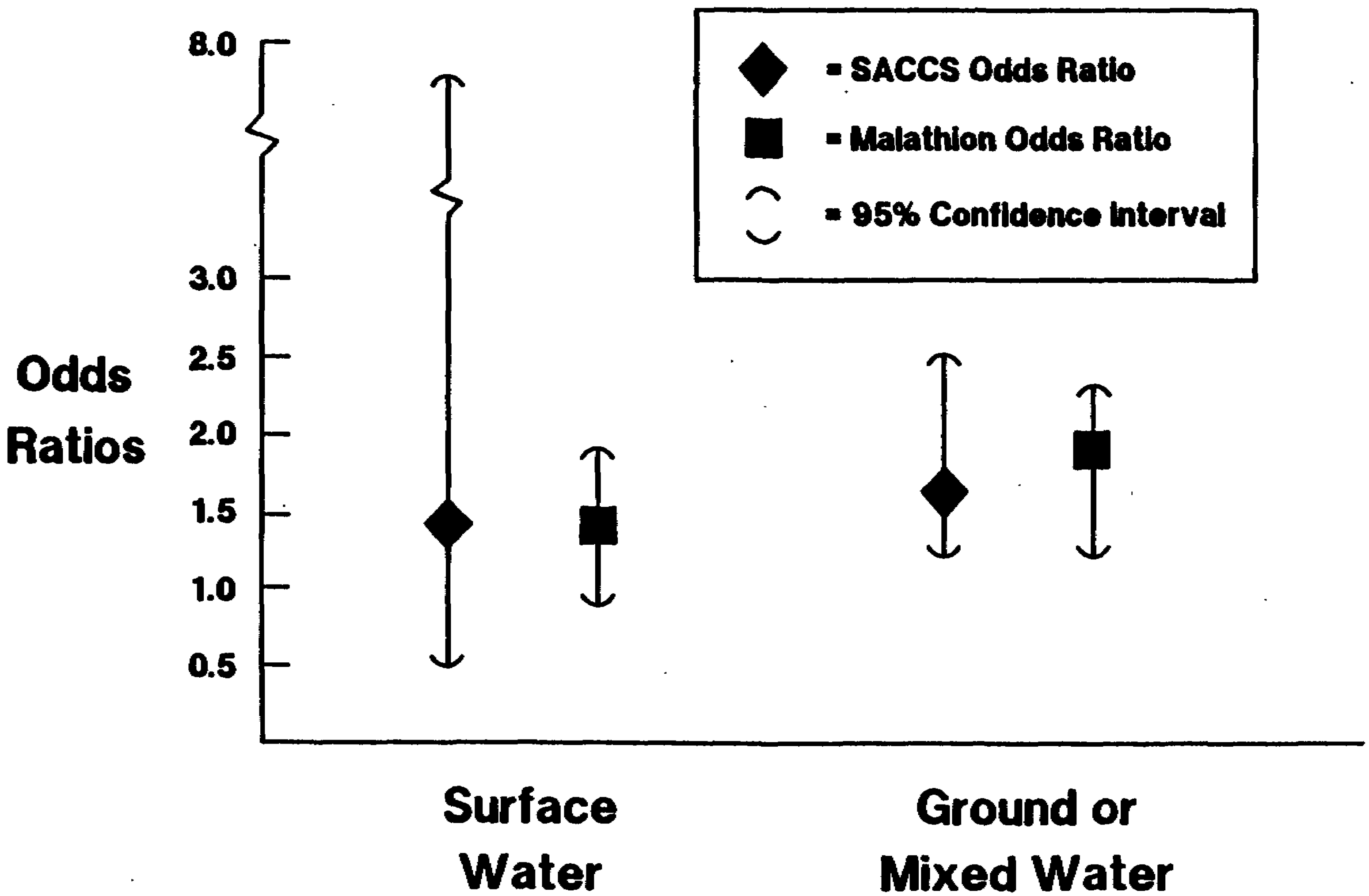
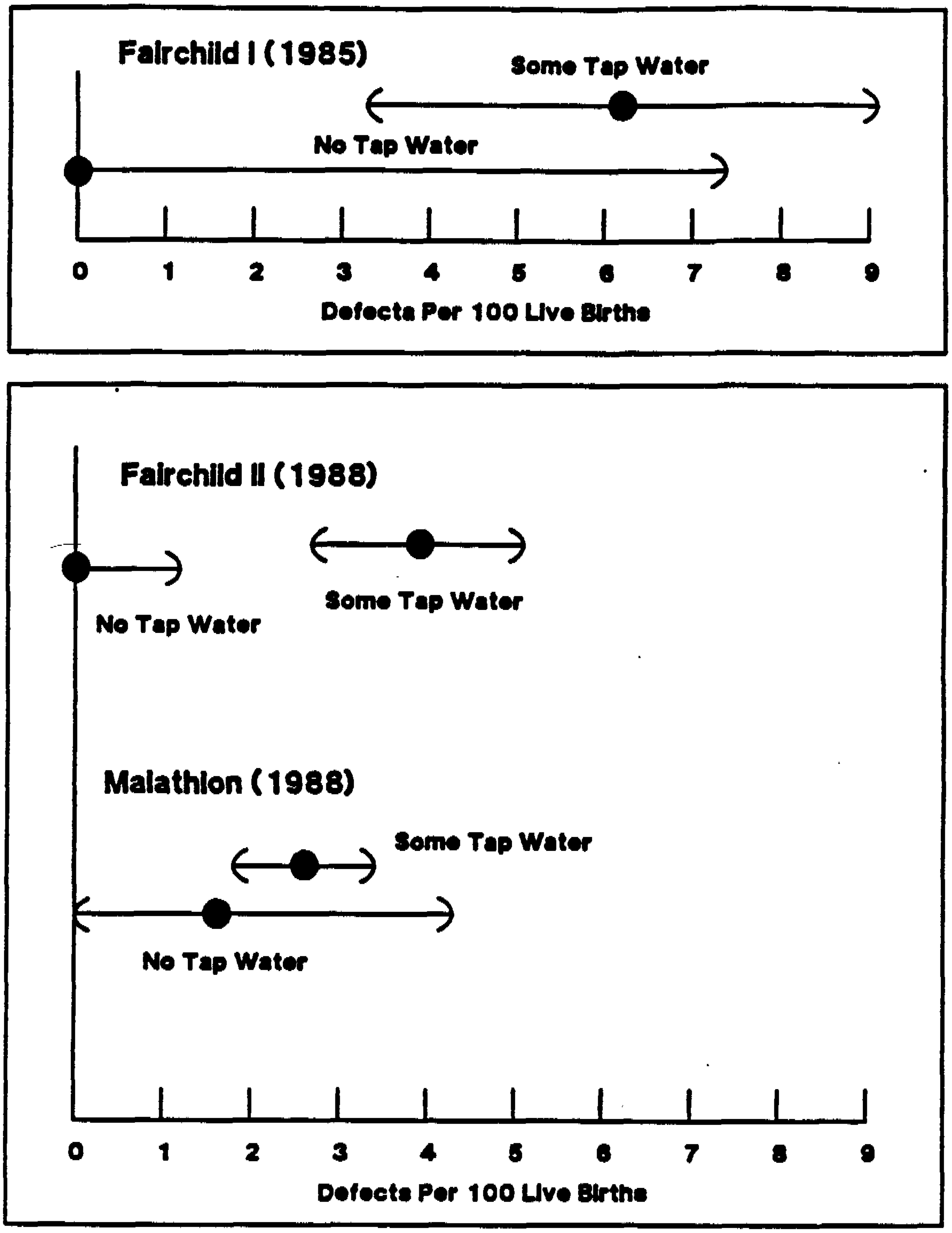


**Figure 1.5 Prevalence of Reportable Birth Defects And 95% Confidence Intervals By Reported Tap Water Use in Three Studies**




• = Pr valenc ( ) = 95% C nfid nce interval

**Figure 1.6 Overall Prevalence of Reportable Birth Defects And 95% Confidence Intervals in Three Studies vs. Expected**

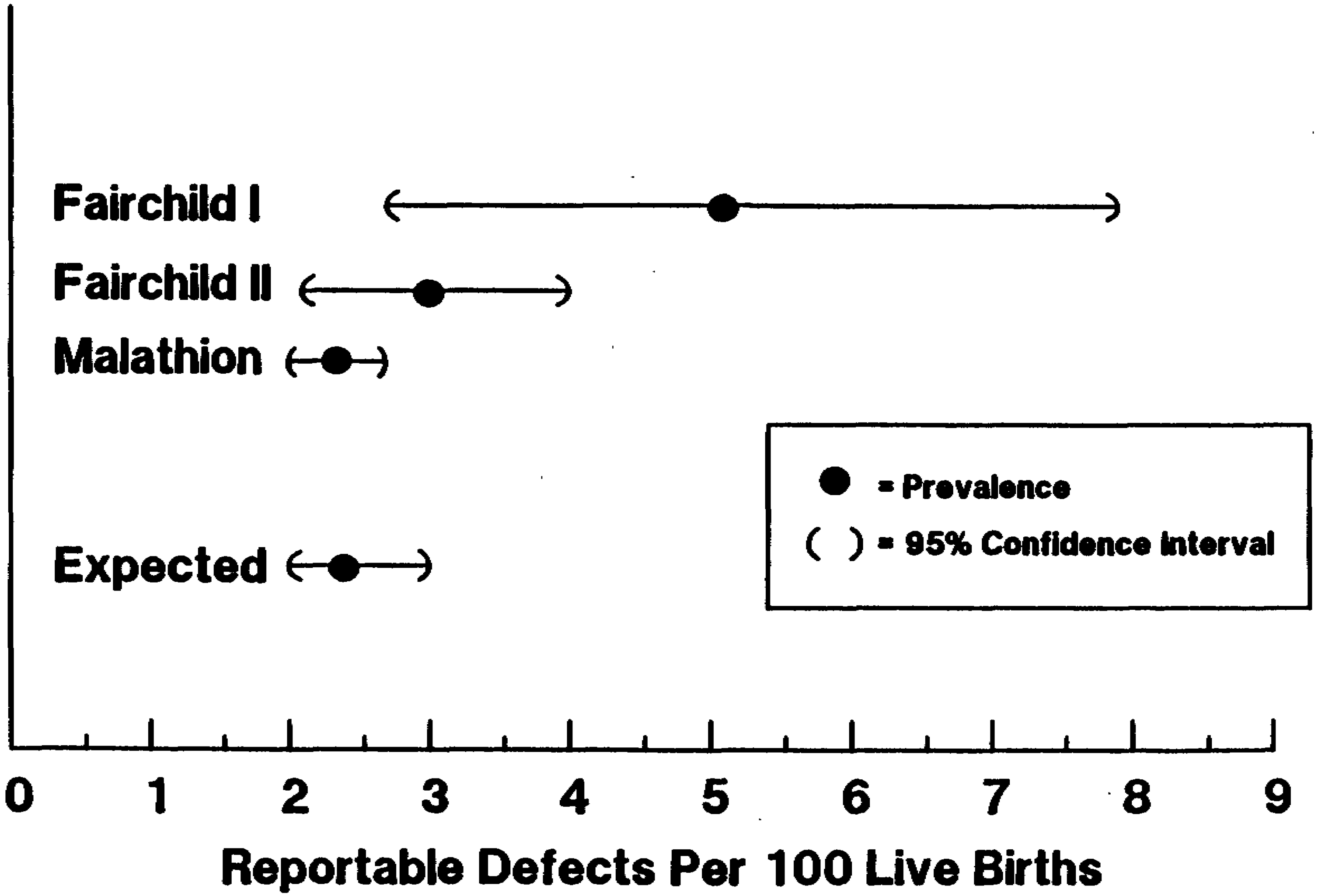


**Figure 1.7 Estimated Prevalence of Cardiac Defects And 95% Confidence Intervals By Reported Use Of Bottled Water vs. Expected**

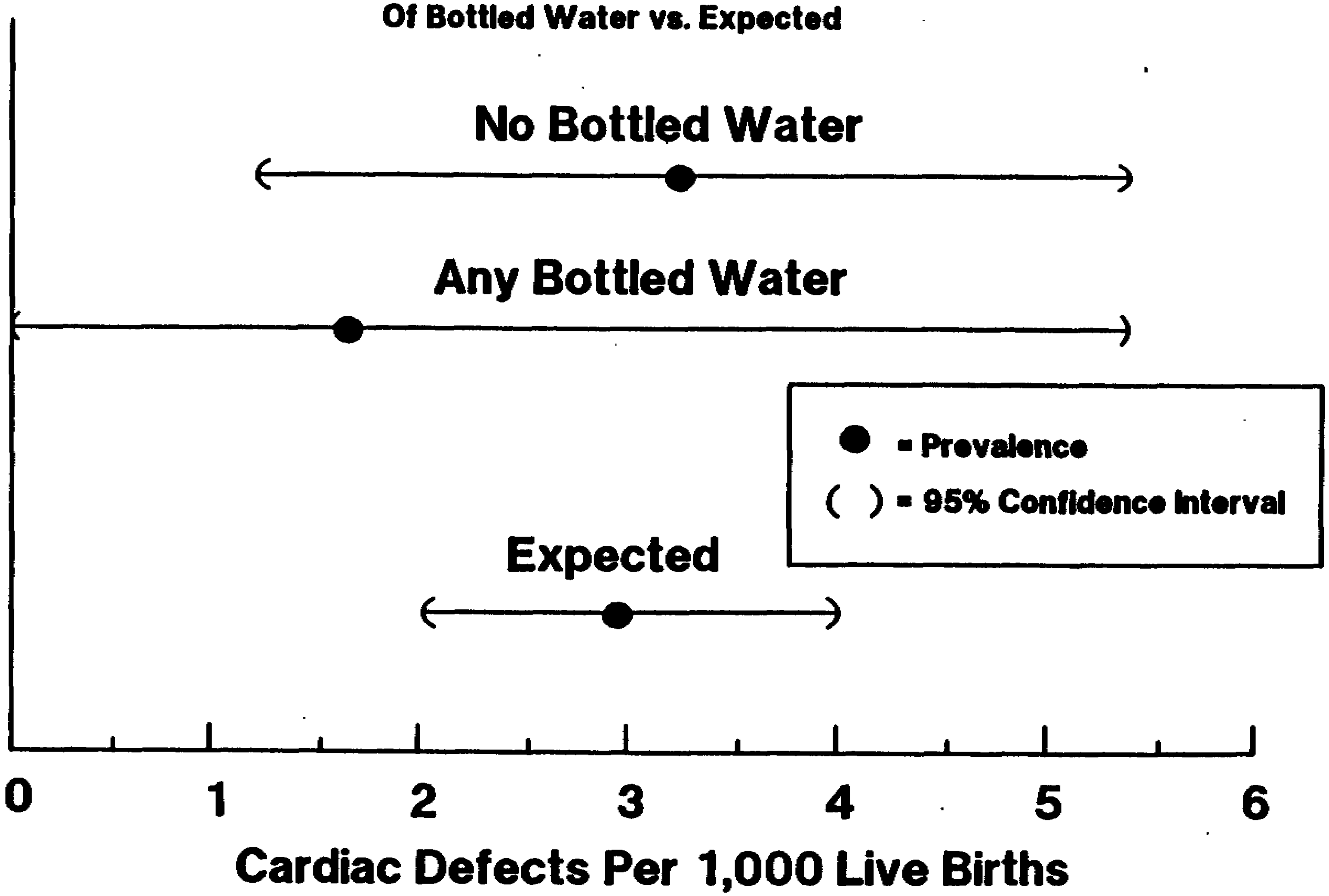
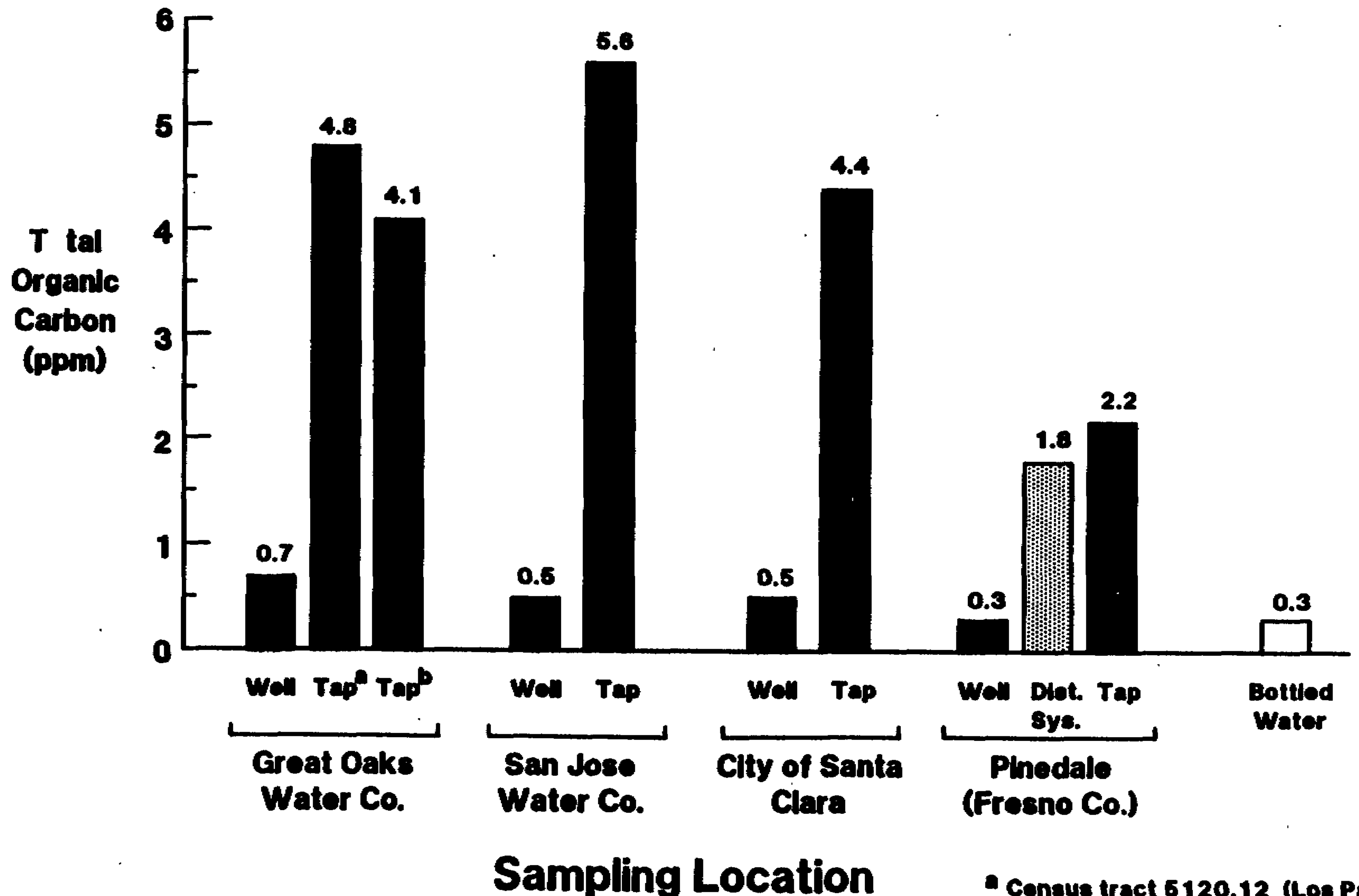


**Figure 1.8 Mean Levels of Total Organic Carbon In Unchlorinated Groundwater in Four Locations and Bottled Water**




[a] Census tract 5120.12 (Los Pas s)
[b] Census tract 5120.11

1.34

SL 032912

**Figure 1.9 Mean Levels of Total Organic Carbon in Chlorinated Surface and Groundwater in Five Locations**

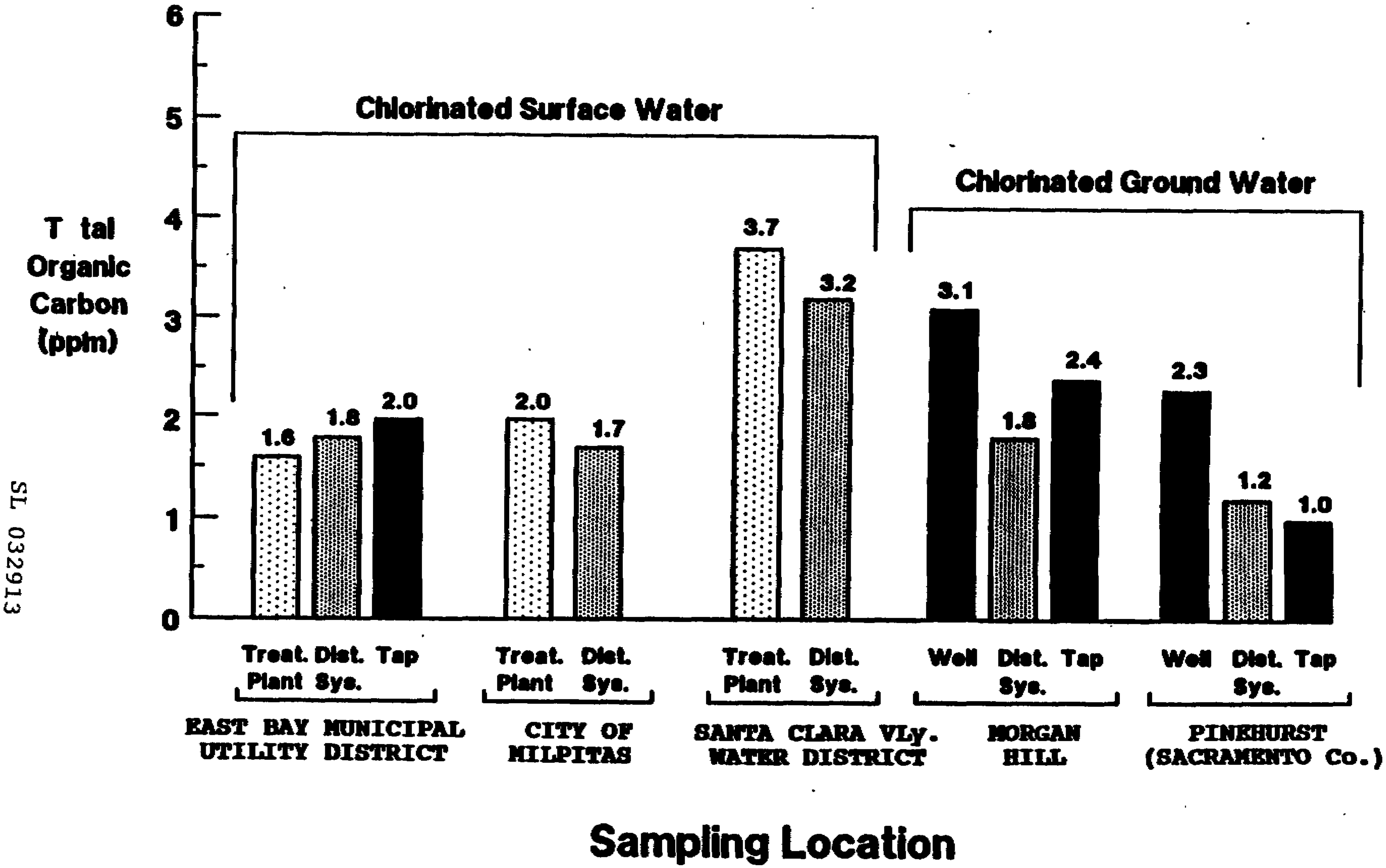
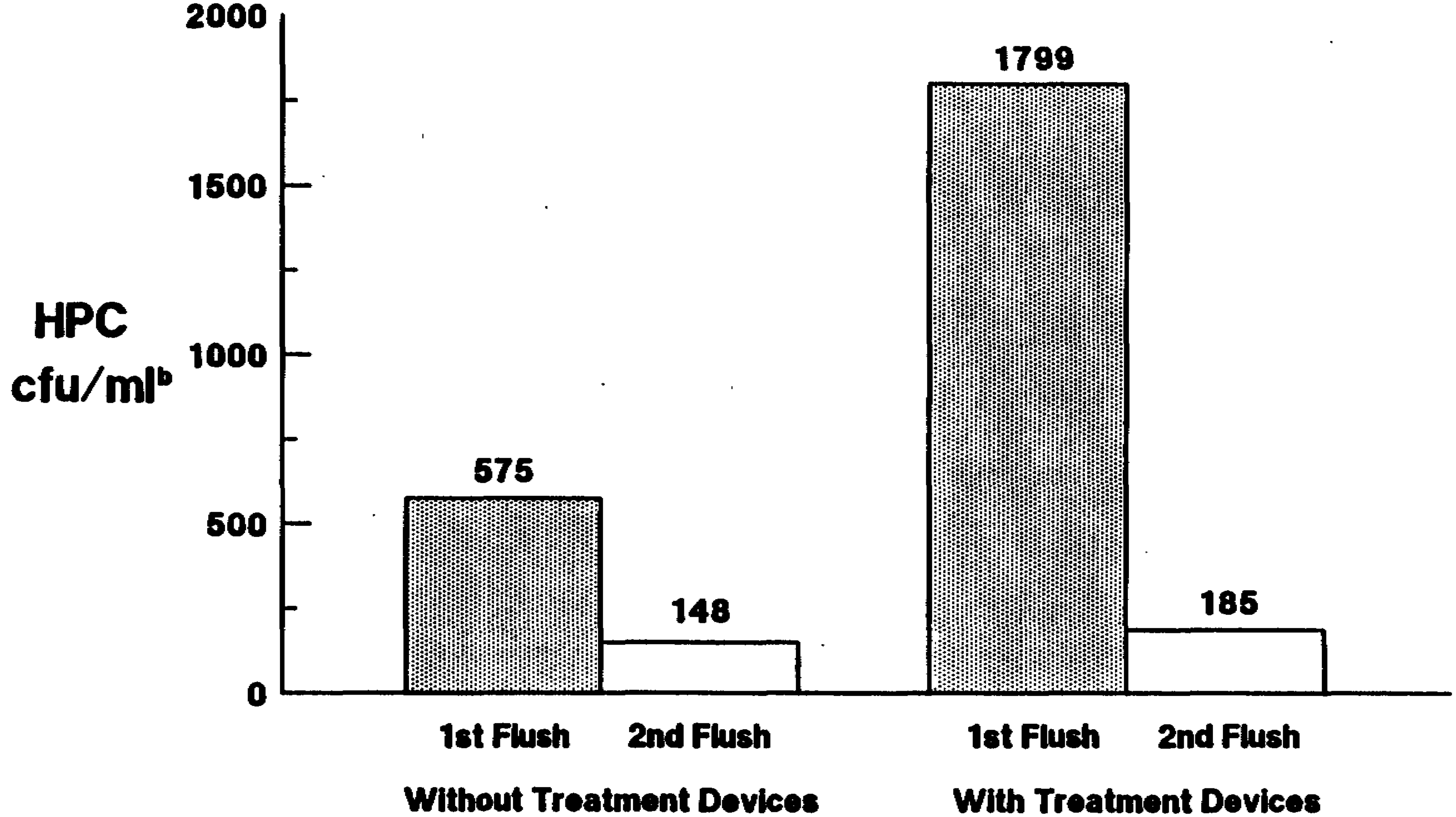


Figure 1.10 Mean Heterotrophic Plate Count [a]




[a] Data from two census tracts in Great Oaks Water Company, one in San Jose Water Company and one in City of Santa Clara.

[b] Colony forming units per milliliter

## Appendix A. Definitions and Abbreviations

Unless otherwise specified the following definitions and abbreviations will be used throughout this report.

SAB: Spontaneous abortion; spontaneous fetal loss before 20 weeks gestation

BD: Anomaly at birth coded as reportable by the California Birth Defects Monitoring Program

Low birth weight: Birth weight of 2500 grams or less on birth certificate

Tap water: Consumption of cold tap water at home reported by mother for first trimester of pregnancy

Bottled water: Consumption of bottled water at home or work reported by mother for first trimester of pregnancy

Showering and bathing: Duration times frequency of showering plus bathing reported by mother during first trimester

N(pregnancies): Number of pregnancies

N(LB): Number of live births

N(SAB): Number of spontaneous abortions

N(BD): Number of birth defects

CI: Confidence interval

CL: Confidence limit

p: Significance probability

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OR: Odds ratio

RR: Relative risk

$OR_{MH}$: Mantel-Haenszel odds ratio

## Appendix B. Definition of Covariates

The following variables have been used in stratified and multivariate analyses throughout this report. Variables not used throughout are defined separately when used. Whenever possible commonly used variables have been divided according to the following categories. Time dependent variables refer to conditions in the first trimester. The base-line category for the construction of dummy variables is underlined.

Nausea: any vs. <u>none</u>

Maternal age: 20 years or less, <u>21-34</u>, 35 or more

Education: <u>less than high school graduate</u>, high school graduate, some college, college graduate

Smoking: <u>none</u>, half a pack a day or less, more

Alcohol: <u>none</u>, 1-3 drinks/week, more

Ethnicity: <u>White (non-Hispanic)</u>, Hispanic, other

Prior fetal loss: <u>none</u>, one, more

Employment: <u>none</u>, any

## Appendix C. Contact Letters t Potential Respondents

### Fairchild I

We need your assistance in a study of great importance to your community. Your name was given to us by you or another member of your household several weeks ago. This was the first phase in a study being conducted by the State Department of Health Services, in collaboration with Santa Clara County Health Department, to determine whether the contamination of water from a well serving the Great Oaks Water District was associated with an increased occurrence of miscarriages, stillbirths, and birth defects. The second phase is now beginning.

The information that we were given indicated that you were pregnant at some time between January 1, 1980 and December 31, 1981, and we would like to interview you concerning this pregnancy. The interview will be conducted, in most cases, by telephone and should not take longer than about 15 to 20 minutes. Your participation in the interview is, of course, entirely voluntary. However, to obtain useful information a high proportion of the women living in the study area who were pregnant in 1980 or 1981 must participate. All information received will be treated as confidential as required by the Health and Safety Code and will be used only in statistical summaries. All forms which identify individuals will be destroyed at the completion of the study.

Available statistics on births are not detailed enough to detect problems of this kind. The special health survey that is being carried out will yield more detailed information and will be suitable for further statistical analysis. The study area includes not only households served by the Great Oaks Water District, but also another area which will serve as a comparison area.

An interviewer will contact you within the next few weeks. If you have any questions please contact project staff by phoning collect (415) 540-2669 or (408) 279-5986. Thank you for your help in this study.

# Fairchild II

We recently received the form from your household in response to the first phase of ur health study. Thank you for your cooperation in returning that informati n t us. The form indicated that you were pregnant sometime between 1980 and 1985. We now would like to interview you concerning your pregnancies.

The interview is usually conducted by telephone. Your participation in the interview is entirely voluntary, and you may terminate the interview at any time. All information received during the interview will be kept confidential as required by the State Health and Safety Code. It will be used only in statistical summaries and no individuals will be identified in any analysis or report. An interviewer will telephone you within the next few weeks to answer any questions you may hav and t schedule an interview.

As we explained in the previous letter, this study is an extension of a recent study f miscarriages and birth defects in Santa Clara County. The original study showed th t in 1980 and 1981 more birth defects and miscarriages occurred in an area f San Jose served by the Great Oaks Water Company than in a similar neighborhood with a different source of water. This new study will cover 1980 to 1985 and will add two neighborhoods to those originally studied. This study will help to clarify the reasons for the previously observed excess of miscarriages and birth defects and will tell us whether this excess still persists.

T obtain useful information, a high proportion of the women living in all the study areas who were pregnant anytime between 1980 and 1985 must participate. We hope you will participate. If you have any questions please write or call us.

We greatly appreciate your help in this study.

Malathion[a]

The Kaiser Foundation Research Institute conducts periodic surveys to provide researchers and the public with information on important health topics. Please help us by answering the questions below and returning this form in the enclosed envelope. No stamp is needed. Your answers will b strictly confidential and will not become part of your medical records.

* Please read each item carefully because the instructions vary from section to section

* Do not hesitate to call us (collect) if you have any questions regarding this survey (415) 428-6730.

---

[a]First paragraph of mailed questionnaire

Cardiac

The Epidemiological Studies and Surveillance Section of the California Department of Health Services is conducting a health study of great importance to you and other residents of Santa Clara County. In a recent study, we found that an unusually high rate of congenital heart defects occurred in 1981 in a particular area of Santa Clara County.

We are conducting a new study to help clarify the causes of the previously observed excess of these birth defects. You have been chosen because a review of vital statistics records indicated that you had a child born in 1981 or 1982. We need your help to conduct the new study. We need your participation whether or not your child had a birth defect. You can help by answering questions ab ut your pregnancy with the child born to you in 1981 or 1982. We would like t ask these questions over the telephone at a time that is convenient for you. The interview will take approximately 15 minutes to complete.

We will be calling you in the near future to arrange a convenient time for a telephone interview. You could assist us greatly by writing down your teleph ne number and the best times to call on the enclosed form and returning it in the stamped pre-addressed envelope. In addition, it would be helpful if you would include your name and address in case the information we have is incorrect and we need to reach you by mail.

All information obtained from you will be kept confidential as required by the State Health and Safety Code and will be used only for this study. Neither you nor your child will be identified in any report of this study. All forms will be destroyed at the completion of the study. If you have any questions concerning the study, please call one of us collect at (415) 540-2828.

Thank you for taking the time to read this letter and to return the form to us.

SACCS

The Department of Health Services is conducting a study in Santa Clara County to evaluate how occupational, environmental and household chemical exposures affect reproductive health. To obtain useful information, we need to interview a large number of women of reproductive age, particularly those who have been pregnant at some time. We would greatly appreciate your participation in this study, which would consist only of an interview.

The interview will be conducted by telephone and will last about 30 minutes. Y u w uld be free to withdraw at any time and you may choose not to answer any question. All information collected during the interview will be kept confidential as required by the State Health and Safety Code. It will be used nly in statistical summaries and no individuals will be identified in any analysis or report.

Enclosed is a brief form, asking for your telephone number, best times to call, and your language preference, (if you don't speak English). It is very important for the success of the study that <u>every</u> woman we contact return this form as soon as possible. We have enclosed a stamped, addressed envelope f r your convenience. An interviewer will telephone you within the next few weeks t answer any questions you may have and to schedule an interview. If you prefer not to be contacted please indicate that on the form.

We hope you will participate in this important study about the reproductiv health of women. If you have any questions, please write or call the investigators below. We would really appreciate your help in this study.

Appendix D. Water Consumpti n Questions Asked in Six Studies

## FAIRCHILD I

I'm going to ask some questions now about the water you drank during this pregnancy or for the three months before the pregnancy.

1. Did you use bottled water at all at home during this pregnancy or for the three months before the pregnancy?

   [ ] YES

   1a. What brand did you use?

   ______________________________

   [ ] NO: SKIP TO QUESTION 3.

2. Did you usually use bottled water at home?

   [ ] YES

   2a. What brand did you use?

   ______________________________

   SKIP TO QUESTION 5.

   [ ] NO

3. How many glasses or cups of cold tap water or beverages made of unheated water did you drink each day, on the average, at home? This should include any beverages made of unheated water such as orange juice, iced tea, or other beverages made from concentrate.

   ______________ a
   GLASSES OR CUPS

4. How many glasses or cups of beverages made from heated tap water did you drink each day, on the average, at home? This should include any beverages that require heating or hot water even though they may be cool when you drink them for example, iced tea that is brewed with hot water, or iced coffee?

   ______________ a
   GLASSES OR CUPS

Now I'm going to ask y u some similar questions about the water you drank at work during this pregnancy r in the three months before th pregnancy.

5. Did you use bottled water at all at work during this pregnancy or for the three months before the pregnancy?

   [ ] YES

   5a. What brand did you use?

   ______________________________

   [ ] NO: SKIP TO QUESTION 7.

6. Did you usually use bottled water at work during this pregnancy or for three months preceding this pregnancy?

   [ ] YES

   6a. What brand did you use?

   ______________________________
   SKIP TO QUESTION 9

   [ ] NO

7. How many glasses or cups of cold tap water or beverages made of unheated water did you drink at work each day, on the average, during this pregnancy or in the three months before the pregnancy? This should include any beverages made f unheated water such as orange juice, iced tea, or other beverages made fr m concentrate.

   ______________ [a]
   GLASSES OR CUPS

8. How many glasses or cups of beverages made from heated tap water did you drink at work each day, on the average, during this pregnancy or in the three months before the pregnancy? This should include any beverages that require heating or hot water even though they may be cool when you drink them, for example, iced t a that is brewed with hot water, or iced coffee?

   ______________ [a]
   GLASSES OR CUPS

[a]Less than one but more than zero recoded to 1.

## FAIRCHILD II

The next group of questions is about the liquids you drank during this pregnancy or for the three months before this pregnancy.

1a. What types of liquids did you usually have each day during this time p riod?

b. About how many glasses, cups or ounces of liquids did you drink per day? Please include all sources of liquids; coffee, tea, soft drinks, juices, water, milk, beer, wine, other liquor, any liquid.

______________________ or [ ] DK

GLASSES OR CUPS
(8 ounces = approx. 1 cup)

c. During just the first trimester of this pregnancy was this amount different?

[ ] YES

How many glasses or cups did you drink per day?

______________________

GLASSES OR CUPS

[ ] NO

[ ] DK

2a. At home, did you use bottled water at all during this pregnancy or for the three months before this pregnancy?

[ ] YES [ ] NO: SKIP TO 3 [ ] DK: SKIP TO 3

b. Did you usually use bottled water at home?

[ ] YES [ ] NO [ ] DK

3a. At hom , ab ut h w many glasses or cups f cold tap water or beverages made f unheated tap wat r did you drink each day? This should include any beverages made f unheated water such as orange juice, iced tea, or other beverages made from concentrate.

________________
GLASSES OR CUPS

or

[ ] NONE: SKIP TO 4.
[ ] DK

b. And during just the first trimester of this pregnancy was this amount different?

[ ] YES

How many glasses or cups did you drink per day?

________________
GLASSES OR CUPS

[ ] NO
[ ] DK

4. IF THE WOMAN DID NOT WORK DURING THIS PREGNANCY OR IN THE 3 MONTHS BEFORE SKIP TO QUESTION 6.

a. And at work, did you use bottled water at all during this pregnancy or for the three months before this pregnancy?

[ ] YES [ ] NO: SKIP TO 5. [ ] DK

b. Did you usually use bottled water at work?

[ ] YES [ ] NO [ ] DK

5a. At work, about how many glasses or cups of cold tap water or beverages made f unheated tap water did you drink each day? This should include any beverages made of unheated water such as orange juice, iced tea, or other beverages made from concentrate.

________________
GLASSES OR CUPS

or

[ ] NONE: SKIP TO 6.
[ ] DK

b. And during just the first trimester of this pregnancy was this amount different?

[ ] YES

How many glasses or cups did you drink per day?

________________
GLASSES OR CUPS

[ ] NO
[ ] DK

## FAIRCHILD IIB

The following questions are about beverage consumption. Some of these are similar t questions that we asked you in the previous interview but will provide us with more specific information. Again, talking about the period from about ____/____ (MO/YR) (to/into) ____/____ (MO/YR): [FROM LMP TO TERMINATION DATE FOR CASES AND FOR FIRST 3 MONTHS OF PREGNANCY FOR LIVE BIRTHS]

(WOMAN WORKED?) YES -------> CONTINUE

NO -------> SKIP TO QUESTION 3

1a. At work, on the average, how many glasses or cups of unheated tap water or drinks made from unheated tap water did you drink per day?

______________
GLASSES OR CUPS

b. At work, how many glasses or cups of hot beverages made from tap water did y u drink per day?

______________
GLASSES OR CUPS

c. At work, how many glasses or cups of bottled water or drinks made from bottled water did you drink per day?

______________
GLASSES OR CUPS

IF DRANK BOTTLED WATER:

d. Was the bottled water carbonated or noncarbonated?

[ ] CARBONATED [ ] NONCARBONATED [ ] BOTH

e. What was the brand name of the bottled water that you drank m st often?

______________________________

[ ] DK

SL 032927

2. The following three questions c ncern you water consumption at home on days when y u went t w rk.

a. On the average, how many glasses or cups of unheated tap water or drinks made from unheated tap water did you drink per day?

________________
GLASSES OR CUPS

b. How many glasses or cups of hot beverages made from tap water did you drink per day?

________________
GLASSES OR CUPS

c. How many glasses or cups of bottled water or drinks made from bottled water did you drink per day?

________________
GLASSES OR CUPS

3a. On non-work days (FOR WOMEN WHO DIDN'T WORK: On a typical day), how many glasses or cups of unheated tap water or drinks made from unheated tap water did you drink at home?

________________
GLASSES OR CUPS

b. On non-work days (FOR WOMEN WHO DIDN'T WORK: On a typical day), how many glasses or cups of hot beverages made from tap water did you drink at home?

________________
GLASSES OR CUPS

c. On non-work days (FOR WOMEN WHO DIDN'T WORK: On a typical day), how many glass s or cups of bottled water or drinks made from bottled water did you drink at home?

________________
GLASSES OR CUPS

IF DRANK BOTTLED WATER:

d. Was the bottled water carbonated or noncarbonated?

[ ] CARBONATED [ ] NONCARBONATED [ ] BOTH

e. What was the brand name of the bottled water that you drank most often?

________________________________________

[ ] DK

SL 032928

f. Was the bottled water delivered to your hom ?

[ ] YES

g. Was the bottled water delivered in a plastic or glass container?

[ ] PLASTIC [ ] GLASS

[ ] NO

4a. I've asked you about water consumption at home (and at work). Were there any other places such as restaurants, clubs, recreational areas, or friends' homes where, at least once a week, you drank tap or bottled water or drinks mad from tap or bottled water?

[ ] YES [ ] NO

IF YES:

| b. What were these places? | c. How often did you drink tap water or drinks made from tap water at ___? | d. How many cups or glasses did you usually drink each time you were there? | e. How often did you drink bottled water or drinks made from bottled water at ________? | f. How many cups or glasses did you usually drink each time you were there? | g. What was the brand name of the bottled water? |
|---|---|---|---|---|---|
| (NAME AND LOCATION) | | | | | |
| ________ | ________ | ________ | ________ | ________ | ________ |
| ________ | ________ | ________ | ________ | ________ | ________ |
| ________ | ________ | ________ | ________ | ________ | ________ |

<u>MALATHION</u>

1. During the first 3 months of this pregnancy, did you drink bottled water either plain or in combination with coffee, tea, orange juice, etc?

   [ ] YES [ ] NO

   IF YES: About how much bottled water did you drink at home and at work?

| | AT HOME | AT WORK |
|---|---|---|
| [ ] NONE | [ ] | [ ] |
| [ ] VERY LITTLE (less than one 8 oz. glass per day) | [ ] | [ ] |
| [ ] MODERATE (1-3 8 oz glasses per day) | [ ] | [ ] |
| [ ] A LOT (4 or more 8 oz. glasses per day) | [ ] | [ ] |

2. Did you also drink tap water during the first 3 months of this pregnancy?

   [ ] YES [ ] NO

   IF YES: Did you drink tap water more or less than bottled water?

   [ ] MORE [ ] LESS [ ] THE SAME

# CARDIAC

I'm now going to ask you some questions about the fluids you drank during the first three months of your pregnancy.

1. On the average how many cups of tea or coffee containing caffeine did y u drink each day during the first three months of your pregnancy:

   Tea? __________ CUPS    Coffee? __________ CUPS

2a. Did you use bottled water at home during the first three months?

   [ ] YES: b. Did you usually use bottled water at home?

   [ ] YES    [ ] NO    [ ] DK

   [ ] NO

   [ ] DK

3. Now I'd like to ask you about how much cold tap water or beverages made fr m unheated tap water such as orange juice or iced tea you drank during these three months of pregnancy.

   During that time, how many glasses of cold tap water did you drink each day:

   a. At home? ____________________ GLASSES OR CUPS PER DAY   or [ ] DK

   b. At work? ____________________ GLASSES OR CUPS PER DAY   or [ ] DK

   c. At other place[a]

| OTHER PLACE | GLASSES OR CUPS PER DAY | DK |
|---|---|---|
| ____________________ | ____________________ | [ ] |
| ____________________ | ____________________ | [ ] |

[a]Asked if respondent previously indicated that, at least twice a week or for one week or more, she spent time in Santa Clara County at a place other than her home or job.

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<u>SACCS</u>

Now I would like to ask about your consumption of coffee and other beverages. During the month <u>before</u> this pregnancy:

1a. How many cups of coffee, excluding decaffeinated coffee, did you usually drink each day?

_______________ [ ] DK
CUPS

b. How many cups of tea, excluding decaffeinated or herbal tea, did you usually drink each day?

_______________ [ ] DK
CUPS

c. How many cans of soda, excluding decaffeinated soda, did you usually drink each day?

_______________ [ ] DK
CANS

2. During the month <u>before</u> this pregnancy, how many glasses of unheated tap water r drinks made from cold tap water, such as juices or iced tea did you usually drink each day:

a. At home? _______________ [ ] DK
GLASSES

b. At work? _______________ [ ] NA, DID NOT WORK OUTSIDE HOME (SKIP Q. 3b.5)
GLASSES

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3a. Did you change your <u>usual</u> consumption of any f these beverages during (the first 20 weeks f) this pregnancy? Please count from your LMP.

[ ] YES [ ] NO [ ] DK

IF YES: b. Did you change your consumption of:

| [REPEAT FOR EACH BEVERAGE] | YES | NO | DK | IF YES: c. During what week did you first change? [BEFORE PREG - 01] | d. How many cups/ cans/glasses) did you drink each day after this change? |
|---|---|---|---|---|---|
| 1. Caffeinated Coffee | 1 | 2 | 3 | ____ WKS | ____ CUPS |
| 2. Caffeinated tea | 1 | 2 | 3 | ____ | ____ CUPS |
| 3. Caffeinated soda | 1 | 2 | 3 | ____ | ____ CANS |
| 4. Tap water at home | 1 | 2 | 3 | ____ | ____ GLASSES |
| 5. Tap water at work? | 1 | 2 | 3 | ____ | ____ GLASSES |

4. Did you usually drink bottled water during (the first 20 weeks of) this pregnancy:

a. At your home?

[ ] YES [ ] NO [ ] DK

b. At your work?

[ ] YES [ ] NO [ ] DK

IF YES TO EITHER:

a. About how many glasses of bottled water did you usually drink each day during (the first 20 weeks of) this pregnancy at home and work combined?

____________________
GLASSES

b. Why did you choose to drink bottled water?

____________________________________________

____________________________________________



SL 032933

## 2. Fairchild I

### Data Collection: Methods and Results

An enumeration was completed in 95% of the 5291 households in two study census tracts, one which received water thought likely to have been contaminated by th Fairchild leak (5120.12) and a second demographically comparable tract receiving water from another source (5120.08). This enumeration was conducted in rder to obtain information on household composition and to ascertain whether any pregnancies had occurred to women in the household during 1980 or 1981. Pregnancies considered eligible for the study were those that had occurred entirely whil the mother resided within the exposed or the control census tract and that had started between January 1, 1980 and December 31, 1981. The women who had been pregnant were interviewed for information concerning the outcome of the pregnancy, demographic and maternal risk factors, possible occupational exposure and exposure to potentially hazardous substances. In addition, they were asked about hot and cold tap water consumption at home and at work and consumpti n f other beverages including bottled water.

In all, 250 pregnancies were ascertained in the exposed census tract and 316 in the control census tract. Completed interviews were obtained for 91.2 percent of the pregnant women in the exposed tract and 86.7 in the control tract. In both areas about two percent of the women refused to be interviewed. Most of the remaining non-respondents had given a telephone number during the hous hold enumeration which was no longer valid at the time of the interview, presumably because they had moved to a different location. Based on vital statistics records, it is estimated that between 40% and 45% percent of total pregnancies occurring in the study areas during 1980-1981 were missed because the women had moved from the area before the study was conducted.

Ectopic pregnancies and twins were not included in the original data analysis. In the reanalysis described here, therapeutic abortions were also eliminated from the data analysis, and if a woman had more than one eligible pregnancy, on was randomly selected for inclusion in the study to avoid the effects of lack of independence f multiple pregnancies f the same woman. After liminating pregnancies that did not meet the requirements described above, there was a total of 349 pregnancies in this analysis compared to 401 pregnancies in the original analysis.

## Spontaneous Abortions

Spontaneous abortions were validated, with the woman's permission, by reviewing medical records, interviewing her physician, or reinterviewing her concerning the circumstances of the reported event. In both the exposed and the contr l tracts, one reported spontaneous abortion was determined to probably have been a false positive. Validation could not be carried to completion in one case reported in the control area and five cases in the exposed area because the women could not be reached by phone or mail or refused the follow-up interview. Medical records of about 25% of the women who had reported no pregnancy during the household enumeration were reviewed through a prepaid health plan. Only one additional spontaneous abortion was ascertained; this was in the exposed area. The data analysis presented here was restricted to the 39 spontaneous aborti ns reported during interview that had been validated as described above after eliminating multiple pregnancies.

In the original analysis potential maternal risk factors had been examined individually and by multiple logistic regression analysis. Maternal risk fact rs for spontaneous abortion considered in the analysis included amount of cold tap water consumed at home during the pregnancy; number of previous pregnancies; number of previous spontaneous abortions; age of mother; amount of smoking; frequency of alcohol consumption; ethnicity; and exposure of the mother to organic solvents, petrochemical products, pesticides, or x-rays during the first trimester of pregnancy. A two-fold excess of spontaneous abortions in the exposed tract had been noted before adjustment for maternal risk factors. The r sults of the multiple logistic regression analysis changed this result very little. Amount of cold tap water consumed and alcohol consumption were the only variables, besides census tract, that showed a statistically significant relationship with the incidence of spontaneous abortions.

A particularly interesting finding in the  riginal study was that the spontane us ab rti n rate increased with increasing amount  f cold tap wat r consumption in both the exposed and the control areas (Figure 2.1). This finding was one factor in the decision to carry out analyses of our other reproductive studies with respect to water exposure.

Upon reanalysis, based on one randomly selected pregnancy per woman, the increase in spontaneous abortion rates with increasing amounts of cold tap water consumed at home is similar to that seen in the original analysis (Table 2.1). The crude and smoothed rates are shown in Figures 2.2 and 2.3. The effect  f amount of tap water was analyzed controlling for use of bottled water, and vice versa. An increasing incidence of spontaneous abortions is seen with increasing amount of tap water within all three categories of bottled water use (Table 2.2). Controlling for bottled water use resulted in an odds ratio of 3.4 ($p=0.003$) for consumption of any amount of tap water. The odds ratio for consumption of bottled water, controlling for amount of tap water, is not significant (odds ratio=1.0, $p=0.97$). No adverse effect of possible exp sure t water as a result of swimming was seen (Table 2.3). Adjustment for possible maternal risk factors was attempted using the Mantel-Haenszel chi square analysis, but the frequency of spontaneous abortions was too small in som categories to obtain meaningful results. However, multiple logistic regression analysis using the same variables and considering water consumption as a three-valued variable resulted in statistically significant odds ratios for the three variables that were significant in the original study, that is, residence in the census tract exposed to contaminated water, the amount of cold tap water c nsumed at home, and consumption of alcoholic beverages during the first trimester  f pregnancy (Table 2.4).

## Birth Defects

Reported congenital anomalies were validated by examination of hospital birth records or by obtaining additional information from the mother or her child's physician. Only defects considered reportable by the California Birth Defects Monitoring Program were included in this analysis. In all, 16 reportable defects were confirmed and are included in this analysis. These included both malformations and deformations.

In the original Fairchild study the rate of rep rted congenital anomalies in the exposed census tract was about three times as high as in the control tract. No unusual pattern was seen in the type of anomalies among births in the exposed tract. Because of the small number of congenital anomalies, no attempt was made t adjust these data statistically for possible maternal risk factors. How ver, such factors were examined on a case-by-case basis and no relationship was seen. The relative risk for congenital malformations in the exposed area was statistic lly significant (RR=3.1, p=0.04, 95% confidence interval 1.1 to 10.4).

Reanalysis of the birth defect data with respect to water consumption gave results similar to those obtained for spontaneous abortions. The rates increased with increasing amount of cold tap water consumption (Table 2.5), and a significant odds ratio was obtained for consumption of tap water controlling f r b ttled water (Table 2.6). No effect of bottled water consumption was seen. The crude and smoothed birth defect rates are shown in Figures 2.4 and 2.5.

T summarize, the amount of consumption of cold tap water and residence in the area exposed to contaminated water are independently related to the risk of spontaneous abortion and birth defects; bottled water does not appear to convey an independent "protective" effect; and exposure to water by swimming is unrelated to the incidence of spontaneous abortions.

One of the questions remaining concerning the results of the original Fairchild study was the actual exposure to contaminated water by the women in the exposed area. It is not known when the contamination started, how much the amount of c ntamination varied over the two year study period, or how much contaminati n w s actually in the water distribution system and the tap water consumed by the w men in the exposed tract. These questions, as well as the relation between amount of cold tap water consumption and the rate of spontaneous abortions in the control as well as the exposed study areas are being addressed in the follow-up studies described in other sections of this report. Findings of this and other studies in the area suggest that the observed association of consumption of tap water and adverse pregnancy outcomes extends outside the original exposed study area and the larger area served by the contaminated water supply.

Table 2.1

Spontaneous Abortion Rates by Tap Water Consumption

| Cold Home Tap Water (glasses/day) | SAB Rate | N (pregnancies) | 95% CI |
|---|---|---|---|
| 0 | 0.0% | 47 | ( 0.0, 7.4) |
| 1[a] | 7.4% | 27 | ( 0.9, 24.1) |
| 2 - 3 | 12.5% | 96 | ( 5.9, 19.1) |
| 4 - 6 | 14.9% | 121 | ( 8.6, 21.2) |
| 7+ | 12.7% | 55 | ( 3.9, 21.5) |
| TOTAL | 11.3% | 346 [b] | ( 8.0, 14.6) |

[a] Includes less than one glass per day.

[b] Excludes three women whose amount of tap water was unknown.

Table 2.2

Spontaneous Abortion Rates by Tap Water and Bottled Water Consumption

| Cold Home Tap Water (glasses/day) | Bottled Water: None | Not Usually | Usually | TOTAL |
|---|---|---|---|---|
| 0 | 0.0% | 0.0% | 0.0% | 0.0% |
| | ( 7)[a] | ( 2) | ( 38) | ( 47) |
| 1[b] | 4.0% | 100.0% | 0.0% | 7.4% |
| | (25) | ( 1) | ( 1) | ( 27) |
| 2+ | 13.7% | 3.4% | 22.7% | 13.3% |
| | (219) | ( 29) | ( 22) | (270) |
| TOTAL | 12.4% | 6.3% | 8.2% | 11.0% |
| | (251) | ( 32) | ( 61) | (344)[c] |

[a] (Number of pregnancies in parentheses)

[b] Includes less than one glass per day.

[c] Excludes five with bottled water use and/or cold tap water use unknown.

Controlling for bottled water

Logit estimate $OR_{MH}$ (any tap water vs. no tap water) = 3.4 (p = 0.003)

Homogeneity chi square - data too sparse

Controlling for tap water

Logit estimate $OR_{MH}$ (any bottled water vs. no bottled water) = 1.0 (p = 0.97)

Homogeneity chi square - (p = 0.02)

Table 2.3

Spontaneous Abortion Rates by Use of Swimming Pools

| | N(SAB) | Rate |
|---|---|---|
| Reported no swimming | 27 | 13.3% |
| Reported swimming | | |
| Great Oaks | 6 | 10.9% |
| Elsewhere | 6 | 7.0% |
| TOTAL | 39 | 11.2% |

Table 2.4

Variables Associated with Risk of Spontaneous Abortion in Multiple Logistic Regression Analysis

| Variable | OR | 95% CI | p |
|---|---|---|---|
| Age < 20 | 2.7 | (0.4, 17.1) | 0.29 |
| Age ≥ 35 | 1.4 | (0.3, 7.4) | 0.67 |
| Some college | 1.4 | (0.5, 3.8) | 0.47 |
| College graduate | 1.7 | (0.6, 4.9) | 0.33 |
| Smoking | | | |
| ≤ 1/2 pack/day | 2.0 | (0.6, 7.1) | 0.26 |
| ≥ about a pack/day | 1.0 | (0.1, 9.2) | 1.00 |
| Alcohol consumption | | | |
| ≤ 1-3 drinks/wk | 1.0 | (0.5, 2.4) | 0.92 |
| ≥ 4 drinks/wk | 11.6 | (1.6, 85.4) | 0.02 |
| Hispanic | 0.5 | (0.1, 4.3) | 0.53 |
| Other non-White | 0.7 | (0.2, 2.4) | 0.62 |
| Previous fetal loss | | | |
| 1 previous fetal loss | 1.1 | (0.4, 3.0) | 0.86 |
| ≥ 2 previous fetal losses | 2.7 | (0.8, 9.0) | 0.10 |
| Employment during pregnancy | 1.7 | (0.7, 3.7) | 0.23 |
| Exposed study area (vs. control) | 2.9 | (1.4, 6.2) | 0.01 |
| Conceived 1981 (vs. 1980) | 1.3 | (0.6, 2.7) | 0.52 |
| Amount of cold home tap water consumed (glasses/day) none, 1-3, 4 or more | 2.2 | (1.2, 4.1) | 0.01 |

Table 2.5

Birth Defect Rates by Tap Water Consumption

| Cold Home Tap Water (glasses/day) | Birth Defect Rate | N (Live Births) | 95% CI |
|---|---|---|---|
| 0 | 0.0% | 47 | (0.0, 7.4) |
| 1[a] | 0.0% | 25 | (0.0, 13.7) |
| 2 - 3 | 6.0% | 84 | (0.9, 11.1) |
| 4 - 6 | 6.8% | 103 | (1.9, 11.7) |
| 7+ | 8.3% | 48 | (2.4, 19.6) |
| TOTAL | 5.2% | 307[b] | (2.7, 7.7) |

[a] Includes less than one glass per day.

[b] Excludes three women whose amount of tap water was unknown.

Table 2.6

Birth Defect Rates by Tap Water and Bottled Water Consumption

| Cold Home Tap Water (glasses/day) | Bottled Water: None | Not Usually | Usually | TOTAL |
|---|---|---|---|---|
| 0 | 0.0% (7)[a] | 0.0% (2) | 0.0% (38) | 0.0% (47) |
| 1[b] | 0.0% (24) | 0.0% (0) | 0.0% (1) | 0.0% (25) |
| 2+ | 7.4% (189) | 3.6% (28) | 5.9% (17) | 6.8% (234) |
| TOTAL | 6.4% (220) | 3.3% (30) | 1.8% (56) | 5.2% (306)[c] |

[a] (Number of live births in parentheses)

[b] Includes less than one glass per day.

[c] Excludes four with bottled water use and/or cold tap water use unknown.

Controlling for bottled water

Logit estimate $OR_{MH}$ (tap water vs. no tap water) = 1.3 (p=0.15)
Homogeneity chi square - data too sparse

C ntrolling for tap water

Logit estimate $OR_{MH}$ (any bottled water vs none) = 0.6 (p=0.48)
Homogeneity chi square - data too sparse

**Figure 2.1 Smoothed Spontaneous Abortion Rates By Tap Water Consumption In Exposed And Control Census Tracts**

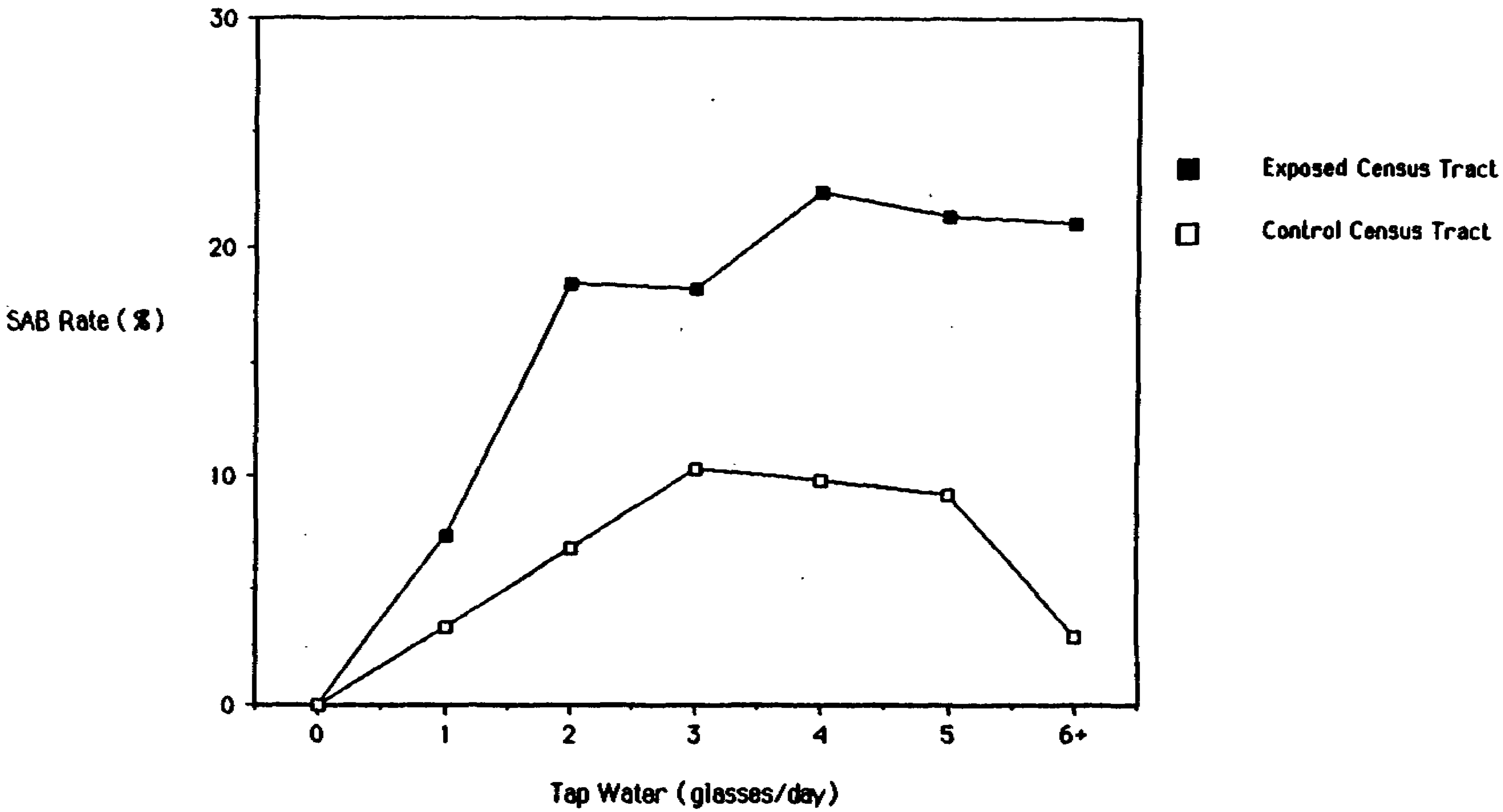

Figure 2.2 Crude Spontaneous Abortion Rates By Tap Water Consumption

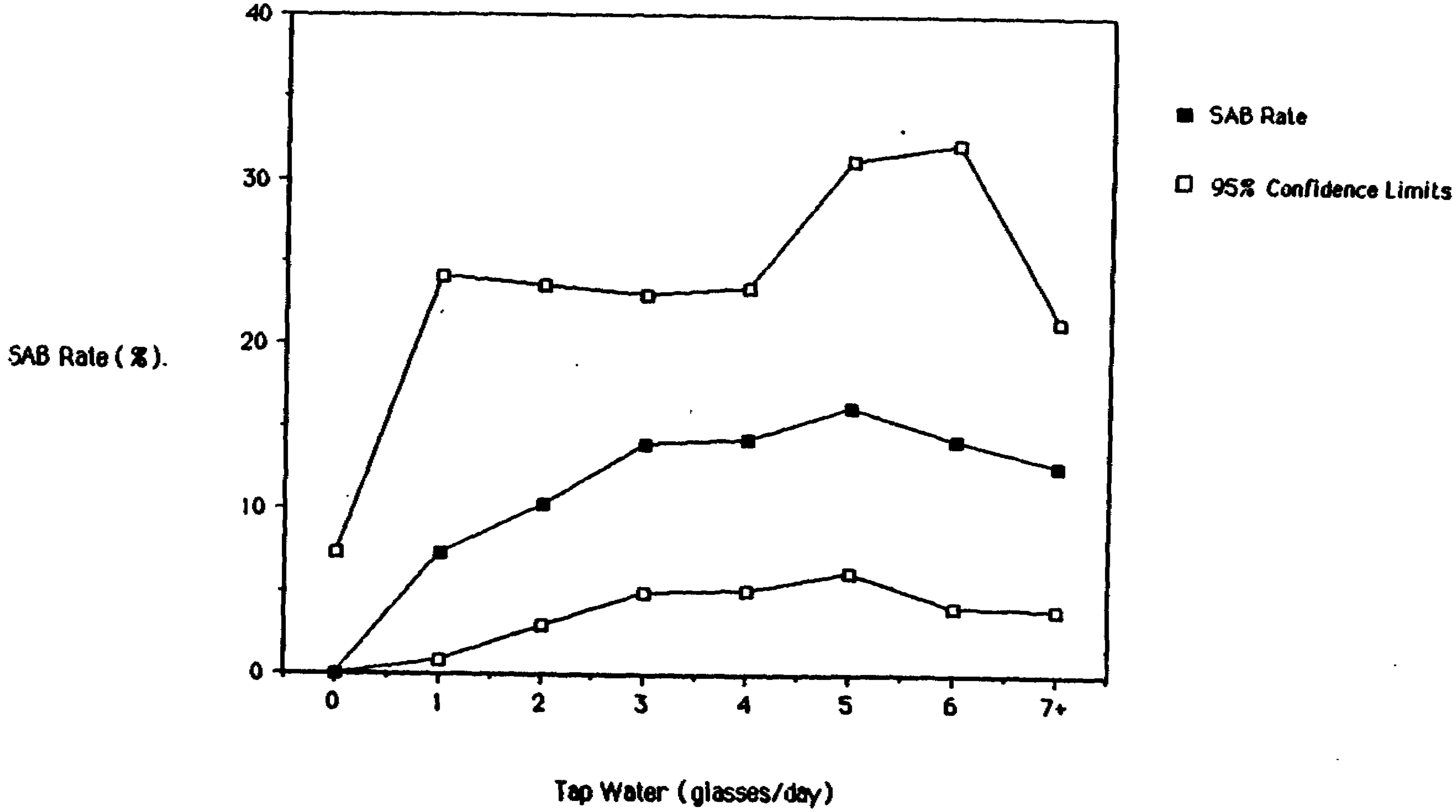

Figure 2.3 Smoothed Spontaneous Abortion Rates By Tap Water Consumption

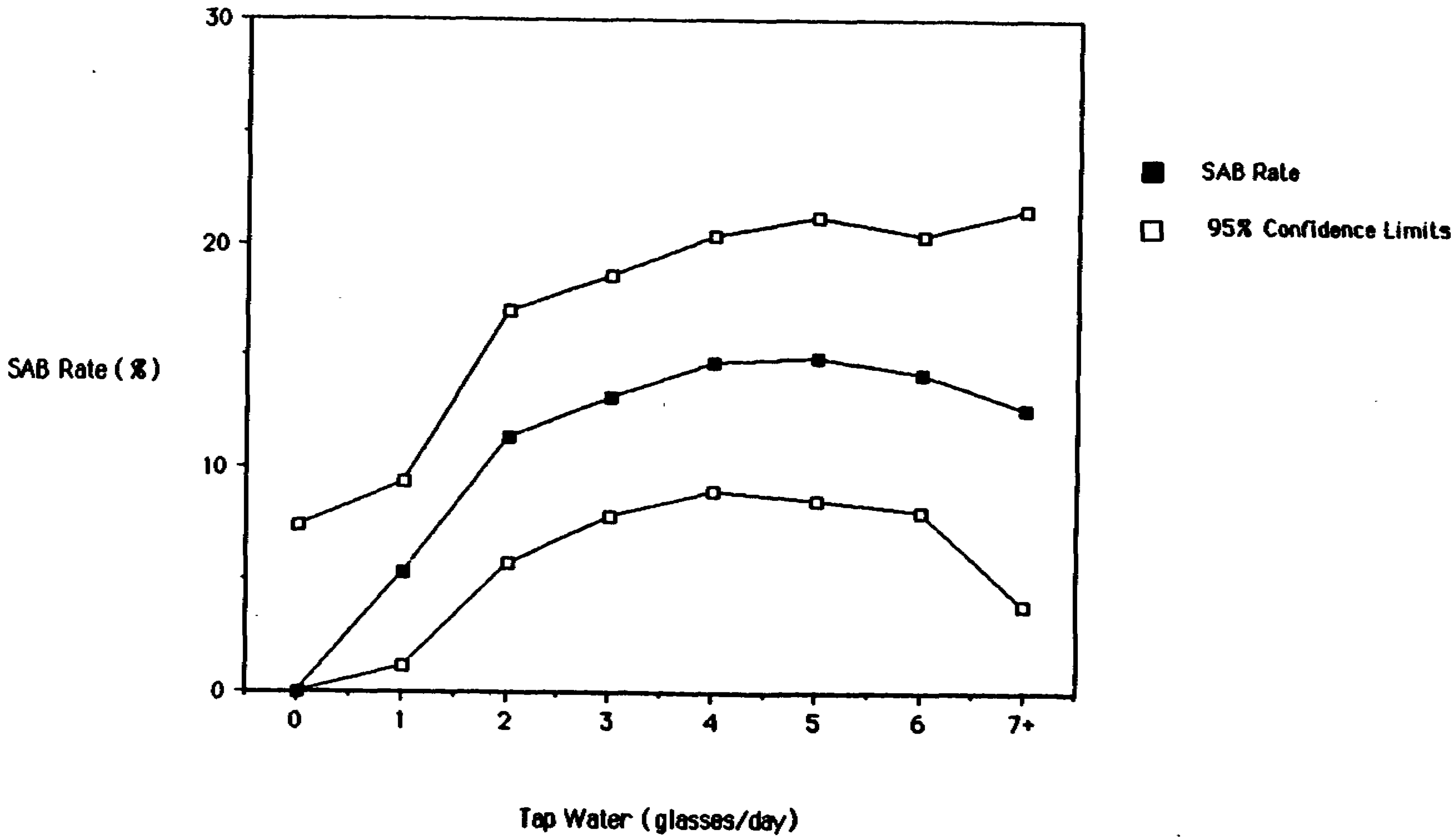

Figure 2.4 Crude Birth Defect Rates By Tap Water Consumption

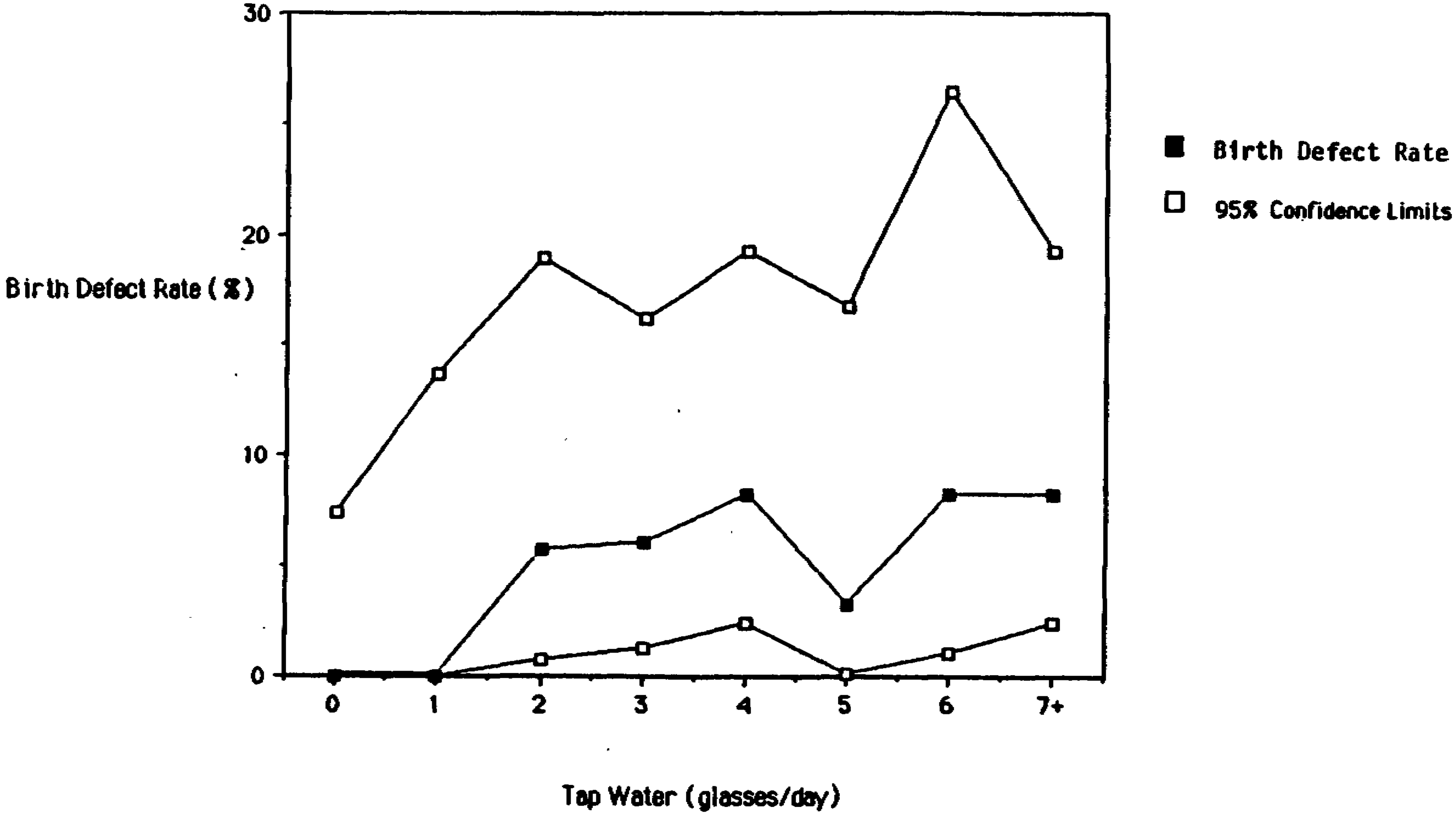




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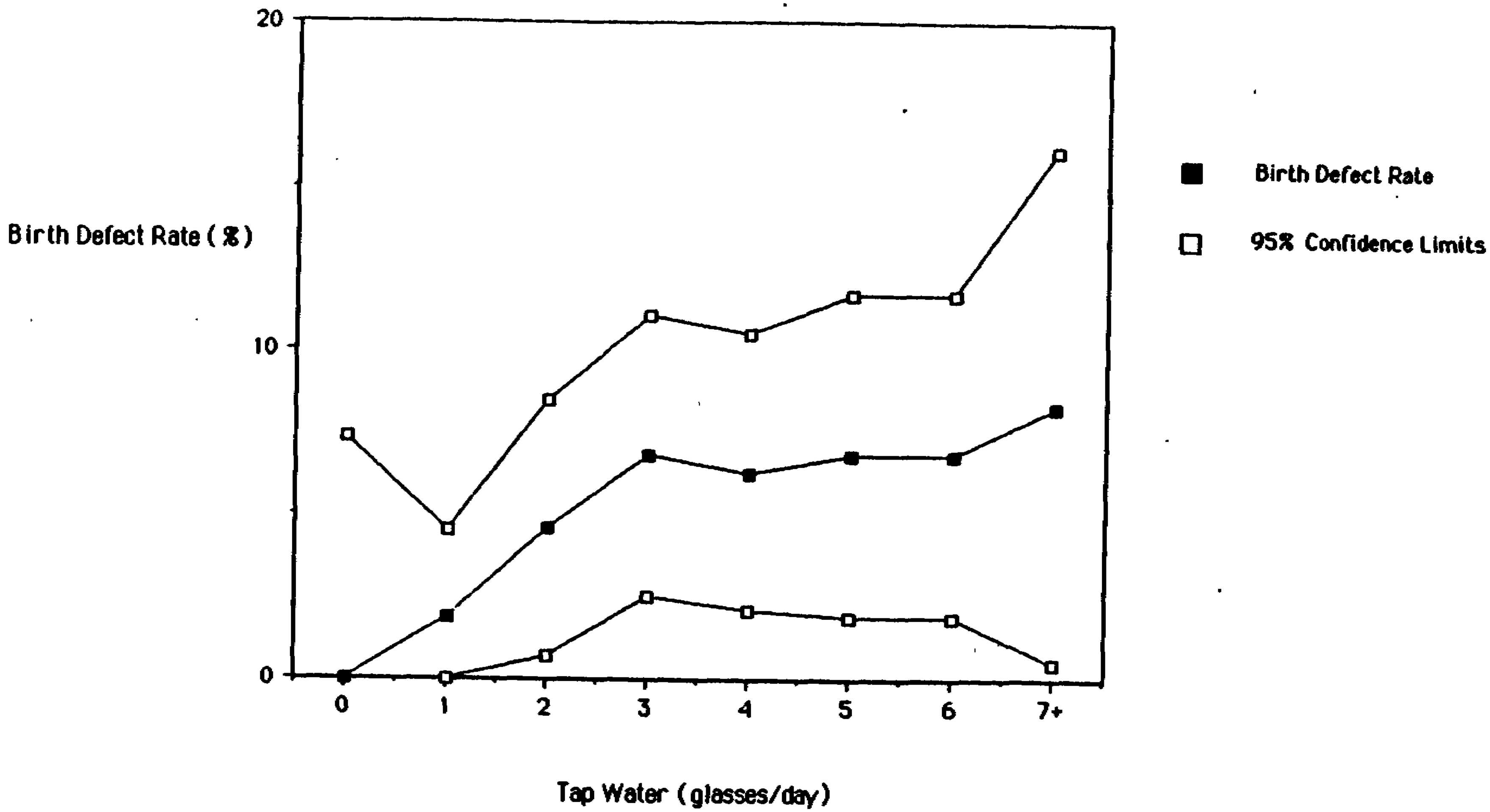
Figure 2.5 Smoothed Birth Defect Rates By Tap Water Consumption



## 3. Fairchild II

### Introduction

Tap water consumption and spontaneous abortion (SAB) rates were positively associated in a California Department of Health Services (CDHS) study of adverse pregnancy outcomes occurring in 1980 and 1981 in two census tracts in Santa Clara County (1). That study (Fairchild I) was conducted to assess whether drinking water contaminated with toxic industrial wastes was likely to be responsible for an excess of adverse pregnancy outcomes. Fairchild I was inconclusive as to the cause of the observed increase of adverse pregnancy outcomes and a follow-up study (Fairchild II) was conducted to resolve remaining questions. This second study demonstrated that adverse pregnancy outcomes occurring in two exposed areas were not likely to be due to contaminated drinking water; that is, the temporal and spatial occurrences of adverse outcomes in two exposed and in two unexposed areas were not consistent with a causal role of the contaminated water (2). However, tap water consumption was again positively associated with SAB rates independent of study area and time period. This report further explores the association of water consumption with SAB, birth defects and low birth weight rates observed in 1980-1985 in four census tracts of Santa Clara County.

### Methods

Details of ascertainment, classification, and validation of pregnancy outcomes are given in (2). Analyses of SAB and low birth weight were based on a single random eligible pregnancy per woman; analyses of defects included all reported eligible live births except twin births.

Water consumption was ascertained through a questionnaire; a copy is included in (2). The respondent was asked how many glasses of cold tap water she drank at home during the pregnancy or in the three months before pregnancy. Sh was als asked if th am unt consumed differed during the first trimester and if so, what was the amount consumed during that time. Similar questions were asked about cold tap water consumed at work if the woman reported employment during her pregnancy. Each woman was also asked if she drank any bottled water at home during her pregnancy or for the three months before. If she responded yes, she was asked if she usually drank bottled water. A similar question was asked about bottled water consumption at work, if applicable. Preliminary analyses were performed for first trimester cold tap water consumption at home, first trimester cold tap water consumption at home and work, bottled water consumption at home, and bottled water use at home and work. Results were generally consistent whether home tap water alone or home and work were considered (see Table 2.12 (2)); only the home tap water results are presented here because the source of home tap water was known while that at work was not. Results for bottled water are presented using reported bottled water use at both home and work because the brands used at either location were not known.

## Results

### Spontaneous Abortion

Analyses of the relationship between spontaneous abortion and tap and bottled water consumption are contained in Tables 3.1-3.12 and Figures 3.1-3.3. There is a modest, non-linear dose response between SAB rate and the number of glasses of cold tap water consumed at home (Tables 3.1 and 3.2). We have shown both the crude rates and rates smoothed by a three-point moving average (Figures 3.1 and 3.2).

Stratified analyses were carried out for a large number of potential covariates (Table 3.3). For all of these covariates except water filter use, the odds ratios (OR) across strata were homogeneous (Table 3.4). The odds ratio for tap water consumption among water filter users was not elevated (0.3) but for non-filter users the OR was 5.7. The increased risk associated with home tap water consumption was seen in all water companies (Table 3.5).

Odds ratios for SAB associated with home tap water consumption were homogeneous across categories of bottled water use, although the OR was lowest among non-drinkers of bottled water (Table 3.6). Overall, the OR for SAB was reduced for women drinking any bottled water compared to those drinking no bottled water (OR =0.4).

The certainty of diagnosis and its possible relationship to the observed association between SAB and water consumption was examined in two ways. Odds ratios were calculated separately for the 47 women with pathologically confirmed SABs and for 44 women who either did not see an MD or whose conceptus was not sent to a pathologist. (The remaining SABs had uncertain pathology confirmation). ORs for tap or bottled water consumption were significant in the two groups but were less marked in pathology confirmed cases (Table 3.7). Additionally, ORs for bottled and tap water consumption were computed for those SABs that were reported but excluded from analysis upon validation (Table 3.8). Similar associations with water use were seen for these SABs.

During the study period (1980-1984), the reported bottled water use increased dramatically from 19.7% to 64.3% (Table 3.9). Similarly the proportion of women reporting no tap water use increased from 5.8% in 1980 to 23.7% in 1984 (Table 3.10). (Data for 1985 is deleted from this presentation because only the first three months of 1985 were included in the study.) Over the five year period, the observed SAB rate in both bottled and non-bottled water drinkers rose somewhat so that the ORs for bottled water by year were quite constant (Table 3.9). This is shown graphically in Figure 3.3. The ORs for cold home tap water consumption were somewhat more variable but did not increase or decrease steadily over the five year period.

A large number of variables were entered into a multiple logistic regression analysis. Estimated ORs and 95% confidence intervals for the full model are presented in Table 3.11. Other models, including those with interactions between study areas and time periods and between cold home tap water consumption and water filter use, are discussed in the full Fairchild II report (2). A complete presentation and discussion of others factors associated with SAB are also presented there (2). Of pertinence here, the OR for SAB associated with any cold tap water at home was increased by this multi-factorial adjustment (OR=6.9). The OR for water filter use around the beginning of pregnancy was 0.4.

In order to examine the hypothesis that increased fluid consumption might be the mechanism by which increased tap water conveyed risk, we looked at the association between SAB and total fluid consumption, except tap water. As shown in Table 3.12, no relationship was seen.

## Birth Defects

The relationship between congenital malformations considered reportable by the California Birth Defects Monitoring Program (CBDMP) and consumption of cold tap water at home is shown in Table 3.13. As shown in Figures 3.4 and 3.5, the dose-response noted for SAB is absent here. The rate of reportable defects in non-tap water drinkers was extremely low (0.4%) and was based on large numbers of births (n=263). Therefore, the odds ratio for tap water drinkers was quite large (22.0), although the overall rate of birth defects in this population (3.1) was not greater than expected based on the rates in the CBDMP. Although the association was technically homogeneous across water companies (Table 3.14; p=0.87), the estimated OR was highest in births among women served by the Great Oaks Water Company.

As with SAB, we looked at the observed association with tap water by certainty of diagnosis (Table 3.15). Here we see that only the definite anomalies are associated with water consumption.

Unlike SAB, there was no association between birth defects and bottled water consumption. The rate of reportable defects in bottled water drinkers (2.7%) was very similar to that in non-drinkers (3.5%). There was no dose-response seen with frequency of bottled water use (Table 3.16). The crude OR of 22 seen for tap water drinking is decreased somewhat after controlling for bottled water consumption (Mantel-Haenszel OR= 6.0) (Table 3.16).

## Low Birth Weight

There was no evidence of an association between low birth weight and either tap or bottled water consumption. The rate of low birth weight in non-tap water drinkers (3.5%) was nearly identical to the rate in the study population (3.4%). The odds ratio for any cold tap water was 0.9 and did not vary by water company. This OR increased slightly when bottled water use was controlled (OR=1.4), reflecting the slightly higher rate of low birth weight in bottled water drinkers. These results are contained in Tables 3.17-3.20.

## Factors Influencing Tap and Bottled Water Consumption

In order to identify women who drank no tap water as distinguished from those who drank no bottled water, a discriminant analysis was performed. Variables entered into this analysis were those listed in Table 3.3. Of these, only four discriminated between these groups (Table 3.21). Bottled water drinkers were most likely to reside in the Great Oaks Water District, to have a pregnancy late in the study period, to be non-smokers, and to fall in the low risk age group (20-34).

## Discussion

Section 10 of this document discusses the potential recall and classification biases as possible explanations for these findings of associations of tap and bottled water use with adverse pregnancy outcomes. It is especially important to remember that first trimester bottled water consumption was not asked and that women reporting live births had from five to seven months longer opportunity to consume bottled water during their pregnancy than women with SAB. This would artificially lower the odds of SAB associated with bottled water use. This kind of "opportunity" bias is not applicable to the tap water questions which did solicit first trimester consumption.

<u>References</u>

1. Epidemiological Studies Section, California Department of Health Services: Pregnancy Outcomes in Santa Clara County 1980-1982: Reports of Two Epidemiological Studies. California State Publications Section. Report 7540-958-1301-5, 1985.

2. California Department of Health Services: Pregnancy Outcomes in Santa Clara County, 1980-1985.

Table 3.1

Spontaneous Abortion Rates by Tap Water Consumption

| Cold Home Tap Water (glasses/day) | SAB Rate | N(pregnancies) | 95% CI |
|---|---|---|---|
| 0 | 3.3% | 214 | ( 0.9, 5.7) |
| 1 | 8.7% | 103 | ( 3.3, 14.2) |
| 2 | 11.4% | 175 | ( 6.7, 16.1) |
| 3 | 10.7% | 150 | ( 5.7, 15.6) |
| 4 | 11.9% | 134 | ( 6.4, 17.4) |
| 5 | 16.3% | 86 | ( 8.5, 24.1) |
| 6 | 8.6% | 58 | ( 1.4, 15.8) |
| 7+ | 13.5% | 96 | ( 6.7, 20.3) |
| TOTAL | 9.8% | 1016 | ( 8.0, 11.6) |

Homogeneity chi square : $p < 0.001$

Table 3.2

Odds Ratios for Spontaneous Abortions
by Tap Water Consumption

| Cold Home Tap Water (glasses/day) | OR | 95% CI |
|---|---|---|
| 0 | 1.0[a] | -- |
| 1 | 2.9 | (1.0, 8.1) |
| 2+ | 4.2 | (1.9, 9.2) |
| Any | 4.0 | (1.8, 9.1) |

[a] Referent group

Table 3.3

Odds Ratios for Spontaneous Abortions by Tap Water Consumption after Adjustment For Potential Confounders

| Variable | $OR_{MH}$ (any cold home tap water vs. none) | Homogeneity Chi Square p |
|---|---|---|
| Alcohol[a] | 4.8 | 0.32 |
| Census tract | 4.2 | 0.55 |
| Education | 4.8 | 0.71 |
| Employment[a] | 4.0 | 1.00 |
| Ethnicity | 3.9 | 0.13 |
| Gravidity | 4.2 | 0.97 |
| Maternal age | 3.9 | 0.64 |
| Month prenatal care began | 5.0 | 0.93 |
| Nausea[a] | 5.9 | 0.60 |
| Ponderal index | 4.8 | 0.32 |
| Prior fetal loss | 4.0 | 0.26 |
| Smoking[a] | 4.6 | 0.58 |
| Water company | 4.2 | 0.50 |
| Water filter use | (see Table 3.4) | 0.04 |
| Year of conception | 4.7 | 0.92 |

| | | |
|---|---|---|
| Unadjusted OR (n=988) | 4.0 | 95% CI (1.8, 9.1) |

[a] First trimester

Table 3.4

Odds Ratios for Spontaneous Abortions by
Tap Water Consumption Stratified by Water Filter Use

| Water Filter Use | OR (any vs. no cold home tap water) | 95% CI | p |
|---|---|---|---|
| Yes | 0.3[a] | (0.04, 2.8) | 0.43 |
| No | 5.7 | (2.3 , 14.3) | < 0.001 |

Water Filter Use

| Cold Home Tap Water Use | Yes: SAB Rate | Yes: N(Pregnancies) | No: SAB Rate | No: N(Pregnancies) |
|---|---|---|---|---|
| Yes | 3.6% | 55 | 12.8% | 709 |
| No | 9.1% | 11 | 2.5% | 200 |

[a]Small sample correction

SL 032958

Table 3.5

Odds Ratios For Spontaneous Abortions by Tap Water Consumption Stratified by Water Company

| Water Company | OR(any vs. no cold home tap water) | 95% CI | p |
|---|---|---|---|
| Great Oaks Water Company | 3.9 | (1.5, 9.8) | 0.003 |
| San Jose Water Company | 2.2[a] | (0.6, 8.3) | 0.18 |
| City of Santa Clara | 8.8[a] | (0.5, 150.9) | 0.04 |
| $OR_{MH}$ | 4.1 | | < 0.001 |

Homogeneity chi square: p=0.50

[a] OR adjusted for small sample size

Table 3.6

Spontaneous Abortion Rates by Tap Water and Bottled Water Consumption

| Cold Home Tap Water (glasses/day) | Bottled Water: None | Not Usually | Usually | TOTAL | OR (any bottled vs. none) |
|---|---|---|---|---|---|
| 0 | 10.0% ( 10)[a] | 0.0% (13) | 3.2% (188) | 3.3% (211) | 0.2[b] |
| 1 | 7.9% ( 38) | 0.0% (10) | 12.5% ( 48) | 9.4% ( 96) | 1.3[b] |
| 2+ | 15.2% (460) | 4.8% (62) | 7.2% (152) | 12.5% (674) | 0.4 |
| TOTAL | 14.6% (508) | 3.5% ( 85) | 5.9% (388) | 10.2% (981) | 0.4 |
| OR (any vs. no home tap water) | 1.1[b] | 1.4[b] | 2.8 | 4.0 | |

$OR_{MH}$ (any vs. no home tap water)
(controlling for bottled water) = 2.65 p= 0.02
Homogeneity chi square p= 0.92

$OR_{MH}$ (any vs. no bottled water)
(controlling for tap water) = 0.45 p= .003
Homogeneity chi square p = 0.43

[a] (Number of pregnancies in parenthesis)
[b] Small sample adjustm nt



SL 032960

Table 3.7

Odds Ratios for Spontaneous Abortions
by Tap Water and Bottled Water Consumption
by Pathology Confirmation Status

| | OR | 95% CI | p |
|---|---|---|---|
| Included in Analysis: Pathology confirmed (n=47) | | | |
| Any vs. No Cold Home Tap Water | 2.5 | (1.0, 6.3) | 0.05 |
| Any vs. No Bottled Water at Home or Work | 0.5 | (0.3, 0.9) | 0.02 |
| Pathology not confirmed (n=44) | | | |
| Any vs. No Cold Home Tap Water | 5.0[a] | (1.2, 20.8) | 0.005 |
| Any vs. No Bottled Water at Home or Work | 0.2 | (0.1, 0.5) | < 0.001 |

[a] Small sample adjustment

Table 3.8

Odds Ratios for Reported Spontaneous Abortions
Designated "Not Validatable" or "Possible" on Validation
by Tap Water and Bottled Water Consumption

| | OR | 95% CI | p |
|---|---|---|---|
| Any vs. No Cold Home Tap Water | 3.6 | (0.5, 27.8) | 0.19 |
| Any vs. No Bottled Water at Home or Work | 0.3 | (0.1, 1.0) | 0.05 |

Table 3.9

Spontaneous Abortion Rates by Bottled Water Consumption by Year

| Year | Women Drinking Any Bottled Water | Spontaneous Abortion Rate: Bottled Water | | Spontaneous Abortion Rate: No Bottled Water | | OR |
|---|---|---|---|---|---|---|
| 1980 | 19.7% | 0.0% | (28)[a] | 5.3% | (114) | 0.3[b] |
| 1981 | 34.9% | 5.3% | (60) | 17.0% | (112) | 0.3[b] |
| 1982 | 47.1% | 3.9% | (80) | 12.2% | (90) | 0.3[b] |
| 1983 | 51.6% | 3.0% | (100) | 13.8% | (94) | 0.2[b] |
| 1984 | 64.3% | 7.8% | (166) | 21.7% | (92) | 0.3 |

[a] (Number of pregnancies in parenthesis)

[b] OR adjusted for small sample size

SL 032963

Table 3.10

Spontaneous Abortion Rates by Tap Water Consumption by Year

| Year | Women Drinking No Cold Tap Water at Home or Work | Spontaneous Abortion Rate | | OR[b] |
|---|---|---|---|---|
| | | No Tap Water | Some Tap Water | |
| 1980 | 5.8% | 0.0% ( 8)[a] | 4.6% (130) | 0.9 |
| 1981 | 9.4% | 6.3% (16) | 13.6% (154) | 1.7 |
| 1982 | 12.6% | 0.0% (21) | 9.0% (145) | 4.4 |
| 1983 | 16.5% | 6.3% (32) | 8.6% (162) | 1.2 |
| 1984 | 23.7% | 3.3% (60) | 15.5% (193) | 4.4 |

[a] (Number of pregnancies in parentheses)

[b] OR adjusted for small sample size

Table 3.11

Multiple Logistic Regression Analysis of Spontaneous Abortion

| Variable | OR | 95% CI | p |
|---|---|---|---|
| Any vs. no cold home tap water consumption[a] | 6.9 | (2.7, 17.7) | 0.0001 |
| Any vs. no nausea[a] | 0.4 | (0.3, 0.7) | 0.0009 |
| Any vs. no employment[a] | 1.0 | (0.6, 1.6) | 0.91 |
| Any vs. no fever[a] | 0.8 | (0.2, 3.0) | 0.80 |
| Maternal age | | | |
| ≤ 20 | 3.3 | (1.4, 10.0) | 0.001 |
| 21 - 34 | 1.0[b] | | |
| 35 + | 2.7 | (1.0, 6.7) | |
| Education | | | |
| ≤ 11 years | 1.0[b] | | 0.37 |
| 12 years (High School grad) | 0.9 | (0.3, 2.7) | |
| 13 - 15 years (some college) | 1.1 | (0.4, 3.2) | |
| ≥ 16 years (college grad or more) | 1.6 | (0.5, 4.9) | |
| Smoking[a] | | | |
| none | 1.0[b] | | 0.65 |
| ≤ 1/2 pack/day | 1.4 | (0.7, 2.8) | |
| 1 or more packs/day | 1.3 | (0.5, 3.4) | |
| Alcohol[a] | | | |
| none | 1.0[b] | | 0.53 |
| 1 - 4 drinks/wk | 1.0 | (0.6, 1.6) | |
| 4 + drinks/wk | 1.8 | (0.6, 5.3) | |

Table 3.11 (C ntinued)

| Variable | OR | 95% CI | p |
|---|---|---|---|
| Ethnicity | | | |
| White (non-Hispanic) | 1.0[b] | | 0.01 |
| Hispanic | 0.9 | (0.4, 2.0) | |
| Other | 0.2 | (0.0, 0.6) | |
| Prior spontaneous fetal loss | | | |
| none | 1.0[b] | | |
| 1 | 1.7 | (0.9, 3.0) | 0.07 |
| 2 or more | 2.4 | (1.0, 5.9) | |
| Water filter use around the beginning of pregnancy | 0.4 | (0.1, 1.5) | 0.19 |
| Census Tract | | | |
| Original Exposed (5120.12) | 1.0[b] | | 0.05 |
| New Exposed (5120.11) | 0.4 | (0.2, 0.8) | |
| Original Control (5120.08) | 0.5 | (0.3, 0.9) | |
| New Control (5053.0204) | 0.5 | (0.3, 1.0) | |
| Time Period | | | |
| 1980-81 | 1.0[b] | | 0.11 |
| 1982-85 | 1.5 | (0.9, 2.6) | |

[a] First trimester

[b] Referent group



SL 032966

Table 3.12

Spontaneous Abortion Rates by Total Liquid Consumption Minus Tap Water

| Liquid[a] (glasses/day) | N(pregnancies) | SAB Rate | 95% CI |
|---|---|---|---|
| 0 | 204 | 10.8% | (6.5, 15.1) |
| 1 | 127 | 7.1% | (2.6, 11.5) |
| 2 | 149 | 10.7% | (5.8, 15.7) |
| 3 | 115 | 11.3% | (5.5, 17.1) |
| 4 | 127 | 11.0% | (5.6, 16.5) |
| 5-6 | 134 | 9.7% | (4.7, 14.7) |
| 7+ | 145 | 9.0% | (4.3, 13.6) |
| TOTAL | 1001 | 10.0% | (8.1, 11.8) |

Homogeneity chi square $p = 0.92$

[a] Total liquids minus tap water at home and work.

Table 3.13

Reportable[a] Malformation Rates by Tap Water Consumption

| Cold Home Tap Water (glasses/day) | N(live births) | BD Rate | 95% CI |
|---|---|---|---|
| 0 | 263 | 0.4% | (0.0, 1.1) |
| 1 | 120 | 5.0% | (1.1, 8.9) |
| 2 | 181 | 3.9% | (1.1, 6.7) |
| 3 | 178 | 2.8% | (0.4, 5.2) |
| 4 | 154 | 3.3% | (0.4, 6.0) |
| 5 | 91 | 4.4% | (0.2, 8.6) |
| 6 | 71 | 2.8% | (0.0, 6.6) |
| 7+ | 113 | 6.2% | (1.8, 10.6) |
| TOTAL | 1171 | 3.1% | (2.1, 4.1) |

[a] California Birth Defects Monitoring Program criteria

Table 3.14

Odds Ratios for Reportable Malformations by Tap Water Consumption by Water Company

| Water Company | Odds Ratio (any vs. no cold home tap water) | 95% CI | p |
|---|---|---|---|
| Great Oaks Water Company | 18.4[a] | (1.1, 303.4) | 0.003 |
| San Jose Water Company | 3.2[a] | (0.2, 56.1) | 0.23 |
| City of Santa Clara | 2.6 | (0.1, 50.1) | 0.28 |
| $OR_{MH}$ | 10.9 | | 0.001 |

Homogeneity chi square: p= 0.87

[a] OR adjusted for small sample size

Table 3.15

Odds Ratios for Birth Conditions Reported by Mother by Tap Water Consumption

| Category Of Reported Condition | OR (any vs. no cold home tap water) | 95% CI | p |
|---|---|---|---|
| Reportable malformation[a] | 22.0 | (1.3, 360.4) | 0.001 |
| Non-reportable anomaly | 1.3 | (0.5, 3.1) | 0.61 |
| Condition other than anomaly[b] | 1.2 | (0.6, 2.5) | 0.65 |

[a] California Birth Defects Monitoring Program criteria

[b] Includes jaundice, respiratory distress, etc.

Table 3.16

Malformation Rates by Tap and Bottled Water Consumption

<u>Bottled Water Use</u>

| Cold Home Tap Water (glasses/day) | None | Not Usually | Usually | TOTAL | OR (any vs. no bottled water) |
|---|---|---|---|---|---|
| 0 | 0.0% (13)[a] | 0.0% (14) | 0.0% (233) | 0.0% (260) | ------- |
| 1 | 10.0% (50) | 0.0% (15) | 2.0% (50) | 5.2% (115) | 0.2[b] |
| 2+ | 2.9% (516) | 8.1% (86) | 4.3% (185) | 3.8% (787) | 2.0[b] |
| TOTAL | 3.5% (579) | 6.1% (115) | 1.9% (468) | 3.3% (1162) | 0.8 |
| OR (any vs. no home tap water) | 1.0[b] | 2.3[b] | 19.5[b] | 21.9 | |

$OR_{MH}$ (any vs. home tap water controlling for bottled water): 6.00, p = 0.002

Homogeneity chi square: p= 1.00

$OR_{MH}$ (any vs. no bottled water controlling for tap water): 1.29, p = 0.42

Homogeneity chi square: p = 0.03

[a] (Number of live births in parenthesis)
[b] Small sample adjustment



SL 032971

Table 3.17

Rates of Low Birth Weight by Tap Water Consumption

| Cold Home Tap Water (glasses/day) | N(live births) | Low Birth Weight Rate | 95% CI |
|---|---|---|---|
| 0 | 198 | 3.5% | (1.7, 7.8) |
| 1 | 82 | 4.9% | (1.5, 12.1) |
| 2 | 145 | 3.5% | (0.92, 7.2) |
| 3 | 128 | 2.3% | (0.35, 6.2) |
| 4 | 127 | 3.2% | (0.83, 7.6) |
| 5 | 79 | 5.1% | (1.4, 12.3) |
| 6 | 49 | 4.1% | (2.3, 18.8) |
| 7 | 13 | 0.0% | (0.0, 19.9) |
| 8 | 43 | 2.3% | (0.57,15.4) |
| 9 | 24 | 0.0% | (0.0, 11.6) |
| TOTAL | 888 | 3.4% | (2.1, 4.3) |

Table 3.18

Odds Ratios for Low Birth Weight by Water Company

| Water Company | OR (Any vs. No Home Tap Water) | p |
|---|---|---|
| Great Oaks Water Company | 0.85 | 0.78 |
| San Jose Water Company | 0.90 | 0.90 |
| City of Santa Clara | 1.1 | 0.92 |
| $OR_{MH}$ | 0.90 | 0.81 |

Homogeneity chi square p=0.98

Table 3.19

Rates of Low Birth Weight by
Bottled Water Consumption

| Bottled Water Home or Work | N(live births) | Low Birth Weight Rate | 95% CI |
|---|---|---|---|
| None | 435 | 3.0% | (1.7, 5.0) |
| Not Usually | 81 | 0.0% | (0.0, 3.6) |
| Usually | 378 | 4.5% | (3.1, 7.7) |

Homogeneity chi square p=0.11

Table 3.20

Rates of Low Birth Weight by Tap and Bottled Water Use

Bottled Water Use (Home or Work)

| Cold Home Tap Water (glasses/day) | None | Not Usually | Usually | TOTAL | OR (any vs. no bottled water) |
|---|---|---|---|---|---|
| 0 | 0.0% ( 9)[a] | 0.0% ( 12) | 4.0% (177) | 3.5% (198) | 1.3 |
| 1 | 0.0% ( 31) | 0.0% ( 8) | 9.3% ( 43) | 4.9% ( 82) | 0.02 |
| 2+ | 3.3% (393) | 0.0% ( 59) | 3.9% (155) | 3.1% (607) | 1.2 |
| TOTAL | 3.0% (433) | 0.0% ( 79) | 4.5% (375) | 3.4% (887) | |
| OR (any vs. no tap water) | 0.28 | 0.19 | 1.3 | 0.94 | 0.81 |

$OR_{MH}$ (any vs. no tap water) controlling for bottled water: 1.4, p=0.53
Homogeneity chi square p=0.90

$OR_{MH}$ (any vs. no bottled water) controlling for tap water: 0.82, p=0.66
Homogeneity chi square p=0.40

[a](Number of live births in parenthesis)

Table 3.21

Factors Discriminating Tap from Bottled Water Drinkers[a]

| Variable | More likely to drink |
|---|---|
| Residence in Great Oaks Water Dist. | No tap |
| More recent pregnancy | No tap |
| Age 20-34 | No tap |
| Smoked during first trimester | No bottled |

Factors not discriminating tap from bottled water drinkers: ethnicity, history of fetal loss, education, alcohol, employment

[a]No tap water vs. no bottled water

Figure 3.1 Crude Spontaneous Abortion Rates By Tap Water Consumption

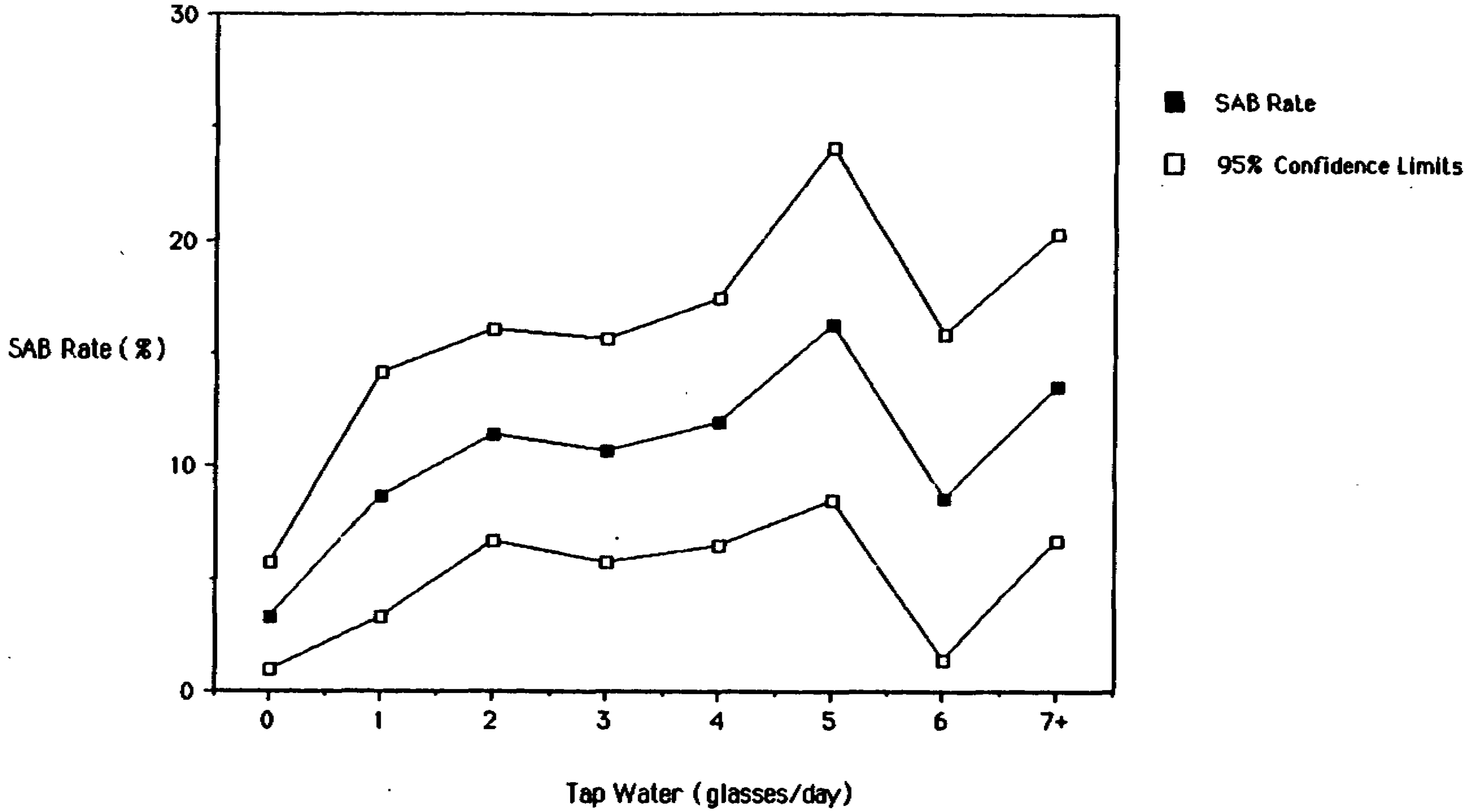


Figure 3.2 Smoothed Spontaneous Abortion Rates By Tap Water Consumption

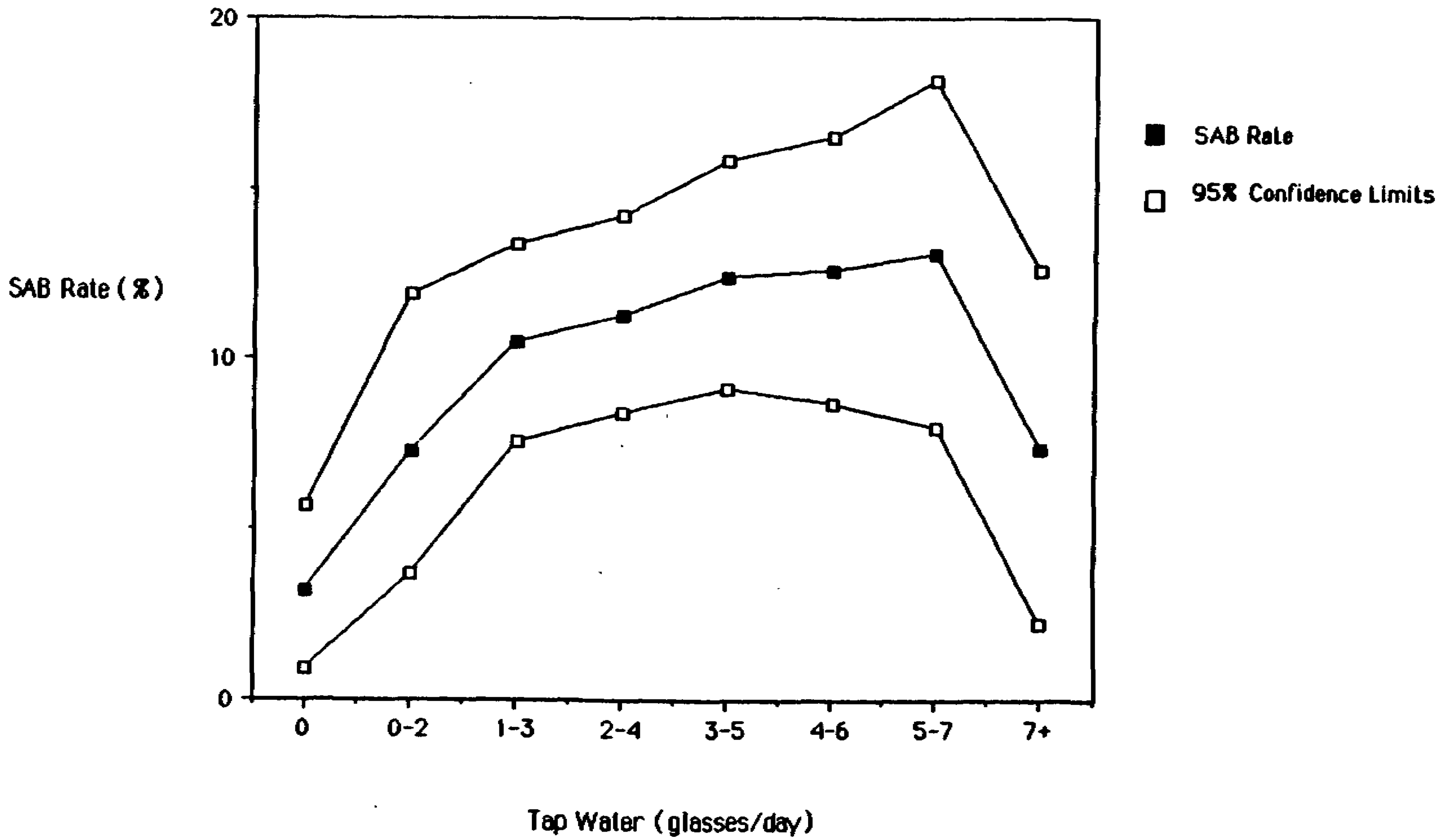
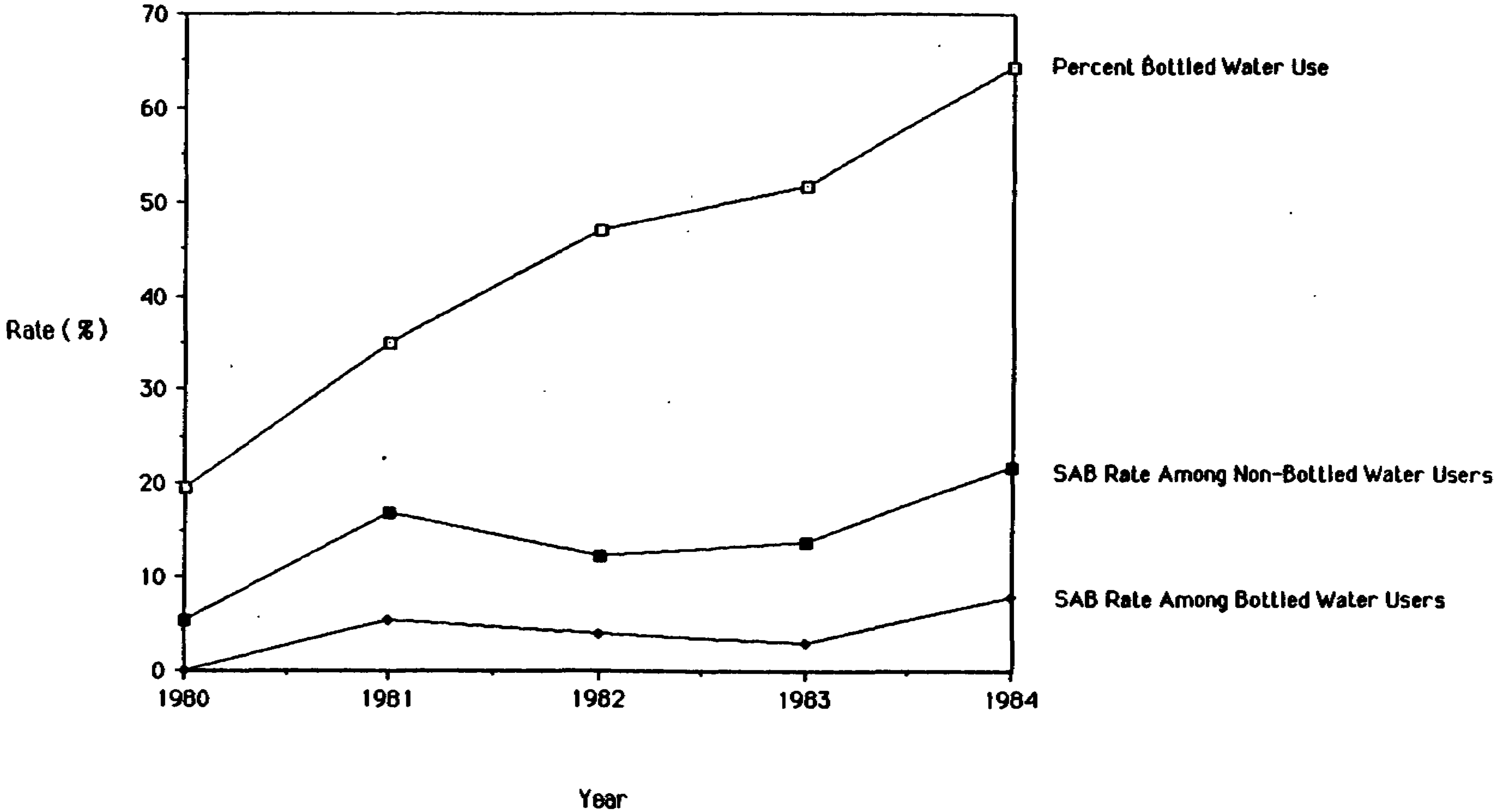


Figure 3.3 Spontaneous Abortion Rates By Bottled Water Use and Year



## Figure 3.4 Crude Birth Defect Rates By Tap Water Consumption

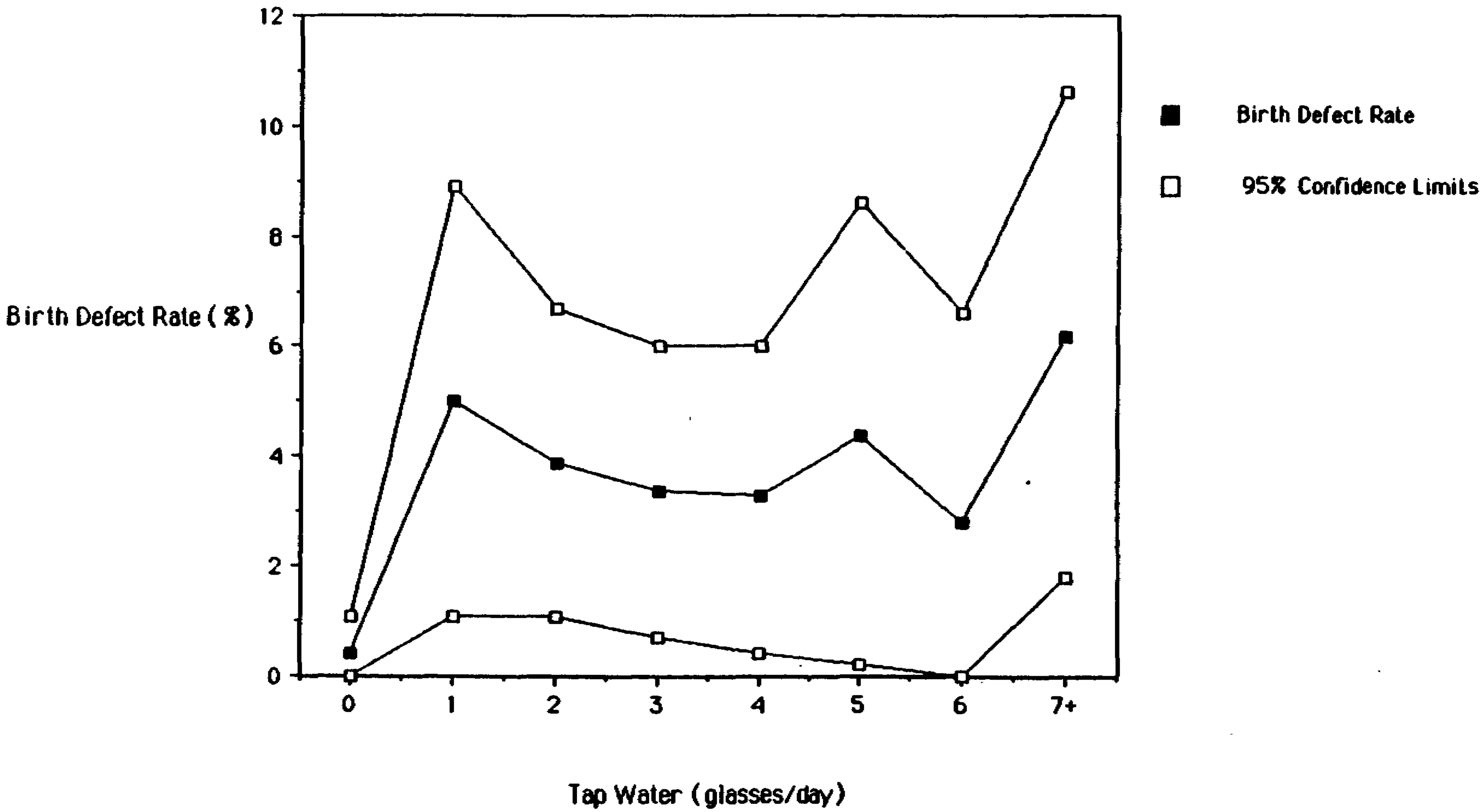
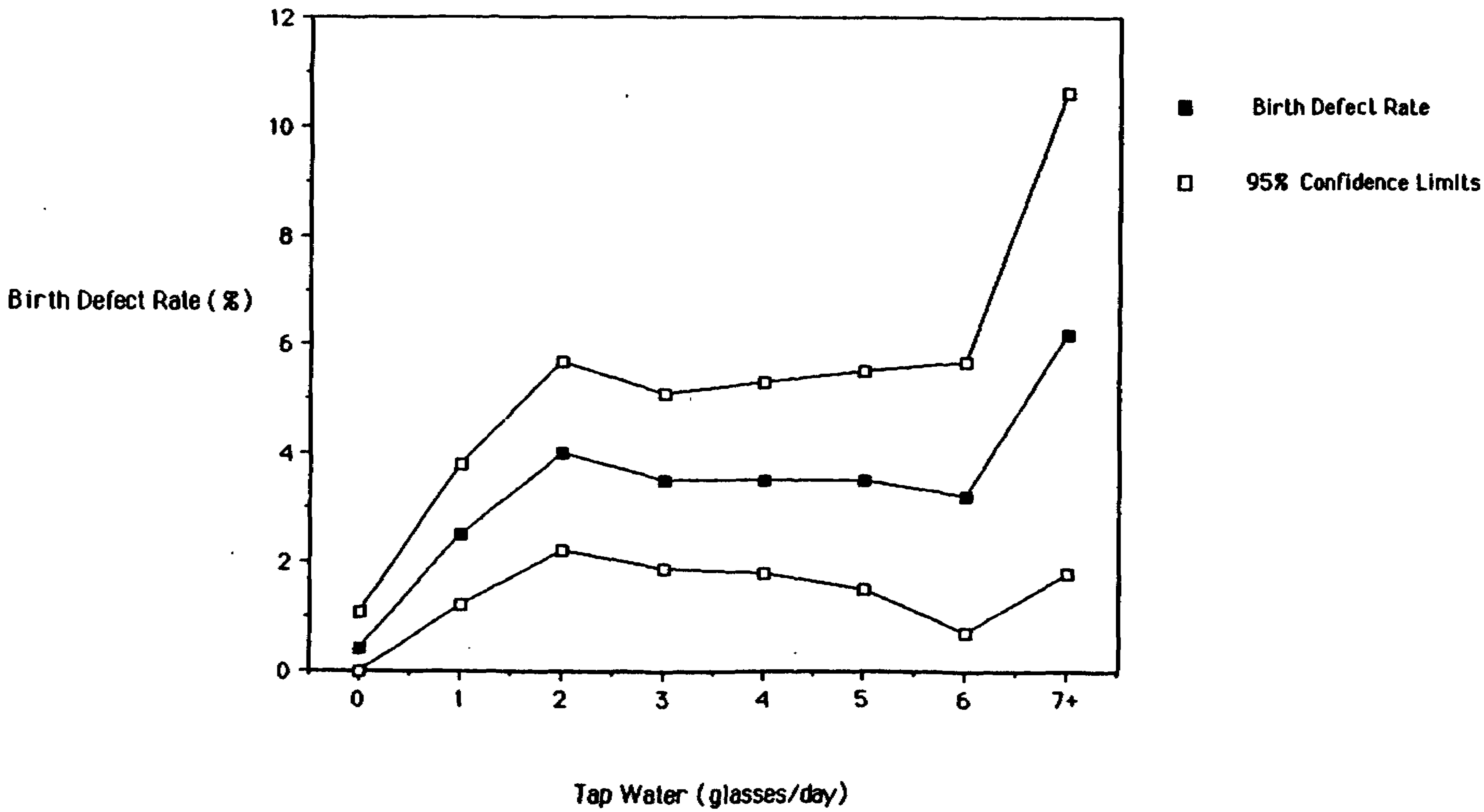


Figure 3.5 Smoothed Birth Defect Rates By Tap Water Consumption



## 4. Fairchild IIA and IIB

### Background

The reinterview of a sample of Fairchild II respondents was conducted for tw reasons. First, the establishment of the National Agency for Toxic Substances and Disease Registries raised the question of whether a study cohort would be willing to cooperate with long-term follow-up and surveillance. In order to address this question, a sample of women with adverse outcomes in Fairchild II as well as an equal number of randomly selected controls were reinterviewed. Second, since these respondents were contacted about their willingness to participate, it was decided to use the opportunity to ask them about frequency and duration of showering and bathing. These questions were asked in several of the other studies, but this issue had come to our attention too late to be included in Fairchild II.

Results from this first reinterview (Fairchild IIA) suggested an association between duration of showering and bathing and spontaneous abortion. Analyses of water-related data in our other studies raised several additional issues. These included the role of water filters (brand, location, type and frequency of service), exercise as a potential confounder, and attitudes and health-related behaviors which might help explain the observed associations. To address these issues, it was decided to reinterview all women with a validated spontaneous abortion or birth defect who had not already been reinterviewed in Fairchild IIA. This reinterview study was called Fairchild IIB.

### Methods

As described, an attempt was made to reinterview all women with at least ne validated adverse outcome from Fairchild II. Spontaneous abortions were identified from the complete Fairchild II data set before a random pregnancy had been selected for analysis. Once selected for reinterview, if a woman had more than one adverse outcome in the study period, one was selected at random to be the subject of the reinterview. A stratified sample of women with no adverse outcomes was also selected. Data from these interviews were merged with data from Fairchild II. The data set used for analysis (Fairchild II, IIA or IIB) varied with the question under study. In addition, responses to the more detailed questions on water consumption included in Fairchild IIB were compared to the less detailed ones from Fairchild II.

## Results

A total of 144 spontaneous abortions, 34 birth defects and 228 live births were included in the samples for these two substudies. The completion rates were quite similar (94.5% and 92.5%) and reflected the excellent participation from the Fairchild study population (Table 4.1). Results on water consumption and spontaneous abortion for Fairchild IIB were very similar to those for Fairchild II, even though Fairchild IIB used a more complex and detailed measure of tap water consumption. Using the Fairchild II tap water questions, the odds rati for spontaneous abortion and tap water consumption was 4.0 compared to 3.8 using the more detailed questions in Fairchild IIB. Therefore, in this section, results on tap and bottled water consumption will not be presented, except in relation to variables collected only in Fairchild IIA and IIB, since results on tap water consumption are presented in Section 3.

Results on spontaneous abortions and total minutes showering and bathing at home are contained and depicted in Table 4.2 and Figure 4.1. A slight trend of increasing risk of spontaneous abortion with duration can be seen among tap water drinkers. The numbers of non-tap water drinkers are too small to determine whether a similar trend is present in this group. The odds rati s for spontaneous abortion associated with amount of showering and bathing, for all women in this substudy (tap water drinkers and non-drinkers) are, to the first decimal place, identical to those for tap water drinkers alone.

In Fairchild IIB we also examined other sources of exposure to water through skin contact or inhalation. These exposures included showering and bathing regularly away from home, bathing others, washing dishes, using a jacuzzi or hot tub, and swimming. None of these exposures was very prevalent, and the results obtained after including them in a total exposure measure were very similar to those obtained using only showering and bathing. Therefore, in order to combine data from both Fairchild IIA and IIB, only duration of showering and bathing was used in these analyses. Duration of showering and bathing (less than 50 minutes per week vs. more than 50 minutes) was later dropped from the multipl 1 gistic regression model (p=0.19) (Table 4.6).

In Fairchild II, women were asked whether they used a filter connected at the tap or sink. Approximately 11% replied affirmatively. As discussed in Section 3, a positive response to this question showed a strong negative association with SAB. Risk of SAB among filter users was similar to the risk in bottled water drinkers, even among women consuming tap water. In Fairchild IIB a number of detailed questions were asked about filter use including location, brand, type, and frequency of servicing. These results are contained in Tables 4.3, 4.4A and 4.4B. Water softeners, most of which were connected in the garage or outside the house (and therefore not included, for the most part, in positive responses to the filter question in Fairchild II), did not appear to convey any protective effect. However, purifiers or other "active" filters did appear to protect, particularly if they were regularly serviced. Numbers were too small to distinguish between reverse osmosis, activated charcoal, or carbon devices.

In order to examine the role of bottled water and its apparently protective effect on spontaneous abortion, women were asked the brand of bottled water they usually drank. Numbers were small because this question was only asked of Fairchild IIB respondents, and the odds ratios were similar across categories (Table 4.5).

A multiple logistic regression analysis was carried out on the Fairchild IIB data set to examine the effect of the added variables (environmental concern, importance of nutrition, exercise, water filter use and multivitamin use) on the relationship between tap water, bottled water, showering and spontaneous abortion. These results are summarized in Table 4.6. For variables common to this analysis and that done for Fairchild II (Table 3.11) results were fairly consistent. In Fairchild IIB the adjusted odds ratio for any cold tap water use was 7.4, compared to 6.9 for Fairchild II. In both analyses, absence of water filter use was associated with greater risk of spontaneous abortion. However, in Fairchild IIB type of water filter was analyzed, and as noted above, only "active" filters showed this relationship. Although maternal age less than 20 or over 35, as well as nausea and smoking, were not retained in the model f r

Fairchild IIB, their coefficients in this analysis were similar to those seen for Fairchild II. In both analyses women of non-White, non-Hispanic ethnicity were at reduced risk of SAB and prior fetal loss was associated with increased risk. In addition, in Fairchild IIB both environmental concern and multivitamin use were examined in relation to risk of SAB. The first was almost equally distributed among women with SAB and normal live births (Table 4.7) while the second was more common among women with live births.

The apparently protective effect of multivitamin use is interesting. It is largely explained by the fact that SABs tend to occur before a woman has th opportunity to begin routine prenatal care and multivitamin use. This can be seen in Table 4.8, where frequency of multivitamin use is shown by length of pregnancy.

Data on exercise and spontaneous abortion appear in Table 4.9. No consistent pattern is seen either overall or when women are stratified on prior fetal loss which might result in limited exercise in subsequent pregnancies.

Unlike spontaneous abortion, no dose-response relationship was seen between duration of showering and bathing and birth defects (Figure 4.2). However, numbers were small and the odds ratios were somewhat elevated for each category over 50 minutes per week (Table 4.10). The effect of filter use on birth defect risk among those drinking tap water is shown in Table 4.11. There is an increased risk of birth defects among the non-filter users (OR=2.8) as compared to the users of any type of filter or softener although the 95% confidence interval is very wide. Numbers were not sufficient to separate types of filters.

No protective effect was seen (OR=1.0) with respect to bottled water consumption and birth defects in this study. This was also examined by brand of bottled water, although numbers were very small (Table 4.12).

In summary, the data from Fairchild IIB are consistent with those from Fairchild II, whenever comparisons are possible. In addition, data from Fairchild IIB suggest that "active" filters, rather than softeners, may be effective in modifying the risk associated with tap water consumption. A modest dose response between SAB and duration of showering and bathing was seen, although this term was not retained as significant in the multiple logistic regression. Possible confounding by exercise, nutritional supplementation and attitudes were also examined and did not explain the associations observed in Fairchild I and II.

Table 4.1

Fairchild IIA and IIB Interview Completion Rates by Pregnancy Outcome

| Fairchild Study | Spontaneous Abortions: Sampled | Spontaneous Abortions: Interviewed | Birth Defects: Sampled | Birth Defects: Interviewed | Live Births: Sampled | Live Births: Interviewed |
|---|---|---|---|---|---|---|
| IIA | 47 | 40 (85.1%) | 5 | 5 (100.0%) | 147 | 143 (97.3%) |
| IIB | 97 | 88 (90.7%) | 29 | 26 ( 89.7%) | 141 | 133 (94.3%) |
| IIA and B | 144 | 128 (88.9%) | 34 | 31 ( 91.2%) | 288 | 276 (95.8%) |
| II | | 211[a] | | 38[b] | | 856[c] |

[a] Total number of definite SABs (including multiple pregnancies per woman)

[b] Total number of reportable birth defects

[c] Total women interviewed without an SAB or birth defect

Table 4.2

Odds Ratios for Spontaneous Abortion by Duration of Showering and Bathing and Tap Water Consumption

Tap Water Consumption[a]

| Duration of Showering and Bathing (min/wk) | Any | | | | | None | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N(SAB) | N(LB) | OR | 95% CI | p | N(SAB) | N(LB) | OR | 95% CI | p |
| 1 ss than 50 | 12 | 49 | 1.0[b] | — | — | 1 | 15 | 1.0[b] | — | — |
| 50- 99 | 42 | 76 | 2.3 | (1.1, 4.7) | 0.03 | 6 | 23 | 3.9 | (0.43, 35.8) | 0.39 |
| 100-149 | 39 | 52 | 3.1 | (1.4, 6.5) | 0.003 | 1 | 12 | 1.3 | (0.07, 22.1) | 1.00 |
| 150+ | 20 | 23 | 3.6 | (1.5, 8.5) | 0.004 | 0 | 4 | 0.0 | — | 1.00 |

[a] Cold tap water at home

[b] Referent group

Table 4.3

Spontaneous Abortions vs. Live Births by
Tap Water Consumption and Water Filter Use

| | Tap Water Consumption[a] | | | |
|---|---|---|---|---|
| | Any | | None | |
| Water Filter Type | N(SAB) | N(LB) | N(SAB) | N(LB) |
| Active[b] and serviced regularly | 0 | 7 | 0 | 1 |
| Softener | 7 | 12 | 0 | 0 |
| Not serviced and/or unknown type | 2 | 2 | 0 | 0 |
| No water filter | 74 | 83 | 3 | 27 |
| TOTAL | 83 | 104 | 3 | 28 |

[a] Includes hot or cold tap water at home.

[b] Reverse osmosis, activated charcoal, or carbon.

Table 4.4A

Comparison of Responses To Questions On Water Filter Use in Fairchild II & IIB[a]

| Fairchild II Filter Use | Fairchild IIB: Softeners | Fairchild IIB: Filters and Purifiers | Fairchild IIB: None |
|---|---|---|---|
| yes | 3 (15.8%) | 9 (60.0%) | 5 ( 2.4%) |
| no | 16 (84.2%) | 6 (40.0%) | 206 (97.6%) |
| Total | 19 | 15 | 211 |

Table 4.4B

Location of Softeners, Filters and Purifiers

| | Softeners | Filters | Purifiers (unknown type) |
|---|---|---|---|
| Tap | 1 | 6 | 0 |
| Under sink | 0 | 5 | 1 |
| Refrigerator | 0 | 1 | 1 |
| Garage/outside house | 18 | 0 | 1 |
| Total | 19 | 12 | 3 |

[a] Women in Fairchild II were asked whether they had a filter connected at sink r tap. In Fairchild IIB women were asked about filter use anywhere, including type and location.

Table 4.5

Odds Ratios for Spontaneous Abortion by Bottled Water Consumption and Brand Name

| | N(SAB) | N(LB) | OR | 95% CI | p |
|---|---|---|---|---|---|
| Alhambra | 7 | 15 | 0.52 | (0.20, 1.3) | 0.17 |
| Other bottled water | 4 | 21 | 0.21 | (0.07, 0.65) | 0.004 |
| Miscellaneous[a] bottled water | 10 | 23 | 0.48 | (0.21, 1.1) | 0.08 |
| No bottled water | 65 | 72 | 1.0[b] | --- | --- |

[a] Includes women who drank (1) bottled water of unknown brand or (2) Alhambra and another known or unknown brand.

[b] Referent group

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Table 4.6

Variables Associated with Risk of Spontaneous Abortion in Multiple Logistic Regression Analysis

| Variable | OR | p |
|---|---|---|
| Any vs. no cold home tap water consumption | 7.4 | 0.0004 |
| Ethnicity | | |
| White (non-Hispanic) | 1.0[a] | |
| Hispanic | 1.1 | 0.88 |
| Other | 0.09 | 0.005 |
| Prior spontaneous fetal loss | | |
| none | 1.0[a] | |
| 1 | 2.6 | 0.09 |
| 2 or more | 8.2 | 0.01 |
| Active water filter[b] use | 0.007 | 0.77 |
| High environmental concern | 3.1 | 0.02 |
| Multivitamin use | 0.26 | 0.01 |

[a] Referent group

[b] Reverse osmosis, activated charcoal, or carbon

Table 4.7

Odds Ratios for Spontaneous Abortion
by Tap Water Consumption and Environmental Concern

| Environmental Concern | N(SAB) | N(LB) | OR (any vs. no tap) | 95% CI |
|---|---|---|---|---|
| High | 57 | 79 | 4.4 | (1.7, 11.6) |
| Low | 26 | 51 | 4.5 | (0.95, 21.8) |
| TOTAL[a] | 83 | 130 | 4.3 | (1.9, 9.8) |

[a]Total does not include SABs and LBs with missing data on environmental concern or tap water consumption.



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Table 4.8

Multivitamin Use by Pregnancy Outcome and Length of Pregnancy

| Outcome (N) | % Multivitamin Use |
|---|---|
| Spontaneous abortion (86) | 61.6 |
| month 1 (10) | 20.0 |
| month 2 (35) | 60.0 |
| months 3-5 (41) | 73.2 |
| Birth defect (26) | 65.4 |
| Live birth (131) | 76.3 |
| TOTAL (243) | 70.0 |

Table 4.9

Odds Ratios for Spontaneous Abortion by Exercise and Prior Fetal Loss

| | Prior Fetal Loss | | | | | | |
|---|---|---|---|---|---|---|---|
| | Any | | | None | | | All |
| Exercise (min/wk) | OR | N(SAB) | 95% CI | OR | N(SAB) | 95% CI | OR |
| 0 | 1.0[a] | 13 | --- | 1.0[a] | 24 | --- | 1.0[a] |
| 1- 29 | --- | 1 | --- | 1.1 | 1 | (0.09, 12.3) | 1.5 |
| 30- 59 | --- | 0 | --- | 1.3 | 3 | (0.28, 5.8) | 0.4 |
| 60- 89 | 1.8 | 4 | (0.17, 20.3) | 0.65 | 4 | (0.19, 2.2) | 0.9 |
| 90-119 | 2.3 | 5 | (0.22, 24.3) | 1.5 | 7 | (0.51, 4.4) | 1.7 |
| 120+ | 0.35 | 3 | (0.06, 2.1) | 1.3 | 20 | (0.63, 2.8) | 1.0 |

[a] Referent group

Table 4.10

Odds Ratios for Birth Defects by Duration of Showering and Bathing and Tap Water Consumption

Tap Water Consumption[a]

| Duration of Showering and Bathing (min/wk) | Any | | | | | None | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N(BD) | N(LB) | OR | 95% CI | p | N(BD) | N(LB) | OR | 95% CI | p |
| less than 50 | 5 | 49 | 1.0[b] | --- | --- | 0 | 15 | 1.0[b] | --- | --- |
| 50- 99 | 13 | 76 | 1.7 | (0.56, 5.0) | 0.44 | 0 | 23 | --- | --- | --- |
| 100-149 | 8 | 52 | 1.5 | (0.46, 4.9) | 0.57 | 0 | 12 | --- | --- | --- |
| 150+ | 5 | 23 | 2.1 | (0.56, 8.1) | 0.30 | 0 | 4 | --- | --- | --- |

[a]Cold tap water at home

[b]Referent group

Table 4.11

Birth Defects vs. Live Births by Tap Water
Consumption and Water Filter Use

| | Drank Tap Water[a] | | Drank No Tap Water | |
|---|---|---|---|---|
| Water Filter | N(BD) | N(LB) | N(BD) | N(LB) |
| Active[b] and serviced regularly | 1 | 7 | 1 | 1 |
| Softener | 0 | 12 | 0 | 0 |
| Not serviced and/or unknown type | 1 | 2 | 0 | 0 |
| No water filter | 22 | 83 | 1 | 27 |
| TOTAL | 24 | 104 | 2 | 28 |

[a] Includes hot or cold tap water at home.

[b] Reverse osmosis, activated charcoal, or carbon.

Table 4.12

Odds Ratios for Birth Defects by
Bottled Water Consumption and Brand Name

| | N(BD) | N(LB) | OR | 95% CI | p |
|---|---|---|---|---|---|
| Alhambra | 5 | 15 | 1.7 | (0.54, 5.5) | 0.35 |
| Other bottled water | 2 | 21 | 0.49 | (0.10, 2.3) | 0.52 |
| Miscellaneous bottled water [a] | 4 | 23 | 0.89 | (0.27, 3.0) | 1.0 |
| No bottled water | 14 | 72 | 1.0[b] | --- | --- |

[a] Includes women who drank (1) bottled water of unknown brand or (2) Alhambra and another known or unknown brand.

[b] Referent group

**Figure 4.1 Odds Ratios For Spontaneous Abortions By Duration Of Showering and Bathing Among Tap Water Consumers**

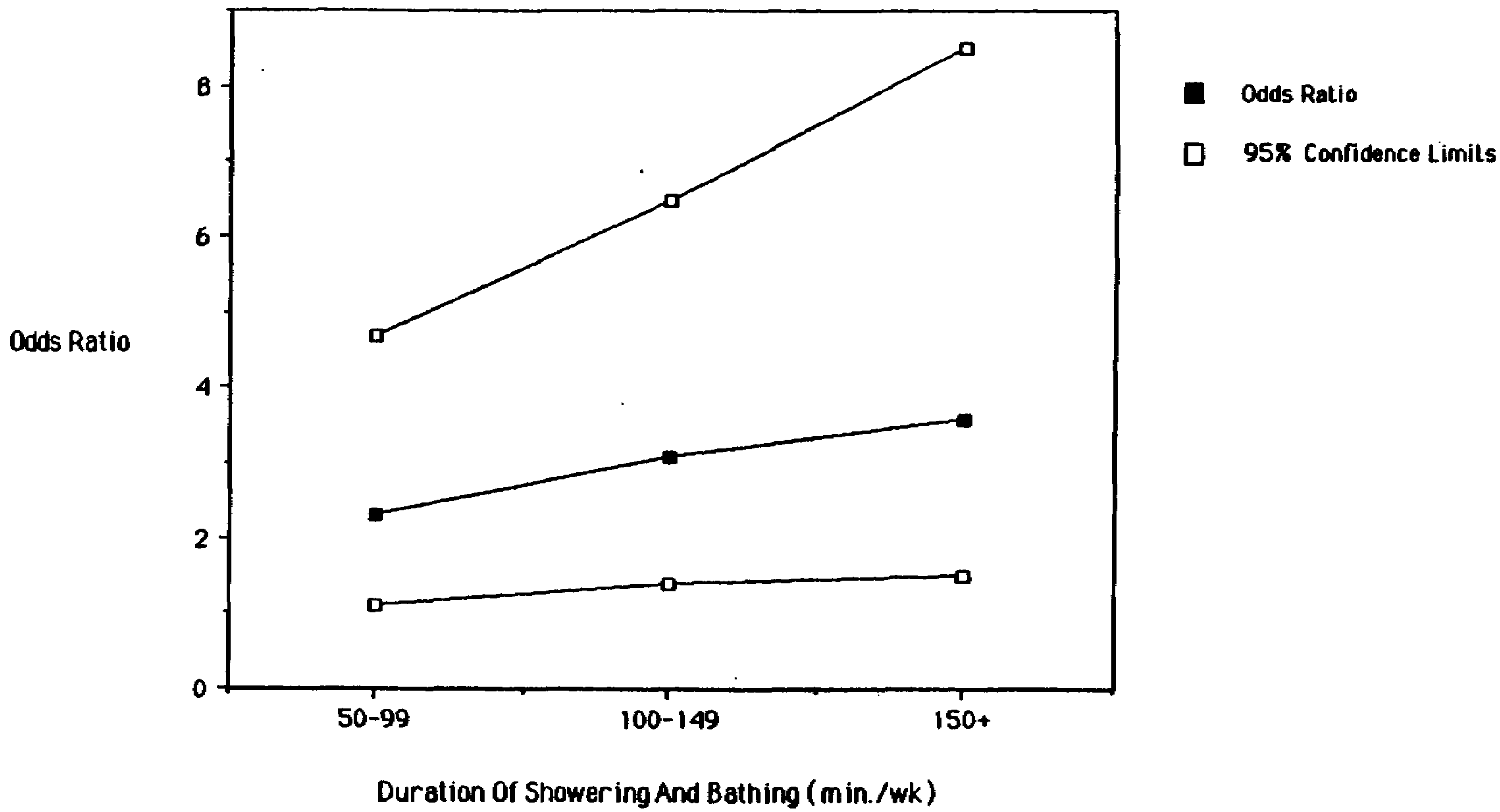
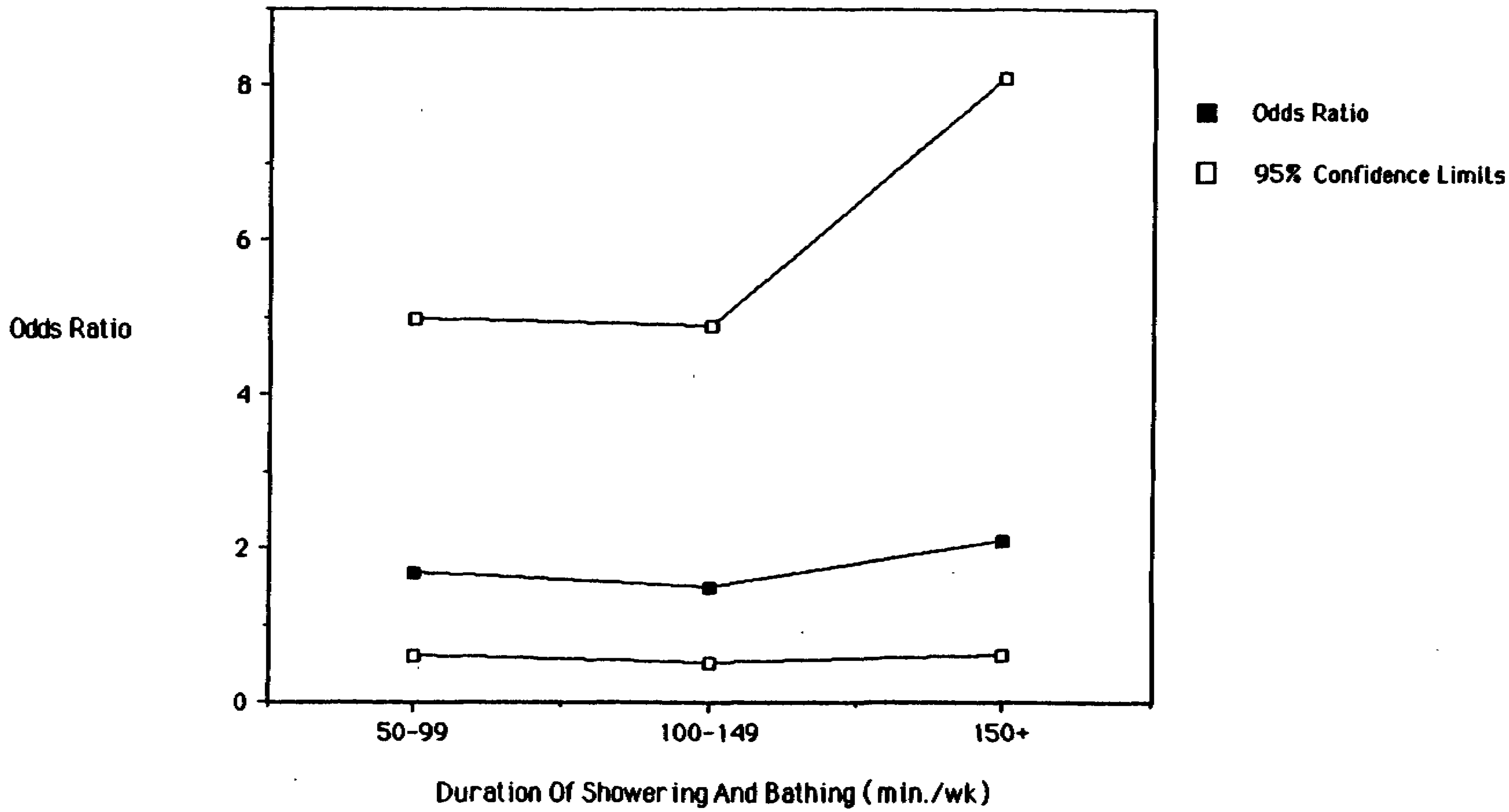


**Figure 4.2 Odds Ratios For Birth Defects By Duration Of Showering And Bathing Among Tap Water Consumers**



## 5. Malathion Study

### A. Background

The data for this investigation were originally collected by the Department of Medical Methods Research of Kaiser Permanente to study the relationship between aerial spraying of Malathion and adverse pregnancy outcomes. The pesticide Malathion was used to eradicate an infestation of the Mediterranean fruit fly in areas of Northern California in 1981-1982. A secondary aim of the study was to examine the relationship between adverse pregnancy outcomes and consumption of tap water.

The study was designed cooperatively by the State of California and Kaiser Permanente; identification of cohort and initial data collection were conducted under the direction of Dr. Diana Petitti. Data linkage, chart reviews, and clean-up of medical and demographic data were undertaken by Ms. Marilyn Goldhaber, also of Kaiser Permanente. The analysis of Malathion exposures was completed by Dr. Duncan Thomas of the University of Southern California, and will be reported separately. Clean-up of residential data was accomplished by Mr. Ed Rappaport, of Dr. Thomas's staff.

The study used a nested case-control design, i.e., cases and controls w re sampled from a cohort of recognized pregnancies. Pregnancies were identified retrospectively at three Kaiser-Permanente Medical Care facilities in Hayward, Santa Clara and Redwood City, based on a pregnancy confirmation visit (at all facilities) or positive pregnancy tests (at Redwood City and Santa Clara only) between September 1, 1981 and June 30, 1982. Elective abortions were excluded from the study. "Cases" were comprised of all ectopic pregnancies, spontaneous abortions, stillbirths, congenital malformations, intrauterine growth retarded infants and neonatal deaths. For precise definitions, see Appendix A. The cases were identified from birth logs, hospital discharge files, medical charts, state birth and fetal death files, and chromosome laboratory data (for anomalies). Congenital malformations were verified by medical abstractors from the

California Birth Defects Monitoring Program. "Controls" were selected by a random systematic (1 in 5) sample from the noncases.

In the analyses described below, neonatal deaths, intrauterine growth retarded infants, and nonreportable anomalies were included in the live births category. This was because: full ascertainment of neonatal deaths using state vital records was never completed; the nonreportable anomalies represented a broad range of conditions including some trivial ones; the small number of intrauterine growth retarded infants showed no association with the water consumption variables and there was no *a priori* reason t pursue analysis of this outcome. The 40 ectopic pregnancies were excluded from further analysis since an ectopic pregnancy is not at risk for any other outcome. The remaining 1893 respondents were comprised of: 474 spontaneous abortions, 144 reportable anomalies, 26 stillbirths, and 1249 live births.

B. Data Collection

Those selected for the case-control study were mailed a questionnaire. After three mailings, telephone interviews were attempted with nonrespondents and with respondents whose questionnaires were incomplete. An 87% response rate was achieved. Table 5.1 summarizes the distribution of outcomes (i) in the original cohort, (ii) among those selected for the case-control study, and (iii) among the respondents to the questionnaire. Twin births and mothers under the age of 18 were excluded.

All mailings and telephone interviews took place between July, 1984 and February, 1985, about two years after the termination of the pregnancies. The mother was asked whether she drank tap water and whether she drank bottled water during the first trimester of her pregnancy. The interview also included questions on other potentially confounding factors such as smoking, alcohol, employment, concern over environmental issues, education and consumption of selected beverages (coffee, tea, soft drinks). The woman's reproductive history was evaluated from her medical chart, including date of last menstrual period (LMP), date of pregnancy termination, mother's age at time of LMP, and numbers of previous pregnancies, live births, miscarriages, elective abortions, etc. Two variables were taken from th



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birth or fetal death certificate: birthweight and gestational age at delivery.

Each woman was also asked to supply a residential history covering the period July 1, 1981 to June 30, 1982 (for the purpose of determining cumulative exposure to Malathion). After the initial analysis of tap water consumption revealed an association with spontaneous abortion in this study and in Fairchild II, the residential data were linked to information on source of water. This linkage involved (1) identifying the address at which the mother resided during the bulk of her first trimester, (2) determining what water company served each residential area, and (3) classifying each water company as to whether it drew from ground water only, surface water only, or a combination of the two (designated "mixed").

C. Methods of Analysis

Spontaneous abortions (SABs) were examined in relation to consumption of tap water as opposed to bottled water. SABs included all involuntary losses up to week 28 from the last menstrual period (LMP) for which no fetal death certificate was filed, and which were not identified as an ectopic pregnancy. Two approaches were taken to the analysis of SABs, corresponding to two aspects of the study design. The first was based on the case-control design: SABs as a group were compared to live births (LBs) without anomalies and the odds ratio (OR) represented the measure of effect. Univariate methods, i.e., stratification, were applied in this analysis to adjust for covariates one-by-one.

For the second approach, each SAB was compared only to those pregnancies under observation at the time of the "failure" (SAB). When time is measured in prespecified intervals, this analysis draws on the fetal lifetable (2, 3, 4). The risk of failing in each time interval is based on examining only those pregnancies which were in the "risk set," i.e., under observation during that interval. As an example, Figure 5.1 depicts the construction of risk sets for three intervals of the lifetable, using a hypothetical cohort of four pregnancies. In week 5, pregnancy #2 contributes a partial week of observation to the risk set, and there are no failures in this week. Week 6 has a complete week of observation from pregnancy #2 and a partial week from pregnancy #1, and again, no failures. In week 7, there are 3 partial weeks and 1 full week of observation, and two failures. Since the two determinants of whether a pregnancy belonged to a given risk set were the time (gestational age) of entry into the study and the time of outcome (birth, spontaneous abortion or stillbirth), women who later miscarried were potential members of the risk set for earlier SABs.

Risk sets were constructed for each week of gestation. Because the full cohort was not used, i.e., covariate information had been collected for only those in the case-control study, individuals and their person-days of observation were weighted using the known sampling fractions for each outcome.

For each interval, the hazard of failing was estimated as: (number of failures) / (person-time at risk). Person-time within each interval was measured in days. For each interval, the conditional probability of failing given survival to that interval, $P(f_i)$, is derived under the assumption that those pregnancies under observation at any point in time are representative of all pregnancies which have survived to that gestational age. To counter potential bias in sparse intervals when subset analyses were being performed, the conditional failure probability was assumed to be exponential rather than linear. Mathematical details are contained in Appendix B. Analogous calculations are made for the hazard and conditional probability of a live birth, $P(\ell_i)$. The conditional probability of "surviving" each interval (i.e., neither failing nor delivering a live birth) is $[1 - P(f_i) - P(\ell_i)]$. Finally, the unconditional probability of failure in each interval is the probability of surviving every previous interval, multiplied by the conditional probability of failure during the interval in question. The cumulative lifetable risk of SAB is the sum of the unconditional failure probabilities over all intervals. Computer programs necessary for these analyses were written in Fortran by one of the investigators (Hertz-Picciotto) and are available on request.

Lifetable risks can be calculated for any specified set of intervals in the gestational period; we have chosen weeks 5 to 20 of gestation because the data are extremely sparse before week 5, and because SABs and stillbirths overlap after week 20 but may differ etiologically. Cumulative risks of SAB have been calculated for different exposure groups and compared. The lifetable thus allows a stratified analysis which incorporates differential entry times.

The use of exact days at risk for estimating the hazard was advocated by Taylor (3). However, other researchers have adopted an approximation which counts women entering or exiting an interval measured in weeks as contributing, on average, 1/2 the interval in person-time (2, 5, 6). For most intervals, we found this approximation to be adequate. It tends t overestimate time at risk, and hence underestimates risk of failure in the early weeks (and "risk" of live birth in the very late weeks), particularly in subset analyses. For most analyses in this data set, the cumulative risk of failure is underestimated by an absolute difference of under 1%, or ab ut a factor of 10% because of this approximation.

As in any stratified analysis, the data become thin in subset analyses. Therefore, to incorporate information on who was at risk as well as simultaneously adjust for multiple potential confounders, a modeling approach was required. The Cox proportional hazards model with time-dependent risk sets, appropriate for accomplishing both, was therefore fitted to these data.

Under this model, the hazard ratio is assumed to be constant over time, comparing those with a risk factor or exposure to those without it. The log of the hazard ratio is expressed as a linear function of the variables in the model. Letting t represent time, the hazard of failure is:

$$\lambda(t) = \lim_{\Delta \to 0} P(\text{failure in } (t, t+\Delta) \mid \text{survival to } t) \;/\; \Delta$$

Thus, the hazard represents the instantaneous conditional risk. For discrete time units, it is approximated by the conditional risk divided by the time unit. The proportional hazards model assumes that the hazard ratio comparing those with a set of risk factors to those without, is constant over time. Mathematically, this proportional hazard assumption is expressed as:

$$\lambda_1(t) = \lambda_0(t) \cdot \exp\left(\sum^{n} \beta_i x_i\right)$$

where subscript ($_1$) represents presence of a risk factor or exposure, ($_0$) represents absence, the $x_i$ are the values of the n covariates, and the $\beta_i$ are the corresponding unknown coefficients.

This model is the time-dependent, cohort analog of logistic regression; that is, in logistic regression the natural logarithm of the odds ratio comparing two groups with covariate vectors $\tilde{x}_1$, and $\tilde{x}_0$ is :

$$\ln OR = \sum_i^n \beta_i \cdot (x_{1_i} - x_{0_i}).$$

Similarly, in Cox regression the natural logarithm of the hazard ratio (HR) comparing the two groups is:

$$\ln HR = \sum_i^n \beta_i \cdot (x_{1_i} - x_{0_i}).$$

The coefficient ($\beta_i$) of each variable represents the relative increase (on a log scale) in risk at any point in time, comparing those with the risk factor to those at baseline for that risk factor. The hazard ratio for indicator variables such as geographic or water source variables is found by exponentiating the coefficient, i.e., HR = $\exp(\beta_i)$, and generally represents, to a very close approximation, the risk ratio at any point in time. The coefficients are estimated using iterative methods for maximizing the partial likelihood. The likelihood is constructed using the rank order of events rather than the absolute failure times (7). The Cox model was fitted using BMDP-2L following the adaptation described in a technical report (8).

An analysis of congenital malformations is also presented, though a full consideration of potential confounders and specific classes of malformations was not conducted. In general, however, the low probability of tap water abstention combined with the rarity of this outcome resulted in (i) low power and (ii) greater sensitivity of the measure of association to misclassification.

## D. Results of Spontaneous Abortion Analyses Using Case-Control Design

For the case-control analysis of SABs, the control group was chosen to include all pregnancies ending in a live birth except those resulting in reportable anomalies. Table 5.2 shows the distribution of SABs and these LBs according to whether the mother drank only tap water, both tap and bottled water, or no tap water during the first trimester of the pregnancy. The crude odds ratio (OR) for having consumed any vs. no tap water, comparing SABs to LBs, was 2.0 with a 95% confidence interval of (1.1, 3.7). Because of the small number of women drinking no tap water, the OR was also calculated comparing those who drank all or mostly tap water vs. those who drank all or mostly bottled water. This yielded an OR of 1.7 (1.2, 2.3).

In an examination of confounders (Table 5.3), SABs were found to differ from LBs with respect to mother's age (SABs were older), nausea (SABs were less likely to experience nausea), gravidity (SABs had more prior pregnancies), prior pregnancy losses (SABs had a higher loss rate), gestational age at entry into the study (SABs entered earlier), environmental concern (SABs were more likely to classify themselves as having 'greater than average' concern) and facility at entry (SABs less frequently attended Hayward). This facility difference was due to the fact that Hayward was the only facility for which pregnancy tests, separate from a pregnancy confirmation visit, were not used as a means of identifying cohort members. SABs did not differ from LBs with respect to ethnicity, smoking, or previous induced abortions. Small differences were observed for alcohol (slightly more alcohol consumed by SABs than by LBs), employment (more SABs were employed) and education (slightly more college graduates among the SABs).

Potential confounders were examined for an association with consumption of tap vs. bottled water, conditional on the outcome (Table 5.4). Among live births, consumption of all or mostly tap water as opposed to all or mostly bottled water was associated with ethnicity and environmental concern. Non-Whites and those with greater than average concern about environmental issues were more likely to drink bottled water. Among SABs, none of the potential confounders was related to water consumption.

Table 5.5 shows the OR adjusted singly for mother's age, race, education, employment, alcohol consumption, cigarette smoking, number of previous miscarriages, gravidity, level of environmental concern, facility at entry and the month of gestation in which she entered the study. In this table, and in the subsequent analyses we have compared women who drank all or mostly tap water to women who drank all or mostly bottled water because the estimates are more stable. No risk factor by itself had an appreciable effect on the OR. For all of these variables, the Mantel-Haenszel adjusted OR for all or mostly tap water consumption was significantly above 1.0, and the risks did not differ significantly between the strata. Similar results with higher ORs were obtained when tap water consumption was categorized as any vs. none, though the p-values were larger (less significant) due t a more skewed distribution of study subjects into the two exposure groups. However, under this classification of tap water consumption, stratification on medical facility of entry revealed strong heterogeneity (Table 5.6). The heterogeneity was partly due to differences in mean gestational age at entry among the three facilities.

To determine whether there was some constellation of factors which together might distinguish the tap water drinkers from the bottled water drinkers, a discriminant function was fitted to these data. No clear pattern of differences emerged (Table 5.7). The strongest predictors were Asian r Black race (with both groups more likely than Whites to drink bottled water), and enrollment at the Santa Clara Kaiser-Permanente facility (wher women were more likely to drink bottled water than were Hayward or Redwood City patients). However, since race was not associated with the outcome SAB, and since the SAB-tap water association was strongest among the Santa Clara women, these associations could not explain the results.

As noted above, concern over environmental issues was positively associated with the outcome SAB. Thirty-one percent of SABs as compared to 26% of LBs had "greater than average" concern. Concern was also negatively associated with the consumption of tap water in both cases and controls. As shown in Table 5.8, some association between tap water consumption and risk of SAB was seen at each level of environmental concern, although there was a pattern of increasing OR with increasing conc rn (from 1.2 at less than average concern to 2.1 at greater than average concern).

### E. Results Using Risk Set Design

These initial analyses suffer from a fundamental problem inherent in fetal loss studies. Because pregnancies come to medical attention at different gestational ages, and because the risk of fetal loss varies by gestational age, the risk of a clinically recognized SAB is highly dependent on gestational age at which medical care is sought. This time will be referred to as age-at-entry. If women who enter the study later differ systematically from those entering earlier with respect to factors affecting risk of an SAB, then the estimated effect measures for any risk factor may be biased.

In this data set of women belonging to a pre-paid health maintenance organization, one half of the pregnancies were identified by the eleventh week post-LMP, or the start of the third month of gestation. Two high risk groups (e.g., pregnant women over the age of 35, and women with two or m re prior fetal losses) tended to enter earlier. As mentioned above, marked differences were seen among the three facilities, with women at the Hayward facility entering on average two weeks later than women attending the other two facilities. This difference was important for analyses comparing geographic areas.

To control for differential age-at-entry, pregnancies ending in an SAB are compared with only those pregnancies in the "risk set," i.e. under observation at the gestational age at which the SAB occurs. Unlike the case-control analysis, stillbirths, reportable anomalies, other live births, and SABs occurring after the SAB in question are all potentially eligible for inclusion in a risk set.

Lifetables were constructed separately for exposure groups defined by tap water consumption. Although women were not asked directly how much tap water they drank, each woman could be classified as having consumed only tap water, mostly tap water, mostly bottled water, or only bottled water. Table

5.9 and Figure 5.2 show the hazard for an SAB in each week of gestation for the all or mostly tap water drinkers and for the all or mostly bottled water drinkers. In almost every week between weeks 5 and 20, tap water drinkers were more likely to miscarry. The difference is most pronounced in weeks 5-11 (measured from the last menstrual period, i.e., true length of gestation is 3-9 weeks). This is also the period of the highest background risk of SAB.

As discussed above, the lifetable assumes that pregnancies under observation are representative of all pregnancies. Some women, however, seek medical care only because they are experiencing symptoms related to miscarriage. To counter the resulting bias, one can exclude such women from the lifetable by including only those who contribute at least two days of observation. The risks derived using this exclusion criterion represent a lower limit on the lifetable risk. At the other extreme, one can include everyone whose pregnancy came to medical attention, even those who are at risk only on the day of termination, and thereby obtain an upper limit. The true risk is likely to lie somewhere between these two. Cumulative lifetable risks f an SAB between weeks 5 and 20 were calculated using both criteria for entering pregnancies into the lifetable. Because the substantive relationships regarding water consumption were not affected by exclusion criteria, f r simplicity, we report lifetable risks using no exclusions.

To analyze the relationship between tap water and risk of SAB, these lifetable risks were derived separately by exposure group (Table 5.10). The risk for all or mostly tap water drinkers was 0.16 compared to a risk for all or mostly bottled water drinkers of 0.09. Those who drank only tap water had a risk of 0.16, while those who drank no tap water had a risk of 0.06.

We also attempted to disentangle the possibly harmful effect of tap water from the possibly protective effect of bottled water by stratifying on amount of bottled water and relative amount of tap water. Unfortunately, women were not asked to quantify their consumption of tapwater. They w re asked whether they drank more or less tap than bottled water. Since most women drank no bottled water, this question was not particularly informative. Tabl 5.11 shows the lifetable risk of SAB for three levels of bottled water consumption (n bottled water, 1-2 glasses, and 3+ glasses per day) calculated separately for those drinking less, or more tap than bottled water (because of small numbers, those reporting equal amounts were lumped with the "more" group). It is difficult to interpret the pattern in each column, since tap water drinkers who drank more than zero glasses of tap water per day could have consumed a larger amount than those who drank more than three glasses per day. However, it is clear that for each level of bottled water consumption the risk of an SAB appears to increase when comparing those drinking less tap water to those drinking more tap water.

The lifetable can correct for differential age-at-entry, but is limited in its usefulness in adjusting for confounders. The number of observations in each stratum limits the number of variables for which one can control. A multivariate analysis which also corrects for differential age-at-entry was achieved by fitting the Cox proportional hazards model to these data. Under this model the ratio of the hazards for an SAB comparing exposed to unexposed pregnancies is expressed as a linear function of all the variables entered into the model. The proportional hazards assumption states that the hazard ratio, comparing those with and without a given set of risk factors, is constant over time.

Based on the examination of confounders and reports from the literature the following variables were entered into the model: consumption of tap water, mother's age ≥35, prior fetal loss, alcohol, education, employment, ethnicity, and smoking. Nausea was not entered into the model because absence of nausea is viewed by some experts as an outward symptom of placental dysfunction, and may therefore be on the causal pathway to a spontaneous abortion. In any case, entering nausea into the model had a negligible effect on the coefficients of any of the retained variables. Gravidity was not entered due to its close correlation with prior fetal loss. Because interviews were conducted on a subset of live births (as compared to 100% of the women whose pregnancies ended in an adverse outcome), some adjustments were necessary for this analysis. Specifically, the same sampling fraction which was applied to the live births during the data-gathering stage was now applied to other outcomes which had been sampled at 100%. This is equivalent to the selection of a random sample f all pregnancies from the original cohort, or a subcohort. For every failure, a risk set is constructed based only on those in the subcohort. This approach is known as a case-cohort analysis (9, 10, 11).

The best fitting model was obtained by stepwise backward elimination, and the only variables which remained in the model were: maternal age ≥35, prior fetal loss, alcohol consumption, tap water consumption, non-White non-Hispanic ethnicity, and education. The selected variables with their coefficients are shown in Table 5.12.

The hazard ratio associated with consumption of tap water was 1.5, with a 95% confidence interval of (1.1, 2.0). A model with interactions between tap water and each of the other variables was also fitted: only the interaction with maternal age remained in the model. However, this model did not provide a significantly better fit than the nested model without interactions. Inclusion of environmental concern, or the interaction between maternal age and tap water, like nausea, had a negligible effect on the coefficients for the water variables.

Goodness of fit comparing the models with and without tap water was assess d using $-2(L_2-L_1)$, where $L_2$ and $L_1$ were the respective log-likelihood functions of the two models. This expression, which was equal to 6.8, has an approximate $\chi^2$ distribution, yielding a p-value for improvement of fit of p=0.009, i.e., a statistically significant improvement. The appropriateness of the proportional hazards assumption was evaluated by inclusion of time-covariate interactions of the form $x_i$*log(time+C), where C was an arbitrary constant. The model with time-covariate interaction terms suggested a small degree of interaction between time and the tapwater effect such that the relationship to failure was strongest at the earliest failure times and declined over time. This is consistent with the week by week comparison of the life table estimates discussed above. The overall fit, however, was not improved by inclusion of these terms ($\chi^2_{(6)} = 1.7$, p=.94).

F. Crude Analysis of Birth Defects

Reportable anomalies (RA), as ascertained by the California Birth Defects Monitoring Program (12), were analyzed using the case-control design, with all other live births providing the controls. Table 5.13 shows the relation between tap water consumption and RA. The odds ratio comparing those who drank any tap water to those who drank no tap water was 1.6, with a 95% confidence interval of (0.6, 4.0). There were only five non-tap water drinkers among the cases, however, and two of these reported drinking no bottled water either. The odds ratio comparing those who drank all or mostly tap water to those who drank all or mostly bottled water was 1.5, with a 95% confidence interval of (0.9, 2.5). There also appeared to be severe underascertainment of anomalies at the Redwood City facility (13). Therefore, stratification on facility of outcome was necessary (Table 5.14). The Mantel-Haenszel adjusted OR was estimated as 1.4, with a 95% confidence interval of (0.8, 2.4). If tap water consumption is related to the risk of a congenital malformation, this study did not have the power to detect it.

G. Exploratory Analyses of Water Source

The residential data collected at the time of the interview were cleaned-up by Mr. Ed Rappaport at the University of Southern California. We linked those residential histories to the LMP, in order to determine a first trimester address for each pregnancy. Addresses were truncated to the nearest 100 in order to protect confidentiality. This could have introduced errors in classification of water company if a block was served by more than one water company. Very few such situations are likely. The water company serving each truncated address was identified. Each water company was classified as to whether it drew from ground water only, surface water only, or a combination of the two (mixed). The classification of mixed includes water companies which blend two sources, as well as those which draw on surface water during some months and ground water during others. Thus, although each pregnancy was associated with a first trimester water company and source, some of those categorized as receiving mixed water may actually have received surface or ground water during their first trimester. It is exp cted that such misclassification would be random with r spect to the pregnancy outcome and therefore would tend to diminish the observed differences between groups.

Three counties accounted for 1839 (97%) of the 1893 pregnancies, and sourc of water was identified for 1807 (98%) of the residents in the three counties. Table 5.15 presents the distribution of pregnancies in these counties by source of water. In two of the counties, there were no women receiving pure ground water, and only 52 women in Santa Clara County received pure ground water.

Lifetable risks of an SAB between weeks 5 and 20 were calculated for tap water drinkers in each county by water source category (see Tables 5.16 and 5.17). These lifetable risks can be compared to those of non-tap water drinkers, also shown in the table. In every category, tap water drinkers have a higher risk than non-tap water drinkers, except for Santa Clara residents served by surface water, whose risk may have been as low as that of non-tap water drinkers. Overall, the risk is higher for women who drank mixed or ground water than for those who drank only surface water, although risks for San Mateo surface water drinkers were also somewhat elevated. Table 5.18 shows the lifetable risks of an SAB for tap water drinkers served by the four water companies with at least 100 women in the study sample. Differences appear to be small.

Comparisons of lifetable risks using the geographic and water source categories should be made with caution because of the potential role of confounders. For example, county of residence was highly associated with maternal age, ethnicity, education, environmental concern, cigarettes, and month of entry. The lifetable only controls for age-at-entry, while several of these variables were significant in the multivariate analysis. The best measures of differences between the geographic and water source categories are obtained using the Cox proportional hazards model.

Subdividing those drinking all or mostly tap water into those receiving any ground water (pure or mixed) vs. those receiving pure surface water, the Cox proportional hazards model was again fitted to these data, using confounders which were previously retained in the model (see above). With all or mostly bottl d water drinkers s rving as referents, the hazard ratio for drinking mainly tap water among residents of areas served by any ground water was 1.7 with a 95% CI of (1.2,2.3); among residents of areas served by surface water only, the hazard ratio was 1.4 with a 95% CI of (1.0,1.9) (see Table 5.19). This model was also fitted with a term for residence in Santa Clara County. When controlling for water type, there was no significant difference between Santa Clara County residents and those living in other counties (Table 5.20). Furthermore, when controlling for water type, the area of residence variables did not contribute significantly to the prediction of SAB. Wh n controlling for county, however, ground water was a significant predictor of SAB. Also, among tap water drinkers, those receiving any ground water were at significantly higher risk (p=.04) than those receiving surface water.

Finally, a model using five dummy variables representing the categories f water source (any ground vs. surface) by county was fitted (Table 5.21). Again, all or mostly bottled water drinkers served as referents. Each f the county by water source variables remained in the model except Santa Clara surface water. For those drinking all or mostly tap water and residing in Santa Clara mixed or ground water areas, the hazard ratio was 1.7 (1.3, 2.2). Tap water drinkers in the other areas had HRs of 1.4 to 1.5. Hazard ratios by geographic area, by water type, and by both are shown in Figure 5.3.

H. Discussion: Bias, Unmeasured Confounders, and Chance

The preceding analyses were aimed at testing a priori hypotheses regarding the relation between consumption of tap water and both congenital malformations and spontaneous abortions. These analyses did not confirm an association with malformations. They did confirm an association with SABs that is statistically significant and cannot be explained by measured confounders. After adjustment for age-at-entry and bottled water consumption, the risk is greater for those who drank more tap than bottled water compared to those who drank less tap than bottled water. The tap water-SAB association remains even after controlling for both age-at-entry and joint confounding by other risk factors. Tap water drinkers whose hom was potentially supplied by any ground water experienced higher risks than those receiving only surface water. Differences between counties were insignificant when water source was controlled for. These findings, if causal, are of public health significance, with effect measures indicating an overall 50% increase in risk for tap water drinkers, or a 33.3% reduction in risk for non-tap water drinkers.

From this study, no conclusion can be drawn as to whether the positive association between tap water consumption and SAB is causal. Factors which could contribute to an artifactual association are discussed below and in Section 10. Artifactual or not, the association may be due to either an unusually low risk in bottled water drinkers or an elevated risk in tap water drinkers. To distinguish between these two alternatives, one would need an external comparison group, using a cohort of pregnancies assembled in a comparable manner in which SABs were medically validated. Most coh rt studies of fetal loss still do not use lifetable methods to correct for time at entry to observation (e.g., 14, 15, 16). While lifetable risks over 15% have been reported, inclusion of pregnancies not medically validated is common (e.g., 2). In addition, cohorts assembled in years during which induced abortions were illegal may not be useful for comparison since induced abortions were often reported as spontaneous. This could explain the higher rates, particularly in the earlier weeks, reported by Shapir et al (5) compared to the weekly rates of the present study. Lifetable risks for SAB in comparable, recently assembled cohorts of medically validated pregnancies appear to be unavailable. Nevertheless, given the risks that have been published, the lifetable risk among non-tap water drinkers in this study appears low.

Alternative explanations for these findings include: confounding by unmeasured risk factors, bias and chance. Potential sources of bias in this study include: selection bias stemming from nonrandom loss to follow-up, from exclusion of elective abortions, or from differential left truncation (i.e., failure of non-tap water drinkers who miscarry to appear for medical care), nonresponse bias, differential recall of water consumption, misclassification of water source, and changes in behavior associated with length of pr gnancy. Several other potential biases were precluded by the risk set analysis or by the cohort design.

Losses to follow-up: All pregnant women appearing at the three Kaiser-Permanente facilities were enrolled in the original cohort. About 5% were lost to follow-up. Although this represents a small fraction, if the joint distribution of water consumption and outcomes in these women was substantially different from those successfully followed, it could result in a spurious finding. One such scenario is shown in Figure 5.4. There is, however, no information regarding whether those lost to follow-up differed from those who were successfully followed.

Elective abortions: Those who sought an elective abortion were ineligible for selection into the case-control study. If these 1600 pregnancies had systematically differed from those who did not choose an abortion with respect to both water consumption and the outcome which would have occurred had an abortion not been induced, the assumption of independence between failure and exits from observation would be violated. It seems unlikely, however, that these pregnancies would have been more or less likely to spontaneously abort had the induced abortion not been conducted. Moreover, including such pregnancies in the lifetable for the whole cohort (i.e., entering them in the denominator during the weeks they were under observation) resulted in lowering the absolute risk of failure by less than 1% (17).

Left truncation: Women who miscarried early in pregnancy and never sought medical care were truncated. Truncation bias could occur if non-tap water drinkers who miscarried failed to seek any medical care at all or sought care outside of Kaiser. The same effect would be produced if tap water drinkers tended to appear for care earlier than abstainers. In particular, media publicity surrounding ground water contamination episodes might impel tap water drinkers to seek prenatal care earlier, so that their SABs would be detected, while tap water abstainers miscarrying at the same gestational age would be truncated. Under this scenario, the lifetable risk estimates could not be validly compared but the hazard ratio estimates provided by the Cox model would still be valid. If such a bias were operating, one would exp ct differences in age-at- ntry by water consumption. However, age-at-entry was identical among the four classes of water consumption: tap only, mostly tap, mostly bottled, only bottled. Furthermore, tap water drinkers who started prenatal care before the media publicity surrounding the Fairchild spill had a similar distribution of age-at-entry as those who started care after the publicity. (See Section 10).

Response: While the proportion responding to the questionnaire did not differ by outcome status (Table 5.1), this marginal independence does not rule out response bias. Whether non-tap water drinkers with SABs were l ss likely to respond than those among the LBs is not known. A clue about non-respondents may be provided by comparing the early respondents, who replied to the mail questionnaire, to the later respondents who were interviewed by telephone. Mail vs. phone respondents did not differ on tap water consumption; SABs were slightly less likely to respond by mail, and the association between tap water and SAB was stronger in the phone respondents than in the mail respondents. If nonrespondents resembled late respondents more than early ones, nonresponse bias may have masked an even stronger association than was observed.

Recall: All interviews, whether by mail or by phone, took place about tw years after the termination of the pregnancy, suggesting the possibility of errors in recall of water consumption. If these errors were random, i.e., if SABs and LBs were equally likely to misclassify their water consumption, either by overreporting or underreporting tap water, then the effect would be to bias the estimated effect measures towards unity (1.0). The true association between water and risk of SAB would then be larger than the measured association. If, however, cases differed from controls in their rates of misclassification, the true risk could be much smaller or larger than what was measured.

Differential recall of exposure could bias the OR away from unity either if cases tended to overreport tap water consumption or if live births tended to underreport tap water consumption, or if both occurred. These scenarios are depicted in Figure 5.5. In order for the OR in this study to have actually been 1.0 the number of tap water abstainers among the SABs who would have had to misclassify themselves as tap wat r drinkers was 12, which is 48% of cell B, the cases who were tap water abstainers. Alternately, the number of tap water drinkers among live births who would have had to misclassify themselves as abstainers was 33, which is only 2.7% of cell C, the controls who were tap water drinkers. Of course the measured OR could have been biased upward by misclassification of both groups. Two pieces of evidence suggest that recall bias was present and may have been of sufficient magnitude to explain the findings.

(1) The questionnaire specifically stated that use of water in hot or cold drinks should be included as water consumed, whether bottled or tap. Therefore, reported consumption of coffee and tea was examined among the twenty-nine women who classified themselves as having consumed neither tap nor bottled water or who had missing values. Fourteen of these women drank four or more cups per week of coffee and tea (combined). Under the assumption that anyone who went to the trouble of making their coffee r tea with bottled water would have been likely to remember and report drinking bottled water, the authors reclassified these women as tap water drinkers (this recoding was done prior to all the analyses reported above). Live births were more likely than SABs to be reclassified from non-tap water consumers to tap water consumers by this recoding. (Nine LBs were reclassified from cell D to cell C while no SABs were moved from cell B to cell A. Some missing values were also recoded.) Thus, before reclassification, the measures of association appeared greater. It is plausible that women who made cold drinks such as juices from frozen concentrate should also be reclassified and that these too would include proportionately more LBs than SABs. However, since the study did not collect this information, it is not possible to identify such women, nor to estimate the magnitude of bias from this misclassification.

(2) Environmental concern was positively associated with SAB. Among LBs, but not among SABs, it was negatively associated with tap water consumption. That is, among the LBs, those with greater than average concern were more likely to have been bottled water drinkers, but among the SABs, environmental concern was not related to type of water consumed. F r the non-tap water drinkers among LBs, the self-reported concern appears to

refl ct an attitude present during the pregnancy which was expressed in a greater probability of tap water abstention. The lack of a difference among the SABs appears to reflect a heightened concern of these tap water drinkers which was a result of the miscarriage. Although the ORs were not significantly different among the three levels of environmental concern, they do increase with increasing level of concern (Table 5.8), suggesting that environmental concern may influence memory or reporting of tap water consumption, resulting in recall bias.

Other circumstantial evidence may also argue for the possibility of recall bias. A higher risk for tap water drinkers, or a lower risk for bottled water drinkers, was observed in all three counties, however, this association was most pronounced among the few (45) residents of Santa Clara County who received ground water. Because the interviews for this study were conducted within 18 months after a widely publicized episode of ground water contamination in Santa Clara County (the Fairchild leak), the magnitude of recall bias may have been stronger among these women. Thus the degree of bias due to differential recall may have varied, and been strongest among those likely to have been the most sensitized to the issue of ground water contamination.

Misclassification of water source: In the exploratory analyses of water source and geographic region, some women may have been misclassified because their home received water from a water company which drew on ground or surface water at different times of the year. Also the degree of mixing differs by water company and calendar time, so that the category of receiving any ground water, mixed or pure, may have been quite heterogeneous. Additionally, some employed women may have consumed the bulk of their tap water at work, which may have had a different source then from home residence. Such misclassification is likely to have been random with respect to outcome and would therefore have tended to bias the measures of association towards unity, i.e., to reduce the apparent differences between groups. The hazard ratios associated with specific water sources may therefore be larger than estimated.

Behavior change: Another type of bias might occur if women tended to change their water consumption habits during pregnancy in one direction, e.g., towards more bottled water. Women who miscarry and therefore have shorter pregnancies would have less opportunity to change to bottled water. Thus the apparent cause-effect relationship would, in actuality be reversed: those with healthier pregnancies have more opportunity to become bottled water drinkers. The questionnaire, on the other hand, sought information on first trimester water consumption. Most SABs occurred in the first trimester so that if women (particularly, non-aborters) changed to bottled water after the first trimester but tended to forget their practices in the earlier part of their pregnancies, such bias is possible. This study collected no data on changes in water consumption practices, and therefore cannot evaluate the magnitude of such a bias.

Of the potential biases discussed above, no evidence is available to evaluate whether losses to follow-up or elective abortions were random or whether there was biased behavior change. The use of risk set analyses precludes biases related to age-at-entry, and furthermore, media publicity appears not to have influenced tap water drinkers to seek care earlier. Thus, left truncation bias seems unlikely. Response bias, if present, is likely to have masked, rather than inflated an association. Similarly, misclassification of water source would have tended to obscure differences between ground and surface water areas. Finally, inconsistencies in reporting of water consumption that were differential with respect to outcome provide evidence for recall bias. Because of the low prevalence of unexposed persons, this bias could be substantial even if only a small number of women misclassified themselves.

The possibility that unmeasured confounders were responsible for this finding seems small. Controlling for previously reported risk factors for SAB--smoking, alcohol, previous pregnancy losses and maternal age--had no influence on the magnitude of the tap water-SAB association. While socioeconomic status was not directly assessed, ethnicity, education and employment also had no effect. Furthermore, where socioeconomic status has been suggested as a risk factor for SAB, reported differences in risks were between the very high and very low social classes (14), the study population in this investigation (members of a health maintenance organization) was unlikely to include women at either end of the spectrum of social class.

The role of chance as an explanation for the water-SAB association must be evaluated with regard to the significance level and the context of this study. The p-values for this association were all significant at the .02 level both before and after adjustment for confounders and regardless of the method of analysis (case-control or case-cohort). The p-values associated with the coefficients for tap water drinkers living at residences in Santa Clara County served by ground water were less than .01 in the multivariate models. Additionally, this analysis was undertaken as a follow-up to an earlier finding, and several other follow-up studies have also been undertaken to test this hypothesis. The backdrop to these investigations is the documentation of contaminated ground water in the general region wh re many members of this study population resided (18, 19, 20).

I. Comments on Methods

The application of modern methods in survival analysis to pregnancy follow-up studies provides a means to control for confounding, differential entry times, and changing risk sets for a non-rare outcome. However, the development of risk models for biomedical applications involving time-dependent data (either risk sets or covariates) took place in the context of cancer survival studies; and hence their use in studies of pregnancy loss may require adaptation. The assumptions of such methods deserve careful scrutiny, for which the following comments provide a starting point.

The first assumption, which also applies to univariate nonparametric methods such as the lifetable, is that entry and exit are independent of outcome. Stated differently, those under observation are assumed to represent a random sample with respect to the ultimate outcome of all pregnancies n t yet terminated. Unlike cancer survival studies, the problem of right censoring is often smaller than the problem of left truncation, i.e., pregnancies which never even come under study because they terminate prior to entry. These are almost exclusively miscarriages, rather than full-term births. To the extent that symptoms which provide a "warning" of imminent miscarriage lead some women to seek m dical attention, the independence assumption certainly does not hold. The use of the two-day exclusion criteria was one way of coping with biased entry. More subtle forms of biased entry/truncation are probably also at play. On the one hand, recent theoretical work in survival analysis supports the consistency of estimators under random left truncation (21); on the other, empirical data generated by new technologies to detect pregnancies earlier in gestation may allow the randomness of left truncation to be evaluated.

The proportional hazards assumption may serve as an adequate description for some variables, but may also detract from uncovering important biologic relationships. For instance, if some risk factors operate primarily during certain windows of time, this assumption may be inappropriate. Attention should be paid to the shape of the underlying hazard function, i.e., most losses occur in a fairly small range of gestational ages. Also, the clustering of losses in certain time intervals may itself pose a problem, since estimation techniques in multivariate models rely on approximations when more than one loss occurs in a single time interval. The loss of precision due to these approximations needs exploration, as do other, possibly additive, risk models.

Finally the motivation for doing a risk-set or time-dependent analysis in pregnancy outcome studies differs from the usual motivation for such analyses. In clinical trials of cancer treatments or in longitudinal mortality studies in the general population, a longer survival time signifies a better outcome. In a pregnancy, a longer time until an SAB occurs is not a more favorable outcome. The real motivation for such an analysis is the staggered entry-times into observation. The implication of this difference has yet to be clarified.

These methodologic issues underscore the need for understanding both the limitations of the statistical tools and the implications of the underlying biology, as reproductive epidemiologists expand their repertoire of analytical methods.

J. Conclusion

The risk of spontaneous abortion was elevated among women who drank mainly tap water in the first trimester, or reduced among women who drank mainly bottled water. A one and a half fold difference remained after adjustm nt not only for multiple potential confounders, but also for the differential distribution of gestational age-at-entry. The risk of SAB for non-tap water drinkers may have been unusually low, though an elevated risk for tap water drinkers could not be ruled out.

If the risk in bottled water drinkers was unusually low, this could have been due to (a) differential recall with live births underreporting tap water consumption, or (b) a protective agent in bottled water. If the risk in tap water drinkers was elevated, this could have been due to (a) differential recall wherein SABs overreported tap water consumption, or (b) a harmful agent in tap water. Tap water drinkers whose source of water included ground water had higher risks than those receiving only surface water when controlling for county alone, or when controlling for multiple potential confounders. Both groups, however, had higher risks than bottled water drinkers, though for surface water the difference was of marginal significance. These observations are consistent with the differential recall hypothesis, or with the hypothesis of a causal association in which the harmful agent or agents were introduced via the distribution system.

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## Appendix A. Definitions of Birth Outcomes

Spontaneous Abortion (SAB) Spontaneous death of the fetus or rejection from the womb before 28 weeks gestation, and in which no fetal death certificate was filed. Included: missed abortion, molar pregnancy and ectopic pregnancy.

Stillbirth (SB) Fetus delivered dead after week 28, or before week 28 and for which a fetal death certificate was filed.

Congenital Anomaly : Live birth with an anomaly coded 740-759 according to the International Classification of Diseases, Ninth Revision. Also includes five pregnancies in which an elective abortion was conducted after a determination of chromosomal anomaly. Anomalies were later divided into:

- Reportable Anomalies (RA), using the California Birth Defects Monitoring Program criteria of reportable anomalies (12) and

- Nonreportable anomalies, which included all others.

Intrauterine Growth Retardation (IUGR): Live birth with weight less than two standard deviations below the mean for the gestational age at birth, and in which no reportable anomaly was found.

Neonatal Death (ND): Death of liveborn child during the first 28 days of life, without RA or IUGR.

Live birth (LB): Liveborn child with no anomaly, no IUGR and no ND.

## Appendix B. Construction of Fetal Lifetables

The construction of fetal lifetables is described in detail by Taylor (3). The lifetable represents the discrete time analogue of the survival function. In the fetal lifetable, time is measured as gestational age; we have used weeks of gestation. The data used to construct the table are:

$d_i$ = number of failures in week i
$b_i$ = number of live births in week i
$t_i$ = number of days-at-risk in week i.

The life table is constructed by calculating the following:

(1) The average daily hazard of dying in week i, conditional on survival to the beginning of that week:

$$qd_i = d_i \div t_i$$

(2) The average daily hazard of a live birth in week i, conditional on survival to the start of week i:

$$rd_i = b_i \div t_i$$

(3) The average probability of a pregnancy surviving a day in week i, conditional on survival to the beginning of the week:

$$pd_i = \exp(-qd_i - rd_i)$$

(4) The probability of a pregnancy surviving into week i+1, conditional on survival to the beginning of week i:

$$p_i = (pd_i)^7$$

(5) The weekly conditional probability of failure:

$$q_i = (1 - p_i) \cdot [qd_i \div (qd_i + rd_i)]$$

(6) The weekly conditional probability of a live birth:

$$r_i = (1 - p_i) \cdot [rd_i \div (qd_i + rd_i)]$$

(7) The cumulative probability of surviving to the beginning of week i:

$$s_i = p_1 \cdot p_2 \cdots p_{i-1} = \prod_{j=1}^{i-1} p_j$$

(8) The unconditional probability of failure in week i:

$$P_i(f) = s_i \cdot q_i$$

(9) The unconditional probability of a live birth in week i:

$$P_i(\ell) = s_i \cdot r_i$$

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(10) The cumulative probability of failure between weeks i and j:

$$P_{i,j}(f) = \sum_{k=i}^{j} P_k(f)$$

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Table 5.1

Distribution of Cohort, Study Sample, Respondents by Outcome[a]

| | Original Cohort | Selected For Case-Control Study | Respondents Case-Control Study | |
|---|---|---|---|---|
| | N | N | N | % |
| Reportable anomaly | 158 | 158 | 139 | (88.0) |
| Spontaneous abortion | 559 | 559 | 474 | (84.8) |
| Ectopic pregnancy | 48 | 48 | 40 | (83.3) |
| Stillbirth | 37 | 37 | 26 | (70.3) |
| Therapeutic abortion with anomaly | 5 | 5 | 5 | (100.0) |
| Nonreportable anomaly | 171 | 171 | 159 | (93.0) |
| Intrauterine growth retardation (IUGR) | 97 | 97 | 78 | (80.4) |
| Neonatal death (NND) in hospital | 14 | 14 | 12 | (85.7) |
| Live birth (no IUGR, anomaly, or NND) | 5987 | 1128 | 1000 | (88.7) |
| TOTAL | 7076[b] | 2217 | 1933 | (87.2) |

[a]Outcomes reported here are mutually exclusive. If a pregnancy outcome could be classified in more than one category, it was placed in the first, in the order listed above.

[b]There were an additional 374 unkn wn outcomes, bringing the total to 7450.

Table 5.2

Spontaneous Abortions and Live Births
by Tap Water Consumption

| | $N(SAB^a)$ | $N(LB^b)$ | Total |
|---|---|---|---|
| (1) Only tap water | 376 | 916 | 1292 |
| (2) Both tap and bottled water | 81 | 261 | 342 |
| (3) No tap water | 13 | 67 | 80 |
| TOTAL | 470 | 1244 | 1714 |

Chi square test for association $p = 0.01$

$OR_{(1 \text{ vs. } 3)} = 2.1$ $(p = 0.01)$

$OR_{(1 + 2 \text{ vs. } 3)} = 2.0$ $(p = 0.02)$

[a] Spontaneous abortions include all fetal losses before 20 weeks and those delivered between 20 and 28 weeks for which no fetal death certificate was filed. Stillbirths, and fetal losses for which no fetal death certificate was filed were not included in this table.

[b] Live births include low birth weights, nonreportable anomalies and neonatal deaths but not those born with reportable anomalies.

Table 5.3

Distribution of Potential Confounders in Spontaneous Abortions and Live Births

| | | Spontaneous Abortion | | Live Birth | | |
|---|---|---|---|---|---|---|
| | | N | (%) | N | (%) | |
| Alcohol | | | | | | |
| | None | 376 | (80) | 1045 | (84) | |
| | 1-3 oz./wk | 67 | (14) | 154 | (12) | p=0.06 |
| | 4-6 oz/wk | 29 | ( 6) | 48 | ( 4) | |
| Gravidity | | | | | | |
| | None | 122 | (26) | 386 | (31) | |
| | 1-2 | 249 | (53) | 659 | (53) | p=0.01 |
| | 3+ | 103 | (22) | 204 | (16) | |
| Nausea | | | | | | |
| | Yes | 282 | (60) | 901 | (72) | |
| | No | 189 | (40) | 345 | (28) | p<0.0005 |
| Maternal age | | | | | | |
| | ≤ 20 | 36 | ( 8) | 138 | (11) | |
| | 21-34 | 363 | (77) | 1027 | (82) | p<0.0005 |
| | 35+ | 75 | (16) | 84 | ( 7) | |
| Ethnicity | | | | | | |
| | Nonwhite, non-Hispanic | 92 | (19) | 255 | (20) | |
| | White, non-Hispanic | 311 | (66) | 801 | (64) | p=0.84 |
| | Hispanic | 71 | (15) | 193 | (16) | |
| Education | | | | | | |
| | < HS graduate | 38 | ( 8) | 94 | ( 8) | |
| | HS graduate only | 112 | (24) | 360 | (29) | p=0.12 |
| | Some college | 181 | (38) | 475 | (38) | |
| | College graduate | 141 | (30) | 319 | (26) | |
| Employment | | | | | | |
| | Not employed | 106 | (22) | 329 | (26) | |
| | Employed | 366 | (78) | 917 | (74) | p=0.09 |
| Smoking | | | | | | |
| | None | 374 | (79) | 982 | (79) | |
| | 1-10 cigs/day | 48 | (10) | 147 | (12) | p=0.36 |
| | 11-20 cigs/day | 41 | ( 9) | 84 | ( 7) | |
| | 21+ cigs/day | 9 | ( 2) | 32 | ( 3) | |

Table 5.3 (Continued)

| | | Spontaneous Abortion | | Live Birth | | |
|---|---|---|---|---|---|---|
| | | N | (%) | N | (%) | |
| Prior fetal loss | | | | | | |
| | 0 | 369 | (78) | 1043 | (84) | |
| | 1 | 79 | (17) | 160 | (12) | p=0.02 |
| | 2+ | 26 | ( 5) | 46 | ( 4) | |
| Previous induced abortions | | | | | | |
| | 0 | 365 | (77) | 997 | (80) | |
| | 1 | 82 | (17) | 195 | (16) | p=0.40 |
| | +2 | 27 | ( 6) | 57 | ( 5) | |
| Environmental concern | | | | | | |
| | < Average | 29 | ( 6) | 114 | ( 9) | |
| | Average | 296 | (63) | 810 | (65) | p=0.03 |
| | > Average | 147 | (31) | 324 | (26) | |
| Facility of entry | | | | | | |
| | Hayward | 137 | (29) | 464 | (37) | |
| | Redwood City | 96 | (20) | 212 | (17) | p=0.005 |
| | Santa Clara | 241 | (51) | 573 | (46) | |

Table 5.4

Proportional Distribution of Potential Confounders by Water Consumption Conditional on Outcome

| | Spontaneous Abortion | | Live Birth | |
|---|---|---|---|---|
| | Mainly Tap | Mainly Bottled | Mainly Tap | Mainly Bottled |
| Maternal age | | | | |
| ≤ 21 | .08 | .04 | .11 | .10 |
| 21-34 | .77 | .75 | .82 | .85 |
| ≥ 35 | .15 | .22 | .07 | .05 |
| Ethnicity | | | | |
| White | .66 | .65 | .66 | .55 |
| Hispanic | .15 | .12 | .15 | .16 |
| Non-White, Non-Hispanic | .19 | .24 | .19 | .29 |
| Education | | | | |
| < High School grad. | .08 | .06 | .08 | .05 |
| High School grad. only | .24 | .20 | .29 | .28 |
| Some college | .38 | .39 | .37 | .43 |
| College grad. | .29 | .35 | .26 | .24 |
| Employment First Trimester | | | | |
| Not employed | .23 | .18 | .27 | .25 |
| Employed | .77 | .82 | .73 | .75 |
| Environmental concern | | | | |
| < Average | .06 | .04 | .10 | .06 |
| Average | .63 | .63 | .66 | .60 |
| > Average | .31 | .33 | .24 | .34 |
| Gravidity | | | | |
| 0 | .24 | .35 | .30 | .35 |
| 1 | .34 | .24 | .34 | .32 |
| 2+ | .42 | .41 | .36 | .33 |
| Previous induced abortions | | | | |
| None | .78 | .71 | .80 | .79 |
| 1 | .17 | .22 | .16 | .15 |
| 2+ | .05 | .08 | .05 | .05 |
| Previous pregnancy loss | | | | |
| None | .79 | .73 | .84 | .84 |
| 1 | .16 | .22 | .13 | .12 |
| 2+ | .05 | .06 | .04 | .05 |

Table 5.4 (Continued)

| | Spontaneous Abortion | | Live Birth | |
|---|---|---|---|---|
| | Mainly Tap | Mainly Bottled | Mainly Tap | Mainly Bottled |
| Alcohol | | | | |
| 0 | .79 | .84 | .84 | .84 |
| 1-3 oz./wk | .14 | .14 | .12 | .12 |
| > 4 oz/wk | .07 | .02 | .04 | .04 |
| Cigarettes | | | | |
| None | .79 | .82 | .78 | .84 |
| < 1/2 pack/day | .11 | .12 | .13 | .10 |
| 1 or more packs/day | .10 | .06 | .10 | .06 |
| Month of Entry | | | | |
| First | .23 | .25 | .19 | .17 |
| Second | .52 | .43 | .35 | .40 |
| Third | .19 | .20 | .25 | .21 |
| After third month | .06 | .12 | .20 | .22 |
| Nausea | | | | |
| Yes | .60 | .59 | .72 | .73 |
| No | .40 | .41 | .28 | .27 |
| Facility of Entry | | | | |
| Hayward Kaiser | .30 | .20 | .39 | .30 |
| Redwood City Kaiser | .20 | .24 | .18 | .14 |
| Santa Clara Kaiser | .50 | .57 | .44 | .57 |

Table 5.5

Odds Ratios for Spontaneous Abortion by Tap Water Consumption[a] Adjusted for Potential Confounders

| Variable | $OR_{MH}$ | p | Chi square Homogeneity(p) |
|---|---|---|---|
| Alcohol[b] | 1.7 | 0.002 | 0.47 |
| Education | 1.7 | 0.002 | 0.74 |
| Employment[b] | 1.7 | 0.002 | 0.53 |
| Environmental concern (see table 5.8) | 1.7 | 0.001 | 0.64 |
| Ethnicity | 1.7 | 0.002 | 0.48 |
| Gestational month-at-entry (into the study) | 1.6 | 0.004 | 0.60 |
| Gravidity | 1.7 | 0.002 | 0.64 |
| Kaiser Facility-at-entry | 1.7 | 0.001 | 0.32 |
| Maternal Age | 1.7 | 0.002 | 0.24 |
| Nausea | 1.7 | 0.002 | 0.88 |
| Prior fetal loss | 1.7 | 0.002 | 0.43 |
| Smoking[b] | 1.7 | 0.002 | 0.87 |
| Crude OR | 1.7 | 0.002 | |

[a] All or mostly tap water vs. all or mostly bottled water

[b] First trimester

Table 5.6

Spontaneous Abortion and Tap Water Consumption
by Facility of Entry

| | Facility | | | | | |
|---|---|---|---|---|---|---|
| | Hayward | | Redwood City | | Santa Clara | |
| Tap Water | SAB | LB | SAB | LB | SAB | LB |
| Any | 134 | 449 | 92 | 205 | 233 | 523 |
| None | 3 | 14 | 4 | 6 | 6 | 47 |
| TOTAL | 137 | 463 | 96 | 211 | 239 | 570 |
| | OR = 1.4 | | OR = 0.67 | | OR = 3.5 | |

Homogeneity chi square p = 0.08

| | Hayward | Redwood City | Santa Clara |
|---|---|---|---|
| Mean gestational age-at-entry (wks) | 12.2 | 10.3 | 10.2 |



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Table 5.7

Factors Discriminating Tap Water
from Bottled Water Drinkers[a]

| Variable | More Likely to Drink: |
|---|---|
| Ethnicity: Black, Asian or other | bottled |
| Santa Clara Kaiser facility | bottled |
| High degree of concern over environmental issues | bottled |
| History of miscarriage | bottled |

Factors Not Discriminating Tap Water
from Bottled Water Drinkers[a]

Maternal age
Education
Alcohol[b]
Smoking[b]
Employment[b]
Gestational age-at-entry
Previous induced abortions
Hayward Kaiser Facility

[a]Drinkers of tapwater only vs. drinkers of bottled water only.

[b]First trimester

Table 5.8

Spontaneous Abortion and Tap Water Consumption
by Environmental Concern

| | Concern | | | | | |
|---|---|---|---|---|---|---|
| | Less Than Average | | Average | | Greater Than Average | |
| | SAB | LB | SAB | LB | SAB | LB |
| All or mostly tap | 27 | 99 | 262 | 680 | 130 | 250 |
| All or mostly bottled | 2 | 13 | 32 | 127 | 17 | 70 |
| TOTAL | 29 | 112 | 294 | 807 | 147 | 320 |
| | OR = 1.2[a] | | OR = 1.5 | | OR = 2.1 | |

[a]Small sample correction, Jewell 1986

Table 5.9

Weekly Hazard Rate for Spontaneous Abortion by Water Consumption (All Counties Combined)

| | All or Mostly Tap | | All or Mostly Bottled | |
|---|---|---|---|---|
| Week | Hazard $\times 10^{-2}$ | Number at Risk | Hazard $\times 10^{-2}$ | Number at Risk |
| 5 | 1.49 | 60 | 0.00 | 17 |
| 6 | 1.33 | 209 | 0.68 | 40 |
| 7 | 1.37 | 404 | 1.22 | 73 |
| 8 | 1.93 | 556 | 0.86 | 100 |
| 9 | 1.59 | 669 | 0.73 | 122 |
| 10 | 2.32 | 771 | 0.76 | 143 |
| 11 | 1.80 | 845 | 1.05 | 159 |
| 12 | 1.68 | 890 | 1.42 | 170 |
| 13 | 0.89 | 943 | 0.89 | 179 |
| 14 | 0.73 | 995 | 0.42 | 186 |
| 15 | 0.50 | 1028 | 0.14 | 193 |
| 16 | 0.51 | 1046 | 0.39 | 200 |
| 17 | 0.30 | 1054 | 0.13 | 203 |
| 18 | 0.17 | 1063 | 0.25 | 204 |
| 19 | 0.32 | 1075 | 0.00 | 208 |
| 20 | 0.22 | 1082 | 0.12 | 212 |

Table 5.10

Lifetable Risk[a] of Spontaneous Abortion by Water Consumption

| All or Mostly: | Tap Water | Bottled Water |
|---|---|---|
| | (1594)[b] | (283) |
| | .16 | .09 |
| | Only Tap Water | No Tap Water |
| | (1408) | (90) |
| | .16 | .06 |

[a] Between weeks 5 and 20, inclusive.

[b] Numbers in parenthesis are total pregnancies in each subgroup prior to applying weights to adjust for sampling probabilities.

Table 5.11

Lifetable Risk[a] of Spontaneous Abortion
By Amount of Bottled Water
and Relative Amount of Tap Water

| Bottled Water (glasses/day) | Amount of Tap Water Relative to Bottled Water: Less | More |
|---|---|---|
| 0 | --- | (1453)[b] |
| | --- | 0.16 |
| 1-2 | (110) | ( 182) |
| | 0.10 | 0.14 |
| 3+ | (134) | ( 38) |
| | 0.08 | 0.16 |

[a] Between weeks 5 and 20, inclusive.

[b] Numbers in parenthesis are total pregnancies in each subgroup prior to applying weights to adjust for sampling probabilities.

Table 5.12

Variables Associated with Risk of Spontaneous Abortion in Cox Proportional Hazards Regression: Best Fitting Model[a]

| | Coefficient (SE) | | Hazard Ratio | p-to remove |
|---|---|---|---|---|
| Tap water consumption[b] | 0.392 | (.162) | 1.48 | 0.015 |
| Prior fetal loss | 0.217 | (.085) | 1.24 | 0.011 |
| Maternal age $\geq$ 35 | 0.542 | (.135) | 1.72 | 0.0001 |
| Alcohol (#oz/wk)[c] | 0.039 | (.018) | 1.04 | 0.026 |
| Non-White, non-Hispanic Ethnicity | 0.195 | (.121) | 1.21 | 0.11 |
| Education (beyond high school) | -0.361 | (.181) | 0.70 | 0.046 |

[a]Variables removed were: employment, cigarette smoking, and Hispanic ethnicity

[b]All or mostly tap water vs. all or mostly bottled water.

[c]The interpretation of the hazard ratio for alcohol is as follows: for each unce of alcohol consumed per week, the risk of SAB at any point in the pregnancy is increased by 4%; consumption of seven ounces per week results in risk $(1.04)^7$=1.38 times that of a nondrinker of alcohol.

Tabl 5.13

Reportable Anomalies and Live Births by Tap Water Consumption

| | N(RA) | N(LB) | Total |
|---|---|---|---|
| (1) Tap water only | 109 | 916 | 1025 |
| (2) Both tap and bottled water | 30 | 261 | 291 |
| (3) No tap water | 5 | 67 | 72 |
| | 144 | 1244 | 1388 |

Test of association p = 0.61

$OR_{(1 \text{ vs. } 3)} = 1.6$ p = 0.32

$OR_{(1+2 \text{ vs. } 3)} = 1.6$ p = 0.33

Table 5.14

Reportable Anomalies and Tap Water Consumption
by Facility of Birth

| | Facility | | | | | |
|---|---|---|---|---|---|---|
| | Hayward | | Redwood City | | Santa Clara | |
| | RA | LB | RA | LB | RA | LB |
| All or mostly tap | 49 | 384 | 14 | 153 | 53 | 404 |
| All or mostly bottled | 5 | 59 | 0 | 23 | 12 | 102 |
| TOTAL | 54 | 443 | 14 | 176 | 65 | 506 |
| | OR = 1.51 | | OR = 2.09[a] | | OR = 1.12 | |

Chi square test for homogeneity p = 0.38

$OR_{MH}$ = 1.37 (0.80, 2.36)

[a]Adjusted for small sample (Jewell, 1986)

Table 5.15

Distribution of Pregnancies[a]
by County and Water Source[b] of First Trimester Residence

| County of Residence | Water Source: Ground | Mixed | Surface | TOTAL |
|---|---|---|---|---|
| Alameda | 0 | 310 | 356 | 666 |
| San Mateo | 0 | 6 | 228 | 234 |
| Santa Clara | 52 | 738 | 117 | 907 |
| TOTAL | 52 | 1054 | 701 | 1807 |

[a]Excludes ectopics, but no other outcomes.

[b]Includes non-tap water drinkers whose residence received water from given source.



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Table 5.16

Lifetable Risk[a] of Spontaneous Abortion by Water Source and County of First Trimester Residence

Tap Water Drinkers[b]

| County | Ground | Mixed | Surface |
|---|---|---|---|
| | ----------------- | Water Source | ----------------- |
| Alameda | (0) | (300)[c] | (348) |
| | | 0.16 | 0.14 |
| San Mateo | (0) | (5) | (222) |
| | | | 0.16 |
| Santa Clara | (45) | (687) | (110) |
| | 0.38 | 0.16 | 0.09 |

| | Non Tap Water Drinkers |
|---|---|
| All Counties | (90) |
| | 0.06 |

[a] Between weeks 5 and 20, inclusive.

[b] Drank any tap water

[c] Numbers in parenthesis are total pregnancies in each subgroup prior to applying weights to adjust for sampling probabilities.

Table 5.17

Lifetable Risk of Spontaneous Abortion
By Water Source of Residence and Water Consumption

| | Water Source of Residence[a] | |
|---|---|---|
| | Any Ground Water | Only Surface Water |
| All or mostly tap water | (901)[b] | (620) |
| | .19 | .14 |
| All or mostly bottled water | (186)[b] | (81) |
| | .09 | .09 |

[a]In the three counties: Alameda, Santa Clara, San Mateo

[b]Numbers in parenthesis are total pregnancies in each subgroup prior to applying weights to adjust for sampling probablilites.

Table 5.18

Lifetable Risk of Spontaneous Abortion for Tap Water Drinkers[a] by Water Company[b]

| | |
|---|---|
| **Surface** | |
| East Bay Municipal Utility District | (159)[c] |
| county: Alameda (all) | 0.15 |
| San Francisco Water District | (493) |
| | 0.13 |
| counties: Alameda (191)<br>San Mateo (221)<br>Santa Clara (78)<br>San Francisco (3) | |
| **Mixed** | |
| Alameda County Water District | (276) |
| county: Alameda (all) | 0.17 |
| San Jose Water company | (477) |
| county: Santa Clara (all) | 0.17 |

[a] Any tap water

[b] Water companies serving 100 or more women in study sample.

[c] Number in parenthesis are total pregnancies in each subgroup prior to applying weights to adjust for sampling probabilities.

Table 5.19

**Variables Associated with Risk of Spontaneous Abortion in Cox Proportional Hazards Regression: Best Fitting Model With Water Source Variables**

| | Coefficient (SE) | Hazard Ratio | p-to-remove |
|---|---|---|---|
| Tapwater drinkers[a]: | | | |
| Ground Water (pure or mixed) | 0.508 (.155) | 1.66 | 0.0011 |
| Surface Water only | 0.324 (.164) | 1.38 | 0.049 |
| Prior fetal loss | 0.207 (.085) | 1.23 | 0.015 |
| Maternal age ≥ 35 | 0.514 (.135) | 1.67 | 0.0001 |
| Alcohol (per oz./wk) | 0.041 (.018) | 1.04 | 0.020 |
| Non-White, non-Hispanic Ethnicity | 0.175 (.122) | 1.19 | 0.15 |
| Education (beyond high school) | -0.326 (.181) | 0.72 | 0.07 |

[a]All or mostly tap water vs. all or mostly bottled water

Table 5.20

Hazard Ratios[a] for Spontan ous Abortion by Water Source and Geographic Area

| | Water Source | | |
|---|---|---|---|
| Geographic Area | Ground | Surface | Overall |
| Santa Clara County | 1.7 | 0.9 | 1.2 (0.8, 1.8)[b] |
| Other Counties | 1.5 | 1.5 | 1.3 (0.9, 1.9) |
| All Counties | 1.7 (1.2, 2.3) | 1.4 (1.0, 1.9) | |

[a]All or mostly tap water vs. all or mostly bottled water.

[b]95% Confidence Intervals.

Table 5.21

Variables Associated with Risk of Spontaneous Abortion
in Cox Proportional Hazards Regression:
Best Fitting Model
With County - Water Source Variables

| | Coefficient (SE) | Hazard Ratio | p-to-remove |
|---|---|---|---|
| Prior fetal loss | 0.210 (.085) | 1.23 | 0.014 |
| Maternal age $\geq$ 35 | 0.515 (.135) | 1.67 | 0.0001 |
| Alcohol (per oz./wk) | 0.046 (.018) | 1.05 | 0.010 |
| Non-White, non-Hispanic Ethnicity | 0.192 (.122) | 1.21 | 0.12 |
| Education (beyond high school) | -0.308 (.182) | 0.74 | 0.090 |
| Tapwater drinkers[a]: | | | |
| Santa Clara County[b]-Ground or Mixed | 0.510 (.137) | 1.67 | 0.0002 |
| San Mateo County - Surface | 0.407 (.175) | 1.50 | 0.020 |
| Alameda County - Mixed | 0.357 (.189) | 1.43 | 0.060 |
| Alameda County - Surface | 0.342 (.173) | 1.41 | 0.049 |

[a]All or mostly tap water vs. all or mostly bottled water.

[b]Santa Clara County surface water drinkers exhibited no excess risk and this variable was therefore eliminated from the model.

Figure 5.1

Construction of Risk Sets for
Hypothetical Cohort of Four Pregnancies

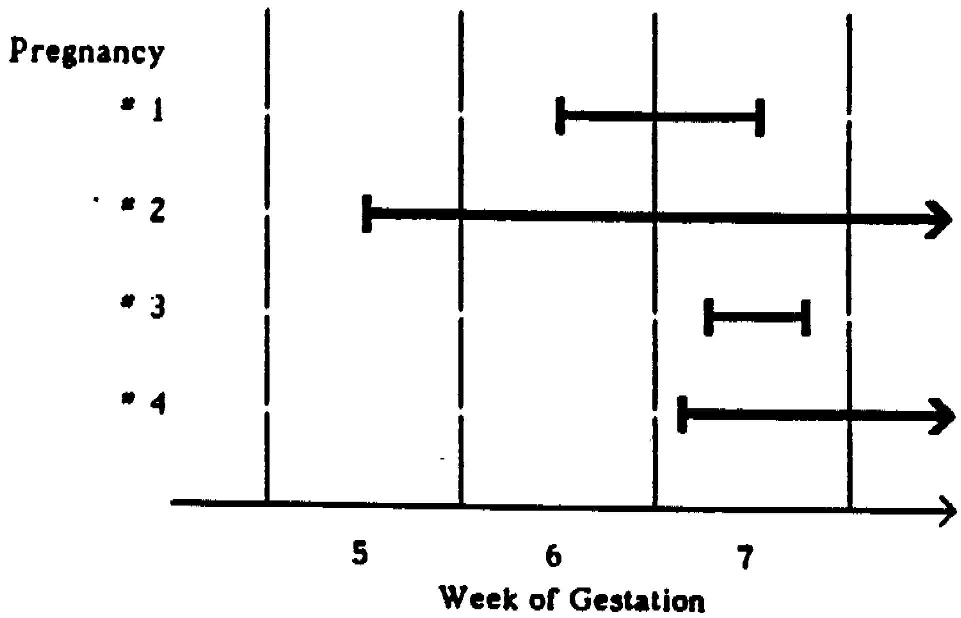
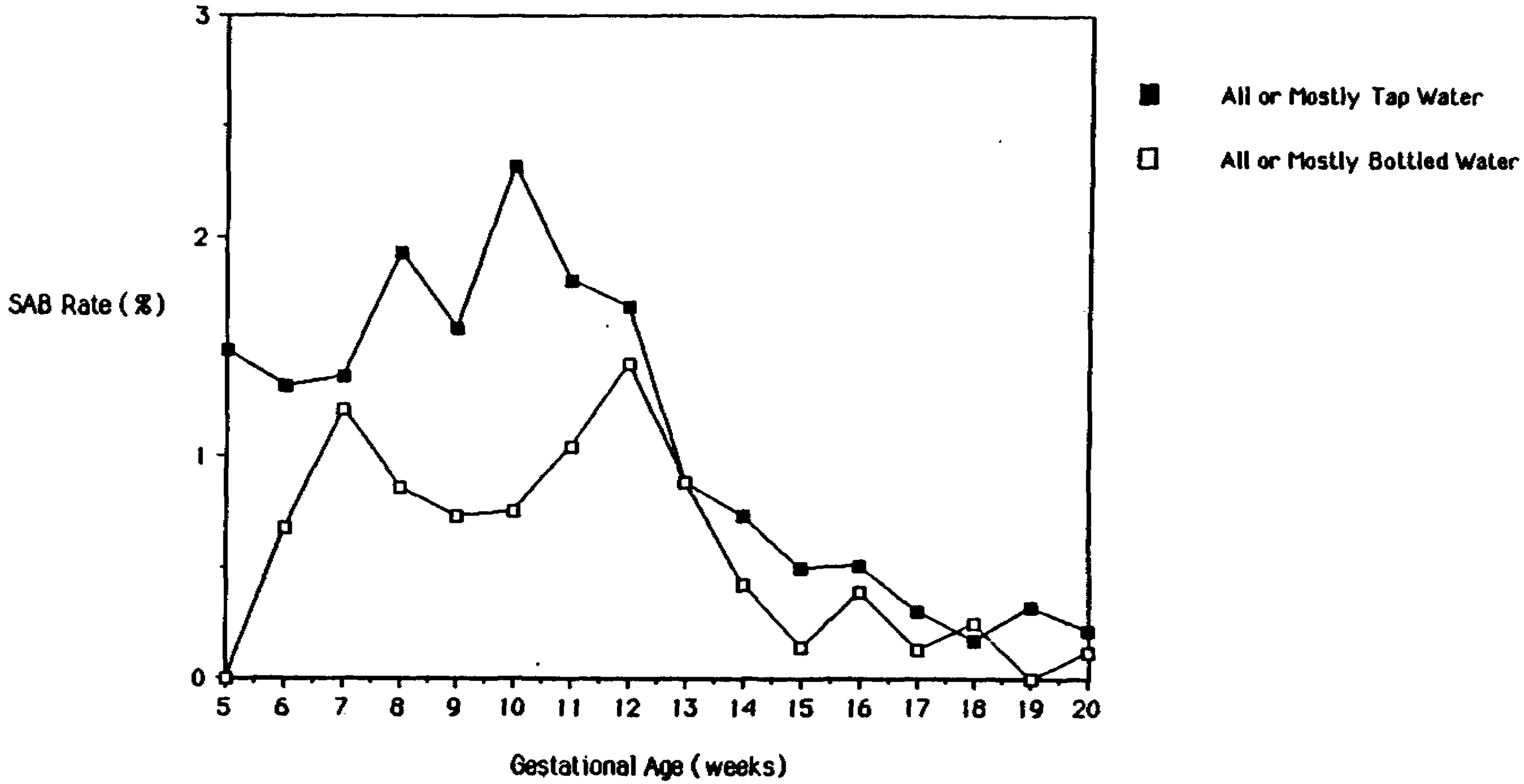
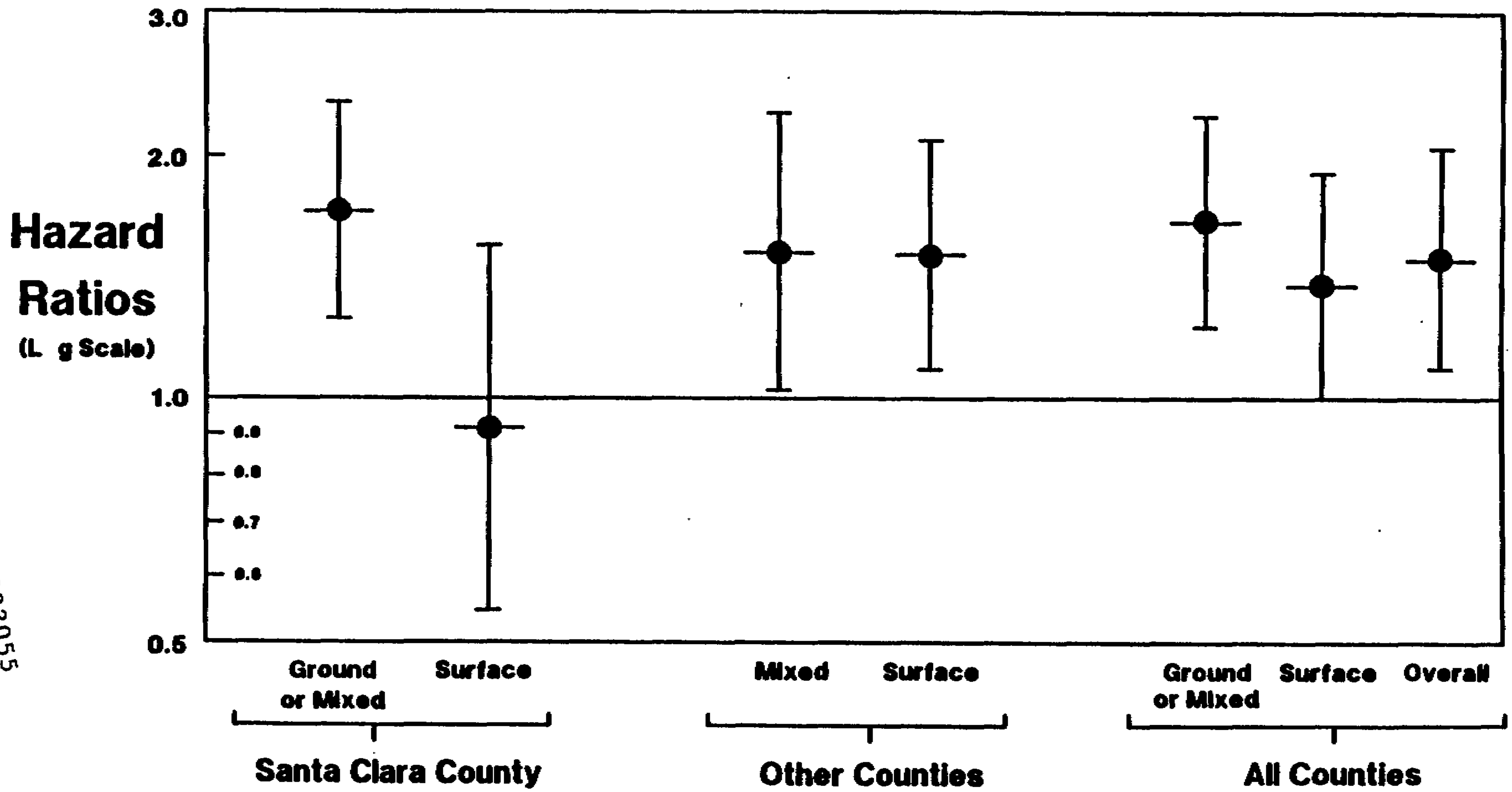


**Figure 5.2 Spontaneous Abortion Rates By Week Of Gestation And Water Consumption**



## Figure 5.3 Hazard Ratios for Spontaneous Abortion Among Tap Water Drinkers By County and Water Source *




* All or Mostly Tap Water vs. All or Mostly Bottled Water

Figure 5.4

## Possible Scenario f r Bias Under Non-Random Loss t  Follow-up

**The Observed Data:**

| | SAB N | SAB % | LB N | LB % |
|---|---|---|---|---|
| tap | 457 | (97) | 1177 | (95) |
| non-tap | 13 | (03) | 67 | (05) |
| | 470 | | 1244 | |

OR=2.0

**Lost to Follow-up:**

374

Hypothetical Distributi n

| SAB | LB | Other |
|---|---|---|
| 80 | 240 | 54 |

(sampled 1 in 5)
48

**Hypothetical Data among Those Lost to Follow-up:**

| | SAB N | SAB % | LB N | LB % |
|---|---|---|---|---|
| tap | 64 | (80) | 45 | (94) |
| non-tap | 16 | (20) | 3 | (06) |
| | 80 | | 48 | |

OR=.26

**Hypothetical Data in Total Population:**

| | SAB | LB |
|---|---|---|
| tap | 521 | 1223 |
| non-tap | 29 | 70 |
| | 550 | 1293 |

OR=1.03

## Figure 5.5

### Two Scenarios of Misclassification Bias Due to Differential Recall

**Observed Table**

| Tap water | SAB | LB |
|---|---|---|
| Any | 457 | 1177 |
| None | 13 | 67 |

OR = 2.0

**General Case**

| | SAB | LB |
|---|---|---|
| Group 1 | A | C |
| Group 2 | B | D |

OR = A/B ÷ C/D

### Hypothetically "True" Tables

If 12 of the 457 in cell A actually belong in cell B, the true OR = 1.0.

| | SAB | LB |
|---|---|---|
| 12 drank no tap water | 445 | 1177 |
| | 25 | 67 |

Or, if 33 of the 67 in cell D belong in cell C, the true OR = 1.0.

| SAB | LB | |
|---|---|---|
| 457 | 1210 | 33 drank tap water |
| 13 | 34 | |

# 6. Cardiac Study

## BACKGROUND

During 1981, the organic solvents 1,1,1-trichloroethane and 1,1-dichloroethylene were detected in the ground water drinking supply of an area of Santa Clara County (SCC) served by the Great Oaks Water Company (GOWC). An epidemiologic investigation conducted by the California Department of Health Services found a 2.5-fold excess prevalence of severe cardiac anomalies in the GOWC area for births occurring in 1981 compar d with births in the remainder of SCC (1). It was subsequently determined that this excess prevalence did not persist for the two succeeding years (1).

A follow-up study was initiated to investigate the occurrence in general of cardiac anomalies in SCC. The objectives of the follow-up study were twofold. The first objective was concerned with determining whether cardiac anomalies among children born only in 1981 were misclassified with respect to exposure to the previously identified water contamination. The findings based on this study objective have been included elsewhere (2). The second objective was broader in its context and pertained to an examination of numerous potential risk factors for congenital cardiac disease. To meet this objective, the study period was expanded to include two additional birth years of data, 1982-83. Among the many potential risk factors investigated was maternal exposure to water in SCC. This report summarizes the analyses related to this particular exposure.

## METHODS

The follow-up study was case-control in design. Children with severe congenital cardiac disease (cases) diagnosed within the first year of life were ascertained by the California Birth Defects Monitoring Program among livebirths in SCC for the period January 1981 through December 1983. The definition of a cardiac anomaly included malformation diagnoses 745-747.9 (International Classification of Diseases-9) made by echocardiogram, catheterization, surgery, or autopsy, except for: septal defects, patent foramen ovale, patent ductus arteriosus in a premature infant (less than 38 weeks), pulmonic stenosis, arrhythmia, or functional murmur, unless any of these was acoompanied by congestive heart failure or any other cardiac anomaly. Septal defects were included if their diagnoses were made by invasive diagnostic procedures (surgery or catheterization). A similar number of controls as cases was identified by random selection from the SCC vital statistics file of livebirths for the same time period as the cases, 1981-83.

The subjects identified and interviewed for this study are presented in Table 6.1. We initially identified 210 cases but 11 were later excluded because they did not meet our diagnostic criteria and one other case was excluded because the address at birth was determined to be out of the county. Among these 198 cases, 16 infants also had Down syndrome and were therefore excluded because of the known increased risk of congenital cardiac disease in this group. Of the 182 cases identified, 147 (80.8%) mothers of these cases were found and interviewed. Of the 210 controls, 176 mothers (83.8%) were found and interviewed. None of the control infants had Down syndrome. Thus, the information in this report is based on data from 147 cases and 176 controls.

The primary reason for either a case mother or a control mother not to have been interviewed was the inability to locate her after extensive tracing efforts. A new control mother was not substituted by resampling the vital statistics files when a control mother was not located. Resampling was not conducted because residences at particular time periods were the variables under examination and it was thought that such a strategy would emphasize mothers in the control group who were more likely to have remained at one address.

Interviews were conducted with mothers of study subjects either over the telephone (85.1%) or in-person (14.9%). The mother of each case or control was queried on her residence address(es), location of her place of employment, and places she frequently visited during the first trimester of her pregnancy with the index child. She was asked about her consumption of drinking water, both tap and bottled sources, for the same time period. The specific questions asked were as follows:

> How much cold tap water or beverages made from unheated tap water such as orange juice or iced tea did you drink during the first three months of pregnancy: At home? At work? At other place?
>
> Did you use bottled water at home during the first three months?
>
> Did you usually use bottled water at home?

She was also asked about the frequency and duration of showering and bathing both at home and at places she frequently visited. In addition, each m ther was asked about numerous other potential risk factors for congenital cardiac anomalies, namely maternal factors such as alcohol consumption, education, employment, age, nausea, race, cigarette smoking, diabetes, epilepsy, and family history of cardiac disease. The length of time between the birth of the child and the interview of the mother ranged between 3.0 and 6.5 years with the mean number of months for cases (mean=56.1 months) and for controls (mean=56.4 months) being approximately the same.

This report presents analyses of the occurrence of cardiac anomalies relative to: maternal water consumption at home (both tap and bottled) and at work (only tap), type of tap water source (i.e., ground, mixed, or surface) supplied to the address at which the mother resided or worked during the first trimester, use of a home water filter, and duration of maternal showering and bathing. Analyses of maternal home tap water consumption were also performed with adjustment for a number of potential confounders. The measure of association used was the odds ratio (OR). Confidence intervals (95%) were calculated using Epistat software (3). When an observed value of an individual cell was less than five, the small sample size adjustment procedure according to Haldane (4) was used. The summary procedure according to Woolf (5) was used to adjust for potential confounders.

## RESULTS

### Water Use At Home

The distribution of cases and controls for all of SCC by maternal consumption of home cold tap water measured in glasses per day is shown in Table 6.2. ORs increased from 0.93 for mothers who drank one glass per day to 1.9 for mothers who drank four or more glasses per day relative to mothers who reported drinking no tap water. However, the 95% confidence interval for each of the ORs included 1.0. An examination across the three birth years of the study period revealed highly elevated ORs for 1981, slightly elevated ORs for 1982, and ORs approximately equal to 1.0 for 1983. These data are shown in Table 6.3. Further, the increasing ORs seen with increasing glasses per day in the total data set was only seen for the stratum of 1981 births. The OR for any tap water (one or more glasses p r day) versus none and cardiac anomalies was 1.5 (0.81, 2.8) for all birth years and was 6.5 (1.1, 37.4) for 1981, 1.8 (0.54, 6.3) for 1982, and 0.77 (0.32, 1.8) for 1983.

Children who were born in 1981 and whose mother had lived in the GOWC area during the first trimester were at risk for exposure to the previously mentioned contaminated water supply. To determine whether these cases were the explanation for the elevated ORs for tap water and cardiac anomalies seen among 1981 births, analyses were performed excluding these cases (n=7) and controls (n=5). The ORs for these analyses were 9.8, 10.3, 9.5, and 19.8 for one, two, three, or four or more glasses per day, respectively. Although these effect estimates were higher than the estimates that included th GOWC area cases, suggesting that the contamination in the GOWC area was not the explanation for the elevated ORs se n among 1981 births, the 95 per cent confidence intervals all included 1.0.

The relation between maternal tap water and cardiac anomalies was examined by adjusting for factors which have been previously reported to be risk factors for cardiac anomalies. For these analyses mothers who consumed one or more glasses per day were compared to mothers who drank no tap water each day during their first trimester. The effect estimates, which are shown in Table 6.4, did not differ greatly from the unadjusted value, OR=1.5. A similar series of analyses (data not shown) performed for individual birth years revealed that the effect estimates for 1982 and 1983 were little affected by these potential confounders. For 1981 data, however, the adjusted ORs were all lower than the unadjusted OR of 6.5. This was particularly true for the OR adjusted for maternal education level (OR=2.8, 95% CI=0.70, 10.8).

Because constituents in water tend to vary by types of water source, e.g., organic solvents are more likely to be found in ground water supplies than in surface water supplies, an analysis of maternal tap water consumption and cardiac anomalies across the three types of water source, i.e., ground, surface, and mixed (a mixture of ground and surface) for each birth year was performed. The water source used for this analysis corresponded to the mother's home address during the first trimester of pregnancy. If a mother had more than one home address during that time and water source type differed across those addresses, water source was considered ground if any address was supplied by a ground water source, while water source was considered mixed if any address was supplied by a mixed source and none were supplied by a ground water source. As is shown in Table 6.5, the ORs for maternal consumption of tap water and cardiac anomalies were found to be larger when the first trimester water source was ground relative to surface for 1981 and 1982 births, but not for 1983 births.

Although information on home water filter use was elicited, the role that water filters play in the potential association between maternal home tap water consumption and cardiac anomalies was unclear from these data due to the small numbers (6 cases and 12 controls) of households that had water filters and the lack of detailed information about the type of filters used. The OR for households with a filter was 0.95 (0.14, 6.5) and the OR for households without a filter was 1.7 (0.84, 3.3).

In an effort to assess whether case mothers differentially report their tap water consumption compared to control mothers, two opinion questions were included in the interview. One asked about how contaminated (i.e., not, somewhat, very, or don't know) the mother perceived her home tap water to be. The other asked whether the mother thought (i.e., no, maybe, yes, or don't know) the water in her community caused birth anomalies. A total of 15 (10.3%) case mothers and nine (5.1%) control mothers thought their tap water was "very" contaminated. Similarly, 58 (40.0%) case mothers and 47 (26.9%) control mothers believed the water in their community caused birth defects. The ORs for maternal tap water consumption and cardiac anomalies across the strata of the responses to these two queries are shown in Table 6.6. The ORs for maternal tap water consumption were higher among mothers who responded that their water was "very" contaminated or responded "yes" to b lief their water causes birth defects relative to mothers who responded "not" and "no", respectively. This was also found for individual birth year strata. The ORs were largest among those mothers who responded "don't know" to the two questions. Distinguishing characteristics of these women are currently being examined.

Further support for the idea that case mothers differentially reported their tap water consumption relative to control mothers was obtained by examining the percentage of cases versus controls by glasses per day of tap water across strata of perception and belief. As is shown in Table 6.7, the percentages of cases and controls across glasses per day within the "not" and "no" strata were similar, whereas within the "very" and "yes" strata 2-4 times more case mothers than control mothers reported to have consumed four or more glasses per day of tap water. A similar relation was found for all birth years, but was slightly more pronounced for 1981 than for 1982 and 1983 births.

Whereas the maternal consumption of home tap water was found to have an OR greater than unity for cardiac anomalies, maternal consumption of bottled water was found to have an OR=0.53 (0.27, 1.0) (for never use versus sometimes or usual use). Similar to the tap water relation, the lowered OR appeared to be determined primarily by the stratum specific OR for 1981 births. The ORs for maternal bottled water consumption and cardiac anomalies by birth year were 0.04 (0.002, 0.64), 0.75 (0.21, 2.6), and 1.1 (0.45, 2.8) for 1981, 1982, and 1983, respectively. These data are displayed in Table 6.8.

As a means of evaluating r utes of exposure to water other than the oral route (possible dermal or inhalation exposure), the length of time spent showering and bathing was examined relative to having a child with cardiac anomalies. No relation was found between the amount of time a mother typically spent in the shower and bath each week at home during her first trimester and having a child with cardiac anomalies (Table 6.9). Analysis by water source type or by year of birth did not change this result. In addition, the average number of minutes per week a mother spent in the bathroom showering, bathing, and after showering or bathing at home was calculated for cases and controls and was found to be similar (cases, m an = 99 minutes; controls, mean = 96 minutes).

## Water Use At Place of Employment

Approximately 63 per cent of case mothers and 63 per cent of control mothers reported that they had worked outside the home (most were employed within the study area) during the first trimester. Among these mothers, no relation was found for maternal cold tap water consumption at work and cardiac anomalies, with ORs of 0.93, 0.58, 2.7, and 0.99 corresponding to one, two, three, or four or more glasses per day relative to no glasses per day. All 95% confidence intervals for these ORs included 1.0. Nor was an association found for any particular water source type. With respect to year of birth, the ORs for maternal tap water consumption (any tap water versus none) at work were 1.2, 0.59, and 1.1 for 1981, 1982, and 1983, respectively.

Water Use At Other Locations In SCC

A total of 20 (13.8 per cent) case mothers and nine (5.2 per cent) control mothers reported consumption of cold tap water at a location in SCC other than at home or at work where they frequently visited (defined as time spent within SCC at least twice a week or for one week or more) during their first trimester. The OR for case mothers who drank any tap water compared to those mothers who drank no tap water was 2.8 (1.3, 6.4). This relation examined by study year strata revealed an OR for 1981 of 4.8 (1.1, 20.8), for 1982 of 2.0 (0.57, 7.0), and for 1983 of 2.1 (0.51, 8.3).

Only 5.4 per cent of case mothers and 8.0 per cent of control mothers indicated they showered or bathed at a place other than at home. The frequency of maternal showering or bathing at places other than at home was unrelated to having a child with cardiac anomalies.

## DISCUSSION

These data showed elevated effect measures for maternal consumption of home cold tap water and cardiac anomalies particularly for births in 1981, less so for births in 1982, and not at all for the most recent study year, 1983. An increasing risk was also found with increasing amount of tap water consumption for 1981 births, but not for 1982 and 1983 births. These elevated ORs remained after adjustment for potential confounders. The elevated ORs seen were for 1981 births occurring countywide and were not explained by case and control mothers who had resided in the GOWC area, an area of known drinking water contamination. Elevated ORs were also found for cardiac anomalies and maternal consumption of tap water at a place other than at home or work. Thes estimates were elevated for all birth years, but were highest for 1981 births. The converse was found with respect to bottled water use. The OR was very small for 1981 births, was slightly less than 1.0 for 1982 births, and was approximately 1.0 for 1983 births.

These findings argue for the presence of an agent(s) in SCC tap water, primarily ground water, around 1980 and 1981 with estimated risks from exposure for cardiac anomalies increasing with increasing amount of water consumed. In contrast, the lack of an association between cardiac anomalies and maternal consumption of tap water at work argues against such an agent in the tap water in SCC. The lack of an association between cardiac anomalies and maternal showering or bathing also argues against the presence of an agent(s) in the water.

Further, there is evidence in these data to suggest that the relations seen between tap water consumption and the occurrence of cardiac anomalies might be a result of differential recall on the part of case mothers (Table 6.7). Among mothers who reported that they thought their water was contaminated or caused birth anomalies, case mothers reported a higher level of tap water consumption (four or more glasses per day) two to four times more frequently than did control mothers. There was some indication that this differential reporting was more pronounced for case mothers who had a child born in 1981. This corresponds to a point in time when publicity regarding the contamination of public water supplies in SCC was greatest.

The apparent protective effect associated with maternal bottled water consumption and cardiac anomalies, seen only for those children born in 1981, may also be due to differential recall. If bottled water contained a protective agent one would expect to see such an effect operating across all birth years rather than the pattern observed in these data. Thus, one might postulate that case mothers (1981) may have underreported their bottled water consumption because they believe tap water caused the anomalies in their child or control mothers (1981) may have overreported their bottled water consumption as an explanation for having an unaffected child. Either scenario may be reasonable given the amount of media attention given to possible water contamination which has occurred in the study area. The data revealed that as many as 40 per cent of case mothers believe that water in their community causes birth defects, whereas 25 per cent of control mothers do. Both of these percentages are very high considering that the scientific community currently estimates that isolated environmental factors explain only about two per cent of the etiology of birth defects (6).

Other methodologic considerations which are pertinent to the interpretation of this study involve the imprecise nature of the questions asked regarding maternal water consumption and the extended length of time between birth of a child and the maternal interview. Either of these could contribute to biased effect estimates. Thus, these data cannot sufficiently distinguish whether there was an agent(s) present in tap water that was related to risk of cardiac anomalies in 1981 or there was differential reporting of water consumption between case and control mothers. Nevertheless, based on the most recent year of birth in this study, 1983, there does not appear to be an increased risk of cardiac anomalies associated with maternal consumption of tap water. Similarly, there does not appear to be a health protective relation betw en maternal bottled water consumption and cardiac anomalies.

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Table 6.1

Subjects Identified and Interviewed for Cardiac Anomalies
Case-Control Study

| | Cases | | Controls | |
|---|---|---|---|---|
| | N | % | N | % |
| Identified | 198 | --- | 210 | --- |
| Excluded, child with Down syndrome | 16 | --- | 0 | --- |
| Not included | | | | |
| Unable to locate | 34 | 18.7 | 30 | 14.3 |
| Mother refused | 1 | 0.5 | 2 | 1.0 |
| Language barrier | 0 | 0 | 2 | 1.0 |
| Total No. Mothers In Study | 147 | 80.8 | 176 | 83.8 |

Table 6.2

Cardiac Anomalies and Home Tap Water Consumption

| Cold Tap Water At Home (glasses/day) | Cases | Controls | OR | 95% CI |
|---|---|---|---|---|
| 0 | 18 | 31 | 1.0[a] | --- |
| 1 | 14 | 26 | 0.93 | (0.39, 2.2) |
| 2 | 27 | 35 | 1.3 | (0.62, 2.9) |
| 3 | 25 | 28 | 1.5 | (0.70, 3.4) |
| 4+ | 61 | 55 | 1.9 | (0.96, 3.8) |
| unk | 2 | 1 | | |
| TOTAL | 147 | 176 | | |

[a]Referent group



SL 033073

Table 6.3

Odds Ratios for Cardiac Anomalies by Home Tap Water Consumption Stratified by Study Year

| | 1981 | | 1982 | | 1983 | |
|---|---|---|---|---|---|---|
| No. Cases | 51 | | 42 | | 54 | |
| No. Controls | 63 | | 47 | | 66 | |
| Maternal Home Tap Water Consumption (glasses per day) | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| 0 | 1.0[a] | --- | 1.0[a] | --- | 1.0[a] | --- |
| 1 | 4.2 | (0.61, 29.1) | 1.9 | (0.29, 12.3) | 0.39 | (0.10, 1.5) |
| 2 | 5.5 | (0.78, 39.3) | 1.6 | (0.37, 6.5) | 0.74 | (0.25, 2.2) |
| 3 | 4.9 | (0.75, 31.6) | 1.9 | (0.40, 8.7) | 1.4 | (0.36, 5.2) |
| 4+ | 10.4 | (1.7, 64.2) | 2.0 | (0.53, 7.4) | 0.87 | (0.32, 2.3) |

[a]Referent group



SL 033074

Tabl 6.4

Odds Ratios for Cardiac Anomalies by Home Tap Water Consumption After Adjustment for Potential Confounders

| Variable | $OR_{Woolf}$ (any vs no home tap water) | 95% CI | Homogeneity Chi square | df | p |
|---|---|---|---|---|---|
| Alcohol | 1.5 | (0.81, 2.8) | 2.9 | 2 | 0.24 |
| Education | 1.4 | (0.74, 2.5) | 2.7 | 3 | 0.44 |
| Employment | 1.5 | (0.79, 2.7) | 0.92 | 1 | 0.34 |
| Maternal Age | 1.5 | (0.81, 2.8) | 0.08 | 2 | 0.96 |
| Nausea | 1.4 | (0.77, 2.7) | 0.95 | 1 | 0.33 |
| Race | 1.4 | (0.73, 2.6) | 2.3 | 2 | 0.32 |
| Smoking | 1.5 | (0.78, 2.7) | 1.0 | 2 | 0.60 |
| Family history | 1.5 | (0.77, 2.8) | 0.66 | 1 | 0.42 |
| Income | 1.4 | (0.74, 2.7) | 4.8 | 2 | 0.09 |
| Maternal diabetes | 1.5 | (0.82, 2.8) | 0.54 | 1 | 0.46 |
| Maternal epilepsy | 1.6 | (0.85, 3.0) | 0.36 | 1 | 0.55 |
| Sex of child | 1.5 | (0.80, 2.7) | 0.01 | 1 | 0.93 |

Unadjusted OR 1.5 (0.81, 2.8)

Table 6.5

Odds Ratios for Cardiac Anomalies by Home Tap Water Consumption
Stratified by Study Year and Water Source

| Maternal Home Tap Water Consumption (any versus none) | 1981 | | 1982 | | 1983 | |
|---|---|---|---|---|---|---|
| | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| Water Source | | | | | | |
| All | 6.5 | (1.1, 37.4) | 1.8 | (0.54, 6.3) | 0.77 | (0.32, 1.8) |
| Ground | 5.9 | (0.76, 46.2) | 3.1 | (0.33,29.1) | 1.7 | (0.07,37.7) |
| Mixed | 6.4 | (0.23,181.8) | 1.3 | (0.33, 4.8) | 0.20 | (0.01, 6.5) |
| Surface | 1.7 | (0.17, 16.6) | 0.60 | (0.22, 1.6) | 1.7 | (0.14,20.5) |



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Table 6.6

Odds Ratios for Cardiac Anomalies by Home Tap Water Consumption[a] Across Responses Concerning Perception Water Is Contaminated and Belief Water Causes Birth Defects

| How contaminated is your tap water? | Cases | Controls | OR | 95% CI |
|---|---|---|---|---|
| Not | 55 | 77 | 1.2 | (0.36, 4.1) |
| Somewhat | 44 | 60 | 0.81 | (0.27, 2.4) |
| Very | 15 | 9 | 2.1 | (0.40, 10.9) |
| Don't know | 31 | 29 | 5.8 | (1.5, 21.9) |

| Does tap water cause birth defects? | Cases | Controls | OR | 95% CI |
|---|---|---|---|---|
| No | 21 | 32 | 0.64 | (0.10, 4.0) |
| Maybe | 44 | 72 | 0.90 | (0.34, 2.4) |
| Yes | 58 | 47 | 2.5 | (0.78, 8.1) |
| Don't know | 22 | 24 | 2.9 | (0.70, 11.7) |

[a]Any tap water versus none.

Table 6.7

Percentage of Case and Control Mothers by Home Tap Water Consumption Across Responses Concerning Perception Water Is Contaminated and Belief Water Causes Birth Defects

| | Mother's Perception of How Contaminated Her Tap Water Is | | | | | |
|---|---|---|---|---|---|---|
| | Not | | Somewhat | | Very | |
| Cold Tap Water At Home (glasses per day) | Case % | Control % | Case % | Control % | Case % | Control % |
| 0 | 7.3 | 9.1 | 15.9 | 13.3 | 26.7 | 44.4 |
| 1 | 12.7 | 6.5 | 6.8 | 25.0 | 6.7 | 33.3 |
| 2 | 21.8 | 26.0 | 25.0 | 21.7 | 6.7 | 0 |
| 3 | 18.2 | 14.3 | 13.6 | 18.3 | 20.0 | 11.1 |
| 4+ | 40.0 | 44.2 | 38.6 | 21.7 | 40.0 | 11.1 |

| | Mother's Belief Water Causes Birth Defects | | | | | |
|---|---|---|---|---|---|---|
| | No | | Maybe | | Yes | |
| Cold Tap Water At Home (glasses per day) | Case % | Control % | Case % | Control % | Case % | Control % |
| 0 | 9.5 | 6.3 | 18.2 | 16.7 | 8.6 | 19.2 |
| 1 | 9.5 | 21.9 | 13.6 | 15.3 | 5.2 | 14.9 |
| 2 | 19.0 | 18.8 | 20.5 | 15.3 | 15.5 | 34.0 |
| 3 | 23.8 | 21.9 | 15.9 | 12.5 | 17.2 | 8.5 |
| 4+ | 38.0 | 31.3 | 31.8 | 40.3 | 53.5 | 23.4 |

Table 6.8

Cardiac Anomalies and Bottled Water Consumption
By Study Year

| Frequency of Bottled Water Use | 1981 Cases | 1981 Controls | 1982 Cases | 1982 Controls | 1983 Cases | 1983 Controls |
|---|---|---|---|---|---|---|
| Never | 50 | 50 | 38 | 41 | 43 | 53 |
| Sometimes/Usually | 0 | 13 | 4 | 6 | 11 | 12 |
| OR[a] | 0.04 | | 0.75 | | 1.1 | |
| 95% CI | (0.002, 0.64) | | (0.21, 2.7) | | (0.45, 2.8) | |

[a]Reflects sometimes/usually users versus never users.

Table 6.9

Odds Ratios for Cardiac Anomalies by Duration of Showering and Bathing

| Duration of Showering and Bathing (min/wk) | Cases | Controls | OR | 95% CI |
|---|---|---|---|---|
| 0-49 | 35 | 35 | 1.0[a] | --- |
| 50-99 | 53 | 69 | 0.77 | (0.43, 1.4) |
| 100-149 | 39 | 46 | 0.84 | (0.45, 1.6) |
| 150+ | 19 | 26 | 0.73 | (0.34, 1.6) |
| TOTAL | 146 | 176 | | |

[a]Referent group

# 7. Spontaneous Abortion Case-Control Study

## INTRODUCTION

The purpose of this study was primarily to examine whether women with spontaneous abortions (SAB) are more likely to have been exposed to solvents during their pregnancy than women with livebirths. It was initiated as one of three follow-up studies to a report of excess adverse reproductive outcomes in a community potentially exposed to solvent-contaminated drinking water (1). That study was conducted to examine community concerns about adverse reproductive outcomes possibly associated with a drinking water well which was found to be contaminated with 1700 ppb 1,1,1-trichloroethane (TCA), leaked from an underground storage tank at Fairchild Camera Company. That well was closed in December 1981. The original survey found a doubling of the rate of SAB in potentially exposed pregnancies during 1980-81, but the timing and distribution of SABs was inconclusive with regards to whether the excess was due to consumption of water from the contaminated well.

This case-control study was designed to examine the broader question of whether solvent exposure during pregnancy is associated with SAB. The study was conducted county-wide and exposures were ascertained at home, work and environmentally. Much other information was obtained during the interview, including data on tap water consumption. When other studies being conducted by the California Department of Health Services (CDHS) indicated a positive association between tap water consumption and SAB, there was great interest in examining this question on a county-wide basis. Although this study had not been completed, the available data were prepared for analysis in order to examine the association of tap and bottled water consumption with spontaneous abortion. The analysis of solvent exposure at home and work will be conducted later, when data collection is complete.

SL 033081

METHODS

Cases in this study are defined as women 18 years old or older, having a spontaneous abortion by 20 weeks gestation, for which a pathology specimen was submitted to a hospital laboratory. Case ascertainment was conducted within six months after pregnancy termination, starting with cases whose last menstrual periods (LMP) occurred during January 1986.

All eleven hospital pathology labs in Santa Clara County participated in the study. Cases were ascertained by trained abstractors reviewing pathology lab report files. Medical charts of potential cases were reviewed to verify that the abortions were spontaneous, not induced, and to obtain the case's address, phone number and certain demographic information. Many of the women who have specimens submitted to hospital labs are seen in the hospitals' OB/GYN clinics or the Emergency Room, but some satellite clinics and private physicians also send specimens to the local hospital. We conducted a survey of county OB/GYNs (67% response) and found that tissue specimens were obtained for 82% of the SABs seen by them and 80% of these were sent to hospital labs, with the remainder sent to private labs. No ascertainment was conducted at private labs for this study.

Controls were selected from Santa Clara County residents who had a live birth, matched to a case by LMP and hospital. The hospital was matched in an attempt to obtain cases and controls from similar demographic and medical practice areas. LMP was matched so that pregnancies of cases and controls would have begun during the same calendar time, thus insuring a similar period of recall and potential for environmental exposure. Three controls per case were identified from birth certificate files, searched at least one month after the expected date of delivery, based on the case's LMP. Name, address, and demographic information were abstracted from the birth certificate.

Cases were asked about events during their entire pregnancy, whereas controls were asked only about the first 20 weeks. The study was designed so that cases and controls would be interviewed at approximately the same time, within a few months of the control's delivery. Thus, they would be recalling events from a similar tim period, although the control's pregnancy would have ended more recently than the case's. (The possible bias introduced by this case-control difference in time from pregnancy termination to interview is being examined in a separate substudy). The interview was conducted using a computer assisted telephone interview (2). It included questions about demographics, residence, pregnancy history, illnesses, diagnostic procedures (e.g. ultrasound), occupation during pregnancy, exposure to solvents at work and home, alcohol, caffeine, tobacco and water intake, and environmental concerns, as well as questions about the demographics and occupation of the father of the pregnancy. A few questions about bottled water use were added shortly after interviewing began so this information was not available for all respondents. The interview was translated and available in Spanish, and some interviews were also conducted in Vietnamese.

To have enough power to examine relatively infrequent solvent exposures, the study goal was to obtain 660 cases and twice as many controls. To accomplish this, over 1000 cases were ascertained. Before interview, subjects were sent a letter explaining the study and asking them to return their phone number and best times to call. These letters were sent out in six batches, approximately one batch per month, as controls became available. Letters were initially sent to cases and two controls per case. Women who did not return the first or second letter were traced by vari us means. The first source was reverse directories and local phone directories, which were searched for the name of the mother and father of the pregnancy. For controls, the medical record of the birth was examined for phone number, employer, or more recent addresses. (Cases had originally been ascertained from medical records, but not controls). In addition, field workers visited some addresses to either speak with the subject or to obtain information from neighbors about her whereabouts. No interviews were conducted in the field. If we discovered that the subject had moved away from the greater San Francisco Bay Area, the subject was considered ineligible and dropped.

Originally, controls were not interviewed until we had obtained agreement from their matched cas . Later the exact matching was dropped, and we attempted to interview all controls wh had agr ed to participate by returning a letter. Additional controls were contacted via tracing procedures, but we did not pursue every control sent a letter if two controls per case had already been interviewed.

At the time this water analysis began, we were in the middle of data collection. So that we did not analyze data from only those respondents most easily contacted, efforts were made to satisfactorily complete interviews in the first four batches. These four batches consisted of the first 1300 women sent letters (out of about 2800 in the entire study). Before analysis, the completed interviews were thoroughly edited to include interviewer comments and to correct data inconsistencies. The completion rates are shown in Table 7.1. We attempted to interview 405 cases and 798 controls in the first four batches (some of the additional exclusions were women for whom the post office returned addresses out of the area). During tracing, an additional 32 cases (7.9%) and 51 controls (6.4%) were found t be ineligible due to a language barrier, having moved out of area, or claiming never to have been pregnant. Of those eligible, 301 cases (80.7%) and 616 controls (82.5%) completed interviews. The refusal rates were similar between cases (9.1%) and controls (11.5%). If a subject refused by letter, we later attempted to convert her by phone. However, we could n t find a phone number for many of the controls, because unlike cases, medical records of controls were not routinely reviewed. This may explain the slightly higher refusal rate among controls. We were unable to contact a larger proportion of cases (10%) than controls (6%).

Because the matching was based on criteria that could pertain to many women, the individual matching was dropped after controls were selected initially, but frequency matching was achieved. The distribution of cases and controls by hospital is nearly identical. The distribution by month of LMP is slightly skewed towards earlier months among controls, and about 12 (5%) cases do not have controls matched by month. However the majority (91%) of respondents had LMPs within a six month period (Feb-July 1986), so there is relatively little time difference between any repondents' LMPs. The matching variables were included in the initial analyses, but do not appear to be confounders and were not retained in the final logistic regression model.

For most consumption questions (tap water, alcohol, smoking), the respondent was asked about her consumption the month before pregnancy, if it changed during pregnancy, and if so, when and to what amount. This information was used to compute average consumption during the first trimester (or the entire pregnancy if shorter). Alcohol consumption is an average of frequency times amount consumed. In the tables that follow, consumption of tap water noted as "none" is actually less than a half glass per day, to correspond to coding practices used during the interview. Questions about bottled water asked whether it was 'usually' consumed during the pregnancy, and included consumption at home or work, and the total daily amount consumed, but did not ask about change. The wording of these questions is contained in Appendix C to Section 1 in this report.

The source (ground, surface, mixed) of tap water was assigned by census tract. The address used to assign census tract in this analysis was that obtained during original case-control ascertainment (e.g. residence at pregnancy termination). Particularly for controls, this may not represent residence during the first trimester of pregnancy. During the interview, addresses were obtained for the time period January 1986 through the current address, but time constraints prevented examination of any data from open-ended questions. Therefore an additional analysis was done including only women who had not moved during this time, assuming the address given would be the same as that found during ascertainment.

Solvent exposure and its relation to spontaneous abortion has not been thoroughly analyzed for this report. However, the distribution of specific chemical exposures at work has been examined and is summarized as exposure to any solvent (primarily chlorinated solvents or those used in electronics industries) and any other hazardous exposure (x-rays, VDTs, anesthetic gases, lead, cancer chemotherapeutics or other self-reported).

RESULTS

Participant Characteristics

Tables 7.2 and 1.3 show the demographic characteristics of the 251 cases and 566 controls analyzed in this report. The proportion of respondents with at least a high school education is similar between cases and controls, but cases were somewhat more likely than controls to be college graduates. Th racial distribution is fairly similar except that cases are slightly less likely to be Hispanic and more likely to be one of the "other" ethnicities. Cases were significantly older than controls and the mean maternal age was about two years higher in cases than controls, reflecting older age as an established risk factor for SAB (3). The mean length of case pregnancies was 10.9 weeks post-LMP. The gestational age distribution was 8.8% (4-6 weeks), 31.9% (7-10 weeks), 41.0% (11-14 weeks), and 18.3% (15-20 weeks), so most SABs occurred during the first trimester with 63% occurring by the twelfth week post-LMP.

Cases were more likely than controls not to be living with the father of the pregnancy. Cases were of higher gravidity than controls and were more likely to have had two or more prior fetal losses. As might be expected many more cases (34%) than controls (1.1%) did not receive prenatal car . However, there was less disparity for having a pregnancy test. Cases were also less likely than controls to have any insurance coverage (including Medi-Cal) for prenatal care. Cases were less likely to have nausea, which may be a sign that pregnancy is not progressing normally. Cases drank more alcohol than controls, but the smoking distribution was fairly similar in cases and controls. The proportions of cases and controls who were employed during pregnancy (about 69%) were very similar, as were the proportions exposed to solvents or other potentially hazardous agents. A large percentage of both cases (55%) and controls (63%) drank some bottled water during pregnancy, but consumption was significantly more prevalent among controls. Tap water consumption was significantly greater in cases (74%) than controls (66%). Interestingly, cases and controls reported similar rates of concern about the quality of their tap water.

## Reported Water Exposure

Among all respondents, 68% drank some tap water, but this varied by certain characteristics (Table 7.3). A larger proportion of Hispanics (75%), women of gravidity three or more (73%), women who were uninsured (77%) and women not very concerned about the quality of their home tap water (83%), drank tap water. Also, women with very short pregnancies (≤ 6 weeks) were less likely to drink any tap water (56%). About 60% of all respondents drank some bottled water. Bottled water use also varied by respondent characteristics and tended to be opposite that noted for tap water drinkers (Table 7.3). In addition, among women who smoked an average of one or more packs of cigarettes per day, only 39% drank bottled water. Women over 35 (47%), and those who did not receive prenatal care (52%) were also less likely to drink bottled water.

Table 7.4 indicates the pattern of tap water consumption at home during the first trimester (14 weeks post-LMP) for cases and controls. There is a significant dose response effect of tap water and SAB, that is strongest with two or more glasses consumed per day, leveling off thereafter. The overall chi square test is statistically significant, as is the crude OR for "any" versus "no" tap water consumption (OR = 1.5, p = .02). If the women coded as drinking '0 glasses' are limited to those who answered they drank no tap water (vs. < 1/2 glass/day), the crude odds ratio for any consumption is 1.4 (p = 0.05).

The source of tap water is shown in Table 7.5A. This data was unavailable for 40 repondents; excluding these, the crude odds ratio for tap water consumption and SAB is 1.6. The majority of respondents lived in areas receiving mixed ground and surface water (85%). Tap and bottled water consumption varied by source; respondents in ground water areas were least likely to drink tap water (60%) and most likely to drink bottled water (73%), whereas those in surface water areas were most likely to drink tap water (78%) and least likely to drink bottled water (44%). This pattern corresponded to the proportion of respondents very concerned about their tap water in each area (60% in ground, 42% in surface). This may be due somewhat to the fact that the contamination reported in 1981 occurred in the well of a company serving ground water, so th r was much negative publicity about ground water. The odds ratios for SAB and tap water consumption do not vary greatly by source, but the association is greatest among mixed area respondents (OR = 1.6).

Because the residence at pregnancy termination may not reflect that during the first trimester, a second analysis was done (Table 7.5B). There were 436 repondents who did not move during the time period for which residence was asked. Among this group the odds ratio for any tap water, irrespective of source, is 1.7 and for bottled water is 0.68. The patterns of varying consumption of tap and bottled water by source, found in the entire study group, is also apparent in this group. However, the association of tap water and SAB was somewhat stronger in the ground water area, for this group of women who had not moved.

The distribution of glasses of bottled water consumed is shown in Table 7.6. Among women who drank any bottled water, there is a substantial proporti n (especially among controls), that drank large amounts (≥ 6 glasses/day). The ORs at the highest consumption levels are significantly less than one. The test for trend is statistically significant. The crude OR for any versus no bottled water consumption is significantly less than one (OR = 0.71, p = 0.02).

The association of SAB and tap water consumption varies by whether bottled water was consumed or not (Table 7.7). Women who did not consume bottled water had a higher OR for tap water consumption (2.1) than those who did drink bottled water (1.2). Tap water and bottled water consumption are negatively correlated as might be expected, but not strongly (r = -0.24).

The association of SAB and water consumption was examined separately for cases whose SAB had occurred by the twelfth week of gestation. This had very little effect on the patterns noted for all cases. The OR for some versus no tap water remains 1.5 (p = 0.05), and the OR for some versus n bottled water is 0.74 (p = 0.09).



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To compare our results and methodology to the other Fairchild follow-up study (Fairchild II), respondents whose pregnancy terminated while living in one of those four study areas were examined. The numbers are very small, with only 19 respondents meeting these criteria (6 cases). The odds ratio (after correction for small sample size) for any tap water consumption and SAB was 4.2 (0.38, 46.7) and for any bottled water consumption is 0.26 (0.03, 2.3). These estimates are rather similar to those in Fairchild II, despite being for more recent pregnancies (1986-87). The proportion of these respondents reporting that they were very concerned about their tap water (47%), was similar to the total group; but of those concerned, only 22% drank any tap water (vs. 53% in the total group), and 89% drank some bottled water (vs. 81% in total group). Excluding these Fairchild respondents from the total study group, yields an OR for tap water and SAB of 1.4, which is still significant ($p \leq 0.05$).

Table 7.8 indicates exposure to water via showering and bathing. Cases tend to have less exposure time than controls, with a significant trend of ORs decreasingly less than one as exposure time increases. This association is not explained by an association of bottled water drinkers taking longer showers (Table 7.3).

<u>Confounder Adjustment</u>

The Mantel-Haenszel odds ratios were calculated for a number of potentially confounding variables (Table 7.9A). None of these variables appear to be important confounders of the tap water and SAB relationship, as there is little change in the OR after adjustment. Hospital and LMP were examined, because they were the matching variables. As indicated, they did not appear to confound the relationship. Education, ethnicity and concern about tap water may be effect modifiers, since they all had p-values less than 0.15 for the homogeneity test. The ORs for tap water and SAB among some of the subgroups are shown in Table 7.9B. The association of tap water consumption and SAB is stronger among women with a high school or lower level of education (OR = 3.1, p = 0.02), of Hispanic ethnicity (OR = 5.2, p = 0.001), and who were not very concerned about the quality of their tap water (OR = 2.5, p = 0.003). In addition, the association is stronger in women of gravidity one (OR - 3.3, p - 0.11) and those who were not nauseous (OR - 1.9, p - 0.02).

Ethnicity and concern were examined in more detail in an attempt to sort out these relationships. Overall, Hispanics were less likely to be very concerned about their tap water (37%), compared to Whites (50%) or other races (53%). As noted previously, Hispanics were also more likely to drink tap water (75%) and slightly less likely to drink bottled water. As with all women, Hispanics who were very concerned were less likely to drink tap water (62%), but their consumption was not curtailed as much as among all women concerned (53% tap drinkers). Among Hispanics, the OR for the tap water and SAB association is elevated at both levels of concern; it is 2.4 among those very concerned and extremely large among those not concerned, with all cases drinking tap water (small sample estimate of OR - 21.9). Th pattern among non-Hispanic Whites is similar to, but less striking than, the overall pattern, with those very concerned having a lower OR (1.2) than women not concerned (1.4). Among women of other races the OR was 0.46 if very concerned and 2.5 if not concerned. Among the 'other' races, Blacks and "others" were more concerned (about 62%) than Asians (50%). Thus, for all races the association between tap water and SAB is strongest among thos not concerned.

An alternative explanation for variation of the effect measure with level of concern might be that women who were concerned, but nevertheless drank some tap water, might drink less (e.g. <2 glasses/day). However, among tap drinkers there was no relationship between the amount consumed and level of concern. Furthermore, among very concerned women there was little difference in the amount of tap water or bottled water consumed between cases and controls. Therefore this explanation is not supported.

The Mantel-Haenszel ORs for bottled water consumption are shown in Table 7.10. Again, none of the variables appear to be strong confounders. Th negative association of SAB and bottled water is stronger among women wh are employed (OR - 0.6, p - 0.008), 20 years old or younger (OR - 0.16, p -0.025) and not nauseous (OR - 0.55, p - 0.02). For comparison to the ethnicity findings with tap water, the ORs by race are; for Hispanics (0.52, p = 0.04), Whites (0.83, p = 0.38) and others (0.63, p = 0.16). The association is again strongest in Hispanics, but is also seen among the other races. There is no difference in the odds ratios by level of concern.

Logistic regression analysis was conducted with a number of factors in the model (Table 7.11). Variables statistically related to SAB are nausea (OR = 0.32), maternal age less than 20 (OR = 0.32), advanced maternal age (OR = 1.9), prior fetal deaths, with a particularly high risk after two or more losses (OR = 3.7) and higher alcohol consumption (OR = 2.4). These associations are consistent with other published studies (3) except for the apparently protective effect of young maternal age. However it should be noted that none of the women in this study were less than 18 years old. The OR for tap water consumption adjusted for the other variables remains at 1.5 (p = 0.06). The absence of nausea may be a symptom of SAB, and concern may result from having an SAB, therefore these variables were removed in one model. After this, the ORs for the other variables remained within 0.1 of the full model estimates, except for two or more fetal deaths, for which the OR is reduced to 3.2. When the hospitals were added to the model as indicator variables, none of them had statistically significant ORs, and the other coefficients changed little. The OR for home tap water consumption remained 1.5 (p = 0.05). The models were run with bottled water instead of tap water and the same variables were significant predictors of SAB. The bottled water OR was increased slightly to 0.77 which was no longer statistically significant (p = 0.16). A model which contained only the significant SAB predictor variables yielded a bottled water OR of 0.75 (p = 0.09).

Because of the differences in the tap water association by race, the three ethnic groups were examined separately. Compared to Whites, Hispanics were generally younger, of higher gravidity with a larger proportion of multiple fetal deaths, less educated and less likely to drink alcohol or smoke. There was also variation by hospital, with about 30% of Hispanics coming from the county public hospital compared to only 5% of Whites. In a logistic regression analysis (tap water model), the variables significantly related to SAB among Hispanics were advanced maternal age (OR = 4.4), nausea (OR = 0.25), and prior fetal deaths (OR for 2 or more = 6.8). The association of SAB and home tap water consumption controlling for the other variables is even stronger than unadjusted (OR = 5.8, p = 0.004), as is tru for bottled water consumption (OR = 0.41, p = 0.06). Therefore, the observation of strong water associations in Hispanics does not appear to be due to any of the potential confounders we measured. The significant predictors of SAB in Whites are the same as in the logistic regression model for all races combined, although the ORs vary somewhat. The adjusted OR for home tap water consumption is 1.4 (p = 0.2) and for bottled water consumption is 0.95. The logistic regression model for "other" ethnicity is quite different with only nausea, prior fetal deaths and smoking one pack of cigarettes or more per day, being significantly related to SAB. The adjusted OR for tap water consumption is 0.71 (p = 0.4) and for bottled water is 0.80 (p = 0.6).

### Interviewing

Interviews for this portion of the study were conducted from April 1986 through January 1987. Slightly more cases than controls were interviewed in the earliest months. The average length of interview was 60 minutes for both cases and controls. About 16 interviewers were involved in interviewing, some of whom had only recently been hired when the stop dat for this portion of the data was determined. Four interviewers conducted fewer than ten interviews and two conducted about 125 interviews each. All interviewers interviewed both cases and controls, except a refusal converter who did only three controls. When the tap water and bottled water associations were adjusted for month of interview, length of interview, and interviewer (stratified into four groups by number of interviews), the Mantel-Haenszel odds ratios were very similar to the unadjusted.

## DISCUSSION

Although the original focus of this case-control study (SACCS) was not to examine water consumption and pregnancy outcome, many detailed questions about consumption were collected. The data were analyzed before data collection was complete, but major efforts were made to include a repres ntative portion of the respond nts, with a satisfactory completion rate, and a large enough sample siz to adequately examine the tap water issue. The data were edited prior to this analysis and potential interviewer bias examined.

The results of this study show a moderate, but statistically significant, association between SAB and reported consumption of tap water or no bottled water. These findings are further strengthened by the observation of significant dose-response relationships for both tap and bottled water. Furthermore, the tap water association is strongest among women who drank no bottled water, suggesting that perhaps bottled water consumption is a protective factor. However, the association between SAB and bottled water weakened somewhat in the logistic regression model. There was a negative association between SAB and water exposure via showering or bathing, which would argue against a solvent contaminant as a cause of the observed association with tap water consumption. Our data are inconclusive with regards to water source.

The findings of this study with regard to water consumption are consistent with others in this report, although of a lesser magnitude. This study shows a dose response effect of tap water that is similar to that of Fairchild II. None of the potential confounders measured affected the associations greatly. As in Fairchild I, the effect of tap water consumption is strongest among women with no prior pregnancies (and thus no prior SABs). The effect of an environmental contaminant on SAB might be expected to be strongest in women with no prior losses, because repeat SABs are more likely to have a physiologic etiology.

There are a few methodologic differences between this study and the others which should be mentioned. The pregnancies in SACCS were much more recent, so exposures may have changed since the Fairchild studies. The cases of SAB are pathology confirmed. While this suggests later SABs, the mean gestational age in SACCS is comparable to that in the other studies. Furthermore, limiting the analysis to SABs of 12 weeks or less did not change the results. The study is conducted county-wide, so it should be most representative of a general county population.

The interview in SACCS asked questions about tap wat r c nsumption before pregnancy and any changes during the first half of pregnancy, so that an average exposure could be calculated based on the length of pregnancy. Thus, it should be more accurate than having the respondent provide "the average." Table 7.12A shows that about 10% of cases changed their home tap water consumption compared to 26% of controls. However, both cases and controls were more likely to increase than decrease consumption. Only 17% of controls who changed (Table 7.12B) reported that the change took place after the second month of pregnancy. Even though 60% of cases had pregnancies which lasted beyond two months, they reported no changes after two months. Among those who decreased consumption, four cases (1.6% of total) and 48 controls (8.5%) stopped drinking tap water altogether. Again, most of these changes occurred in the first two months (80% of controls and all cases). We might assume that these women began drinking bottled water, but this is a small proportion of total bottled water drinkers (3% and 13.5% respectively). If the proportion of controls who stopped drinking tap water each month is applied to the number of cases still pregnant that month, w would expect 17 cases to have stopped drinking tap water, but only four did so. In addition, six controls started drinking tap water during pregnancy (five during first two months), but no cases did so (2 expected).
In summary, controls do not appear to be changing water consumption more than cases due to greater opportunity, during their longer pregnancy.

Examining the association between SAB and tap water before pregnancy (Table 7.13) yields an OR of 1.4 (1.0, 2.1), whereas the association based on consumption only after any change has an OR of 1.8 (1.3, 2.6). This suggests that the interpretation of these associations in other studies may vary, depending on the manner in which consumption is ascertained in a particular study. Unless specified, as was done in SACCS, it is not clear what level women would report if they changed consumption. Furthermore, this reporting may depend on their pregnancy outcome. For example, controls with full term pregnancies may tend to report levels after the change, whereas cases may report consumption before the change or average it over their shorter pregnancy. If consumption of cases 'before' is compared to controls 'after', the OR for any tap water would be 2.0.

Additional differences between this study and the others in this report include; a large proportion of both cases and controls who drank bottled water, and, among bottled water drinkers, a large proportion (54%) who also drank some tap water. Cases and controls were similarly concerned about the quality of their tap water.

Of all the studies in this report, SACCS seems to be the one least subject to recall bias; both because respondents were not told that water consumption was of particular interest and because subjects throughout the county were less likely to be aware of the publicity surrounding the original localized water contamination. Risk factors noted among these cases are the same as those commonly found in published studies (3), supporting the representativeness of this study group.

There may be a possibility of selection bias in this study, if pathology specimens are obtained more readily by some segments of the population than others. However, the demographic characteristics of this study group are similar to those in the other county wide case-control study (Cardiac). Concerned, educated women might be more likely to save a specimen or seek medical care for symptoms of an SAB. However, these women drank less tap water, so we would expect this to bias results towards the null value. Cases and controls were fairly similar by race and concern, but cases were slightly better educated.

Another explanation for the observed association between reported water consumption and SAB may be confounding. None of the many variables we examined altered the associations. However, there may be an as yet unidentified confounder. The associations are stronger among Hispanics and less educated women, so perhaps there is a socioeconomic factor involved. If so, we might expect a difference by insurance coverage or employment. The association of tap water and SAB among insured women (OR = 1.5) was stronger than among non-insured (OR = 1.2). The association was also stronger among women who worked. Average income (1980 Census) of the census tract of residence, at pregnancy termination, was examined to further explore possible socioeconomic effects. There was no significant difference in the distribution by case/control status, bottled water, r tap water consumption. Middle class census tracts ($25,000 - 30,000) tended t include fewer tap water consumers, but they also included the largest proportion of very concerned respondents. Adjusting for income (4 levels), yielded odds ratios similar to the unadjusted; 1.6 for tap water and 0.73 for bottled water. The associations were strongest in the lowest income (<$20,000) areas (ORs=2.9, p=.01 and 0.63, p=.3 for tap and bottled water respectively). These findings are not due to an association between race and income, as they are even stronger among Whites. However, it must be remembered that individual household income during pregnancy was not asked in this study. Potential biases are discussed in more detail in Section 10 of this report.

In conclusion, this study shows a moderate association of SAB with water consumption that is consistent with the other studies in this report. The association can not be readily explained by the many variables examined, and should be studied further.

## References


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2. Sawtooth Software Inc., Ketchum, Idaho.

3. Kline J and Stein Z. Spontaneous Abortion, in: Perinatal Epidemiology. Bracken M., ed. Oxford University Press, London, 1984; pp. 23-51.

Table 7.1

Completion Rates for SACCS Respondents, Batches 1-4

| | Cases | | Controls | |
|---|---|---|---|---|
| | N | % | N | % |
| Sent Letters (Batches 1-4) | 422 | | 875 | |
| Returned Letters | 135 | 32.0 | 415 | 47.4 |
| Attempted Interviews | 405 | | 798 | |
| Ineligible[a] | 32 | 7.9[b] | 51 | 6.4[b] |
| Refusals[c] | 34 | 9.1[d] | 86 | 11.5[d] |
| Not located or not reached | 38 | 10.2[d] | 45 | 6.0[d] |
| Completed | 301 | 80.7[d] | 616 | 82.5[d] |
| Analysis | | | | |
| Excluded (before bottled water data added) | 32 | 8.6[d] | 14 | 1.9[d] |
| Analyzed (for water) | 251 | 73.6[e] | 566 | 77.2[e] |

[a]Ineligible due to language other than English or Spanish, moved away from San Francisco Bay Area or claimed never pregnant.

[b]Percent of attempted interviews.

[c]Refusals include those by letter.

[d]Percent of eligible (eligible=attempted-ineligible).

[e]Percent of eligible minus the early interviews which did not ask bottled water questions. Other interviews are unavailable due to computer and editing complications, presumed unbiased.

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Table 7.2

Characteristics of Cases and Controls

| | Cases | | Controls | |
|---|---|---|---|---|
| | No. | % | No. | % |
| Education | | | | |
| Less than High School | 43 | 17.1 | 102 | 18.0 |
| High School Graduate | 63 | 25.1 | 164 | 29.0 |
| Some College | 69 | 27.5 | 161 | 28.5 |
| College Graduate | 76 | 30.3 | 139 | 24.6 |
| Ethnicity | | | | |
| White | 138 | 55.0 | 297 | 52.6 |
| Hispanic | 52 | 20.7 | 144 | 25.5 |
| Asian | 43 | 17.1 | 90 | 15.9 |
| Black | 8 | 3.2 | 16 | 2.7 |
| Other | 10 | 4.0 | 18 | 3.2 |
| Maternal Age[a] | | | | |
| <20 | 8 | 3.2 | 48 | 8.5 |
| 21-34 | 196 | 78.1 | 470 | 83.0 |
| 35+ | 47 | 18.7 | 48 | 8.5 |
| Marital Status[a] | | | | |
| Married or together | 216 | 86.1 | 526 | 92.9 |
| Single, never married | 24 | 9.6 | 28 | 5.0 |
| Other | 11 | 4.4 | 12 | 2.1 |
| Gravidity[a] | | | | |
| 1 | 13 | 5.2 | 158 | 28.0 |
| 2 | 76 | 30.3 | 154 | 27.3 |
| 3 | 60 | 23.9 | 125 | 22.1 |
| 4+ | 102 | 40.6 | 128 | 22.7 |
| Prior Fetal Loss[a] | | | | |
| 0 | 156 | 62.2 | 447 | 79.0 |
| 1 | 66 | 26.3 | 93 | 16.4 |
| 2+ | 29 | 11.6 | 26 | 4.6 |
| Prenatal Care[a] | | | | |
| Yes | 164 | 65.6 | 560 | 98.9 |
| No | 86 | 34.4 | 6 | 1.1 |
| Month of Pregnancy Test[a] | | | | |
| None | 33 | 13.2 | 21 | 3.7 |
| First (1-6 weeks) | 158 | 63.0 | 342 | 60.4 |
| Second (7-10) | 47 | 18.7 | 144 | 25.4 |
| Third or later | 13 | 5.2 | 59 | 10.4 |



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Table 7.2 (Continued)

| | Cases No. | Cases % | Controls No. | Controls % |
|---|---|---|---|---|
| Insurance Coverage[a] | | | | |
| Yes | 212 | 84.5 | 511 | 90.3 |
| No | 39 | 15.5 | 55 | 9.7 |
| Nausea[a] | | | | |
| Yes | 128 | 51.2 | 417 | 73.7 |
| No | 122 | 48.8 | 149 | 26.3 |
| Alcohol[a] | | | | |
| <0.5 drinks/wk | 147 | 58.8 | 386 | 68.2 |
| 1-3 drinks/wk | 71 | 28.4 | 146 | 25.8 |
| 4+ drinks/wk | 32 | 12.8 | 34 | 6.0 |
| Cigarette Smoking | | | | |
| 0 | 188 | 74.9 | 456 | 80.6 |
| ≤1/2 pk/day (1-12) | 37 | 14.7 | 70 | 12.4 |
| ≥ 1 pk/day (13+) | 26 | 10.4 | 40 | 7.1 |
| Employment | | | | |
| Yes | 173 | 69.2 | 389 | 68.7 |
| No | 77 | 30.8 | 177 | 31.3 |
| Solvent Exposure | 51 | 20.3 | 99 | 17.5 |
| Other Hazards (X-ray, VDT, lead, etc.) | 117 | 46.6 | 229 | 40.5 |
| Tap Water Consumption[a] | | | | |
| Some | 184 | 74.2 | 371 | 66.0 |
| None | 64 | 25.8 | 191 | 34.0 |
| Bottled Water[a] | | | | |
| Some | 138 | 55.0 | 357 | 63.1 |
| None | 113 | 45.0 | 209 | 36.9 |
| Concern about Tap Water | | | | |
| Very | 109 | 43.4 | 275 | 48.6 |
| Somewhat | 65 | 25.9 | 131 | 23.1 |
| Not | 74 | 29.5 | 152 | 26.7 |
| Don't Know | 3 | 1.2 | 8 | 1.4 |

[a]Chi-square comparing case and control distribution has p-value $\leq 0.05$.

Table 7.3

Proportion Who Drank Tap and Bottled Water by Demographic Characteristics

| | Percent that drank any Tap Water[a] | Percent that drank Bottled Water[b] |
|---|---|---|
| **Education** | | |
| Less than High School | 71.1 | 51.0 |
| High School Graduate | 68.6 | 61.2 |
| Some College | 68.0 | 63.9 |
| College Graduate | 67.3 | 62.8 |
| **Ethnicity** | | |
| White | 68.8 | 59.5 |
| Hispanic | 75.3 | 56.1 |
| Asian | 62.6 | 67.7 |
| Black | 45.8 | 66.7 |
| Other | 64.3 | 67.9 |
| **Maternal Age** | | |
| ≤20 | 67.9 | 60.7 |
| 21-34 | 68.1 | 62.5 |
| 35+ | 71.6 | 47.4 |
| **Marital Status** | | |
| Married or together | 68.6 | 61.2 |
| Other | 67.6 | 54.7 |
| **Gravidity** | | |
| 1 | 64.1 | 64.3 |
| 2 | 64.0 | 69.6 |
| 3+ | 72.8 | 54.0 |
| **Prenatal Care** | | |
| Yes | 68.5 | 61.7 |
| No | 68.1 | 52.2 |
| **Insurance Coverage** | | |
| Yes | 67.4 | 62.1 |
| No | 77.4 | 48.9 |
| **Nausea** | | |
| Yes | 68.7 | 62.2 |
| No | 68.2 | 57.2 |
| **Alcohol** | | |
| <0.5 drinks/wk | 69.3 | 58.4 |
| 1-3 drinks/wk | 66.2 | 65.9 |
| 4+ drinks/wk | 69.2 | 62.1 |

Table 7.3 (Continued)

| | Percent that drank any Tap Water[a] | Percent that drank Bottled Water[b] |
|---|---|---|
| **Cigarette Smoking** | | |
| None | 68.1 | 61.7 |
| ≤1/2 pk/day (1-12) | 71.4 | 67.3 |
| ≥ 1 pk/day (13+) | 68.2 | 39.4 |
| **Employment** | | |
| Yes | 67.9 | 66.9 |
| No | 69.7 | 46.9 |
| **Showering/Bathing** | | |
| 0- 49 mins/wk | 67.1 | 62.1 |
| 50- 99 mins/wk | 70.4 | 57.6 |
| 100-149 mins/wk | 67.7 | 62.6 |
| ≥ 150 mins/wk | 67.0 | 62.0 |
| **Concern about Tap Water** | | |
| Very | 52.6 | 80.7 |
| Some or none | 82.7 | 42.7 |

[a]Overall, 68.5% of repondents drank some tap water (n=555).

[b]Overall, 60.6% of respondents drank some bottled water (n=495).

Table 7.4

Odds Ratios For Spontaneous Abortion by Tap Water Consumption

| Home Tap Water[a] (glasses/day) | Case | Control | OR | 95% CI[b] |
|---|---|---|---|---|
| 0 | 64 | 191 | 1.0 [b] | ---- |
| 1 | 24 | 64 | 1.1 | (0.62, 2.0) |
| 2 | 47 | 77 | 1.8 | (1.1, 3.0) |
| 3 | 43 | 78 | 1.6 | (1.0, 2.7) |
| 4 | 22 | 52 | 1.3 | (0.68, 2.3) |
| 5 | 18 | 42 | 1.3 | (0.66, 2.5) |
| 6+ | 30 | 58 | 1.5 | (0.88, 2.7) |
| TOTAL | 248 | 562 | | |

$\chi^2 = 17.7$, $p = 0.013$ $\chi^2_{trend} = 7.3$, $p < 0.01$

[a] Average consumption during first trimester, including any changes in habit. ("0" is actually less than half a glass/day, other categories are also rounded off).

[b] Referent group

Table 7.5A

Odds Ratios for Spontaneous Abortion by Tap Water Consumption Stratified by Water Type

| Water Type | Tap Water (glasses/day) | Case | Control | OR | 95% CI |
|---|---|---|---|---|---|
| Ground | 1+ | 12 | 32 | | |
| | 0 | 7 | 23 | 1.2 | (0.42, 3.6) |
| Mixed | 1+ | 146 | 304 | | |
| | 0 | 47 | 159 | 1.6 | (1.1, 2.4) |
| Surface | 1+ | 9 | 23 | 1.4 | (0.24, 7.8) |
| | 0 | 2 | 7 | 0.88[a] | (0.15, 5.5) |
| Mantel-Haenszel | OR = 1.6 p = 0.012 | | | | |

Table 7.5B

Water Type Among Women Who Did Not Move[b]

| Water Type | Tap Water (glasses/day) | Case | Control | OR | 95% CI |
|---|---|---|---|---|---|
| Ground | 1+ | 8 | 16 | 2.7 | (0.50, 19.9) |
| | 0 | 3 | 16 | 1.9[a] | (0.47, 7.7) |
| Mixed | 1+ | 88 | 162 | 1.6 | (0.96, 2.7) |
| | 0 | 29 | 86 | | |
| Surface | 1+ | 5 | 14 | 1.8 | (0.13, 5.7) |
| | 0 | 1 | 5 | 0.83[a] | (0.12, 5.4) |
| Mantel-Haenszel | OR = 1.7 p = 0.02 | | | | |

[a]Corrected for small sample size.

[b]Same address between January 1986 and date of interview, so lived at this address during first trimester.

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Table 7.6

Odds Ratios for Spontaneous Abortion by
Bottled Water Consumption

| Bottled Water[a] (glasses/day) | Case | Control | OR | 95% CI |
|---|---|---|---|---|
| 0 | 113 | 209 | 1.0[b] | ------ |
| 1 | 14 | 38 | 0.68 | (0.34, 1.4) |
| 2 | 25 | 43 | 1.1 | (0.60, 1.9) |
| 3 | 33 | 68 | 0.90 | (0.54, 1.5) |
| 4 | 27 | 61 | 0.82 | (0.48, 1.4) |
| 5 | 8 | 41 | 0.36 | (0.15, 0.84) |
| 6+ | 31 | 106 | 0.54 | (0.33, 0.87) |
| TOTAL | 251 | 566 | | |

$\chi^2 = 14.4$ $p < 0.05$ $\chi^2_{trend} = 8.7$ $p \leq 0.005$

[a] Usual consumption during pregnancy (cases) or first 20 weeks (controls), at home and work.

[b] Referent group



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Table 7.7

Odds Ratios for Spontaneous Abortion by
Tap Water and Bottled Water Consumption

| | No Bottled Water | | Any Bottled Water | |
|---|---|---|---|---|
| Tap Water Use | Case | Control | Case | Control |
| Any | 106 | 185 | 78 | 186 |
| None | 6 | 22 | 58 | 169 |
| | OR=2.1 (0.83, 5.3)<br>p=0.11 | | OR=1.2 (0.82, 1.8)<br>p=0.32 | |

Summary OR= 1.3, p= 0.11

Tap Water Crude OR = 1.5, p = .02

Bottled Water Crude OR = 0.71, p = 0.03

Table 7.8

Odds Ratios for Spontaneous Abortion
by Duration of Showering and Bathing

| Duration of Showering and Bathing (Min/wk)[a] | Case | Control | OR | 95% CI |
|---|---|---|---|---|
| 0 - 49 | 50 | 95 | 1.0[b] | ------ |
| 50 - 99 | 99 | 203 | 0.93 | (0.60, 1.4) |
| 100 - 149 | 79 | 191 | 0.79 | (0.50, 1.2) |
| ≥ 150 | 23 | 77 | 0.57 | (0.31, 1.1) |
| TOTAL | 251 | 566 | | |

$\chi^2 = 4.6$ $p = 0.20$ $\chi^2_{trend} = 4.2$ $p = 0.04$

[a] Only asked number baths/week; assumed 10 minutes to get total exposure. For showers, minutes were asked.

[b] Referent group

Table 7.9A

Odds Ratios for Spontaneous Abortion and Home Tap Water Consumption after Adjustment for Potential Confounders

| Variables | $OR_{MH}$ (any cold home tap water vs. none) | Chi square for homogeneity p |
|---|---|---|
| Alcohol | 1.5 | 0.42 |
| Education | 1.5 | 0.13[a] |
| Employment | 1.5 | 0.36 |
| Ethnicity | 1.5 | 0.03[a] |
| Gravidity | 1.4 | 0.45[a] |
| Marital Status | 1.5 | 0.69 |
| Maternal Age | 1.5 | 0.62 |
| Month Prenatal Care Began | 1.6 | 0.59 |
| Nausea | 1.5 | 0.30[a] |
| Prior Fetal Loss | 1.4 | 0.62 |
| Smoking | 1.5 | 0.83 |
| Concern About Tap Water (very vs. some/none) | 1.4 | 0.02[a] |
| Showering/Bathing | 1.5 | 0.54 |
| Solvent Exposure (work) | 1.5 | 0.16 |
| Other Hazardous Exposure | 1.5 | 0.86 |
| Insurance Coverage | 1.4 | 0.65 |
| Hospital | 1.5 | 0.91 |
| Month of LMP | 1.5 | 0.54 |

[a]Sub-group OR's shown in Table 7.9B (not all have significant p-value for homogeneity).

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Table 7.9B

Odds Ratios for Spontaneous Abortion and Home Tap Water Consumption by Potential Confounder Sub-groups

| Factor | OR | p |
|---|---|---|
| Education | | |
| Less Than High School | 3.1 | 0.017 |
| High School graduate | 2.1 | 0.03 |
| Some College | 1.2 | 0.58 |
| College graduate | 1.0 | 0.97 |
| Ethnicity | | |
| Hispanic | 5.2 | 0.001 |
| White | 1.3 | 0.22 |
| Other | 1.1 | 0.75 |
| Gravidity | | |
| First | 3.3 | 0.11 |
| Second | 1.2 | 0.56 |
| Third or more | 1.4 | 0.13 |
| Nausea | | |
| Yes | 1.3 | 0.25 |
| No | 1.9 | 0.02 |
| Concern about Home Tap Water | | |
| Very Concerned | 1.0 | 0.97 |
| Somewhat or Not | 2.5 | 0.003 |

Table 7.10

Odds Ratios for Spontaneous Abortion by Bottled Water Consumption after Adjustment for Potential Confounders

| Variables | | | $OR_{MH}$ (any bottled water vs. none) | Chi square for homogeneity p |
|---|---|---|---|---|
| Alcohol | | | 0.70 | 0.33 |
| Education | | | 0.71 | 0.94 |
| Employment | | | 0.71 | 0.13 |
| Yes | OR = 0.60 | p = 0.008 | | |
| No | OR = 1.0 | p = 0.98 | | |
| Ethnicity | | | 0.70 | 0.44 |
| Gravidity | | | 0.76 | 0.72 |
| Marital Status | | | 0.73 | 0.75 |
| Maternal Age | | | 0.75 | 0.16 |
| ≤ 20 yrs | OR = 0.16 | p = 0.025 | | |
| 21-34 yrs | OR = 0.82 | p = 0.26 | | |
| ≥ 35 yrs | OR = 0.68 | p = 0.35 | | |
| Month Prenatal Care Began | | | 0.70 | 0.73 |
| Nausea | | | 0.73 | 0.13 |
| Yes | OR = 0.89 | p = 0.59 | | |
| No | OR = 0.55 | p = 0.02 | | |
| Prior Fetal Loss | | | 0.72 | 0.44 |
| Smoking | | | 0.73 | 0.52 |
| Concern About Tap Water (very vs. some/none) | | | 0.75 | 0.91 |
| Showering/Bathing | | | 0.72 | 0.38 |
| Insurance Coverage | | | 0.73 | 0.29 |
| Hospital | | | 0.71 | 0.15 |
| Month of LMP | | | 0.69 | 0.57 |

Crude OR = 0.71 (1.1, 2.1) p = 0.02

Table 7.11

Logistic Regression Analysis for Spontaneous Abortion and Tap Water Consumption

| Factor | OR | p |
|---|---|---|
| Alcohol | | |
| Moderate (1-3 gls/wk) | 1.3 | 0.20 |
| High (4 + gls/wk) | 2.4 | 0.004 |
| Education | | |
| Less Than High School | 1.1 | 0.75 |
| Some College | 1.2 | 0.35 |
| College graduate | 1.4 | 0.13 |
| Employment | 0.95 | 0.77 |
| Ethnicity | | |
| Hispanic | 1.0 | 0.90 |
| Other | 1.3 | 0.26 |
| Home Tap Water | 1.5 | 0.06 |
| Maternal Age | | |
| ≤ 20 years | 0.32 | 0.01 |
| ≥ 35 years | 1.9 | 0.01 |
| Nausea | 0.32 | < 0.0001 |
| Prior fetal loss | | |
| one | 2.2 | 0.0001 |
| two or more | 3.7 | < 0.0001 |
| Smoking | | |
| ≤ 1/2 pack (1-12 cigs)/day | 1.3 | 0.31 |
| - 1 pack/day or more | 1.6 | 0.16 |
| Concern (very) | 0.93 | 0.67 |

Table 7.12A

Changes in Tap Water Consumption During Pregnancy

| Change | Case N | Case % | Control N | Control % |
|---|---|---|---|---|
| Increased | 19 | 7.6 | 90 | 16.0 |
| Decreased | 7 | 2.8 | 62 | 11.0 |
| No Change | 224 | 89.6 | 412 | 73.0 |

$X^2$=28.8 p<.001

Table 7.12B

Change in Tap Water Consumption by Direction of Change and Month

| Month | N(cases)[a] | Increase Case | Increase Control | Decrease Case | Decrease Control |
|---|---|---|---|---|---|
| First (6 weeks) | 251 | 15 (79.0%) | 38 (43.7%) | 2 (33.3%) | 33 (53.2%) |
| Second (7-10 weeks) | 229 | 4 (21.0%) | 32 (36.8%) | 4 (66.7%) | 20 (32.3%) |
| Third[a] (11-14 weeks) | 149 | 0 | 11 (12.6%) | 0 | 4 ( 6.5%) |
| Fourth or later | 46 | 0 | 6 ( 6.9%) | 0 | 5 ( 8.1%) |
| $X^2$ | | 9.57 p = 0.05 | | 11.75 | p = 0.02 |

[a]Number of cases still pregnant at start of interval (all controls were pregnant during each time period).

Table 7.13

Association of Tap Water Consumption and Spontaneous Abortion Before and After Changes in Consumption

| Tap Before[a] Change | Case | Control |
|---|---|---|
| Any | 186 | 379 |
| None | 63 | 186 |

OR = 1.4 (1.0, 2.1)

| Tap After[b] Change | Case | Control |
|---|---|---|
| Any | 182 | 337 |
| None | 67 | 228 |

OR = 1.8 (1.3, 2.6)

[a] "Before" is asked as one month before the LMP until a change occurs, or throughout the pregnancy or first 20 weeks, if no change.

[b] "After a change" includes those whose use was unchanged.

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## 8. Reproductive Toxicology of Water Contaminants

Environmental exposure to chemicals as a cause of early pregnancy loss is just beginning to be investigated and understood (1). Of the agents currently known to produce spontaneous abortions and/or malformations in humans very few are environmental chemicals.

Agents that produce spontaneous abortions (abortifacients) and agents that produce malformations (teratogens) are frequently discussed together in developmental toxicology (2, 3). Animal studies have shown that high doses f teratogens usually cause death of the embryo (which leads to abortion in humans) and malformation while lower doses may lead to growth retardation, delayed development and other developmental toxicity (4). The majority of known human developmental toxins listed in Table 8.1 were identified when well-defined exposures occurred in limited numbers of women (case histories) (2). Subsequently, epidemiological and animal research established their developmental toxicity.

A few environmental chemicals, including primarily industrial solvents, are currently being investigated in epidemiological studies as potential human developmental toxicants (Table 8.2).

A much larger number of chemicals can be considered suspect human developmental toxicants on the basis of developmental toxicity demonstrated in routine animal testing. There is some information on animal developmental toxicity for the majority of chemicals on the EPA "Priority Pollutant" list, which includes the most commonly detected water contaminants. Water soluble priority pollutants with known developmental toxicity in animals are listed in various compilations of animal reproductive toxicology studies (5, 6). In most cases such effects occur when very high doses are given during pregnancy. Thus, relevance for low level chronic environmental exposure in humans (as would occur with contaminated drinking water) is unclear. Unlike cancer-causing chemicals, developmental toxicants are thought not to exert their effects until exposures reach a definable threshold level. Exceptions to this could include mutagens that affect gametes or bioaccumulative chemicals.

In addition to chemical contaminants, water contains a variety of metals and minerals (trace elements), many of which are naturally occurring, with concentrations that vary by geographical region. However, trace element concentrations can also be affected by pollution, particularly with heavy metals (7). The metal and mineral content of water is important because dietary trace element deficiencies are known from animal studies to produce developmental toxicity (8) (Table 8.3). In some cases, excess of one trace element can lead to deficiency of another through competition for absorption and tissue receptors. Trace element content of drinking water has been investigated as a factor affecting birth defect incidence in some areas of Britain and Canada (9, 10), but no associations have been confirmed.

Other agents present in drinking water and potentially related to abortion induction are microorganisms (Table 8.4) (11) and radioactive substances (12). Water districts routinely screen water supplies for radioactive emissions (alpha and beta particles and uranium) and microorganisms (coliform bacteria and turbidity measures). In addition, viral infections (which are most commonly associated with abortion) are not known to be transmitted via drinking water. However, nutritional and immune system function could be influenced by water contaminants and secondarily affect the incidence of subclinical or localized infection (13). In addition, toxins produced by microorganisms are potential abortifacients (14).

While the agent responsible for differential abortion rates in the current studies is unknown, the work to date has identified some highly probable characteristics:

-- water soluble (cold tap water effect)
-- absorbable via the oral route (cold tap water effect)
-- removable by charcoal filter (filter effect)
-- effective at low exposure level or bioaccumulative (analytical data)

and possibly:

-- volatile and/or skin absorbable (weak shower effect)

At the same time, scientific understanding of developmental toxins leads to some conclusions about p ssible characteristics of human abortifacients:

-- mutagenic or with alkylating ability

-- cross placenta readily and/or selectively concentrate in fetus

-- interfere with cell division

-- cause metabolic/nutritional disruption

-- interfere with production of trophic factors and cell membranes

Together, these considerations are useful in eliminating many potential candidates for responsible agents. Trace elements, for example, are not typically volatile/skin absorbable. Heavy metals and some classes of pesticides are minimally soluble in water. Routine water treatment eliminates many known infectious agents. Most bioaccumulative substances are lipid rather than water soluble. Such considerations need to be combined with planned water analysis studies that attempt to identify potentially responsible agents. Some potential candidates (known or suspected developmental toxins, water soluble, volatile) that have not yet b en included in water analyses thus far are: glycol ethers (2-ethoxyethanol, 2-methoxymethanol) (15), ketone solvents (2-butanone, methyl pentanone, cyclohexanone) (16), aliphatic hydrocarbons (17), dimethylformamide (5), carbon disulfide (18), ethylene oxide (19), and methyl chloride (20).

An exciting and unique opportunity is opened by the work done to date to increase our knowledge about links between environmental exposure and early human reproductive loss, a subject that has created concern without producing the necessary scientific understanding to address that concern (21). A fairly large body of information and theory is available from developmental toxicology to guide this process, although the responsible agent cannot be deduced from the limited analytical and exposure data generated thus far. One method for further exploring these findings is by animal testing using the water sources in question (see Appendix A for proposed study protocol).

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## Table 8.1

### Some Agents With Known or Suspected Human Abortifacient or Teratogenic Effects

<u>Drugs</u>

<u>known</u>

alcohol
thalidomide
diethylstilbestrol
antineoplastics (several)
anticonvulsants (valproate, diphenylhydantoin, trimethadione)
anticoagulants (warfarin)
antibacterials (quinine, chloroquin, kanamycin)
antifolate (aminopterin)
retinoids (several)

<u>suspected</u>

anesthetic gases (halothane)
oral antidiabetic drugs

<u>Environmental Chemicals</u>

<u>known</u>

lead
methyl mercury

<u>suspected</u>

PCBs

Table 8.2

Chemicals Currently Being Studied as Human Abortifacients/Teratogens

| Chemical | |
|---|---|
| tetrachloroethylene | (22, 23) |
| methylene chloride (and related solvents) | (24) |
| toluene (and related solvents) | (25, 26) |

Table 8.3

Metals and Minerals Associated with Embryotoxic and Teratogenic Effects in Humans and/or Animals (7, 8)

| Metal excess | Mineral deficiency |
| --- | --- |
| lead (animals & humans) | zinc (animals & humans) |
| methyl mercury (animals & humans) | copper (animals) |
| cadmium (animals) | manganese (animals) |
| selenium (animals) | magnesium (animals) |

Table 8.4

**Microorganisms/Infections Associated with Embroyotoxic and Teratogenic Effects in Humans (17)**

Viral

| | |
|---|---|
| cytomegalovirus | rubella |
| herpes simplex | rubeola |
| influenza | vaccinia |
| mumps | varicella-Zoster |
| poliomyelitis | variola |

Bacterial

syphilis
listeriosis

Parasitic

toxoplasmosis

Rickettsial

Coxiella laurnetti (Q fever)

Appendix A. The Effect of Water Source on Reproductive Outcome in Sprague-Dawley Rats

## Introduction

Based on recent epidemiological data collected by the California Department of Health Services, it has been observed that in certain geographical locations of the state there is an association between the frequency of abortions and the consumption of tap water. Based on this observation, it has been suggested that there may be a causal link between the consumption of some city waters and adverse reproductive outcome in select human populations of Northern California. Specifically, based on retrospective interviews of women characterized by either recent successful pregnancies or abortions, it was observed that pregnant individuals who consumed tap water in certain geographical regions had a higher incidence of abortion than women in the same geographical regions who had consumed bottled waters during pregnancy. There are at least five possible explanations for the above observation. First, tap water in certain geographical regions may contain a reproductive toxin which in humans may lead to an increased risk of abortion. Second, some bottled waters may contain factors which promote a successful pregnancy in a subpopulation of women. Third, a combination of the first two possibilities may exist. Fourth, the observation of an association between the consumption of tap water and increased abortion risk may be spurious. Fifth, the association of healthy pregnancy outcome and consumption of bottled waters may represent a bias recall.

The purpose of the proposed grant is to evaluate the first three possibilities using the pregnant rat as an animal model. The fourth and fifth possibilities in our opinion need to be evaluated through additional interviews of the risk population groups. In particular, prospective studies are needed to evaluate the possibility of bias recall with regard to bottled versus tap water consumption.

## Experimental protocol

Two hundred virgin Sprague-Dawley female rats weighing between 180 and 200 grams will be purchased from a commercial vendor. Sprague-Dawley rats have been chosen because this strain has reliable reproductive patterns, a low frequency of spontaneous resorptions and is one of the most commonly used strains in teratology studies. Rats will be housed individually in stainless steel cages in a controlled environment (temperature = 23°C) with a 12 hr light/dark cycle. The animals will be allowed free access to a commercial rat chow throughout the experimental study. During a one week acclimation period all animals will receive distilled deionized water as their sole drinking source. Glass bottles will be used with stainless steel sippers. After the acclimation period, rats will be mated using stock-fed Sprague-Dawley males. Mating will be confirmed by the presence of both sperm plugs and sperm in a vaginal smear (day 0 of pregnancy). Animals which are not mated after a three week period will be removed from the study.

Following mating, the rats will be assigned to one of 6 water groups: 1) control distilled deionized water; 2) water collected from homes in the Great Oaks area in which an individual resides who reported both the consumption of tap water during pregnancy and had an abortion; 3) water collected from homes in the Great Oaks area in which an individual resides who reported both the consumption of tap water during pregnancy and had a successful pregnancy outcome; 4) water collected from homes in an area outside the Great Oaks area in which an individual resides who reported both the consumption of tap water during pregnancy and had an abortion; 5) water collected from homes in an area outside the Great Oaks area in which an individual reported both the consumption of tap water during pregnancy and had a successful pregnancy outcome; 6) Alhambra bottled water. All rats will have the same type of watering system. The pregnant rats will be assigned to their water groups in a sequential manner, starting with water group 1. That is, the first pregnant rat will be assigned to water group 1, the second pregnant rat to water group 2, etc. At the time of water group assignments the animals will be numbered using a random number table. Prior to the completion of the analysis of the reproduction data for each dam, only the personnel involved with the daily feeding and weighing of the animals will be aware of the animal codes. The cage racks utilized in our animal rooms hold six cages per row and there are six rows per rack. In the proposed study, the placement of the cages will be: top row, water groups 1-6; second row, water groups 2-1; third row, water groups 3-2, etc. Throughout pregnancy, data on water intake will be collected daily and maternal weight gain will be measured every three days. Animals will be examined daily by the PI for any obvious signs of toxicity.

Groups 1-6 will contain 30 rats each. (Two hundred, rather than 180, female rats will be ordered to allow for the fact that about 10% of the rats will normally be resistant to breeding.) For groups 2-5, the tap water used for each group will represent a pool of water collected from five households. Aliquots of water from each household will be stored frozen for future investigation if the consumption of any of the pooled water sources are found to pose a reproductive hazard. Water from the households will be collected in 5 gallon acid-washed carboys and stored frozen until use. The water will be thawed at room temperature and refrozen up to four times. All animals will receive fresh water every other day. It is estimated that water will be collected from each of the households a maximum of four times. The water will be collected by members of the Principal Investigator's laboratory.

On day 20 of gestation, all animals which are mated will be weighed and killed by overexposure to ether. Laparotomies will be performed, the uterus removed and weighed. Implantation sites will be counted, and the number of resorptions and live fetuses recorded. Live fetuses will be removed from both the left and right horns of the uterus, cleaned, examined for external malformations, measured for crown-rump length and weighed. To minimize the possibility that horn position may be a variable in the proposed study, only fetuses from the right horn will be examined for skeletal and soft tissue malformations. The second and fourth fetuses in the distal portion of the right horn will be placed in 70% ethanol for future staining with alizarin red and alcian blue for skeletal and connective tissue examination (Aliverti et al., 1979); the first and third fetuses in the distal portion of the right horm will be placed in Bouin's fixative for examination of internal tissues by a modified version of Wilson's razor blade technique (Barrow and Taylor, 1968). The personnel (2) involved in the assessment of fetal malformations (soft tissue and skeletal) will be blind to water group assignments.

The following data on reproductive outcome will be collected: number of implantations; number of resorptions; number of live fetuses; weight and crown-rump length of all live fetuses; presence of gross external malformations in live fetuses; presence of soft tissue and/or skeletal malformations in four fetuses per litter.

Pregnant animals judged to be moribund by the PI will be killed. Blood, liver and kidney samples will be collected from these dams for subsequent laboratory tests. The uterine horn will be removed and analyzed with regard to implantation sites, resorption number and condition of any viable embryos/fetuses. Any pregnant animals which are found dead will be necropsied and data will be collected regarding the number of implantation and resorption sites.

<u>Data analysis</u>

Treatment effects will be evaluated with parametric or nonparametric statistics as appropriate. Group comparisons will be based on the litter as the unit of analysis. The following 5 major hypotheses will be tested in this experiment:

1. Relative to control water (group 1), independent of the reported success of pregnancy outcome, tap water collected from homes in the Great Oaks area (groups 2 & 3) contains a reproductive toxin.

2. Relative to tap water collected from homes in the Great Oaks area in which both the consumption of tap water during pregnancy and a successful pregnancy were reported (group 3), tap water collected from homes in which tap water consumption during pregnancy and an abortion were reported (group 2) contains a reproductive toxin.

3. Relative to control water (group 1), tap water collected from homes outside the Great Oaks area in which both the consumption of tap water during pregnancy and an abortion were reported (group 4) contains a reproductive hazard.

4. Relative to tap water collected from homes outside of the Great Oaks area in which both the consumption of tap water during pregnancy and a successful pregnancy were reported (group 5), tap water collected from homes in this area in which both consumption of tap water during pregnancy and an abortion were reported (group 4) contains a reproductive hazard.

5. Relative to control water (group 1), bottled water (group 6) contains factors which are beneficial to pregnancy outcome.

<u>Study duration</u>

The study will require approximately 6 months with 1 month lead time. An interim report will be filed halfway through the project and the final report will be submitted within 15 days of the completion of the analysis of the experimental data.

## Follow-up studies

If the results from the initial studies support the hypothesis that there is a reproductive toxin in tap water collected from certain geographical areas, studies will be designed to determine the nature of the toxin. The basic approach in these studies will be to evaluate a number of filtration processes with regard to the potential amelioration of the teratogenic effects of the water. A detailed experimental design for this type of project will be included as part of our final report.

If the results from the initial study do not support the hypothesis that there is a reproductive toxin in tap water collected from the putative risk geographical area, there are two possibilities: first, the results are correct, that there are no reproductive toxins in the water; second, the results are incorrect, and that the reproductive toxin was not detected due to a low exposure of the rat to the toxin. The second possibility can in part be tested for by conducting a follow-up study in which the exposure to the test waters can be lengthened to include a period prior to pregnancy and exposure during lactation. In addition to the lengthening of exposure time, exposure intensity to the putative toxin can be increased by the use of aerosol chambers providing a fine mist of the different water sources. Alternatively, exposure intensity may be increased by concentrating the putative toxin in the water (probably by the use of freeze-drying) and feeding the concentrate during pregnancy. A detailed experiment for the above type of studies will be provided as part of our final report.

While it could be argued that the above "follow-up" studies should be incorporated into our initial experimental design, logistically this would be very difficult and, in our opinion, the cost would be prohibitive. In contrast, following the completion of the experiment outlined in this grant, there is a good possibility that the number of water sources which need to be tested in the follow-up studies can be reduced.

References

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## 9. Past and Future Water Testing

### Introduction

There are two principal sources of water used in the areas under study; water from public systems and bottled water. Both sources are regulated by the Department of Health Services and are subject to certain standards of water quality.

The public systems that serve Santa Clara, Alameda, and San Mateo counties obtain their water from both surface water and groundwater. The surface water sources are derived from the Sierra Nevada, the Sacramento River-Delta system and local reservoirs. With the exception of some of the City of San Francisco (CSF) s urces, these surface sources are chemically treated, filtered and chlorinated. Certain CSF sources are not filtered but all are chlorinated. The groundwat r s urces are derived from a number of distinct aquifers that underlie the three c unties. With the exception of some that are disinfected, most of the groundwater sources do not receive treatment.

Public water systems are required to meet those water quality and monitoring regulations adopted by the State of California in 1977 and revised in 1981. These regulations, shown in Tables 9.1 through 9.4, are at least as stringent as those established by the U.S. Environmental Protection Agency (EPA) pursuant t the federal Safe Drinking Water Act. In addition to these regulations, in 1984, public water systems that use groundwater sources were required under Assembly Bill 1803 (AB 1803) to monitor their sources for selected unregulated organic chemical contaminants.

Suppliers of bottled water are required to meet the water quality and monitoring requirements set by the Federal Food & Drug Administration (Appendix A) and the State of California (Appendix A).

There are three public water systems that serve the four census tracts studied in Fairchild I and II. They include the Great Oaks Water Company (GOWC), which serves the two study areas, and the San Jose Water Company (SJWC) and the City f

Santa Clara (CSC) which serve the tw control areas. There are also three companies that are th major suppliers of b ttled water within Santa Clara County. These companies are assumed to be the predominant sources of bottled water used by residents in the study areas.

Each bottled water company provides treatment of their source water. Alhambra uses groundwater from a well on their property. The water is treated by sand filtration, reverse osmosis, degasification, deionization and ozonation. Minerals are added for flavor and taste. Black Mountain uses water from a spring on their property. The water is treated by sand, carbon and paper filtrati n and ozonation. Sierra Springs uses East Bay Municipal Utilities District water. The water is treated by carbon filtration, softening cartridge filtration, membrane filtration, reverse osmosis and ozonation.

Source Sampling

Table 9.5 summarizes selected water quality data for the period of time indicated for water supplied by the three public water systems and the three bottled water companies cited above. In addition, Table 9.5 also contains water quality data on the two public water systems, East Bay Municipal Utilities District (EBMUD) and the City of San Francisco, that are the major suppliers of surface water t those women surveyed in the Malathion study and who used the Hayward and Redwood City Kaiser facilities. The constituents shown in Table 9.5 are normally used by sanitary engineers to characterize the quality of a drinking water supply.

Table 9.5 indicates that, in general, the well waters can be characterized as moderately hard, and are typical of California groundwater. However, as th range in concentrations of several constituents (i.e., hardness, calcium, magnesium) shows, there is substantial variation in water quality among w lls. By contrast the surface water used by EBMUD and CSF is significantly different in quality from the well water. While the well water is moderately hard, the surface waters are considered soft as indicated by the lower levels of hardness, calcium and magnesium.

GOWC, SJWC, and CSC also sampled all their wells in 1984-85 for volatile organic chemical (VOC) contaminants as part of the AB 1803 groundwater monitoring pr gram. A list of the ch micals that were m nit r d is c ntained in Appendix B. Tabl 9.6 summarizes th results. Only in water from wells used by SJWC were any VOCs detected. As Table 9.6 indicates, none of the three VOCs detected were above State Action Levels. Since the completion of this program, continuous monitoring for VOCs has been a part of the total monitoring program instituted by all three systems. The frequency of monitoring is at least one sample per well per year.

Monitoring for certain pesticides was also conducted under the 1803 program. The pesticides were selected based on information obtained from historical us records maintained by the California Department of Food & Agriculture, field surveys, and through discussions with the Santa Clara County Agricultural Commissioner. No pesticides were detected in the wells sampled.

Because of the concern that existing monitoring will not detect non-volatile organic chemical contaminants, some radionuclides (i.e., radon), and many bacterial organisms, the Department designed a sampling program (see Appendix C) t expand the existing water quality data base. Samples of water were collected from the highest producing wells within the GOWC, SJWC, and CSC systems, the three bottled water companies, a well near GOWC used to monitor contaminated groundwater (Fairchild San Jose), treated water from EBMUD, and a representative well within the Pinedale Water Company (PWC) system. PWC serves the community of Pinedale where a previous study by the Department has shown the spontaneous abortion rate to be normal. It is important to note that these were one-time samples and ongoing water quality may vary from the results shown.

Water samples were analyzed for Total Organic Carbon (TOC), Total Organic Halides (TOX), radon, and heterotrophic plate count (HPC). TOC is an indication of the total concentration of organic material in a water sample. TOX measures the total amount of chlorinated and other halogenated organic material. Radon is a volatile radionuclide found in groundwater. Coliform and fecal coliform are bacteria that are common to the gut of warm-blooded animals and are an indication f possible contamination from human wastes. HPC detects a broad spectrum f bacteria which are normal flora in soil and water. It is an indication of th general bacterial content of a water supply. HPC was determined using two growth media, tryptone glucose yeast extract (TGY) and R2A agar. The results are shown in Tabl 9.7. They indicate that levels of TOC, TOX and radon in the public water systems and the bottled water were low. The highest TOC and TOX levels wer from the EBMUD system. As previously indicated, EBMUD uses surface water sources that receive inputs of natural organic matter (i.e., vegetation) resulting in increased TOC. The utility also chlorinates the water producing TOX in the form of chlorinated byproducts (e.g. trihalomethanes). Since GOWC, SJWC, and CSC do not chlorinate, halogenated compounds would not be expected in their well waters. Although the radon levels in the well waters from the study area were higher than in the bottled waters and EBMUD water, they are well below the median radon concentration (approximately 1000 pCi/l) of well waters that have been previously sampled in California, and below the radon level in the water from the PWC well. There is currently no drinking water standard for radon.

Each of the public systems and bottled waters met the requirements for coliform bacteria. Two of the bottled waters, Black Mountain and Sierra Springs, had elevated levels of HPC. There are no standards for HPC although the EPA has used 500 colonies per milliliter as a guidance level for HPC. Some bacterial genera whose members include opportunistic human pathogens (i.e., Pseudomonas speci s) can be detected by HPC. There is concern that a high HPC could indicate excessive levels of organisms that may adversely affect susceptible individuals such as infants, the elderly, or those compromised by illness. Several bacterial species were detected in the samples but attempts to identify other types of organisms present were not successful. The Departments' Food and Drug Branch collected additional samples of Black Mountain Spring Water for bacteriological analysis. Three five-gallon containers were sampled. The results indicated that the coliform tests were negative in the three samples. The HPC (TGY) levels were negative for two of the samples and 2,800 per milliliter for the third sample. Further sampling is being conducted to determine the reason for the variation in the HPC levels. It can be seen from these data that there is no unusual chemical or bacteriological characteristic common to all the water sources in these study areas.

## Tap Water Sampling

In addition to the above mentioned sampling, the Department conducted a sampling of water at household taps to determine if there are any water quality changes imparted during the delivery f water to the c nsumer (see Appendix D for the sampling protoc l). The sampling was conducted at 48 sampling sites (i.e., private homes) within the four census tracts studied in Fairchild I and II. As previously indicated, these census tracts are served by three public water systems. They include the Great Oaks Water Company (GOWC), which serves the two study areas, and the San Jose Water Company (SJWC) and the City of Santa Clara (CSC) which serve the two control areas.

Samples were collected in the early morning before any water had been used by the residents. This procedure, which resulted in water standing in the househ ld piping for several hours, was intended to indentify any contaminants that were permeating through the pipes or leaching from the pipe materials. Households that employed point-of-use treatment devices were also sampled to determine the effect of these devices on water quality. Water samples were to be analyz d for TOC, TOX, trace metals, lead and copper, total and fecal coliform bacteria, and HPC. Unforseen problems in the laboratory, however, prevented the analysis for c pper and HPC (R2A) from being carried out.

Table 9.8 summarizes the tap sampling results. TOC levels were significantly higher than the average TOC levels found in the sources used by GOWC [average TOC = 0.7 milligrams per liter (mg/l)], SJWC (average TOC = 0.5 mg/l), CSC (average TOC = 0.5 mg/l), and in the bottled waters (average TOC = 0.3 mg/l). TOC levels averaged highest in the census tract served by SJWC (average TOC = 5.6 mg/l). The TOC was somewhat lower in the census tract served by CSC (average TOC = 4.4 mg/l) and by GOWC (average TOC = 4.1 mg/l and 4.8 mg/l). However, there was n significant differences found in the TOC levels between the four census tracts.

The point-of-use treatment devices that were sampled did not appear to consistently remove the TOC from the water. Of the eight devices sampled, only one showed a removal of greater than 50 percent and four showed an increase in TOC levels after treatment. Information on the maintenance of these devices was not available; therefore, conclusions on the effectiveness of these devices cannot be made at this time.

The reason for this increase in TOC is not clear. The most likely hypothesis is that the TOC is related to the growth of a microbiological flora on the pipe wall. Microbial growths ar not uncommon in water distribution pipes particularly where water s urces do not require disinfection as is the case with these three water systems. The HPC results also suggest that there are bacterial growths present. Many tap samples showed the presence of heterotrophic bacteria. It is important to note that there is no reason to believe that these bacteria are linked to reproductive problems. The highest levels were found in the first water drawn from the tap and from taps with point-of-use devices. Levels were much reduced after the water had been allowed to run. Only one sample for fec l coliform organisms, an indication of contamination from human wastes, was p sitive. Follow-up samples to confirm that result were negative, suggesting that the initial finding was an artifact.

The chemical makeup of the TOC has not been establised. With the exception f a few samples from households served by SJWC and CSC, there were no halogenated rganic chemicals detected as evidenced by the TOX results. The finding of TOX in these samples was the result of chlorinated surface water being used to supplement groundwater supplies in certain areas served by both water systems at the time of the sampling. The general lack of measureable TOX indicates that the increase in TOC was not the result of industrial solvents, which have contaminated some groundwater in the area. Additional work using more s phisticated analytical techniques has begun in an attempt to separate and identify individual chemicals that contribute to the TOC content.

T determine if this increase in TOC levels is common to all water systems, sampling of selected water systems in the San Francisco Bay area and in other parts of the state has begun. The water systems selected include those supplying chlorinated surface water and chlorinated groundwater as well as systems using unchlorinated groundwater. The preliminary results suggest that water systems with chlorinated supplies do not show an increase in TOC levels from source to tap while those with unchlorinated supplies do. Additional sampling is being conducted to confirm this observation.

The results of the lead analysis indicate that there were no lead levels above the drinking water standard of 50 micrograms per liter (ug/l). The average level of lead in all four census tracts was 6 ug/l. It dces not appear from these results that leaching of lead from plumbing pipe is a problem.

Table 9.1

Maximum Contaminant Levels
Inorganic Chemicals

| Constituent | Maximum Contaminant Level, mg/l |
|---|---|
| Arsenic | 0.05 |
| Barium | 1. |
| Cadmium | 0.010 |
| Chromium | 0.05 |
| Lead | 0.05 |
| Mercury | 0.002 |
| Nitrate (as $NO_3$) | 45. |
| Selenium | 0.01 |
| Silver | 0.05 |

Table 9.2

Maximum Contaminant Levels
Organic Chemicals

| Constituent | Maximum Contaminant Level, mg/l |
|---|---|
| (a) Chlorinated Hydrocarbons | |
| Endrin | 0.0002 |
| Lindane | 0.004 |
| Methoxychlor | 0.1 |
| Toxaphene | 0.005 |
| (b) Chlorophenoxys | |
| 2,4-D | 0.1 |
| 2,4,5--TP Silvex | 0.01 |
| (c) Trihalomethanes | 0.1 |

Table 9.3

Limiting Concentrations For Fluoride

| Annual Average of Maximum Daily Air Temperature | | Fluoride Concentration mg/1 | | | |
|---|---|---|---|---|---|
| Degrees Fahrenheit | Degrees Celsius | Lower | Optimum | Upper | Maximum Contaminant Level |
| 53.7 and below | 12.0 and below | 0.9 | 1.2 | 1.7 | 2.4 |
| 53.8 to 58.3 | 12.1 to 14.6 | 0.8 | 1.1 | 1.5 | 2.2 |
| 58.4 to 63.8 | 14.7 to 17.6 | 0.8 | 1.0 | 1.3 | 2.0 |
| 63.9 to 70.6 | 17.7 to 21.4 | 0.7 | 0.9 | 1.2 | 1.8 |
| 70.7 to 79.2 | 21.5 to 26.2 | 0.7 | 0.8 | 1.0 | 1.6 |
| 79.3 to 90.5 | 26.3 to 32.5 | 0.6 | 0.7 | 0.8 | 1.4 |

Table 9.4

MCL Radioactivity

| Constituent | Maximum Contaminant Level, pCi/l |
|---|---|
| Combined Radium-226 and Radium-228........ | 5 |
| Gross Alpha particle activity............. (including Radium-226 but excluding Radon and Uranium) | 15 |
| Tritium.................................. | 20,000 |
| Strontium-90............................. | 8 |
| Gross Beta particle activity............. | 50 |

Table 9.5

Selected Water Quality Data, 1980-1987[a]

| Water Supplier | K, mg/l | Alkalinity mg/l | Hardness mg/l | Ca mg/l | Mg mg/l | As mg/l | Na mg/l | Cl mg/l | $No_3$ mg/l | $SO_4$ mg/l |
|---|---|---|---|---|---|---|---|---|---|---|
| | Constituent Median (Range) | | | | | | | | | |
| GOWC | NA | 224 (206-280) | 268 (234-397) | 47 (38-85) | 35 (25-50) | .01 (ND-.013) | 21.5 (17-30) | 16 (12-28) | 9.5 (6-23) | 41 (33-62) |
| SJWC | 1.1 (0.5-1.7) | 265 (172-379) | 324 (218-459) | 57 (14-82) | 42 (25-66) | ND | 20.5 (16-39) | 32 (24-55) | 17 (3-30) | 58 (28-114) |
| CSC | 1.2 (1.2-1.3) | 216 (186-245) | 227 (120-303) | 60.5 (48-90) | 17 (13-23) | ND | 26.5 (21-37) | 22 (15-38) | 7 (2-38) | 38.5 (25-63) |
| Alhambra | NA | NA | NA | 0.7 (0.5-0.7) | 0.8 (0.6-0.8) | ND | 3.85 (3.8-3.9) | 3.45 (3.4-3.5) | ND | 3.25 (3.11-3.4) |
| Sierra Springs | NA | 6 | 1 | NA | NA | NA | NA | 2 | ND | 1 |
| Black Mountain | 0.7 (0.6-3.3) | 112 (106-115) | 116 (106-128) | 18 (14-21) | 17.5 (16-19) | 0.001 | 14.8 (13.9-17.3) | 17.6 (16.7-24) | 1.9 (0.4-3.1) | 17.2 (15.8-22.6) |
| CSF | 1.0 (0.8-1.3) | 58.3 (43-66) | 72 (54-80) | 15 (12-20) | 7.1 (5.8-7.9) | ND | 5.6 (2.3-9.5) | 8 (4-17) | 1.6 (1.0-1.8) | 5.6 (1.5-25) |
| EBMUD | 0.8 (0.77-0.95) | 40.5 (24-53.5) | 41.5 (28-59.5) | 11.8 (9.5-20) | 3.1 (3.1-4.6) | ND | 2.2 (2-26) | 3 (3-12) | ND (ND-0.3) | 3 (2.2-40) |

NA - Not Available
ND - Not Detected
[a]Water quality data from Water Supplier Monitoring Reports.

TABLE 9.6

Volatile Organic Chemical Data

| Water Supplier | Chemical | Concentration ppb Median (Range) | Action Level ppb |
|---|---|---|---|
| GOWC | ND | | |
| SJWC | 1,1,1-trichloroethane | 1.2 (0.5-3.4) | 200 |
| | 1,1,2-trichloro-1,2,2-trifluoroethane | 2.5 (0.6-5.8) | 18,000 |
| | tetrachloroethylene | 1.15 (0.7-1.6) | 5 |
| CSC | ND | | |

Table 9.7

Pregnancy Outcome Studies Sampling Results

San Jose Water Company (43-011)
September 14, 1987

| WELL NAME | TOC mg/l | RADON pCi/l | BACTERIA coliform (MPN 100 ml) | BACTERIA fecal coliform (MPN 100 ml) | HPC/ml | TOX ug/l | VOC ug/l |
|---|---|---|---|---|---|---|---|
| Senter Road | | | | | | | 1,1,1-TCA : 2.0 (D.L. = 0.5) |
| Berryessa #1 | | | | | | | EPA 601 : N.D. (D.L. = 0.5) |

Table 9.7 (Continued)
Pregnancy Outcome Studies Sampling Results

San Jose Water Company (43-011)
November 4, 1987

| WELL NAME | | TOC mg/l | RADON pCi/l | BACTERIA coli-form (MPN 100 ml) | BACTERIA fecal coliform (MPN 100 ml) | BACTERIA HPC TGY cfu/ml | BACTERIA HPC R2A cfu/ml | TOX ug/l | VOC ug/l |
|---|---|---|---|---|---|---|---|---|---|
| 1. Willow Glen | #1 | 0.4 | | | | | | | |
| 2. | #2 | 0.5 | | | | | | | |
| 3. | #3 | 0.5 | | | | | | | |
| 4. | #4 | 0.4 | 420±50<br>470±50<br>360±50<br>410±50 | <2.2 | <2.2 | 1 | 20 | <15 | EPA 601 : N.D.<br>(D.L. = 0.5) |
| 5. | #5 | 0.4 | | | | | | | |
| 6. Control (Malone #2) | | 0.4 | 430±50<br>440±50 | <2.2 | <2.2 | <1 | <1 | <15 | EPA 601 : N.D.<br>(D.L. = 0.5) |
| 7. Malone | #1 | 0.5 | | | | | | <15 | |
| 8. Malone | #2 | 0.4 | 440±40<br>460±50 | <2.2 | <2.2 | <1 | 3 | | |
| 9. Tully | #1 | 0.4 | | | | | | | |
| 10. | #2 | 0.5 | | | | | | | |
| 11. | #3 | 0.5 | | | | | | | |
| 12. | #4 | 0.4 | 340±40<br>350±40 | <2.2 | <2.2 | 1 | 6 | <15 | |

Table 9.7 (Continued)
Pregnancy Outcome Studies Sampling Results

San Jose Water Company (43-011)
November 4, 1987

| WELL NAME | | TOC mg/l | RADON pCi/l | BACTERIA coli-form (MPN 100 ml) | fecal coliform (MPN 100 ml) | HPC TGY cfu/ml | HPC R2A cfu/ml | TOX ug/l | VOC ug/l |
|---|---|---|---|---|---|---|---|---|---|
| 13. Cottage Grove | #3 | 0.4 | | | | | | | |
| 14. | #4 | 0.4 | | | | | | | |
| 15. | #6 | 0.4 | | | | | | | |
| 16. | #7 | 0.5 | 380±40<br>370±50 | <2.2 | <2.2 | <1 | 27 | <15 | |
| 17. Senter | | 0.5 | | | | | | | |

Table 9.7 (Continued)
Pregnancy Outcome Studies Sampling Results

San Jose Water Company (43-011)
November 22, 1987

| WELL NAME | | TOC mg/l | RADON pCi/l | BACTERIA coli-form (MPN 100 ml) | BACTERIA fecal coliform (MPN 100 ml) | HPC/ml | TOX ug/l | VOC ug/l |
|---|---|---|---|---|---|---|---|---|
| 1. Blossom Hill | #1 | 0.6 | | | | | | |
| 2. | #4 | 0.6 | | | | | | |
| 3. | #5 | 0.6 | | | | | | |
| 4. | #6 | 0.5 | | | | | | |
| 5. Control (B.H. #1) | | 0.6 | | | | | | |
| 6. Branham | #1 | 0.7 | | | | | | |
| 7. | #2 | 0.6 | | | | | | |
| 8. | #3 | 0.8 | | | | | | |
| 9. | #4 | 0.7 | | | | | | |
| 10. Bryan | #1 | 0.6 | | | | | | |
| 11. | #2 | 0.7 | | | | | | |
| 12. | #4 | 0.5 | | | | | | |
| 13. | #5 | 0.5 | | | | | | |
| 14. Foxworthy | #1 | 0.6 | | | | | | |

Table 9.7 (Continued)
Pregnancy Outcome Studies Sampling Results

San Jose Water Company (43-011)
November 22, 1987

| WELL NAME | | TOC mg/l | RADON pCi/l | BACTERIA coli-form (MPN 100 ml) | fecal coliform (MPN 100 ml) | HPC/ml | TOX ug/l | VOC ug/l |
|---|---|---|---|---|---|---|---|---|
| 15. Koch | #1 | 0.5 | | | | | | |
| 16. | #2 | 0.4 | | | | | | |

Table 9.7 (Continued)

Pregnancy Outcome Studies Sampling Results

Great Oaks Water Company (43-022)
October 21, 1987

| WELL NAME | TOC mg/l | RADON pCi/l | BACTERIA coli-form (MPN 100 ml) | BACTERIA fecal coliform (MPN 100 ml) | HPC TGY cfu/ml | HPC R2A cfu/ml | TOX ug/l | VOC ug/l |
|---|---|---|---|---|---|---|---|---|
| 1. No. 7 | 0.8 | 460±30<br>470±30 | <2 | <2 | 2 | 6 | <15 | |
| 2. No. 11 | 0.8 | 380±30<br>380±30 | <2 | <2 | 2 | 54 | <15 | |
| 3. No. 16 | 0.8 | 420±30<br>420±40 | <2 | <2 | <1 | 5 | <15 | |
| 4. Control (#16) | 0.8 | 390±40<br>400±40 | <2 | <2 | 1 | 5 | <15 | |
| 5. No. 3 | 0.7 | | | | | | | |
| 6. No. 4 | 0.7 | | | | | | | |
| 7. No. 10 | 0.6 | | | | | | | |
| 8. No. 12 | 0.7 | | | | | | | |

Table 9.7 (Continued)

Pregnancy Outcome Studies Sampling Results

Fairchild - San Jose
October 21, 1987

| WELL NAME | TOC mg/l | RADON pCi/l | BACTERIA coli-form (MPN 100 ml) | BACTERIA fecal coliform (MPN 100 ml) | HPC TGY cfu/ml | HPC R2A cfu/ml | TOX ug/l | VOC ug/l |
|---|---|---|---|---|---|---|---|---|
| 1. WCC-20-B | 1.6 | 370±30<br>370±30<br>380±30<br>400±30 | <2 | <2 | 2300 | 9700 | 2530 | $CHBrCl_2$ : 0.8<br>1,1-DCA : 20.0<br>1,2-DCA : 0.7<br>1,1-DCE : 159<br>Trans-1,3 Dichloropropene : 1.1<br>PCE : 4.2<br>1,1,1-TCA : 5922.0<br>TCE : 0.6<br>Freon : None detected |
| 2. WCC-20-B-TB# | | | | | | | <15 | |

#TB: Trav l Blank

Table 9.7 (Continued)

Pregnancy Outcome Studies Sampling Results

City of Santa Clara (43-012)
October 27, 1987

| WELL NAME | TOC mg/l | RADON pCi/l | BACTERIA coli-form (MPN 100 ml) | fecal coliform | HPC TGY cfu/ml | HPC R2A | TOX ug/l | VOC ug/l |
|---|---|---|---|---|---|---|---|---|
| 1. No. 14 | 0.5 | $380\pm30$<br>$370\pm40$ | <2.2 | <2.2 | <1 | 5 | <15 | |
| 2. No. 21 | 0.5 | $430\pm30$<br>$450\pm40$<br>$410\pm40$<br>$410\pm40$ | <2.2 | <2.2 | <1 | 2 | <15 | |
| 3. No. 28 | 0.4 | $480\pm40$<br>$460\pm40$ | <2.2 | <2.2 | 1 | 230 | <15 | |
| 4. Control (No. 14) | 0.4 | $450\pm40$<br>$480\pm40$ | <2.2 | <2.2 | 2 | 3 | <15 | |
| 5. No. 7 | 0.4 | | | | | | | |
| 6. No 12 | 0.5 | | | | | | | |
| 7. No. 22-02 | 0.4 | | | | | | | |
| 8. No. 25 | 0.5 | | | | | | | |

Table 9.7 (Continued)

Pregnancy Outcome Studies Sampling Results

East Bay Municipal Utility District
October 21, 1987

| WATER SUPPLIER | TOC mg/l | RADON pCi/l | BACTERIA coli-form (MPN 100 ml) | BACTERIA fecal coliform (MPN 100 ml) | BACTERIA HPC TGY cfu/ml | BACTERIA HPC R2A cfu/ml | TOX ug/l | VOC ug/l |
|---|---|---|---|---|---|---|---|---|
| 1. EBMUD Tap | 1.2 | 60±130<br>-40±140 | <2.2 | <2.2 | 1 | 680 | 62 | $CHCl_3$ : 15.8<br>$CHBrCl_2$ : 0.53 |

Table 9.7 (Continued)

Pregnancy Outcome Studies Sampling Results

Pinedale Community Services District
November 9, 1987

| WELL NAME | TOC mg/l | RADON pCi/l | BACTERIA coliform (MPN 100 ml) | BACTERIA fecal coliform (MPN 100 ml) | HPC TGY cfu/ml | HPC R2A cfu/ml | TOX ug/l | VOC ug/l |
|---|---|---|---|---|---|---|---|---|
| 1. Well #7 | 0.3 | 1530±90 | <2.2<br><2.2 | <2.2<br><2.2 | 1<br><1 | 27<br>35 | | EPA 601 : N.D.<br>(D.L. = 0.5) |

Table 9.7 (Continued)
Pregnancy Outcome Studies Sampling Results

Bottled Water Companies
(Various)

| WATER SUPPLIER | TOC mg/l | RADON pCi/l | BACTERIA coli-form (MPN 100 ml) | BACTERIA fecal coliform (MPN 100 ml) | BACTERIA HPC TGY cfu/ml | BACTERIA HPC R2A cfu/ml | TOX ug/l | VOC ug/l |
|---|---|---|---|---|---|---|---|---|
| 1. Alhambra 10-21-87 | <0.3 | - 1±150<br>-50±170<br>-60±150<br>20±160 | <2.2 | <2.2 | <1 | 1 | <15 | $CHCl_3$ : 0.96 |
| 2. Black Mountain 10-21-87 | 0.4 | - 3±180<br>-30±160 | <2.2 | <2.2 | 20,000 | 35,000 | <15 | $CHCl_3$ : 0.52 |
| 3. Sierra Springs 11-10-87 | 0.3 | | <2.2 | <2.2 | <1 | 50,000 | | |

Table 9.8

Tap Water Sampling Results

| Water System | Census Tract | TOC mg/l | TOX ug/l | Bacteria (MPN 100 ml) coliform | Bacteria (MPN 100 ml) fecal coliform | HPC (TGY) cfu/ml | Lead ug/l |
|---|---|---|---|---|---|---|---|
| | | Average (Range) | Median (Range) | Median (Range) | | Median (Range) | Median (Range) |
| SJWC | 5120.08 | 5.6 (4.3-8.9) | <11.0 (<11.0-120) | <2.2 (<2.2-2.2) | <2.2 (<2.2-2.2) | 735 (<1-11,000) | 6 (<1-19) |
| GOWC | 5120.11 | 4.8 (3.1-6.3) | <11.0 | <2.2 (<2.2->16) | <2.2 (<2.2-5.1) | 145 (1.0-8,600) | 4 (<1-10) |
| GOWC | 5120.12 | 4.1 (1.3-5.4) | <11.0 | <2.2 | <2.2 | 255 (1.0-32,000) | 4.5 (<1-11) |
| CSC | 5053.0204 | 4.4 (3.6-5.1) | <11.0 (<11.0-86) | <2.2 | <2.2 | 450 (3.0-6,600) | 5 (2-18) |

## PART 103—QUALITY STANDARDS FOR FOODS WITH NO IDENTITY STANDARDS

Subpart A—General Provisions

Sec.
103.3 Definitions.
103.5 General principles.

Subpart B—Standards of Quality

103.35 Bottled water.

AUTHORITY: Secs. 401, 403, 701, 52 Stat. 1046 1048 as amended, 1055-1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 341, 343, 371), unless otherwise noted.

### Subpart A—General Provisions

**§ 103.3 Definitions.**

(a) A "lot" is:

(1) For purposes of determining quality factors related to manufacture, processing, or packing, a collection of primary containers or units of the same size, type, and style produced under conditions as nearly uniform as possible and usually designated by a common container code or marking, or in the absence of any common container code or marking, a day's production.

(2) For purposes of determining quality factors related to distribution and storage, a collection of primary containers or units transported, stored, or held under conditions as nearly uniform as possible.

(b) A "sample" consists of 10 subsamples (consumer units), taken one from each of 10 different randomly chosen shipping cases to be representative of a given lot, unless otherwise specified in a specific quality standard in this part.

(c) An "analytical unit" is the portion(s) of food taken from a subsample of a sample for the purpose of analysis.

[42 FR 14325, Mar. 15, 1977]

**§ 103.5 General principles.**

(a) The quality of a food depends upon numerous characteristics including but not limited to the levels of microorganisms and such physical factors as turbidity, color, flavor, and odor. Such characteristics are indicative of the quality of the raw materials and ingredients, the degree of quality control used in manufacture, processing, and packing, and the conditions of distribution and storage. The diversity of raw materials, food processing, and distribution practices, as well as the variation in quality factors important to consumers, requires that individual standards of quality be established for different types of food.

(b)(1) The label of a food that fails to meet the requirements of an applicable standard of quality promulgated pursuant to this part shall bear the general statement of substandard quality specified in § 130.14(a) of this chapter in the manner and form therein specified; but in lieu of such general statement of substandard quality, the label may bear the alternative statement, "Below Standard in Quality———", the blank to be filled in with whichever of the following are applicable:

(i) "Contains Excessive Bacteria".

(ii) "Excessively Turbid".

(iii) "Abnormal Color".

(iv) The phrase specified in the applicable standard of quality to describe any other quality deviation.

(2) The statement of substandard quality shall appear on the principal display panel or panels and shall immediately and conspicuously precede or follow, without intervening written, printed or graphic matter, the name of the food.

(c) Product descriptions included in a standard of quality promulgated pursuant to this part are intended only to designate the class of foods to which the standards apply, and are not standards of identity for the products involved. Should a standard of identity later be established for any of these foods, the standard of quality will be recodified to appear in the same part of the regulations.

(d) The food characteristics included in a standard of quality published in this part relate only to the quality of the food and not to compliance with any of the adulteration provision of section 402 of the act. Compliance with a standard of quality promulgated pursuant to this part does not excuse failure to observe either the requirement of section 402(a)(4) of the act that food may not be prepared, packed, or held under insanitary conditions, or the provisions of Parts 110 and 129 of this chapter requiring that food manufacturers must observe current food manufacturing practices. For example, evidence obtained through factory inspection indicating such a violation renders the food unlawful, even though the food contains levels of microorganisms lower than those prescribed by an applicable standard.

(e) The Commissioner of Food and Drugs, either on his own initiative or on behalf of any interested person who has submitted a petition, may establish, amend, or repeal, under Subpart B of this part, a regulation prescribing a standard of quality for a food pursuant to Part 10 of this chapter.

[42 FR 14325, Mar. 15, 1977, as amended at 42 FR 15673, Mar. 22, 1977; 44 FR 12172, Mar. 6, 1979]

## Subpart B—Standards of Quality

### § 103.35 Bottled water.

(a) *Definitions.* (1) "Bottled water" is defined as water that is sealed in bottles or other containers and intended for human consumption. Bottled water does not include mineral water or any food defined in § 165.175 of this chapter.

(2) "Trihalomethane" (THM) means one of the family of organic compounds, named as derivatives of methane, wherein three of the four hydrogen atoms in methane are each substituted by a halogen atom in the molecular structure.

(3) "Total Trihalomethanes" (TTHM) means the sum of the concentration in milligrams per liter of the trihalomethane compounds (trichloromethane [chloroform], dibromochloromethane, bromodichloromethane and tribromomethane [bromoform]), rounded to two significant figures.

(b) *Microbiological quality.* Bottled water shall, when a sample consisting of analytical units of equal volume is examined by the methods described in applicable sections of "Standard Methods for the Examination of Water and Wastewater," 15th Ed. (1980), American Public Health Association, which is incorporated by reference (copies may be obtained from the Division of Food Technology, Bureau of Foods (HFF-210), 200 C St., SW., Washington, DC 20204, or may be examined at the Office of the Federal Register, 1100 L St., NW., Washington, DC 20408), meet the following standards of microbiological quality:

(1) *Multiple-tube fermentation method.* Not more than one of the analytical units in the sample shall have a most probable number (MPN) of 2.2 or more coliform organisms per 100 milliliters and no analytical unit shall have an MPN of 9.2 or more coliform organisms per 100 milliliters; or

(2) *Membrane filter method.* Not more than one of the analytical units in the sample shall have 4.0 or more coliform organisms per 100 milliliters and the arithmetic mean of the coliform density of the sample shall not exceed one coliform organism per 100 milliliters.

(c) *Physical quality.* Bottled water shall, when a composite of analytical units of equal volume from a sample is examined by the method described in applicable sections of "Standard Methods for the Examination of Water and Wastewater," 15th Ed. (1980), which is incorporated by reference (the availability of this incorporation by reference is given in paragraph (b) of this section), meet the following standards of physical quality:

(1) The turbidity shall not exceed 5 units.

(2) The color shall not exceed 15 units.

(3) The odor shall not exceed threshold odor No. 3.

(d) *Chemical quality.* (1)(i) Bottled water shall, when a composite of analytical units of equal volume from a sample is examined by the methods described in paragraph (d)(1)(ii) of this section, meet standards of chemical quality and shall not contain chemical substances in excess of the following concentrations:



73-077 O—86——3

*Substance—Concentration in Milligrams per Liter*

| | |
|---|---|
| Arsenic | 0.05 |
| Barium | 1.0 |
| Cadmium | 0.01 |
| Chloride | 250.0 |
| Chromium | 0.05 |
| Copper | 1.0 |
| Iron | 0.3 |
| Lead | 0.05 |
| Manganese | 0.05 |
| Mercury | 0.002 |
| Nitrate (N) | 10.0 |
| Phenols | 0.001 |
| Selenium | 0.01 |
| Silver | 0.05 |
| Sulfate | 250.0 |
| Total dissolved solids | 500.0 |
| Zinc | 5.0 |
| Organics: | |
| Endrin (1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-Octa-hydro-1,4-endo, endo-5,8-dimethano naphthalene) | 0.0002 |
| Lindane (1,2,3,4,5,6-hexachloro-cyclohexane, gamma isomer) | 0.004 |
| Methoxychlor (1,1,1-trichloro-2,2-bis(p-methoxy-phenyl) ethane | 0.1 |
| Total Trihalomethanes | 0.10 |
| Toxaphene ($C_{10}H_{10}Cl_8$—technical chlorinated camphene, 67-69 percent chlorine) | 0.005 |
| 2,4-D (2,4-dichlorophenoxyacetic acid | 0.1 |
| 2,4,5-TP Silvex (2,4,5-trichlorophenoxypropionic acid | 0.01 |

(ii) Analyses conducted to determine compliance with paragraph (d)(1)(i) of this section shall be made in accordance with the methods described in the applicable sections of "Standard Methods for the Examination of Water and Wastewater," 15th Ed. (1980), or "Methods for Chemical Analysis of Water and Wastes," Environmental Monitoring and Support Laboratory, EPA-600/4-82-055, March 1983, U.S. Environmental Protection Agency, both of which are incorporated by reference. Analyses for organic substances shall be determined by appropriate methods described in "Methods for Organochlorine Pesticides in Industrial Effluents" and "Methods for Chlorinated Phenoxy Acid Herbicides in Industrial Effluents," November 28, 1973, which are incorporated by reference, and "Part I: The Analysis of Trihalomethanes in Finished Waters by the Purge and Trap Method," Method 501.1 and "Part II: The Analysis of Trihalomethanes in Drinking Water by Liquid/Liquid Extraction," Method 501.2 in 40 CFR Part 141, Appendix C (45 FR 68672; November 29, 1979). The availability of these incorporations by reference are given in paragraph (b) of this section.

(2)(i) Bottled water packaged in the United States to which no fluoride is added shall not contain fluoride in excess of the levels in Table 1 and these levels shall be based on the annual average of maximum daily air temperatures at the location where the bottled water is sold at retail.

TABLE 1

| Annual average of maximum daily air temperatures (° F) | Fluoride concentration in milligrams per liter |
|---|---|
| 53.7 and below | 2.4 |
| 53.8-58.3 | 2.2 |
| 58.4-63.8 | 2.0 |
| 63.9-70.6 | 1.8 |
| 70.7-79.2 | 1.6 |
| 79.3-90.5 | 1.4 |

(ii) Imported bottled water to which no fluoride is added shall not contain fluoride in excess of 1.4 milligrams per liter.

(iii) Bottled water packaged in the United States to which fluoride is added shall not contain fluoride in excess of levels in Table 2 and these levels shall be based on the annual average of maximum daily air temperatures at the location where the bottled water is sold at retail.

TABLE 2

| Annual average of maximum daily air temperatures (° F) | Fluoride concentration in milligrams per liter |
|---|---|
| 53.7 and below | 1.7 |
| 53.8-58.3 | 1.5 |
| 58.4-63.8 | 1.3 |
| 63.9-70.6 | 1.2 |
| 70.7-79.2 | 1.0 |
| 79.3-90.5 | 0.8 |

(iv) Imported bottled water to which fluoride is added shall not contain fluoride in excess of 0.8 milligram per liter.

(e) *Radiological quality.* (1) Bottled water shall, when a composite of ana-



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lytical units of equal volume from a sample is examined by the methods described in paragraph (e)(2) of this section, meet standards of radiological quality as follows:

(i) The bottled water shall not contain a combined radium-226 and radium-228 activity in excess of 5 picocuries per liter of water.

(ii) The bottled water shall not contain a gross alpha particle activity (including radium-226, but excluding radon and uranium) in excess of 15 picocuries per liter of water.

(iii) The bottled water shall not contain beta particle and photon radioactivity from manmade radionuclides in excess of that which would produce an annual dose equivalent to the total body or any internal organ of 4 millirems per year calculated on the basis of an intake of 2 liters of the water per day. If two or more beta or photon-emitting radionuclides are present, the sum of their annual dose equivalent to the total body or to any internal organ shall not exceed 4 millirems per year.

(2) Analyses conducted to determine compliance with paragraph (e)(1) of this section shall be made in accordance with the methods described in the applicable sections of "Standard Methods for the Examination of Water and Wastewater," 15th Ed. (1980), and "Interim Radiochemical Methodology for Drinking Water," Environmental Monitoring and Support Laboratory, EPA-600/4-75-008 (Revised), March 1976, U.S. Environmental Protection Agency, both of which are incorporated by reference. The availability of these incorporations by reference is given in paragraph (b) of this section.

(f) *Label statements.* Bottled water, the quality of which is below that prescribed by this section, shall be labeled with a statement of substandard quality as follows:

(1) When the microbiological quality of bottled water is below that prescribed by paragraph (b) of this section, the label shall bear the statement of substandard quality specified in § 103.5(b).

(2) When the physical, chemical, and/or radiological quality of bottled water is below that prescribed by paragraphs (c) through (e) respectively of this section, the label shall bear the statement of substandard quality specified in § 103.5(b) except that, as appropriate, instead of or in addition to the words "Contains Excessive Bacteria" the following statement(s) shall be used:

(i) "Excessively Turbid", "Abnormal Color", and/or "Abnormal Odor" if the bottled water fails to meet the requirements of paragraph (c) (1), (2), and/or (3), respectively, of this section.

(ii) "Contains Excessive Chemical Substances", if the bottled water fails to meet any of the requirements of paragraph (d) of this section. The specific chemical(s) may be declared in lieu of the words "Chemical Substances" in the statement "Contains Excessive Chemical Substances". When a specific chemical is declared, that name by which the chemical(s) is designated in paragraph (d) of this section shall be used. Example: "Contains Excessive Copper".

(iii) "Excessively Radioactive" if the bottled water fails to meet the requirements of paragraph (e) of this section.

(g) *Adulteration.* Bottled water containing a substance at a level considered injurious to health under section 402(a)(1) of the act is deemed to be adulterated, regardless of whether or not the bottled water bears a label statement of substandard quality prescribed by paragraph (f) of this section.

(Secs. 401, 403(h), 410, 701(e), 52 Stat. 1046-1047 as amended, 70 Stat. 919 as amended, 88 Stat. 1694 (21 U.S.C. 341, 343(h), 349, 371(e)); secs. 409, 701(e), 706, 70 Stat. 919 as amended, 72 Stat. 1784-1788 as amended, 74 Stat. 399-407 as amended (21 U.S.C. 348, 371(e), 376))

[42 FR 14325, Mar. 15, 1977, as amended at 44 FR 12172, Mar. 6, 1979; 46 FR 41037, Aug. 14, 1981; 47 FR 11821, Mar. 19, 1982; 49 FR 10090, Mar. 19, 1984]

## PART 104—NUTRITIONAL QUALITY GUIDELINES FOR FOODS

### Subpart A—General Provisions

Sec.

104.5 General principles.
104.19 Petitions.



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Assembly Bill No. 170

## CHAPTER 639

An act to repeal Chapter 7.5 (commencing with Section 4040) of Part 1 of Division 5 of, and to add Article 6.5 (commencing with Section 26591) to Chapter 5 of Division 21 of, the Health and Safety Code, relating to health.

[Approved by Governor September 14, 1987. Filed with Secretary of State September 15, 1987.]

LEGISLATIVE COUNSEL'S DIGEST

AB 170, Killea. Health: bottled, vended, hauled, and processed water.

(1) Existing law does all of the following:

(a) Requires the State Department of Health Services to adopt and enforce such regulations as it determines are reasonably necessary to ensure that all bottled water, as defined, and vended water which is sold or otherwise distributed in the state is pure, wholesome, potable, and contains no inorganic chemicals or organic chemicals including pesticides and plasticizers in concentrations which may have an adverse effect on public health and safety.

(b) Prohibits any person from operating a water-bottling plant, as defined, in this state except pursuant to a license issued by the department.

(c) Prohibits any bottled water produced in an out-of-state water-bottling plant from being sold or distributed within this state unless either the out-of-state bottler or the distributor has first obtained an out-of-state bottler's or distributor's license.

(d) Prohibits any person from owning or operating any water-vending machine except pursuant to a license issued by the state.

(e) Requires the department to charge and collect a fee for each license applied for which is required to be an amount reasonably necessary to produce sufficient revenue to enforce the provisions relating to bottled and vended water.

(f) Requires the department to require each bottler, distributor, or vendor of bottled water, each owner or operator of any water-vending machine, and each applicant for a license to make specified tests and authorizes the department to require any bottler, distributor, or vendor of bottled water, any owner or operator of a water-vending machine, or any applicant for a license to make tests for any substance at any time when the department believes the substance may be present in the water source and threaten the public health and safety.

(g) Requires the department, upon a determination by the department that a particular water source is subject to potential



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contamination, to notify the bottler, distributor, vendor of bottled water, or the owner or operator of any water-vending machine who is required, with certain exceptions, to conduct an analysis, as prescribed, of the water source at issue, and if evidence of contamination is found, authorizes the department to take various actions.

(h) Prescribes labeling requirements for each container of bottled water sold in the state and each water-vending machine located in this state.

(i) Makes any violation of these provisions or of any regulation adopted pursuant to these provisions a misdemeanor.

(2) This bill would repeal all of these provisions and reenact them with various substantive changes as part of the Sherman Food, Drug, and Cosmetic Law. It would do all of the following:

(a) Revise the definitions of the terms "bottled water" and "water-vending machine" and add definitions of the terms of "water hauler," "retail water treatment plant," "private water source," and "private water source operator."

(b) Provide for the regulation by the department of water from water haulers, water from retail water treatment plants, and water from private sources.

(c) Expand the coverage of the provisions of existing law described in (1) (a), above, to include water haulers, operators of water treatment plants and private water source operators.

(d) Establish an annual license fee for a water-bottling plant or out-of-state bottled water distributor, water-vending machine, water hauler, retail water treatment plant operator, and private water source operator and require the department to charge and collect a prescribed fee for each department evaluation of a water-vending machine model or a retail water treatment plant to determine compliance with specified standards.

(e) Require the fees described in (2) (d) to be adjusted annually as prescribed.

(f) Require that all testing of bottled water, bottled water sources, water distributed by water haulers, water treatment plants, and water from vending machines be done by specified laboratories.

(g) Revise the definitions of the terms "mineral water," and "purified water" for purposes of provisions relating to the labeling of bottled water or vended water.

(h) Eliminate the existing misdemeanor penalty described in (1) (i), and make any violation of the above provisions of existing law described in (1), above, or of the additional provisions which would be enacted by the bill, or of any regulation adopted pursuant thereto, punishable as a misdemeanor with prescribed penalties or, under specified circumstances, as a felony with prescribed penalties. The bill would, therefore, impose a state-mandated local program.

(3) The California Constitution requires the state to reimburse local agencies and school districts for certain costs mandated by the

state. Statutory provisions establish procedures for making that reimbursement.

This bill would provide that no reimbursement is required by this act for a specified reason.

*The people of the State of California do enact as follows:*

SECTION 1. Chapter 7.5 (commencing with Section 4040) of Part 1 of Division 5 of the Health and Safety Code is repealed.

SEC. 2. Article 6.5 (commencing with Section 26591) is added to Chapter 5 of Division 21 of the Health and Safety Code, to read:

Article 6.5. Bottled, Vended, Hauled, and Processed Water

26591. (a) "Bottled water," means any drinking water or other water defined in Section 26594, which is placed in bottles or other containers for drinking, culinary, or other purposes involving a likelihood of the water being ingested by humans.

(b) "Water-bottling plant" means any facility in which bottled water is produced.

(c) "Water-vending machine" means any self-service device which, upon insertion of a coin, coins, or token, or upon receipt of payment by other means, dispenses servings of water in bulk, without the necessity of refilling the machine between each operation.

(d) "Water hauler" means any of the following:

(1) Any person who hauls water in bulk by truck, rail ship, barge, or other vehicle for drinking, culinary, or other purposes involving a likelihood of the water being ingested by humans.

(2) Any person who hauls water in bulk by truck, rail, ship, barge, or other vehicle to any water-vending machine.

(3) Any person who hauls water in bulk by truck, rail, ship, barge, or other vehicle to or from any water-bottling plant or any retail water treatment plant.

"In bulk," as used in this subdivision, means containers having capacities of 25 gallons or greater.

(e) "Retail water treatment plant" means any place, other than a water-bottling plant, water-vending machine, or public water system, where water is processed or treated in any manner and is sold or given away at the treatment plant in customer's containers for drinking, culinary, or other purposes involving a likelihood of the water being ingested by humans.

(f) "Private water source" means a nonmunicipal, noncommunity-owned, privately owned source of water which meets the requirements of an approved source for bottled water as defined in Section 129.3 of Title 21 of the Code of Federal Regulations.

(g) "Private water source operator" means any person who sells, delivers, or gives away water from a private water source to a water-bottling plant, water-vending machine, water hauler, retail water treatment plant, or to any person.

26592. (a) The department shall adopt and enforce the regulations it determines are reasonably necessary to ensure that all bottled water, vended water, water from water haulers, water from retail water treatment plants, and water from private water sources which is sold or otherwise distributed in this state is pure, wholesome, potable, and contains no inorganic chemicals or organic chemicals, including pesticides and plasticizers in concentrations which may have an adverse effect on public health and safety. The regulations shall include, but not be limited to, all of the following:

(1) Minimum standards for the sanitary production and distribution of bottled, vended, and hauled water, and water from retail water treatment plants and private water sources within this state. The standards shall include, but not be limited to, all of the following:

(A) Standards for the sanitary production, packaging, and distribution of bottled water shall not be less stringent than those standards prescribed by Part 110 and Part 129 of Title 21 of the Code of Federal Regulations.

(B) Standards to ensure that, prior to bottling, bottled water shall be subject to effective germicidal treatment by ozone, ultraviolet, or an equivalent disinfection process approved by the state department. The standards developed pursuant to this category for bottled water which contains carbon dioxide shall prescribe that sufficient compliance includes meeting the microbiological requirements described in Section 103.35 of Title 21 of the Code of Federal Regulations.

(C) Standards to ensure that dispensers for bottled water, which are furnished by the water bottler or distributor shall be delivered to the consumer's premises in a clean, sanitary condition, protected from dust or other contamination.

(D) Standards to ensure that ollas or other water-holding dispensers, both refrigerated and nonrefrigerated, shall be examined for cleanliness each time the dispenser is serviced by the representative of the distributor or bottler. When necessary, these dispensers shall be sanitized in place or returned to the bottler or distributor for cleaning or sanitizing before reuse according to the methods described in Part 129 of Title 21 of the Code of Federal Regulations.

(E) Standards for sanitary transfer of water from any source to storage or vehicle tanks, and from storage or vehicle tanks to customer owned or used storage tanks, vehicles, or other containers, or to water-vending machines, retail water treatment plants, or to water bottling plants.

(F) Standards for water quality and for sanitation of vehicle tanks, storage tanks, and distribution systems used by water haulers.

(G) Standards for sanitation and processing of water by retail water treatment plants.

(H) Standards for protection and sanitation of private water sources.

(2) Quality standards for bottled water, mineral water, vended water, water distributed by water haulers, water from retail water treatment plants, and water from private water sources. The quality standards of bottled water, including mineral water, vended water, water distributed directly to consumers by water haulers, water from retail water treatment plants, and water distributed directly to consumers from private water sources shall not be less stringent than those standards prescribed by Section 103.35 of Title 21 of the Code of Federal Regulations, except that mineral waters shall exceed 500 milligrams per liter of total dissolved solids. The quality standards shall include all drinking water maximum contaminant levels and may include any additional standards that the department determines are reasonably necessary to protect public health and safety. In addition, bottled water shall not exceed 10 parts per billion of total trihalomethanes or five parts per billion of lead unless the department establishes a lower level by regulation. Notwithstanding any other provision of law, the quality standards shall ensure that bottled water, vended water, water from retail water treatment plants, water distributed by water haulers, and water from private water sources contain no inorganic or organic chemicals, including pesticides and plasticizers, in concentrations which may have an adverse effect on public health and safety.

Mineral water producers which bottle 5,000 gallons, or less, per week shall have until January 1, 1989, to comply with the quality standards for bottled water pursuant to this paragraph. Mineral water producers may present to the State Department of Health Services data on consumption of mineral water and the health effects of inorganic elements which may be present as listed in the bottled water quality standards of Part 103.35 of Title 21 of the Code of Federal Regulations.

(3) Polycarbonate resins manufactured after January 1, 1988, and intended for use in fabricating containers for water products defined in this article shall not contain in excess of three parts per million residual methylene chloride or in excess of 200 parts per million residual monochlorobenzene unless the department establishes a lower level by regulation. For the purpose of monitoring compliance with this section, the concentration of methylene choride and monochlorobenzene shall not exceed one part per billion in water. "Polycarbonate resins" mean the substances defined by Section 177.1580 of Title 21 of the Code of Federal Regulations except as modified by this section.

(4) Minimum standards of design, construction, and sanitation for any water-vending machine. Those water-vending machines, other than coin-operated self-service devices, from which any operator or

customer dispenses unit servings in bulk may be exempted by the department from the requirements of subparagraphs (G), (M), and (O). The minimum standard shall include, but not be limited to, all of the following:

(A) Provide that water-vending machines shall be in compliance with the construction and performance standards established by the department or by an independent authority approved by the department.

(B) Provide that all water-vending machines shall be designed and constructed to permit easy cleaning and maintenance of all exterior and interior surfaces.

(C) Provide that water-vending machines shall have all parts and surfaces which come into contact with the water constructed of approved, corrosive-resistant and nonabsorbent material capable of withstanding repeated cleaning and sanitizing treatment.

(D) Provide that water-vending machines shall have a recessed or guarded corrosion-resistant dispensing spout.

(E) Provide that water-vending machines be designed so all treatment of the vended water by distillation, ion exchange, filtration, ultraviolet light, reverse osmosis, mineral addition, or any other acceptable process is done in an effective manner.

(F) Provide that water-vending machines shall have an effective system of handling drip, spillage, and overflow of water.

(G) Provide that water-vending machines shall have a backflow prevention device approved by the department for all connections with the water supply.

(H) Provide for disinfecting vended water by ultraviolet light or other method approved by the department prior to delivery into the customer's container.

(I) Provide that water-vending machines shall be equipped with monitoring devices designed to shut down operation of the machine when the disinfection unit fails to function.

(J) Provide that water-vending machines shall be equipped with a self-closing, tight-fitting door on the vending compartment.

(K) Provide that water-vending machines shall comply with the American Water Works Association (AWWA) specifications for granular activated carbon if used in the treatment of potable water (AWWA B604-74).

(L) Provide that water-vending machines shall be maintained in a clean and sanitary condition, free from dirt and vermin.

(M) Provide that water-vending machines shall be connected to a state approved and regulated public water supply.

(N) Provide that water-vending machines shall be located in an area that can be maintained in a clean condition and in a manner that avoids insect and rodent harborage.

(O) Provide that the water-vending machine shall be equipped with monitoring devices designed to shut down the labeled purified water delivery system if treatment of water by the machine does not result in a total dissolved solids content of less than 10 milligrams per liter in the purified water.

(5) Standards for labeling and advertising of bottled water, vended water, water distributed by a water hauler, water from a retail water treatment plant, and water from private water sources.

(6) Standards for processing bottled water through a line or lines used for any other food product.

(b) The department, upon the request of a local health officer, may authorize the local health officer to implement and enforce those provisons of this chapter which relate to water-vending machines, and retail water treatment plants under the terms and conditions specified by the department.

26592.1. Each bottler, distributor, or vendor of bottled water, each owner or operator of a water-vending machine, each water hauler, each operator of a retail water treatment plant, and each private water source operator shall obtain a bacterial analysis by an approved laboratory of water so bottled, distributed, or sold at such times as may be required by regulations of the department. The analysis shall be submitted to the department indicating whether the water is pure and wholesome. Analyses of vended water or water from retail water treatment plants shall be submitted to the local health officers if the local health officers are authorized by the department pursuant to subdivision (b) of Section 26592.

26592.2. No water shall be sold or otherwise distributed which has been produced in any water-bottling plant, vended by any water-vending machine, hauled by any water hauler, processed by any retail water treatment plant or distributed by any private water source operator which does not at least satisfy the minimum standards adopted by the department for the production and quality of the water.

26592.3. No water-vending machine shall be used in this state which does not at least satisfy the minimum standards adopted by the department.

26592.4. The department shall require that each water-vending machine, retail water treatment plant, water hauler vehicle and facility, and private water source be maintained in a clean and sanitary condition at all times.

26593. (a) No person shall operate a water-bottling plant, operate a private water source, or be a water hauler in this state except pursuant to a license issued by the department. If a person has a valid water-bottling plant license issued by the department, additional licenses for a private water source operator or for a water hauler based and operating at the same address, or for an out-of-state bottled water distributor shall not be required.

(b) No person shall own or operate a water vending machine or a retail water treatment plant except pursuant to a license issued by the department or to a permit issued by a local health department.

26593.1. No bottled water produced in an out-of-state bottling plant shall be sold or distributed within this state unless either the out-of-state bottler or the distributor shall have first obtained an out-of-state bottler's or distributor's license.

26593.2. (a) The department shall charge and collect a fee for each license applied for in accordance with the fee schedule in Table 1, which shall be an amount reasonably necessary to produce sufficient revenue to enforce the provisions of this article. The fees collected shall be adjusted annually as required by Section 113. New applicants for a bottled water license or for an out-of-state distributors license shall pay Category 2 fees for the first license year.

(b) The water-bottling plant and out-of-state bottled water distributor categories shall be determined by dividing by 52 the number of gallons produced or shipped into California during the previous year. If the result is an average of 5,000 gallons or less per week, the firm is Category 1. If the average exceeds 5,000 gallons per week, the firm is Category 2.

Table 1
License Fees

| License Class | Annual Fee |
|---|---|
| Water-Bottling Plant or Out-of-State Bottled Water Distributor | |
| Category 1 | $300 |
| Category 2 | 850 |
| Water-Vending Machine | 10 |
| Water Hauler | 300 |
| Retail Water Treatment Plant | 300 |
| Private Water Source Operator | 300 |

(c) The owners or operators of each water-bottling plant, retail water treatment plant, private water source, each water hauler in California and bottlers or distributors of water bottled out-of-state shall make application for a license on forms provided by the department. Applications and license fees shall be submitted for each calendar year.

(d) Each water-vending machine owner or operator shall make application each calendar year for a license for all machines on forms provided by the department. A decal or seal provided by the department indicating a license fee has been paid shall be affixed in a prominent place to each water-vending machine in service.

26593.3. The department may deny any license application or revoke or suspend any license issued for cause. The department shall inform the person of any denial, revocation, or suspension in writing, stating with particularity reasons for the denial, revocation, or suspension.

"Cause," as used in this section, means a violation of any provision of this chapter or any regulation adopted pursuant thereto.

26593.4. The department shall charge and collect a fee for each department evaluation of a water-vending machine model or a retail water treatment plant to determine compliance with standards established by this article. The fee shall be three hundred dollars ($300) and shall be adjusted annually as required by Section 113.

26593.5. The department shall require each bottler, distributor, or vendor of bottled water, each owner or operator of any water-vending machine, each water hauler, each retail water treatment plant operator, each private water source operator, and each applicant for a license, to test for all substances necessary to establish conformance to standards adopted pursuant to Section 26592 at the times and frequencies the department may reasonably establish.

26593.6. (a) Water bottlers shall monitor annually all approved water sources for the presence of volatile organic compounds of potential public health concern, as specified by the United States Environmental Protection Agency in Tables 2 and 14 contained in Volume 50 of the Federal Register on pages 46904, 46923, and 46924 on November 13, 1985, or as reasonably specified by the department as a condition of licensure.

(b) In lieu of source water monitoring required by this section, a water bottler may document that the source monitoring required by this section is conducted by another entity approved by the department.

(c) Detection of a volatile organic compound, except trihalomethanes, for which source monitoring is required pursuant to this section shall be followed immediately by a program of periodic monitoring by the water bottler to confirm the presence or absence in the source water of the volatile organic compound. If the volatile organic compound is confirmed to be present in the source water the water bottler shall use granular activated carbon treatment or an equivalent treatment operated in accordance with good manufacturing practices as provided in Section 129.80 of Title 21 of the Code of Federal Regulations until the time that the concentration of the volatile organic compound does not exceed one part per billion, a United States Food and Drug Administration level, or a department action level for drinking water, whichever is less.

(d) The department may exempt any water bottler from the monitoring requirements of this section for any source as to which the bottler can make a showing satisfactory to the department that the source (1) does not contain the volatile organic compound for which monitoring is required and (2) is not vulnerable to contamination by the volatile organic compound because for surface water sources the compounds are not applied, manufactured, stored, disposed or shipped upstream, and for groundwater sources, the compounds are not applied, manufactured, stored, disposed, or shipped in the ground water recharge basin.

26593.7. Notwithstanding any other provisions of this article, the department may require any bottler, distributor, or vendor of bottled water, any owner or operator of a water-vending machine, any water hauler, any retail water treatment plant operator, any private water source operator, or any applicant for a license to test and submit results to the department for any substance, including organic chemical contaminants, at any time which the department believes the substance may be present in the water source and threaten the public health and safety.

26593.8. (a) Upon a determination by the department that a particular water source is subject to potential contamination, the department shall notify the bottler, distributor, or vendor of bottled water, the owner and operator of any water-vending machine, any water hauler, any retail water treatment plant operator, or any private water source operator of the specific contaminants or class of contaminants which pose a potential health risk.

(b) Within 90 days after notification by the department, the bottler, distributor, vendor of bottled water, the owner and operator of any water-vending machine, any water hauler, any retail water treatment plant operator, or any private water source operator shall conduct an analysis of the water source and submit the results of the analysis to the department.

(c) If evidence of contamination is found, the department may, by order, require the bottler, distributor, vendor of bottled water, or the owner and operator of any water-vending machine, any water hauler, any retail water treatment plant operator, or any private water source operator to conduct a source and product water analysis for the contaminants of concern in accordance with conditions specified by the department. The water analysis shall be conducted and reported on an annual basis, unless the department finds that reasonable action requires either more frequent or less frequent analysis.

(d) The department may, by order, require the bottler, distributor, vendor of bottled water, the owner and operator of any water-vending machine, any water hauler, any retail water treatment plant operator, or any private water source operator to reduce or eliminate the concentration of any chemical which the department determines may have an adverse effect on public health and safety. Until an enforceable standard has been established for a chemical which may have an adverse effect on human health, the department may require treatment techniques to reduce the concentration of the contaminants which require treatment necessary, in the department's judgment, to prevent known or anticipated adverse effects on the health of persons. The treatment system shall be designed to meet criteria designated by the department or by an independent authority approved by the department.

(e) The department may grant variances from the requirements of subdivision (d), if the bottler, distributor, vendor of bottled water, the owner and operator of any water-vending machine, any water hauler, any retail water treatment plant operator, or any private water source operator demonstrates either of the following:

(1) That the prescribed treatment technique is not necessary to protect the health of consumers because its raw water source is not subject to, nor is it likely to be subject to, significant chemical contamination.

(2) An alternative treatment technique is at least as efficient in lowering the level of contaminants to be controlled.

26593.9. All testing of bottled water, bottled water sources, water distributed by water haulers, water from retail water treatment plants, and water from vending machines shall be done by laboratories approved by the department, laboratories certified by the United States Environmental Protection Agency, laboratories certified by the primary enforcement authority in states which have been granted primacy by the United States Environmental Protection Agency, or laboratories certified (accredited) by a third-party organization acceptable to a primacy state.

26594. (a) Each container of bottled water sold in this state, each water-vending machine, and each retail water treatment plant located in this state shall be clearly labeled in an easily readable format. Bottled water may be labeled "drinking water," notwithstanding the source or characteristics of the water, only if it is processed pursuant to the Food and Drug Administration Good Manufacturing Practices contained in Section 103.35 and Parts 110 and 129 of Title 21 of the Code of Federal Regulations, Sections 12235 to 12285, inclusive, of Title 17 of the California Administrative Code, and any other requirements established by the department pursuant to Sections 26593.5, 26593.6, and 26593.7. Any vended water and any water from retail water treatment plants may be labeled "drinking water," notwithstanding the source or characteristics of the water, only if it is processed pursuant to Article 10 (commencing with Section 27650) of Chapter 4 of Division 22 and any other requirements established by the department pursuant to Sections 26593.5, 26593.6, and 26593.7.

(b) In addition to the requirements of subdivision (a), if a bottler, distributor, water hauler, retail water treatment plant operator, private water source operator, or vending machine operator provides information in the labeling or advertising of bottled water or vended water, stating or implying it is the product of a specific source of water or treated in a specific manner, the source or treatment shall be clearly labeled in an easily readable format. In order to be so labeled, the source or treatment shall conform to the following criteria:

(1) "Artesian well water" means water from a well tapping an aquifer in which the water level will stand above the bottom of the

confining bed of the aquifer, and in which the hydraulic pressure of the water in the aquifer is greater than the force of gravity. Artesian well water shall not be altered by the addition or deletion of minerals or by blending it with water from a nonartesian well water source, except that artesian well water may be filtered and shall be treated with ozone or an equivalent disinfection process. Any water which satisfied the designation of this paragraph may be labeled "artesian well water."

(2) "Fluoridated water" means water containing naturally occurring or added fluoride. The label shall specify whether it is naturally occurring or added fluoride. Any water which meets the designation of this paragraph shall contain not less than 1.0 milligrams per liter fluoridization and otherwise comply with the Food and Drug Administration quality standards set forth in Section 103.35(d)(2) of Title 21 of the Code of Federal Regulations.

(3) "Mineral water" means bottled water or vended water containing more than 500 milligrams per liter of total dissolved solids and originating entirely from an underground source, which may be a well, artesian well, or spring. Bottled or vended mineral water may be derived from a natural orifice or from a bore hole adjacent to the natural orifice. If it is derived from a natural orifice or from a bore hole adjacent to the natural orifice, the water shall be from the same underground stratum and be of the same quality and composition as the water derived from the natural orifice without external force. Mineral water may not be altered by the addition or deletion of minerals or by blending it with water from another source, except that mineral water may be filtered and shall be treated with ozone or an equivalent disinfection process approved by the department and shall be treated to reduce the concentrations of any naturally occurring substance which exceeds the bottled water safety standards established by the department. Mineral water may be collected and transported by pipes, tunnels, trucks, or similar devices. Any water which meets the criteria of this paragraph may also be labeled "natural mineral water."

(A) Mineral water which contains carbon dioxide as it emerges from the source and is bottled directly with its entrapped gas, or, the gas is mechanically separated from the water and later reintroduced into the water at the time of bottling shall be labeled "naturally carbonated" or "naturally sparkling."

(B) Mineral water which contains carbon dioxide, other than that naturally occurring in the source product, shall be labeled with the words "carbonation added" or "carbon dioxide added" when the carbonation is obtained from a natural or manufactured source.

(4) "Mineralized water" means bottled or vended water which meets the requirements of "mineral water" except that the water contains added minerals.

(5) "Natural water" means bottled or vended spring, artesian well, or well water which is unmodified by mineral addition or

deletion, except "natural water" may be filtered and shall be sanitized with ozone or an equivalent disinfection process and treated to reduce the concentration of any substance which exceeds safety standards established by the state department.

(6) "Naturally sparkling water" means bottled water or vended water with a carbon dioxide content from the same source as the water. "Sparkling," "carbonated," or "carbonation added" means bottled water or vended water which contains carbon dioxide.

(7) "Purified water" means water produced by distillation, deionization, reverse osmosis, or other method meeting the definition of purified water in the 21st edition of the United States Pharmacopeia. Water which meets the designation of this paragraph, and is vaporized, then condensed, may be labeled "distilled water."

(8) "Spring water" means water which issues by natural forces out of the earth at a particular place. Bottled or vended spring water may be derived from the natural orifice or from a bore hole adjacent to the natural orifice. If it is derived from the natural orifice by external force or from a bore hole adjacent to the natural orifice, the water shall be from the same underground stratum and be of the same quality and composition as the water derived from the natural orifice without external force. Spring water may not be altered by the addition or deletion of minerals or by blending it with water from a nonspring water source, except that spring water may be filtered and shall be treated with ozone or an equivalent disinfection process. Spring water may be collected and transported by pipes, tunnels, trucks, or similar devices.

(9) "Well water" means water from a hole bored into the ground which taps the water of an aquifer, except that well water may be filtered and shall be treated with ozone or an equivalent disinfection process. Well water may not be altered by the addition or deletion of minerals or by blending it with water from a nonwell water source.

(10) Notwithstanding any other provision of this section, water from a public water system which is unprocessed by the bottler or vendor shall be labeled as "unprocessed public drinking waters."

26594.2. Except as provided in paragragh (3) of subdivision (b) of Section 26594, any bottled water or vended water, the quality of which is below the quality required by this article, shall be labeled with a statement of substandard quality, as prescribed by Section 103.35 of Title 21 of the Code of Federal Regulations.

26594.3. Any bottler, distributor, vendor of bottled water, or owner or operator of any water-vending machine, whose corporate name or trademark contains the words "spring" or "springs," or any derivative of either of these words, or "well," "artesion well," or "natural" shall label each bottle or vending machine with the source of the water in typeface at least equal to the size of the typeface of the corporate name or trademark, if the source of the bottled or vended water is different from the source stated in the corporate name or trademark.

26594.4. (a) A bottled water, as defined in Section 26594, with natural or added carbonation, may be prepared with added flavors, extracts, essences, or fruit juice concentrates derived from a spice or fruit and comprising less than 1 percent by weight of the final product. The final product shall contain no sweeteners, or additives other than the flavors, extracts, essences, or fruit juice concentrates and carbon dioxide and shall be designated on labels and in advertising as follows:

(1) The common or usual name of the characterizing flavor shall accompany the designation of the bottled water product type as defined in subdivision (b) of Section 26594.

(2) The product may be designated as "natural" only if it meets the requirements for the designation as defined in paragraphs (5) and (6) of subdivision (b) of Section 26594, and naturally derived flavors, extracts, or essences are used.

(b) Products labeled pursuant to this section shall comply with all other provisions of this article. Products with one type or one source of bottled water that are labeled pursuant to this section shall not be blended with water that is not bottled water or that is of another bottled water type.

26594.5. The department, prior to issuing a license, shall review all labels prepared pursuant to this article, and may require any changes in order to comply with the provisions of this article.

SEC. 3. No reimbursement is required by this act pursuant to Section 6 of Article XIII B of the California Constitution because the only costs which may be incurred by a local agency or school district will be incurred because this act creates a new crime or infraction, changes the definition of a crime or infraction, changes the penalty for a crime or infraction, or eliminates a crime or infraction.

O

Appendix B. Chemicals Monitored During Well Sampling

## PURGEABLE ORGANIC ANALYSES
## (VOLATILES)

| | | |
|---|---|---|
| LABORATORY NAME: | REPORT PREPARED BY: (SIGNATURE) | DATE OF REPORT: |
| SYSTEM NAME: | | NUMBER: |
| WELL NAME AND/OR NUMBER: | STATE WELL NUMBER: | |
| DESCRIPTION OF SAMPLING POINT: | | |
| NAME OF SAMPLER: | SAMPLER EMPLOYED BY: | |
| DATE/TIME SAMPLE COLLECTED: | DATE/TIME SAMPLE RECEIVED @ LAB: | DATE ANALYSES COMPLETED: |
| TEST METHODS: | Were all the constituents listed below quantified? | |

| CONSTITUENT | REPORTING UNITS | STORET CODE | ANALYSES RESULTS | DETECTION LIMIT |
|---|---|---|---|---|
| Benzene | ug/l | 34030 | | |
| Bromodichloromethane | ug/l | 32101 | | |
| Bromoform | ug/l | 32104 | | |
| Bromomethane | ug/l | 34413 | | |
| Carbon tetrachloride | ug/l | 32102 | | |
| Chlorobenzene | ug/l | 34301 | | |
| Chloroethane | ug/l | 34311 | | |
| 2-Chloroethylvinyl ether | ug/l | 34576 | | |
| Chloroform | ug/l | 32106 | | |
| Chloromethane | ug/l | 34418 | | |
| | ug/l | | | |
| Dibromochloromethane | ug/l | 32105 | | |
| 1,2-Dichlorobenzene | ug/l | 34536 | | |
| 1,3-Dichlorobenzene | ug/l | 34566 | | |
| 1,4-Dichlorobenzene | ug/l | 34571 | | |
| Dichlorodifluoromethane | ug/l | 34668 | | |
| 1,1-Dichloroethane | ug/l | 34496 | | |
| 1,2-Dichloroethane | ug/l | 34531 | | |
| 1,1-Dichloroethene | ug/l | 34501 | | |
| trans-1,2-Dichloroethene | ug/l | 34546 | | |
| 1,2-Dichloropropane | ug/l | 34541 | | |
| cis-1,3-Dichloropropene | ug/l | 34704 | | |

WELL NAME AND/OR NUMBER ____________________

PURGEABLE ORGANIC ANALYSES (Continued)



| CONSTITUENT | REPORTING UNITS | STORET CODE | ANALYSES RESULTS | DETECTION LIMIT | |
|---|---|---|---|---|---|
| trans-1,3-Dichloropropene | ug/l | 34699 | | | |
| Ethyl benzene | ug/l | 34371 | | | |
| Methylene chloride | ug/l | 34423 | | | |
| Methyl Ethyl Ketone | ug/l | 81595 | | | |
| Methyl Isobutyl Ketone | ug/l | 81596 | | | |
| 1,1,2,2-Tetrachloroethane | ug/l | 34516 | | | |
| Tetrachloroethene | ug/l | 34475 | | | |
| Tolu ne | ug/l | 34010 | | | |
| 1,1,1-Trichloroethane | ug/l | 34506 | | | |
| 1,1,2-Trichloroethane | ug/l | 34511 | | | |
| Trichloroethene | ug/l | 39180 | | | |
| Trichlorofluoromethane | ug/l | 34488 | | | |
| Vinyl chloride | ug/l | 39175 | | | |
| Xylenes | ug/l | 81551 | | | |

Note any unidentified peaks below

SL 033174

# BASE/NEUTRALS AND ACIDS
# ORGANIC ANALYSES

| | | |
|---|---|---|
| LABORATORY NAME: | REPORT PREPARED BY: (SIGNATURE) | DATE OF REPORT: |
| SYSTEM NAME: | | NUMBER: |
| WELL NAME AND/OR NUMBER: | | STATE WELL NUMBER: |
| DESCRIPTION OF SAMPLING POINT: | | |
| NAME OF SAMPLER: | SAMPLER EMPLOYED BY: | |
| DATE/TIME SAMPLE COLLECTED: | DATE/TIME SAMPLE RECEIVED @ LAB: | DATE ANALYSES COMPLETED: |
| TEST METHODS: | Were all the constituents listed below quantified? | |

BASE/NEUTRAL EXTRACTABLES

| CONSTITUENT | REPORTING UNITS | | STORET CODE | ANALYSES RESULTS | DETECTION LIMIT | |
|---|---|---|---|---|---|---|
| Acenaphthene | ug/l | | 34205 | | | |
| Acenaphthylene | ug/l | | 34200 | | | |
| Anthracene | ug/l | | 34220 | | | |
| Aldrin | ug/l | | 39330 | | | |
| Benzo(a)anthracene | ug/l | | 34526 | | | |
| Benzo(b)fluoranthene | ug/l | | 34230 | | | |
| Benzo(k)fluoranthene | ug/l | | 34242 | | | |
| Benzo(a)pyrene | ug/l | | 34247 | | | |
| Benzo(ghi)perylene | ug/l | | 34521 | | | |
| Benzyl butyl phthalate | ug/l | | 34292 | | | |
| β-BHC | ug/l | | 39338 | | | |
| δ-BHC | ug/l | | 34259 | | | |
| Bis(2-chloroethyl)ether | ug/l | | 34273 | | | |
| Bis(2-chloroethoxy)methane | ug/l | | 34278 | | | |
| Bis(2-ethylhexyl)phthalate | ug/l | | 39100 | | | |
| Bis(2-chloroisopropyl)ether | ug/l | | 34283 | | | |
| 4-Bromophenyl phenyl ether | ug/l | | 34636 | | | |
| Chlordane | ug/l | | 39350 | | | |
| 2-Chloronaphthalene | ug/l | | 34581 | | | |



SL 033175

WELL NAME AND/OR NUMBER ____________________

BASE/NEUTRALS AND ACIDS (Continued)



| CONSTITUENT | REPORTING UNITS | STORET CODE | ANALYSES RESULTS | DETECTION LIMIT |
|---|---|---|---|---|
| 4-Chlorophenyl phenyl ether | ug/l | 34641 | | |
| Chrysene | ug/l | 34320 | | |
| 4,4'-DDD | ug/l | 39310 | | |
| 4,4'-DDE | ug/l | 39320 | | |
| 4,4'-DDT | ug/l | 39300 | | |
| Dibenzo(a,h)anthracene | ug/l | 34556 | | |
| Di-n-butylphthalate | ug/l | 39110 | | |
| 1,3-Dichlorobenzene | ug/l | 34566 | | |
| 1,2-Dichlorobenzene | ug/l | 34536 | | |
| 1,4-Dichlorobenzene | ug/l | 34571 | | |
| 3,3'-Dichlorobenzidine | ug/l | 34631 | | |
| Dieldrin | ug/l | 39380 | | |
| Diethyl phthalate | ug/l | 34336 | | |
| Dimethyl phthalate | ug/l | 34341 | | |
| 2,4-Dinitrotoluene | ug/l | 34611 | | |
| 2,6-Dinitrotoluene | ug/l | 34626 | | |
| Di-n-octylphthalate | ug/l | 34596 | | |
| Endosulfan sulfate | ug/l | 34351 | | |
| Endrin aldehyde | ug/l | 34366 | | |
| Fluoranthene | ug/l | 34376 | | |
| Fluor ne | ug/l | 34381 | | |
| Heptachlor | ug/l | 39410 | | |
| H ptachlor epoxide | ug/l | 39420 | | |
| Hexachlorobenzene | ug/l | 39700 | | |
| Hexachlorobutadiene | ug/l | 34391 | | |
| Hexachloroethane | ug/l | 34396 | | |
| Indeno(1,2,3-cd)pyrene | ug/l | 34403 | | |
| Isophorone | ug/l | 34408 | | |
| Naphthalene | ug/l | 34696 | | |
| Nitrobenzene | ug/l | 34447 | | |
| N-Nitrosodi-n-propylamine | ug/l | 34428 | | |
| PCB-1016 | ug/l | 34671 | | |
| PCB-1221 | ug/l | 39488 | | |
| PCB-1232 | ug/l | 39492 | | |
| PCB-1242 | ug/l | 39496 | | |

SL 033176

WELL NAME AND/OR NUMBER ______________________________

BASE/NEUTRALS AND ACIDS (Continued)



| CONSTITUENT | REPORTING UNITS | STORET CODE | ANALYSES RESULTS | DETECTION LIMIT | |
|---|---|---|---|---|---|
| PCB-1248 | ug/l | 39500 | | | |
| PCB-1254 | ug/l | 39504 | | | |
| PCB-1260 | ug/l | 39508 | | | |
| Phenanthrene | ug/l | 34461 | | | |
| Pyr ne | ug/l | 34469 | | | |
| Toxaphene | ug/l | 39400 | | | |
| 1,2,4-Trichlorobenzene | ug/l | 34551 | | | |
| **ACID EXTRACTABLES** | | | | | |
| 4-Chloro-3-methylphenol | ug/l | 34452 | | | |
| 2-Chlorophenol | ug/l | 34586 | | | |
| 2,4-Dichlorophenol | ug/l | 34601 | | | |
| 2,4-Dimethylphenol | ug/l | 34606 | | | |
| 2,4-Dinitrophenol | ug/l | 34616 | | | |
| 2-Methyl-4,6-dinitrophenol | ug/l | 34657 | | | |
| 2-Nitrophenol | ug/l | 34591 | | | |
| 4-Nitrophenol | ug/l | 34646 | | | |
| Pentachlorophenol | ug/l | 39032 | | | |
| Phenol | ug/l | 34694 | | | |
| 2,4,6-Trichlorophenol | ug/l | 34621 | | | |
| **ADDITIONAL EXTRACTABLE PARAMETERS** | | | | | |
| Benzidine | ug/l | 39120 | | | |
| α-BHC | ug/l | 39337 | | | |
| γ-BHC | ug/l | 39340 | | | |
| Endosulfan I | ug/l | 34361 | | | |
| Endosulfan II | ug/l | 34356 | | | |
| Endrin | ug/l | 39390 | | | |
| Hexachlorocyclopentadiene | ug/l | 34386 | | | |
| N-Nitrosodimethylamine | ug/l | 34438 | | | |
| N-Nitrosodiphenylamine | ug/l | 34433 | | | |

SEB-SD
DLB-5/84
REV-5/85

# AGRICULTURAL CHEMICALS
# AND MISCELLANEOUS ORGANIC ANALYSES

| | | |
|---|---|---|
| LABORATORY NAME: | REPORT PREPARED BY: (SIGNATURE) | DATE OF REPORT |
| SYSTEM NAME: | | NUMBER |
| WELL NAME AND/OR NUMBER: | STATE WELL NUMBER: | |
| DESCRIPTION OF SAMPLING POINT: | | |
| NAME OF SAMPLER: | SAMPLER EMPLOYED BY: | |
| DATE/TIME SAMPLE COLLECTED: | DATE/TIME SAMPLE RECEIVED @ LAB: | DATE ANALYSES COMPLETED: |

| CONSTITUENT | REPORTING UNITS | STORET CODE | ANALYSES RESULTS | DETECTION LIMIT |
|---|---|---|---|---|
| Endrin | ug/l | 39390 | | |
| Lindane | ug/l | 39782 | | |
| Methoxychlor | ug/l | 39480 | | |
| Toxaphene | ug/l | 39400 | | |
| 2,4 - D | ug/l | 39730 | | |
| 2,4,5 - TP Silvex | ug/l | 39045 | | |
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Appendix C. Department of Health Services Sampling Scheme

DPS

State of California — Department of Health Services

# Memorandum

To : Dr. Raymond Neutra
Dr. Shanna Swan
ESSS

Date : October 16, 1987

Subject: Pregnancy Outcome Studies

From : Dr. David P. Spath DMV for
PWSB

Dr. Michael Volz DMV
SRL

Pursuant to our meeting on October 14, 1987, attached find the proposed sampling/analysis scheme (Table 1) in support of the Pregnancy Outcome Studies (Santa Clara Co.). As you know, because of the compressed time frame, it will be difficult to coordinate logistics in conjunction with this activity so that modifications may be necessary.

Please note the following:

SAMPLING:

1. Through its Inorganics Unit, SRL plans on providing 8 oz. glass sampling containers to collectors of TOC samples.

2. Through its Organics Unit, SRL intends to furnish VOC kits to collectors of VOC samples. In addition, two (2) VOC kits per sample will be made available to HML for TOX analyses as required. All kits are to contain travel blanks.

3. The Radiochemistry Unit and PWSB will make available Rn sampling kits and/or containers to collectors of Rn samples. PWSB's current Rn survey will be held in abeyance during the Santa Clara Co. investigation.

4. The Biologics Unit will provide sterile bacteriological bottles to collectors.

SCHEDULING:

1. PWSB plans on well water sampling at Fairchild and at the Great Oaks Water (GOW) Co. on or about 10/21/87. Sampling materials will be needed from SRL on 10/20/87.

   The Fairchild sample will require analyses for: TOC, VOC, Rn, Bacteria, and TOX.

   There will be seven (7) well water samples plus one (1) duplicate taken from GOW Co. All eight (8)

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samples will be analyzed for TOC. Three (3) samples and the one (1) duplicate also will be analyzed for VOC if necessary (PWSB to verify monitoring records), Rn, Bacteria and TOX.

2. PWSB plans on well water sampling from the City of Santa Clara on or about 10/27/87. Sampling materials will be needed from SRL by 10/26/87.

3. Bottled water samples will be provided to SRL and HML by PWSB.

4. Surface water samples will be taken by SRL and PWSB and be provided to SRL and HML.

5. The control groundwater from Pinedale Water Company (Fresno Co.) will be provided by PWSB.

The next meeting is scheduled for Wednesday, 10/28/87, at 10:30 a.m. in Rm. 458 of the Main Building.

cc: Dr. Fuhs (DL)
Mr. Rogers (PWSB)
Dr. Tamplin (SRL)
Mr. Simmons (HML)

Table 1. Proposed Sampling/Analysis Scheme in Support of Pregnancy Outcome Studies

| Water Sample | Type | Number* | Sampling/Analysis** TOC | VOC | Rn | Bacteria | TOX |
|---|---|---|---|---|---|---|---|
| A. | Wells | 46 | + | | | | |
| B. | Wells | 10 (***) | (+) | (+) | + | + | + |
| C. | Bottled Water | 4 | + | + | + | + | + |
| D. | Surface Water | 2 | + | + | + | + | + |
| E. | Fairchild Site | 1 | + | + | + | + | + |
| F. | Control Ground-Water | 1 | + | + | + | + | + |

* Well waters are from non-chlorinated groundwater; Bottled water is from Alhambra, Sierra Spring, and Black Mountain and consists of one or more types of plastic containers depending upon volume, i.e., polycarbonate for 5 gallons and polyethylene for 1 gallon; surface waters are both chlorinated (SFWD and EBMUD); control groundwater will be from Pinedale Water Company (Fresno Co.).

** Sampling is to be initiated or or after 10/21/87; TOC analysis for all organic C compounds including glycol ethers and non-volatiles like p-CBSA; VOCs by EPA M 601; Rn analyses by liquid scintillation counting; bacterial enumeration for total- and fecal coliform bacteria and for others by both HPC and R2a techniques; TOX in non-purgeable mode, by HML; all other analyses by SRL.

*** Subset of (A); for QA purposes, one replicate well sampling for each of the three water systems will be made thus resulting in a total of 13 well samples; a selection of representative wells to be sampled has been made based on production information (i.e., those wells that contribute the greatest amount of water to the water system's demand over time) and the aquifer characteristics (i.e., confined vs unconfined zones). The number of wells to be sampled for bacterial enumeration may be limited, however, by availability of R2a media. Should high concentrations of Rn or bacteria be detected in the representative well water samples, sampling of the remaining wells for that constituent will be considered; VOC data on all 46 wells, however, currently exist thus obviating the need for additional VOC sampling; TOC will be determined for all 46 wells as part of (A).

VOCs on wells to be run only if monitoring data within the last 2 yrs is unavailable from PWSB.

Appendix D. Tap Sampling Protocol

I. There will be 48 sampling sites (i.e., private homes) within four census tracts identified by Epidemiological Studies & Surveillance Section (ESSS). Sites will be selected within each census tract as close to each other as possible to reduce total sampling time. ESSS personnel will contact homeowners to conduct a presampling interview and work with Public Water Supply Branch (PWSB) staff to arrange a time schedule for sampling. ESSS will identify those sites where well-maintained as well as non-maintained carbon filters are used. ESSS will also identify sit s where other types of filtration devices (i.e., reverse osmosis) are used. ESSS and PWSB will complete the sampling schedule and transmit the schedule to the Sanitation & Radiation Laboratory (SRL) and the Hazardous Materials Laboratory prior to the c mmencement of sampling.

II. All samples will be collected by field engineers (2) from PWSB and Santa Clara County Health Department sanitarians. A maximum of six sites will be collected per day. A presampling workshop will be held to acquaint personnel with the protocol requirements.

III. Four samples will be collected from each site. There will be two different sampling sequences depending upon the existence of carbon filters or reverse osmosis devices at the site.

A. Sampling Sequence Where No Carbon Filter or Reverse Osmosis Device Used

1. The first sample will be collected from the kitchen tap. The sample will be collected immediately after the tap is turned on. A volume of 250 ml will be collected in a clean sterile glass bottle. After the sample is collected the tap will be turned off. This sample will reflect any water quality changes imparted by the faucet and faucet plumbing.

2. The second samples will be collected at the kitchen tap. Another sample container identical to that used in (A)(1) will be made ready. Immediately after the kitchen tap is again turned on, a sample volume of 250 ml will be collected. After the second 250 ml sample is collected the tap again will be turned off. Four 40 ml clean glass vials will be made ready. The tap will be turned on and the vials carefully filled to

overflowing. Agitation during the filling of the vials will be av ided. Th vials will be capped in a way to prevent any headspace. These samples will reflect any water quality changes imparted by the home plumbing.

3. The third sample will be collected from a running shower using sterile four ounce plastic bacti bottles. The sampler will turn on the bathtub water (do not turn on the shower) and adjust the water to a normal showering temperature. This will be done by touch and will be subject to the discretion of the sampler. The shower then will be turned on, allowed to run for 10 seconds and a sample will be collected in a sterile bacti bottle. At those sites without bathtubs or where the bathtub and shower are separate, the shower first will be turned on and the water temperature adjusted as described above. As soon as the water temperature is adjusted the sample will be taken. This sample will reflect any bacteriological changes imparted by the shower plumbing.

B. Sampling Sequence Where Carbon Filter Used

1. The first sample will be collected at the tap at which the carbon filter or reverse osmosis device is attached. A 250 ml sample will be collected in a container identical to that used in (A)(1). This sample will reflect any water quality changes imparted by the faucet, faucet plumbing and carbon filter or reverse osmosis device and the amount of organic chemical matter removed by the carbon filter or reverse osmosis device.

2. The second samples will be collected at a different tap (preferably the bathroom). A sample will be collected in another container identical to that used in (A)(1). First, the tap will be turned on and 250 ml will be run to waste. The sampler will then collect 250 ml. The tap will be turned off. Four 40 ml clean glass vials will be made ready. The tap will be turned on again and samples will be collected in the vials in accordance with (A)(2). This sample will reflect any water quality changes imparted by the home plumbing and the organic chemical content of the water prior to treatment with the carbon filter reverse osmosis device.

3. A sample of shower water will be collected in accordance with (A)(3).

C. Travel Blanks

1. A separate set of travel blanks will be carried with the sample containers to be used at ach sampling site.

2. Each s t of separate travel blanks will consist of one 250 ml sterile glass b ttle and tw 40 ml clean glass vials all of which are filled with organic free water. The water in the 250 ml bottle shall have been sterilized.

3. The travel blanks will be prepared by SRL.

D. Sample Transportation and Sample Handling in th Laboratory

1. All samples immediately will be placed in an iced storage container until delivered to the laboratory.

2. All samples will be delivered to SRL. Upon receipt at the laboratory, the samples will be handled by SRL personnel with assistance from the sample collector in the following manner.

a. Samples collected in accordance with (A)(1) and (B)(1) will be handled in the following manner. A subsample from the 250 ml sample collected pursuant to (A)(1) will be apportioned into a sterile bacti bottle provided by th laboratory for bacteriological analyses. The subsample remaining in the 250 ml bottle will be acidified and retained for metals analysis. Two subsamples from the 250 ml sample collected pursuant to (B)(1) will be apportioned as follows: 1) approximately 55 ml into a sterile bacti bottle provided by the laboratory for bacteriological analysis, and 2) 50 ml into a clean glass bottle for total organic carbon (TOC) analysis. The remaining subsample in the 250 ml bottle will be acidified and retained for metals analysis. The 40 ml vials will be delivered by SRL to Art Hudson in HML for total organic halide (TOX) analysis.

b. Samples collected in accordance with (A)(2) and (B)(2) will be handled in the following manner. Two subsamples from the 250 ml sample collected pursuant to (A)(2) or (B)(2) will be apportioned as follows: 1) approximately 55 ml into a sterile bacti bottle provided by the laboratory for bacteriological analysis, and 2) 50 ml into a clean glass bottle for TOC analysis. The remaining subsample in the 250 ml bottle will be acidified and retained for metals analysis. The 40 ml vial samples will be delivered to Art Hudson in HML for (TOX) analysis.

c. Samples collected in accordance with (A)(3) and (B)(3) will undergo bacteriological analysis.

IV. Ten per cent f the samples, and at least one per sampling batch, will be collected in duplicate and analyzed as required to fulfill Quality Assurance (QA) requirements. In addition, QA in the laboratory will include positive and negative controls for bacteriological analysis, and replicate matrix spike recoveries for metals and TOC analysis to support precision and accuracy statements.

V. All samples will be delivered to SRL on or before 12 noon of the same day that they are collected. All samples will be kept refrigerated prior to analyses.

VI. Samples will be analyzed by SRL/HML by the following methods.

A. TOC will analyzed according to EPA Method 415.1.

B. Trace metals, lead and copper, will be quantified by EPA Methods 239.2 and 220.1, respectively (Methods for Chemical Analysis of Water and Wastes EPA-600/4-79-020).

C. Bacterial population densities will be enumerated by the heterotrophic plate count (HPC) pour plate and R2a and spread plate agar technics, respectively (Standard Methods for the Evaluation of Water and Wastewater, 16th Edtn., 1985, APHA.AWWA.WPCF).

D. TOX will be measured by EPA Method 9020 (Test Methods for Evaluating Solid Waste; Physical/Chemical Methods, 3rd Edtn., 1986).

## 10. Potential Sources of Bias and Confounding

The studies presented in this report may be subject to bias for a number of reasons. The exposures under study are self reported and ascertained after pregnancy outcome is known. The studies were conducted at a time when there was considerable concern about water quality and the Fairchild studies had suggested that pregnancy outcomes might be related to tap water consumption. The study of sp ntaneous abortion (SAB) may be subject to additional biases due to the fact that a large proportion of these cases are never medically validated and that cas  ascertainment is related to the time the woman seeks prenatal care. Finally, the differential opportunity for exposure in cases of SAB and mothers of live born infants is of concern. We will discuss these potential biases and the evidence in these studies that each was operating. Three related issues are als  discussed: 1) the absence of a decline in SAB rates over time despite an increase in tap water abstention, 2) how rates in these studies compare with rep rted rates of adverse pregnancy results and 3) the possibility of a hidden c nfounder which might explain the observed associations.

### 10.1 Biased availability for study

### 10.11 Biased awareness of early pregnancy loss

A non-tap water drinker (or bottled water drinker) could be hypothesized to be a person (perhaps a busy professional) who would overlook a missed period and be unlikely to have an early pregnancy test or seek medical care for h r pregnancy or SAB. Such a person would not be included in the cohort of recognized pregnancies which were analyzed in the Malathion study, nor would she appear in the Fairchild studies. She would also have been missed by the negative validation carried out for the first Fairchild study, since that looked only at pregnancies for which a woman had sought medical care. The presence of such women in these study populations would result in a deficit of spontaneous abortions among bottled water drinkers and a spuriously low rate of spontaneous abortions in this group.

This scenario seems unlikely for several reasons. First, we looked at gestational age at SAB by tap and bottled water use. In the Malathion study

23.1% of sp ntaneous ab rtions in tap water abstainers ccurred at or before the eighth week, compared to 15.3% in the tap water drinkers. This is contrary to what one would expect if bottled water drinkers tended to obtain pregnancy confirmation later than tap water drinkers. Secondly, the use of bottled water increased from 20% to 70% between 1980 and 1985 in the Fairchild study areas, while the rate of SAB among bottled water drinkers remained low. If failure to recognize early SABs was an explanation for th low rates in bottled water users, women who switched to bottled water must lso have become less accurate in reporting early pregnancy loss. This seems highly unlikely.

10.12 Biased rates of cooperation

One might hypothesize that the "busy bottled water drinker" with an adverse pregnancy outcome would be less willing to be interviewed. This behavior w uld also result in a deficit of adverse outcomes among bottled water drinkers. We evaluated this hypothesis in two ways. First, in order to characterize bottled water drinkers, we carried out several discriminant analyses. In the Malathion study, bottled water drinkers were more likely t be non-White, and particularly Asian (Table 5.7), and neither in this study nor in Fairchild II (Table 3.21) did educational level or work during pregnancy discriminate between tap and bottled water drinkers. Thus, we f und no evidence supporting the "busy bottled water drinker" stereotype. Second, in Fairchild II we looked at the number of attempts necessary to interview the respondents as a function of bottled water consumption (Table 10.1). There is no indication that bottled water drinkers were more difficult to recruit than tap water drinkers. Thus, there is no evidence suggesting that bottled water drinking cases would have been selectively missed because of differential rates of cooperation.

10.13 Biased migration prior to study onset

One might hypothesize that a person with prior adverse pregnancy outcomes wh was aware of the reported association between tap water consumption and reproduction would be more likely to have moved away prior to the onset of our studies. One piece of evidence against this bias comes from the Malathion study. In this study, in which women were enr lled through p sitive pregnancy t sts and schedul d prenatal visits, about 50% were enrolled before December 1981, when the Fairchild leak became known. There were no differences between 1981 and 1982 entrants with respect to prior fetal loss. Nor did the Fairchild publicity cause women to enter prenatal care earlier. The mean gestational age at entry for cases of SAB was 5.5 in both 1981 and 1982 study entrants, and 6.9 and 7.0 among women with live births in 1981 and 1982 respectively.

Therefore, it does not appear that a bias with respect to availability for study was operating in these data.

10.2 Opportunity bias

Since spontaneous abortions occur early in pregnancy, women who abort may not have had time to change from tap to bottled water use. Thus, the observed "protective effect" of bottled water could, in whole or part, be due to the fact that mothers of live births had more opportunity to adopt this behavior. We call this "opportunity bias". We have shown that this bias is operating with respect to use of prenatal vitamins. Before stratifying on length of pregnancy, use of prenatal vitamins appears to protect against spontaneous abortion. However, after controlling for length of pregnancy, it is clear that this association is an artifact of opportunity bias (Table 4.8); that is, SAB prevented multivitamin use, rather than the reverse. Could the same bias be operating with respect to bottled water?

Unlike prenatal vitamin use, which is usually begun after the first prenatal visit, most women drink water before they become pregnant, and many are advised to increase water consumption during pregnancy. This can be seen in Table 7.12A which shows that more women increased than decreased tap water consumption after they became pregnant. Nevertheless, women who suspected a problem with their water might have decreased their tap water consumption during pregnancy as a health protective measure.

In SACCS women were asked about their water consumption in the month before pregnancy and whether it changed during pregnancy. (See Appendix D to Section 1 for the exact wording of these questions.) Data on direction and month of change are shown in Tables 7.12A and 7.12B. As can be s en, controls changed their tap water consumption more frequently than cases. Opportunity bias could arise because of the differential time available to change behavior in cases and controls. Most women who changed did so in the first or second month of pregnancy (85% of controls who changed and 100% of cases). Was the lack of change after that time among cases due to the fact that their pregnancies had terminated? No. Even though 60% of SABs occurred after the second month, no cases changed their water consumption after the second month. Thus, it does not appear that opportunity bias is operating here.

## 10.3 Biased recall of disease

In a cohort study, an exposed subject might be more likely to report an adverse outcome, while an unexposed subject might fail to report such an outcome. However, this is an unlikely source of bias in our studies for several reasons. First, an association between water and adverse pregnancy outcome is seen in the Malathion Study in which 96% of the cohort was followed to a validated pregnancy outcome. Second, to eliminate false positives, adverse outcomes were medically validated in all of our studies. Third, the negative validation conducted for the first Fairchild study found that the "unexposed" were not more likely to underreport SABs or birth defects then the "exposed."

## 10.4 Biased recall of exposure

In all the studies presented here, the degree and type of water consumed was ascertained after pregnancy outcome. Because of the publicity concerning water contamination and pregnancy outcome in Santa Clara County and particularly in the area serviced by the GOWC, one might expect a greater awareness of tap water consumption among those with adverse pregnancy outcomes than among those without. For example, a non-tap water drinker with an adverse outcome might report a small amount of water used (say for brushing her teeth) and be classified as a tap water user, while a woman with a normal live birth might omit mentioning such use. We will now discuss several issues which relate to the plausibility of this source of bias in our studies.

10.41 How many misclassifications must be invoked to explain our results?

There are two kinds of misclassification which are of particular concern. The first, occurring with probability p(1), occurs when unexposed cases are misclassified as exposed. The second, occurring with probability p(2), ccurs when exposed controls are misclassified as unexposed. How large would these probabilities have to be to account for the observed associations reported here?

We first consider p(1). We have calculated the number of subjects in Fairchild II who would have to be reclassified in order for SAB rates to be constant across tap water strata (Table 10.2). Of the 100 SABs, 93% rep rted drinking some tap water. If only 78% of women had actually consumed tap water, SAB rates would have been similar regardless of the amount of tap water was consumed. In order for this to happen, 16 women must have been misclassified with respect to exposure. How likely is this? On the one hand, the number of SABs who are non-tap water drinkers would have to increase from 7 to 22, or by 300%, which seems unlikely. On the other hand, this represents a misclassification of only 16% of cases, which is plausible. We have carried out similar calculations for each of our studies and present the results in Table 10.3. The number of hypothetically misclassified cases ranges from 7 to 20 adding up to a total of 72 cases across all studies. This represents a total of 6.9% of all cases. Although this scenario requires a misclassification of between 31% and 100% of unexposed cases, the absolute number of women misclassified is small and represents only 3%-24% of the cases in each study.

10.42 The shift in distribution required

The hypothetical redistribution of cases shown in Table 10.2 is not confined to a shift from "no tap water" to "one glass per day." Rather, a shift primarily from "none" to "2 or more glasses" must be hypothesized. This weighs against recall bias as an explanation of our findings since it would be harder for a woman to forget drinking 2+ glasses of water a day than 1 glass or less.

10.43 Environmental concern in relation to the water associations

The relationship between environmental concern and the observed associations was examined because of the assumed relationship between the likelihood of recall bias and concern about tap water quality. In Fairchild IIB the OR f r tap water was independent of concern (Table 4.7). In the Malathion study there was a somewhat increasing OR for tap water with increasing concern (Table 5.8). In SACCS, there was no association with tap water in the "very concerned" (OR=1.0, p=.97) compared to a significant association in those less concerned (OR=2.5, p=.02) (Table 7.9B).

In the Cardiac study the OR was greatest in the 21% of cases and 16% of c ntrols who were uncertain whether their water was contaminated (OR=5.8). H wever, aside from this group, there was an increasing OR with increasing concern or belief that tap water caused birth defects (Tables 6.6 and 6.7).

Thus, it is possible that recall bias can explain some or all of the association between reported tap water consumption and cardiac anomalies, which are very severe, and not consistently account for the association between tap water consumption and spontaneous abortions.

10.44 Variation of the association by geography, type of water source and year

The association between tap water consumption and spontaneous abortion was stratified by geographic location, water source and calendar year. We assume that if recall bias was operating, it was strongest in women who were pregnant in 1980-81 and living in the "exposed" Fairchild study areas and that this bias would decrease with increasing time and distance. Under these hypotheses, ORs should be greater for respondents in Santa Clara County, and particularly in areas served by the GOWC. This should be seen most clearly in pregnancies which began before the contaminated well was shut down at the end of 1981.

The data on this are conflicting. In the Malathion study, among women living in Santa Clara County, the OR for tap water is greater for subjects who entered the study in 1981 than for those who entered in 1982. (ORs were 2.9 vs. 1.7 respectively.) However, no such difference over time is seen for the other tw counties. Moreover, for 1981 and 1982 entrants combined, the association with tap water did not differ by county (Table 5.20).

In Fairchild II, the associations between spontaneous abortions and bottled water use or tap water abstention changed very little over time. (Table 3.9 and 3.10). Furthermore, the water utility with the highest OR in that study was Santa Clara (OR=8.8) which was farthest from Great Oaks (Table 3.5).

We also examine the cardiac defect rates by time and water source. As can be seen in Table 6.5, the strongest association is seen in 1981. The association is weaker in 1982 and not seen in 1983. In the ground water areas which include (but are not limited to) the Great Oaks Service Area, the association is somewhat greater. The elevated rates in ground water drinkers in 1981 and 1982 could argue for either recall bias or a causal relationship between ground water contamination and cardiac defects.

Thus, an examination of this association by geographic area, water source and year does not resolve the question of the role of recall bias.

### 10.45 Certainty of diagnosis

The strength of the association between tap water and adverse pregancy outcome was examined in relation to the certainty of diagnosis. One might expect a causal relationship to be strongest in the most certain diagnoses. Here too, the evidence is conflicting. On the one hand, the association between water and birth defects is seen only in reportable defects, not minor defects or other conditions reported by the mother (Table 3.15), which argues against the association being the result of recall bias. On the other hand, spontaneous abortions classified as doubtful or possible showed an association similar to that seen for pathologically confirmed SABs (Table 3.7). This argues in favor of recall bias if one believes that only medically confirmed cases are true spontaneous abortions.

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10.46 Biased recall of filter use

Data on filter use weigh against recall bias as an explanation of the water findings. Misclassification of filter use is less likely, particularly when such details as brand, type, location and frequency of service were ascertained. It would also be necessary to postulate misclassification in users of filters but not water softeners since the latter devices were not associated with any "protective effect". Nonetheless, the number of cases ne would need to postulate as misclassified in order to remove the association between SAB and absence of filters among tap water drinkers would be relatively few.

10.47 Exposure recall bias in non-cases

We have also calculated the amount of reclassification of controls from unexposed to exposed which would be necessary in order that SAB rates be constant across strata (p(2)). In the cross-sectional studies, p(2) must be large. Since p(2) is applied to a large number of normal pregnancies this implies an implausibly large number of misclassified subjects. This number is not as large in the case-control studies. Interestingly, the scenario of misclassified "normals" is different from that for misclassified cases when the prevalence of tap water abstention increases over time. In the former, the rate in the exposed remains constant over time, while the rate in the unexposed falls. This does not fit the observed data.

10.5 Did SAB rates change as tap water abstention increased over time?

The frequency of tap water abstention between 1980 and March 1985 is shown in Table 10.4. While the prevalence of abstention rose from 6% to 22% (and the use of "some bottled water" from 20% to 70%), the SAB rate in tap water abstainers remained low and averaged 4.1%. The rate of SABs in tap water drinkers was about three times as great as that in abstainers throughout the time period. As the prevalence of abstainers increased, one might expect the crude SAB rate to have fallen if bottled water use, or tap water abstention, truly prevented SABs. We calculated what the crude SAB rate would have been if the rate in abstainers had remain d 4.1% and the rate in tap water drinkers remained 10%. In fact, the crude rate w uld nly have fallen from 10.3% t 8.7% between 1980 and 1984. We d not have the statistical power to decide whether a change of this magnitude actually occurred.

10.51 <u>What pattern in SAB rates over time would be expected if recall bias was operating</u>

What pattern in rates would be expected if the observed association between SAB and tap water consumption was due to unexposed cases misclassifying themselves as exposed? In Table 10.5 we show one scenario for a 10% abstention rate and one for a 30% rate. These calculations assume that there is no association between SAB and tap water consumption: the rate of SAB is assumed to be 9.1% for users and non-users alike. We assume a 50% misclassification rate among the unexposed cases. If the abstention rate is 10%, this reclassification results in five cases being transferred from the unexposed to the exposed category. However, when more women abstain, a larger number of unexposed cases must be reclassified. Therefore, as the abstention rate increases in both cases and non-cases, the rate of SAB in abstainers remains unchanged, while the spuriously high rate in tap water drinkers is further increased. At the same time the crude rate remains at 9.1%.

How well do the data in Table 10.4 conform to the scenario in Table 10.5? The answer is, fairly well. While the rate of abstention increased, the rate of SAB among abstainers remained low and the rate in tap water drinkers increased somewhat. This is evidence in support of misclassification as an explanation of these findings. Once again, the data set does not have the power to conclusively distinguish between the pattern expected under the recall bias hypothesis and that expected under the causal hypothesis.

10.52 <u>How do rates in these studies compare to those seen in other studies?</u>

If the apparent association between tap water abstention and adverse pregnancy outcomes was due to some deleterious substance in ground water throughout the Santa Clara basin, one would expect the SAB and birth defect rates f r the county to be somewhat higher than th se reported elsewhere.

H wever, if the phenom n n was due to xposure recall bias or to some causal factor which was present universally, the verall rates for the county would be similar to rates seen elsewhere. What pattern is actually seen?

The prevalence of all defects reported in the Fairchild II study area is slightly higher than that seen by the California Birth Defects Monitoring Program for the five Bay Area Counties in 1983 (3.3% vs 2.5%). However, even if this elevation were real, it does not appear to extend throughout the county, since the prevalence of birth defects in all of Santa Clara County (2.4%) was not high.

How do the rates for SABs in our studies compare to rates seen in other studies? This question is more difficult since methodologies for ascertaining SABs vary considerably. In our studies, all SABs are medically validated and a random pregnancy is selected per woman, both of which lead to lower overall SAB rates than those usually reported. Rates of SAB from several studies are shown in Table 10.6. However, in most of these, SABs are not medically validated and multiple pregnancies are included.

The comparison of SAB rates between studies is made more difficult by the sensitivity of the estimate of the SAB rate to time prenatal care began. This can be avoided by using life table methods. This was done in the Malathion study and results are presented by county and water type in Table 5.16. Tap water abstainers (in all counties combined) had a cumulative risk f SAB of 6% which is lower than usually reported for life table rates which are about 50% greater than the crude rates.

## 10.6 <u>The role of confounding</u>

Could the observed association be due to a hidden confounder, some health protective factor (or constellation of factors) related to tap water abstention which decreased SAB risk? In order to reconcile the presence of such a confounder with the pattern observed in Table 10.4, one must postulate that when a woman abstained from tap water use she also changed her behavior with respect to this hidden factor. Alternatively, one must postulate that early in the study, when tap water abstention rates were low, the "p tential abstainers" (th s wh abstained later in the study) had alr ady adopted this hyp thetical health pr t ctive behavior but their low rate of SAB was hidden in the higher rates of the tap water drinkers with which they were grouped. One would need to additionally postulate that the new recruits to tap water abstention each year came almost exclusively from this low risk group. Alternatively, one could invoke some factor highly correlated with tap water abstention which reduced the risk of miscarriage. A whimsical example might be avoiding the strain of bending over to drink water from the tap. All of these scenarios seem unlikely.

In all these studies we have controlled for a wide variety of confounders including many which might be related to healthful behaviors: alcohol use, smoking, time prenatal care began and, in Fairchild IIB, vitamin use, concern for nutrition and exercise. None of these can account for the observed associations.

We have not asked about income because this is a sensitive area in which respondents are reluctant to give information. However, it is not likely that socio-economic status is the hidden confounder which could explain these findings. First, education, which is correlated with income is not a predictor of SAB and does not confound the SAB-tap water relationship. Second, socio-economic status is unlikely to be correlated with active water filters but not softeners. The only evidence in favor of this variable as a confounder is that the 12% of women in SACCS whose prenatal care was not covered by insurance were less likely to drink bottled water than those who were insured (49% vs 62%). However, the OR for tap water and SAB, after controlling for insurance was very similar to the crude OR (1.4 vs 1.5).

Any hypothesized confounder would have to be more strongly associated with both SAB and tap water abstention than are these two variables to each other. This is highly unlikely, since the strongest known risk factors for SAB, such as advanced maternal age and prior fetal loss have associations with SAB similar in magnitude to the association seen in these studies for tap water abstention. For these reasons, a "hidden confounder" is not a likely hypothesis to explain the findings of these studies.

CONCLUSION

This section has examined sources of bias and confounding which are most likely in these studies. We conclude that the observed associations are not easily explained in terms of availability bias, opportunity bias or biased recall of disease. The presence of a constellation of uncontrolled confounders is always possible, but seems unlikely given the evidence. Biased recall of exposure does remain a distinct possibility for explaining the findings in these studies.

Unf rtunately, the available evidence does not allow us to prove or disprove that the results are due solely to bias and/or confounding. For this reason, and because the implications of these studies are so serious, they should be foll wed up by prospective studies in which tap water and bottled water use patterns are ascertained prior to pregnancy termination. Only in this way can the possibility of recall bias be eliminated.

Table 10.1

**Availability of Respondents**
**As a Function of Bottled Water Use[a] (Fairchild II)**

| Number of attempts before interviewing respondent | Bottled Water Use: Yes N | Yes % | No N | No % | All N | All % |
|---|---|---|---|---|---|---|
| 1 | 6 | 29 | 14 | 17 | 20 | 19 |
| 2-3 | 6 | 29 | 31 | 37 | 37 | 36 |
| 4+ | 9 | 43 | 38 | 46 | 46 | 45 |
| TOTAL | 21 | 101[b] | 83 | 100 | 103 | 100 |

[a]Among those with SAB.

[b]T tal does not equal 100 because of rounding.



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Table 10.2

Number of Cases of Spontaneous Abortion Which Must be Misclassified With Respect to Exposure in Order That SAB Rates Be Constant Across Tap Water Strata (Fairchild II)

| | Observed | | | Hypothetical | | | |
|---|---|---|---|---|---|---|---|
| Tap water (glasses/day) | N(pregnancies) | N(SAB) | SAB Rate | N(pregnancies) | N(SAB) | SAB Rate | N(Observed-Hypothetical) |
| 0 | 214 | 7 | 3.3 | 229 | 22 | 9.6 | -15 |
| 1 | 103 | 9 | 8.7 | 104 | 10 | 9.6 | -1 |
| 2+ | 699 | 84 | 12.1 | 683 | 68 | 10.0 | +16 |
| TOTAL | 1016 | 100 | 9.8 | 1016 | 100 | 9.8 | 0 |

Tabl 10.3

Number and Percent of Unexposed Cases in Each Study Which Must be Misclassified in Order that SAB Rates Be Constant Across Tap Water Strata

| Study | N(Type of cases) | N(misclassified) | % Cases misclassified | % Unexposed misclassified |
|---|---|---|---|---|
| Fairchild I | 39 (SAB) | 7 | 18.0 | 100 |
| Fairchild II | 100 (SAB) | 16 | 16.0 | 68 |
| Fairchild II | 38 (BD) | 9 | 23.7 | 68 |
| Malathion | 474 (SAB) | 12 | 2.5 | 48 |
| C rdiac | 148 (BD) | 8 | 5.4 | 31 |
| SACCS | 248 (SAB) | 20 | 8.1 | 31 |
| TOTAL | 1047 | 72 | 6.9 | 45 |

Table 10.4

SAB Rates and Tap Water Consumption by Year (Fairchild II)

| | % Abstaining From Tap Water | SAB Rate in Abstainers % (N) | SAB Rate in Tap Water Drinkers % (N) | Overall SAB % (N) |
|---|---|---|---|---|
| 1980 | 5.8 | 0.0 ( 8) | 4.6 (130) | 4.4 (138) |
| 1981 | 9.4 | 6.3 (16) | 13.6 (154) | 12.9 (170) |
| 1982 | 12.6 | 0.0 (21) | 9.0 (145) | 7.8 (166) |
| 1983 | 16.5 | 6.3 (32) | 8.6 (162) | 8.3 (194) |
| 1984[a] | 22.2 | 4.3 (70) | 16.7 (246) | 13.9 (316) |
| TOTALS | 14.9 | 4.1 (147) | 11.4 (837) | 10.3 (984) |

[a]Includes the first three months of 1985.

Table 10.5

Expected Disease Rates With a 50% Exposure Misclassification
In Cases While The True Abstention Rate Increases
From 10% to 30%

| Tapwater Use | 10% ABSTENTION SAB Truth | 10% ABSTENTION SAB Reported | 10% ABSTENTION Non-SAB Truth | 30% ABSTENTION SAB Truth | 30% ABSTENTION SAB Reported | 30% ABSTENTION Non-SAB Truth |
|---|---|---|---|---|---|---|
| Any | 90 | 95 | 900 | 70 | 85 | 700 |
| None | 10 | 5 | 100 | 30 | 15 | 300 |
| P(SAB/Tap) | 0.091[a] | 0.095[b] | | 0.091 | 0.108 | |
| P(SAB/No Tap) | 0.091 | 0.048 | | 0.091 | 0.048 | |

[a] True P(SAB/Tap) = 90/(90 + 900) = 0.091

[b] Reported P(SAB/Tap) = 95/(95 + 900) = 0.095



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Table 10.6

Summary of Selected Studies of Spontaneous Abortion Rates Assessed by Retrospective Interviews

| Author | Group Studied | Definition of Spontaneous Abortion | SAB Rate |
|---|---|---|---|
| CDHS | Residents living near the Purity Dumpsite in Fresno County, CA, and controls (interview of any adult respondent in the household) | Fetal loss any time, SAB not validated, contains multiple pregnancies/woman | 8.0 in exposed<br>9.7 in control |
| CDHS | Women living near the McColl dumpsite in Fullerton, CA, and control women | Fetal loss ≤20 weeks, SAB not validated, contains multiple pregnancies/woman | 8.5 in exposed<br>6.9 in control |
| Hemminki, et al (1982) | Women engaged in sterlizing instruments with chemical agents in hospitals, and control hospital workers | Not stated | 11.3 in exposed<br>10.6 in control |
| Smith (1982) | Wives of 2,4,5-T chemical applicators and control wives | Not stated | 8.6 in exposed<br>9.3 in control<br>(Excludes therapeutic abortions in denominator) |
| Himmelberger, et al (1978) | Women anesthesiologists, nurse anethetists, women operating room pers nnel | Fetal loss ≤20 weeks | 14.0 (Excludes therapeutic abortions in denominator) |