AN INVESTIGATION OF SPONTANEOUS ABORTIONS FOLLOWING A METAM SODIUM SPILL INTO THE SACRAMENTO RIVER

California Department of Health Services, Environmental Health Investigations Branch

March 1993

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EXECUTIVE SUMMARY

On July 14, 1991, shortly before 10 p.m., a tank car derailed and released 19,000 gallons of the herbicide metam sodium into the Sacramento River six miles north of the town of Dunsmuir in Northern California. Local residents were exposed to the toxic by-products, mainly methylisothiocyanate. A community-based health survey focusing on chronic effects including pregnancy outcomes was conducted in April 1992 in the Dunsmuir area. A total of 969 households (81%) participated.

Since metam sodium has been associated with increased incidence of fetal loss in animals and there had been anecdotal reports of spontaneous abortions following the spill, the relationship between spontaneous abortion (fetal loss before 20 weeks gestation) and possibility of exposure was examined. Seventy-four pregnancies were reported during the study period (7/90-2/92). A follow-up interview was conducted (October 1992) to confirm pregnancy information and obtain permission to review the medical records of women who reported a spontaneous abortion.

A woman was considered exposed if she resided in or visited the spill area during the time of greatest potential exposure (July 15 to July 16, 1991). Based upon this exposure definition and the date of the last menstrual period, four groups were defined: fetus exposed in the first trimester, fetus unexposed in the first trimester, post-spill conception in an exposed woman, and post-spill conception in an unexposed woman.

Five spontaneous abortions were reported during the April 1992 survey among fetuses exposed in the first trimester. One spontaneous abortion has been confirmed to date giving a confirmed spontaneous abortion rate of 14% (1/7). If all five were confirmed the rate would be 45% (5/11). The rates of reported and confirmed spontaneous abortion in the unexposed group (26%, 21%), in the exposed post-spill conception group (26%, 23%) and in the unexposed post-spill conception group (20%, 20%) were similar.

Using only confirmed spontaneous abortions, this study does not show a higher rate of spontaneous abortion among fetuses exposed in the first trimester. Including the four unconfirmed spontaneous abortions exposed in the first trimester increases the rate above the unexposed, but the statistical confidence interval around this rate is very wide. The higher than usual rates of confirmed spontaneous abortion even in unexposed groups and a review of birth certificates suggests that women whose pregnancies ended in live births did not all participate in our study.

Due to the inherent limitations of epidemiological studies, we cannot determine whether the elevated rate of reported spontaneous abortion among fetuses exposed in the first trimester was due to exposure to the by-products of metam sodium. Other factors such as imprecise reporting of exposure and pregnancy ending date, chance, differential recall of missed menstrual periods in the unconfirmed spontaneous abortions, under-ascertainment of live births and spontaneous abortions, and stress generated by the spill could have influenced the rate.

DHS will make another attempt to confirm the reported but unconfirmed spontaneous abortions.
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An Investigation of Spontaneous Abortions Following a Metam Sodium Spill into the Sacramento River

On July 14, 1991, shortly before 10 p.m., several cars of a Southern Pacific train derailed at the Cantara Loop on the Upper Sacramento River, six miles north of the town of Dunsmuir in Northern California. In all, 19,000 gallons of the herbicide metam sodium were spilled into the Sacramento River. The chemical plume traveled 45 miles downstream, killing nearly all aquatic life and exposing residents to the chemical and its volatile by-products. The California Department of Health Services (DHS) has previously reported on the acute health effects of the chemical spill. The purpose of this report is to describe the investigation of pregnancy outcomes among women who participated in a community-based health survey in April 1992 and in a follow-up interview in October 1992.

Background

Description of the Incident and Initial DHS Response

Dunsmuir, with a population of 2,129, is the largest town on the affected segment of the river and is the nearest to the spill site (Figure 1). It is believed that the plume of metam sodium passed through Dunsmuir in the early morning hours of July 15.

The DHS investigation of acute health effects showed that 14% of Dunsmuir city residents sought medical care in the month following the spill. Symptoms were consistent with exposure to irritant gases and included eye, respiratory, gastrointestinal, and skin irritation.

Reproductive Toxicology of Metam Sodium and By-Products

Metam sodium when mixed with water is believed to rapidly decompose to methylisothiocyanate (MITC) and hydrogen sulfide. Other less common by-products include methylamine and carbon disulfide. A review of the toxicological literature on metam sodium found an increased number of fetal losses and birth defects (neural tube defects) occurring in pregnant rats and rabbits exposed to...
Air monitoring for MITC began on July 17th, the third day following the spill. The highest measured amount of MITC in Dunsmuir for a 12-hour period was taken on July 18 and was 4 to 5 ppb. This measurement was well below the one-hour (720 ppb) and 24-hour (30 ppb) action levels for developmental toxicity.

Since air measurements for MITC in Dunsmuir were not available, OEHHA estimated MITC levels for the first two days, July 15 and 16, for different exposure situations. For the first 12 hours after the spill, a short term exposure of a few minutes to one hour for individuals within 300 feet of the river would have produced a maximum exposure estimate of 140 to 1600 ppb of MITC. For a longer exposure of several hours and possibly up to one day, levels could have ranged from 15 to 200 ppb during the first day after the spill in the Dunsmuir area. These estimated exposure levels apply to individuals living near the river and the actual exposures for Dunsmuir residents who lived as far as 1,500 feet from the river are likely to have been much lower.

Thus, the estimated maximum one-hour exposure level (140 to 1600 ppb) contained the one-hour developmental toxicity action level of 720 ppb. In addition, anecdotal reports of spontaneous abortions following the spill were received by DHS staff.

**DHS Health Investigations**

In the months following the spill, residents continued to report health problems they felt were related to the spill. These included reports of new and/or continuing respiratory problems, skin rashes, joint pain, diarrhea, sensitivity to chemicals, mood changes, fatigue, and vision problems. Residents also continued to express concern about the occurrence of spontaneous abortions and possible birth defects.

**Birth Defects**

The DHS's Birth Defects Monitoring Program conducted an investigation to determine whether any excesses in birth defects occurred among children born to women potentially exposed to the spill during their pregnancy. Among 100 deliveries, one baby was identified with a structural birth defect which affected the gastrointestinal system. In California, three of every 100 babies have a reportable birth defect. Thus, one baby with a birth defect out of 100 deliveries is lower than expected.

**Community-Based Health Survey**

To address concerns regarding continuing health problems and pregnancy outcomes, DHS's Environmental Health Investigation Branch conducted a health survey in the Dunsmuir area in April 1992. The survey collected information from one adult who responded for all other household members. The survey collected demographic information for each household, asked where each individual was during the first three days following the spill, and asked about the occurrence of certain health problems and pregnancy outcomes.
and income were asked for each household. Questions on both acute and long-term health problems were also asked but are not part of this report.

**Follow-Up Interview**

In October 1992, trained interviewers made an effort to conduct a follow-up interview with each woman who had a reported pregnancy. During the interview, each woman was asked to either confirm or clarify where she had been from 10 p.m. on July 14 to 8 p.m. on July 25, 1991. She was then asked her total number of pregnancies, number of SABs, and how many times she had been pregnant with an LMP beginning on or after July 1, 1990. For each pregnancy in the time period, she was asked for the date of her LMP, pregnancy outcome, number of weeks the pregnancy lasted, the date the pregnancy ended, and if and how much she smoked during the pregnancy.

If the pregnancy ended in a live birth, the name of the child, place of delivery and birthweight were asked. If the pregnancy ended in a SAB, the woman was asked whether she had a positive pregnancy test, had seen a doctor to confirm the pregnancy, had an ultrasound, had passed tissue during the SAB and had seen a doctor following the SAB. These women were also asked to allow DHS to examine their medical records regarding the pregnancy which ended in a SAB.

**Data Analysis**

All reported pregnancies with a known outcome were included in these analyses whether or not a follow-up interview was conducted. Twin pregnancies were included as two pregnancies. Information provided by the woman in the interview took precedence over information provided in the survey since the survey response was sometimes given by a family member or friend and was of a less detailed nature.

A woman was considered exposed if she resided in or visited Dunsmuir, Mt. Shasta, Castella, or Lakehead (spill area) on July 15 and/or July 16, 1991 for any amount of time. Based upon existing and estimated air levels of MITC, July 15 to 16 represented the period of greatest potential exposure. The woman's presence in the spill area was determined from information provided in the follow-up interview or if not available, from the survey.

The exposure information and the calculated LMP date were used to place each pregnancy into one of four groups for analysis. The date of the woman's LMP was calculated by subtracting the number of weeks the pregnancy lasted from the date the pregnancy ended. The four groups are: fetus exposed in the first trimester, fetus unexposed in the first trimester, post-spill conception in an exposed woman, and post-spill conception in an unexposed woman (Table 1). While most SABs occur during the first trimester, a SAB can occur up to 20 weeks gestation thus, exposure during the first 20 weeks was also examined. The rate of SAB (proportion of pregnancies ending in a SAB) was calculated for confirmed and reported SABs in each of the four groups. Exact 95% binomial confidence intervals (CI) were obtained for each rate. However, since the exposed
Assessment of Information Provided by a Proxy

The pregnancy information collected in the survey was provided either by the woman herself or by a proxy (family member or friend). Information provided by a proxy may be less reliable. In particular the proxy may have been unaware of a pregnancy during the study period. Therefore, a sample (10%) of the women whose names were provided and who were reported by a proxy to have no pregnancies during the study period (n=145) were interviewed to verify their non-pregnancy status.

For women with a reported pregnancy who participated in the follow-up interview, the following information was compared with that provided in the survey by a proxy: exposure, calculated LMP and ending date, and pregnancy outcome.

RESULTS

Data Collection

Community-Based Health Survey

A total of 1,192 households were contacted, and 969 (81%) completed the April 1992 survey; of these 969 households, 111 (11%) participated anonymously. Among the non-respondents, 94 (8%) refused, and 129 (11%) were never at home when contacted.

Initial analysis of the survey data identified 79 possible pregnancies reported for 68 women. This included two sets of twins (three non-SABs, one SAB) and four pregnancies which were reported to have ended in therapeutic abortions. Two therapeutic abortions took place prior to the spill and two following the spill. All therapeutic abortions were excluded from the follow-up interview and subsequent analyses.

Of the remaining 75 pregnancies, the name of the woman was withheld for 11 pregnancies (9 women). These 11 anonymous pregnancies resulted in seven non-SABs and four SABs. These four SABs could not be confirmed but were included in some of the analyses.

Follow-Up Interview

The follow-up interview attempted to collect information on all 64 pregnancies for which the name of the mother was provided. One reported pregnancy resulting in a live birth was found to have begun prior to the study period and was excluded. Interviews were completed for 47 of the remaining 63 pregnancies (73%); 33 non-SABs and 14 confirmed SABs. Five women refused to participate (five non-SABs); nine women could not be reached by telephone or letter (11 pregnancies: seven non-SABs, three SABs, and one unknown outcome). Since the outcome for one pregnancy remained unknown following the interview, this pregnancy was then excluded from the analyses (Figure 2). Among women reporting live births, the participation rate in the follow-up...
Figure 2. Status of Pregnancies Reported in April 1992

Pregnancies reported in April 1992 survey
n = 79

Removed from Analysis

4 therapeutic abortions

Name Provided
n = 64

Non-Participant
n = 16

Participant
n = 47

Name Withheld
n = 11

Phone interview October 1992

Removed from Analysis

1 pregnancy with ineligible LMP† date

Removed from Analysis

1 unknown outcome (pregnancy ≤ 20 weeks)

1 live birth
n = 1

11 live births
1 pregnancy
≥ 20 weeks
3 SABs*
n = 15

31 live births
2 pregnancies
≥ 20 weeks
14 SABs*
n = 47

3 live births
4 pregnancies
≥ 20 weeks
4 SABs*
n = 11

Final Dataset

53 non-SABs
46 live births
7 pregnancies ≥ 20 weeks
21 SABs*
14 confirmed
7 unconfirmed
n = 74

* SABs = Spontaneous abortion; pregnancy ending before 20 weeks gestation.
† LMP = last menstrual period
### Table 2. Analysis of Confirmed Spontaneous Abortions Categorized by Exposure in the First Trimester

<table>
<thead>
<tr>
<th>Exposure Group</th>
<th>Exposed 1st Trimester</th>
<th>Unexposed 1st Trimester</th>
<th>Exposed Post-Spill</th>
<th>Unexposed Post-Spill</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed SABs</td>
<td>1</td>
<td>7</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Non-SABs</td>
<td>6</td>
<td>26</td>
<td>17</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>7</td>
<td>33</td>
<td>22</td>
<td>5</td>
</tr>
<tr>
<td>Spontaneous Abortion Rate</td>
<td>14%</td>
<td>21%</td>
<td>23%</td>
<td>20%</td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td>(0.58)</td>
<td>(9.39)</td>
<td>(8.45)</td>
<td>(1.72)</td>
</tr>
</tbody>
</table>

### Table 3. Analysis of All Reported Spontaneous Abortions Categorized by Exposure in the First Trimester

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<th>Exposed Post-Spill</th>
<th>Unexposed Post-Spill</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Reported SABs</td>
<td>5</td>
<td>9</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Non-SABs</td>
<td>6</td>
<td>26</td>
<td>17</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>35</td>
<td>23</td>
<td>5</td>
</tr>
<tr>
<td>Spontaneous Abortion Rate</td>
<td>45%</td>
<td>26%</td>
<td>26%</td>
<td>20%</td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td>(17-77)</td>
<td>(13-43)</td>
<td>(10-48)</td>
<td>(1-72)</td>
</tr>
</tbody>
</table>

1. Exposed 1st Trimester: Last menstrual period 4/15/91 through 7/16/91 and mother/fetus in Dunsmuir during 7/15/91 to 7/16/91.
2. Unexposed 1st Trimester: Last menstrual period 7/1/90 through 7/16/91 and mother/fetus not exposed in the first trimester or pregnancy ended before exposure.
3. Exposed Post-Spill: Last menstrual period 7/17/91 through 2/29/92 and mother was in Dunsmuir during 7/15/91 to 7/16/91.
4. Unexposed Post-Spill: Last menstrual period 7/17/91 through 2/29/92 and mother was not in Dunsmuir during 7/15/91 to 7/16/91.
5. Confirmed SABs: Spontaneous abortion was confirmed through medical record review or physician review of the follow-up interview information.
6. Non-SABs: Pregnancy ended in a live or still birth or lasted at least 20 weeks gestation.
7. All Reported SABs: Spontaneous abortion may or may not have been confirmed.
When only confirmed SABs were examined, no increased risk was observed for exposure in the first trimester. However, when all reported (confirmed and unconfirmed) SABs were examined, an elevated rate was observed for exposure in the first trimester, although the confidence interval was wide and this finding could be due to chance alone. It would have taken eight of the 11 exposed pregnancies to have ended in a SAB (for a rate of 73%) in order for the result to achieve statistical significance at the 95% confidence level. The small population in Dunsmuir precluded our ability to obtain "statistically significant" results for any observed rate less than 73%.

It is possible that risk of SAB could have been increased by stress generated by the spill. Stress has been associated with an increase in some reproductive outcomes, but research to date on the relationship between stress and SAB is limited.

Confirmed and reported unexposed and post-spill SAB rates were similar. However, both the unexposed rate for confirmed SABs (21%) and for all reported SABs (26%) are higher than unexposed rates reported in two other DHS studies which used similar ascertainment methods. In these studies, the rates for confirmed SABs range from 7-10% and for reported SABs the rates range from 9-11%.

The higher SAB rates, even among the unexposed pregnancies (many of which ended before the spill), may be due to a number of reasons. One possibility is under-ascertainment of live births. Indeed review of the 1991 birth certificate data suggested that not all of the live births were identified during the April 1992 survey. This may be due to refusal to participate in the April 1992 survey, absence from home at the time of the survey, or movement out of the area prior to the survey. In addition, the design of the study limited our ability to examine other possible risk factors which may increase the risk of SAB. These include maternal illness and medication use, contraceptive use, nutrition, parental occupation or environmental exposures, and socioeconomic characteristics.

It is possible that the April 1992 survey did not ascertain all the SABs that occurred in the study population. Women may have refused to participate, may have been away from home, moved from the area or failed to recognize an early fetal loss.

CONCLUSIONS

Although a possible increase in the SAB rate among pregnancies exposed in the first trimester cannot be confirmed it should not be discounted. However, women who were exposed and subsequently became pregnant do not appear to be at increased risk of SAB.

Using only confirmed SABs, this study does not show a higher rate of SAB among fetuses exposed in the first trimester. Including the four unconfirmed SABs exposed in the first trimester increases the rate above the unexposed, but the confidence intervals are wide and overlap. The higher rates of confirmed SAB even in unexposed groups and the review of birth certificates suggest that not all women whose pregnancies ended in live births participated in our study.


* SABs = Spontaneous abortion; pregnancy ending before 20 weeks gestation.
† LMP = last menstrual period

Revised April 22, 1993.
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<tr>
<td>Confirmed SABs</td>
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<td>7</td>
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<tr>
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<td>6</td>
<td>26</td>
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<td>5</td>
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<tr>
<td>Spontaneous Abortion Rate</td>
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