

HEALTH CONSULTATION

PRELIMINARY HEALTH REVIEWS IN RANCHO CORDOVA, SACRAMENTO COUNTY, CALIFORNIA

AEROJET-GENERAL CORPORATION RANCHO CORDOVA, SACRAMENTO COUNTY, CALIFORNIA [CERCLIS NO. CAD980358832](#)

September 2, 1998

Prepared By:

California Department of Health Services
Under Cooperative Agreement with the
Agency for Toxic Substances and Disease Registry

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HEALTH CONSULTATION

PRELIMINARY HEALTH REVIEWS IN RANCHO CORDOVA, SACRAMENTO COUNTY, CALIFORNIA

AEROJET-GENERAL CORPORATION RANCHO CORDOVA, SACRAMENTO COUNTY, CALIFORNIA

STATEMENT OF ISSUE

The Environmental Health Investigations Branch (EHIB), within the California Department of Health Services (CDHS), under a cooperative agreement with the Agency for Toxic Substances and Disease Registry (ATSDR), is conducting [public health assessment](#) activities on the Aerojet-General Corporation (Aerojet) [Superfund](#) site in Sacramento County, California (See [Figure 1](#)). A preliminary public health assessment written in December 1988 recommended that when additional environmental information and data became available, ATSDR would make another assessment ([1](#)). A site review and update written in March 1993 also recommended a public health assessment be conducted when more data became available ([2](#)).

This [health consultation](#) is one in a series that will be performed as part of the ATSDR enhanced public health assessment process at this site. During this process, data and information on the release of hazardous substances and their impact on public health will be evaluated. Five health consultations on perchlorate [exposure](#) in the drinking water supply have recently been written as part of this series ([3-7](#)). In this health consultation, we will focus on three preliminary reviews of health outcome data gathered on individuals living in areas potentially affected by the perchlorate-contaminated drinking water. These reviews focus on specific health outcomes related to biologically-plausible effects from exposure to perchlorate and surveys performed at the request of concerned residents. These reviews include: data from the Genetic Disease Branch of CDHS pertaining to neonatal hypothyroidism, hospital discharge data from the Office of Statewide Health Planning and Development (OSHPD) of CDHS pertaining to goiter, agranulocytosis and aplastic anemia and information from the California Cancer Registry for cancer in general, and specifically for cancers of the thyroid and blood cells.

BACKGROUND

Aerojet began operation in the Rancho Cordova area of California in 1951. Since that time, Aerojet has manufactured liquid and solid propellants for military and commercial rocket systems and has fabricated, assembled, tested and rehabilitated rocket engines ([1](#)). In addition, between 1974 and 1979, Cordova Chemical Company, a wholly-owned subsidiary of Aerojet, manufactured paint components, herbicides, and pharmaceutical products within the facility boundaries. Over the years, Aerojet and Cordova Chemical disposed of hazardous waste by burial, open dumping, discharge into unlined ponds, and injection into deep underground wells ([1](#)). Monitoring demonstrated perchlorate in the groundwater,

which was thought to have arisen from ammonium perchlorate, a main component of solid rocket fuel. In addition to the natural migration of perchlorate-contaminated groundwater from the site, Aerojet has been reinjecting water treated to remove trichloroethylene, but still contaminated with perchlorate, back into the groundwater at the site's western and northern boundary. Some of these discharges, including perchlorate, moved off-site of the Aerojet facility boundary ([Figure 1](#)) and contaminated several drinking water wells of the Arden Cordova Water District ([7](#)). The Regional Water Quality Control Board (RWQCB), the lead regulatory agency, is also investigating other potential sources of the perchlorate, such as the McDonnell Douglas or Purity Oil sites.

The Arden Cordova Water Service is composed of two distinct systems, the Arden System and the Cordova System ([Figure 1](#)). These systems are not interconnected (i.e., the wells located in the Cordova System serve only the Cordova System customers). The Cordova System has been impacted by the perchlorate contamination, whereas the Arden System is located several miles west of the contamination and thus it is unlikely that it will ever be affected ([7](#)). The Cordova System supplies water to 11,650 connections, approximately 36,500 customers, mostly family residences and commercial businesses ([8](#)). It is believed that perchlorate first contaminated wells in the Cordova System sometime in the late 1980s; however, it was not until February 1997 that the distribution of water from affected wells was stopped. Currently, drinking water wells 13, 15 and 16 remain closed (due to levels of 220, 95 and 210 parts per billion (ppb) perchlorate, respectively). Additionally, three wells which initially were closed in April 1997 [wells 11 and 14 (4.4 ppb perchlorate each) and well 19 (6.8 ppb perchlorate)] have been reopened and are again serving customers, as of June 1997 ([7](#)). A prior health consultation concluded that a completed exposure pathway to perchlorate-contaminated drinking water for residents and employees served by the Arden Cordova Water District existed and that this water may have posed a health hazard to exposed individuals during the length of time that these wells were in use ([7](#)).

Currently, there remains much debate over the health effects related to perchlorate [ingestion](#) and considerable uncertainty pertaining to the levels of perchlorate which are believed to be of danger to the public health. At present, the U.S. Environmental Protection Agency (U.S. EPA) has a provisional oral [reference dose \(RfD\)](#) for perchlorate compounds (0.0001 mg/kg/day) which is an estimate of a daily exposure to the human population that is likely to be without appreciable [risk](#) of deleterious effects during one's lifetime ([10](#)). However, this level may be a more conservative estimate by a factor of 1000 due to toxicological uncertainties involved. Additionally, the detection limit for perchlorate in drinking water was just recently decreased by the availability of more advanced methods of testing, so that wells which were previously thought to be uncontaminated were more recently found to contain small amounts of perchlorate. These factors may have contributed to the appearance that people may have been receiving perchlorate-contaminated drinking water for almost ten years without any prior health agency response.

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APPENDIX A

Responses to Comment

The initial draft of this health consultation was released to the site team after a presentation of the data at the site team meeting on December 11, 1997. The period of written comment extended from that time until January 15, 1998. Only one formal comment was received from the site team participants and was from Aerojet. That letter has been reproduced and included below.

Aerojet Comment

We have the following comment on the "Actions Planned" section which suggests the possibility of exposure modeling in regard to a possible study of neonatal thyroid levels. The CDHS draft demonstrates that neonatal hypothyroidism was not increased in incidence in the areas of interest. In the "unexposed" area, CDHS found only four cases of neonatal hypothyroidism reported in twelve years, so there is little likelihood of doing any meaningful epidemiologic study of hypothyroidism, given so few cases available. Undertaking such a study to further evaluate neonatal thyroid hormone levels with mothers divided into groups according to maternal perchlorate intake as modeled by ATSDR raises many methodological concerns, including:

1. There is uncertainty as to the accuracy and validity of the exposure modeling as a means to distinguish "exposed" from "unexposed" groups, and no way to measure the validity. We believe that an exposure assessment would be very speculative. We refer you generally to Aerojet's comments in our letter of October 13, relative to exposure assumptions. Your October 16 draft consultation also notes difficulties with attempting such an evaluation. Even if one could accurately model past concentrations in particular wells, there must be adequate information on consumption and a host of other factors to make the evaluation potentially useful.

2. It is difficult to interpret differences in mean thyroid hormone levels in populations if almost all of the values are within normal limits and there is no excess number of persons with clinically significant abnormal values.

3. The consultation document points out the importance of other factors, such as deficiencies of Thyrotropin Releasing Factor and Thyroid Stimulating Hormone, aplasia or hypoplasia of the thyroid gland, and iodine deficiency. The CDHS has not indicated how any potential study will deal with these other factors.

4. Finally, the utility and interpretation that may be given to population differences in thyroid

hormone levels when such levels are still within normal bounds is questionable.

Aerojet Comment

On page one, paragraph two, Aerojet comments, "The October 16, 1997 draft states a belief that perchlorate first contaminated wells in the Cordova system "as early as 1987" which is an assumption which we think should not be stated as such."

EHIB Response

To the best of our understanding, perchlorate may have first contaminated drinking water wells in this area sometime during the late 1980s. The objectionable statement referring to 1987 was cited from a prior health consultation performed by ATSDR in 1993. We have not been given information to contradict this statement, but have elected to change the statement to reflect the possible uncertainty in the date of first contamination. This statement will now read "It is believed that perchlorate first contaminated wells in the Arden Cordova system sometime in the late 1980s."

Aerojet Comment

In the following line also on page one, Aerojet comments, "We are also concerned about the statement at page 3 that water "may have posed a health hazard" and the absence of any language that notes that CDHS believes that health impact was unlikely. (See Aerojet's October 13 letter at pages 8 and 9.)".

EHIB Response

We see no reason to amend our assertion that water containing perchlorate may have posed a health hazard. Water free of this substance would most certainly not pose a health hazard (from perchlorate). However, levels of perchlorate found in several wells in the Arden Cordova water district were substantially above the USEPA's acceptable provisional reference dose range (4-18 ppb). On the basis of this data we believe that the statement is accurate and that the water indeed may have posed a health hazard. We did not feel that any inclusion of language implying that the health department believed that health impact was unlikely was warranted because not all aspects of perchlorate-related health outcomes could be measured by our preliminary health outcome studies and those that were studied were extensively commented upon in the appropriate discussion section.

Aerojet Comment

Based on the studies' preliminary results wherein no significant health effects were found in the potentially affected population, and the uncertainties of how other factors would also impact the observable health impacts, it appears reasonable to conclude that modeling of potential perchlorate uptake is not warranted. However, if CDHS intends to undertake the exposure evaluation described, it is our understanding Aerojet's input will be included in the evaluation of methods to be used and developing the assumptions and approach to be taken.

We were asked by parties during the presentation of this data at an Aerojet Site Assessment Team meeting in Rancho Cordova on December 11, 1997 to rerun our data on neonatal hypothyroid cases and restrict the suspected exposure period from 1990 through 1995 or 1996 and the affected zip code to 95670 only. This seemed reasonable since there was some consensus in this meeting that the estimated time of exposure was too broad and the area of exposure was more limited than we previously thought. I have included the results of the original analyses and the additional analyses below for comparison:

Table 1: Neonatal hypothyroidism status for potentially-exposed and unexposed zip codes in California, 1985-1996.

Exposure Status/Location	Hypothyroid Cases (<u>expected cases</u>)	Total Screens
Rancho Cordova (exposed)*	4 (3.76)	11,814
Rancho Cordova (unexposed)**	6 (6.41)	20,135
Rest of State (unexposed)	2,068 (-)	6,494,193

* includes zip codes 95670, 95742, 95655 and 95827

** includes zip codes 95628, 95608, 95864 and 95662

Table 1a: Neonatal hypothyroidism status for potentially-exposed zip code 95670 versus the rest of the state, California, 1990-1996.

Exposure Status/Location	Hypothyroid Cases (<u>expected cases</u>)	Total Screens
95670 (exposed)	4 (1.84)	5,217
Rest of State (unexposed)	1391 (-)	3,954,281

Odds Ratio = 2.18

95% Confidence Interval (0.85 - 5.6)

Fisher's Exact p-value = 0.115

As can be seen from the above tables, the results are different depending on when it is estimated that individuals consumed potentially perchlorate-contaminated water. If we consider the data from [table 1a](#), then in fact, individuals were shown to be over two times more likely to have given birth to a child with confirmed clinical hypothyroidism with maternal residence in zip code 95670 during 1990-1996 as compared to births throughout the state. However, these results were not statistically significant and may in fact be unrelated to perchlorate exposure. This information does make it more important to follow-through with an exposure assessment for perchlorate contamination of the area's drinking water supply, which will in turn allow for improved analyses of the relationship of drinking water and health parameters.

There are four sections on page two which deal with methodological difficulties in designing a study which would measure the effects of maternal perchlorate ingestion (via drinking water) and neonatal thyroid hormone status.

We agree with the comments provided by Aerojet regarding the potential difficulties and limitations of exposure modeling, confounding factors and interpretation of results. We do not feel that these difficulties should prevent us from attempting to perform these studies however, but they must and will be

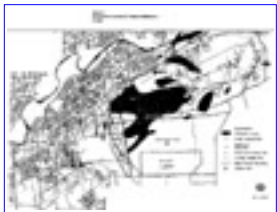
considered in the designing of the study and the interpretation of any results which are ultimately obtained. We look forward to further comments and suggestions from Aerojet regarding future evaluations.

Table 2: Neonatal thyroid hormone values (T4) per suspected exposure group, 1985-1996.

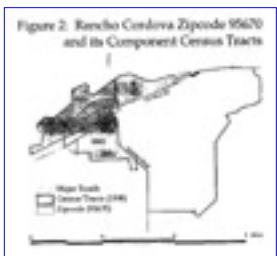
Exposure Status	Number <u>of Screens</u>	Mean	Median	Standard <u>Deviation</u>
Exposed	11,773	15.04	14.6	4.57
Unexposed	20,077	15.27	14.9	4.57
Rest of State	6,479,190	14.77	14.4	4.38

Table 2a: Neonatal thyroid hormone values (T4) from the suspected exposure zip code 95670 versus the rest of the state, California, 1991-1995.

Exposure Status	Number <u>of Screens</u>	Mean	Median	Standard <u>Deviation</u>
95670 (Exposed)	3,708	15.79	15.4	4.78
Rest of State	2,851,284	15.03	14.7	4.56



[Figure 1. Perchlorate Groundwater Plume in Relation to Aerojet](#)



[Figure 2. Rancho Cordova Zipcode 95670 and its Component Census Tracts](#)

¹ The OSHPD maintains a computerized data base of all discharges to California hospitals for each year. Pertinent patient information found in this data base includes: primary diagnosis with listings of additional diagnoses, demographics and treatments performed while hospitalized.

² The CCR is the statewide population-based cancer surveillance system which gathers information on all cancers diagnosed in California since 1988 (excluding basal and squamous cell carcinomas of the skin and carcinoma in situ of the cervix). Hospitals and physicians are required by law to refer information to the CCR's network of ten regional registries which perform analyses and conduct studies on this data.

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Figure 1
Facility's Groundwater Plume in Relation to
Aerofel

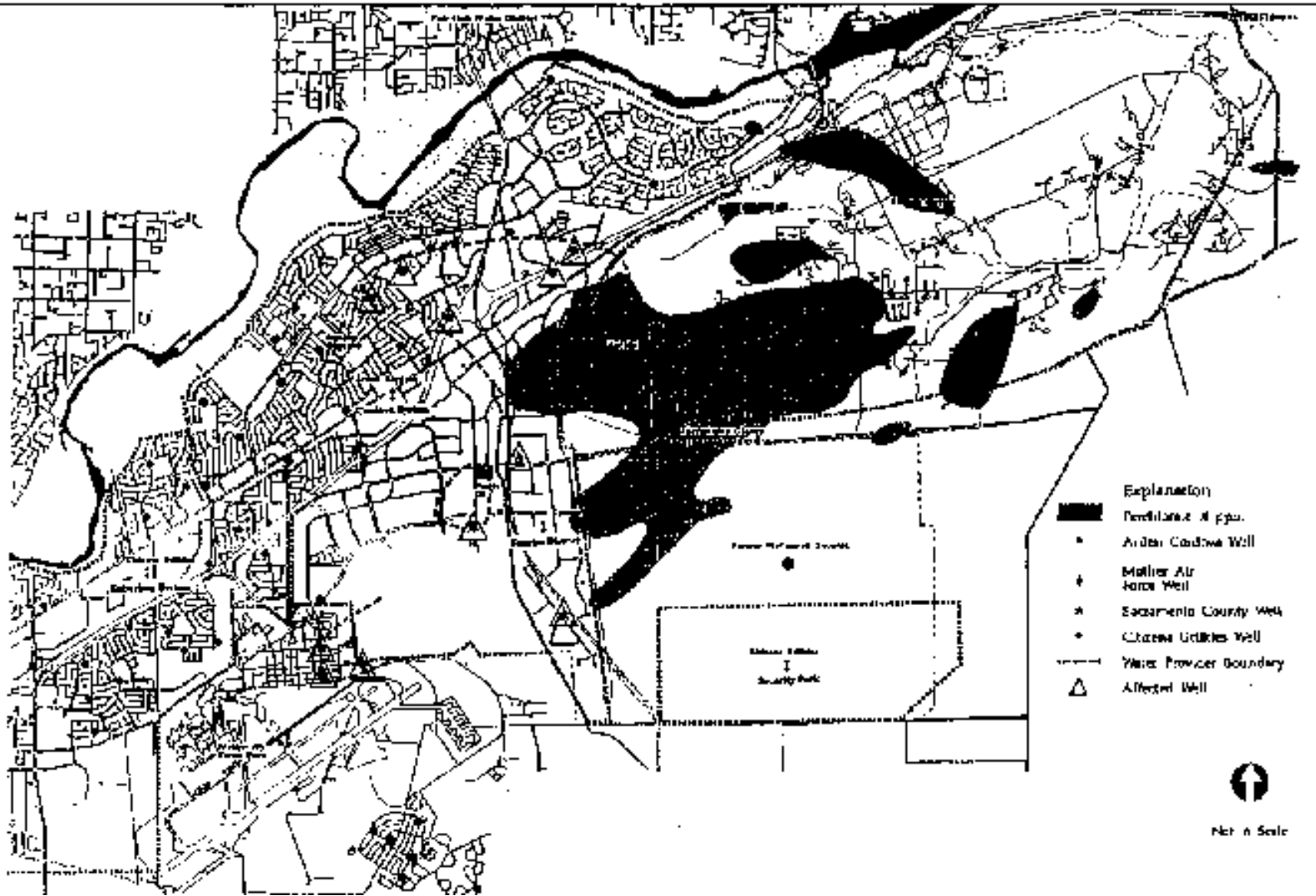
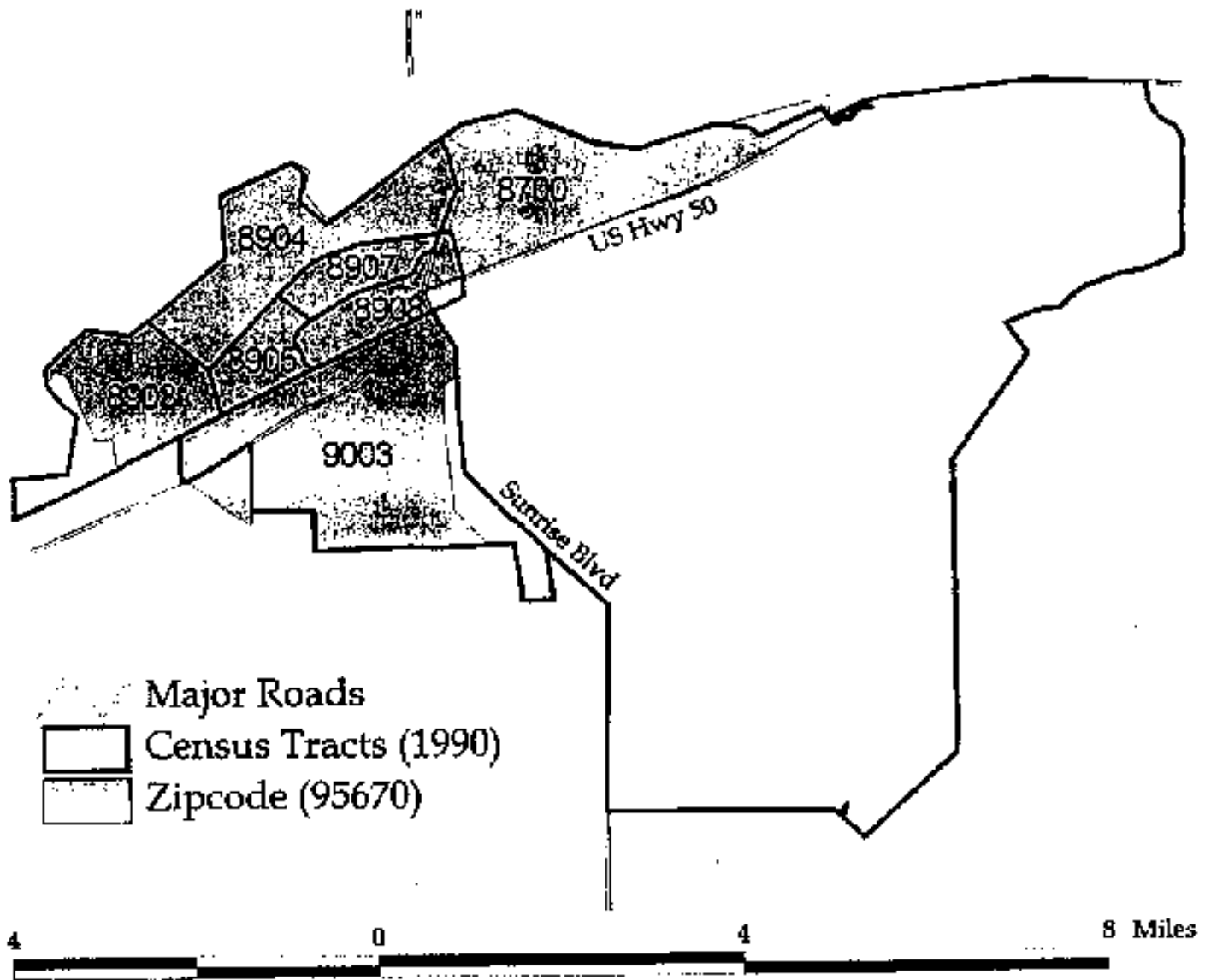


Figure 2: Rancho Cordova Zipcode 95670 and its Component Census Tracts



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CONCLUSION

The preliminary information which was reviewed included: neonatal thyroid hormone levels, goiter, agranulocytosis, aplastic anemia, all cancers, thyroid cancers and leukemia in individuals residing in zip codes near Aerojet (which were used as a proxy for exposure to perchlorate) during the assumed time period that perchlorate contaminated the Arden Cordova drinking water system. Investigation found that:

- mean neonatal thyroid hormone levels were higher in the suspected exposed zip codes than the corresponding statewide rates (lower mean levels would have suggested a possible effect of perchlorate);
- there was no increase in cases of neonatal hypothyroidism in the exposed zip codes than expected;
- the OSHPD data base was not considered a useful source of information for assessing the incidence of goiter;
- there was no increase in the rate of hospitalizations for agranulocytosis;
- cases of aplastic anemia in a suspected perchlorate-exposed zip code were higher than the statewide rate, but most of the cases in the affected area were related to other likely causes, such as chemotherapy, radiation or AIDS infection;
- rates for all cancers, thyroid cancers, and leukemias were not higher than the expected rates, based on statewide figures.

The major handicap with these preliminary studies was the limitation imposed by the lack of good exposure measurements in the affected population. It is unclear at this time exactly when the perchlorate groundwater plume first contaminated the drinking water supply of the Arden Cordova System. Thus, the time periods analyzed may have been too broad. The other difficulty with using zip codes as proxies for exposure is that there are more refined dose-reconstruction techniques used in hydrological modeling, which may better determine which neighborhoods or streets received contaminated water. Here again, one must assume that zip codes are much less reflective of actual exposure to perchlorate-contaminated drinking water and that the actual number of exposed persons may be much smaller. Finally, the other difficulty with assessing these health outcome surveys is that perchlorate is not specific for producing thyroid dysfunction or hematological abnormalities. Thus, any case that was ascertained may have other, more likely causes.

PUBLIC HEALTH RECOMMENDATIONS AND ACTIONS

The Public Health Recommendations and Action Plan (PHRAP) for this site contains a description of actions taken, to be taken, or under consideration by ATSDR and CDHS at and near the site. The purpose of the PHRAP is to ensure that this health consultation not only identifies public health hazards, but also provides a plan of action designed to mitigate and prevent adverse human health effects resulting from exposure to hazardous substances in the environment. The CDHS and ATSDR will follow-up on this plan to ensure that actions are carried out.

Actions Completed

1. CDHS performed preliminary surveys of health outcomes related to known or suspected effects of perchlorate ingestion by individuals in zip codes nearby to the site.
2. CDHS prepared a fact sheet about perchlorate and health. CDHS made this fact sheet available to the affected water purveyors, including the Arden Cordova Water Service to provide to their customers.

Actions Planned

1. The Air Force and the Perchlorate Work Group are sponsoring an investigation into fate and transport questions regarding perchlorate. They will investigate the skin permeability of perchlorate.
2. The Air Force and the Perchlorate Work Group are sponsoring a series of animal investigations to address some of the information lacking in perchlorate toxicology. Several animal toxicology studies will be funded to review the genetic and neurological toxicity of perchlorate.
3. ATSDR will conduct an exposure investigation and will model perchlorate contamination of the Arden Cordova drinking water supply.
4. ATSDR and CDHS will conduct an epidemiological investigation reviewing the association between exposure to perchlorate-contaminated drinking water and neonatal thyroid levels.

Recommendations for Further Action

1. CDHS and ATSDR will continue communicating with the Arden Cordova Water System customers about the perchlorate issue.

REFERENCES

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APPENDIX

Table 1: Neonatal hypothyroidism status for potentially-exposed and unexposed zip codes in California, 1985-1996.

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Table 2: Neonatal thyroid hormone values (T4) per suspected exposure group, 1985-1996.

Exposure Status	<u>Number of Screens</u>	Mean	Median	<u>Standard Deviation</u>
Exposed	11,773	15.04	14.6	4.57
Unexposed	20,077	15.27	14.9	4.57
Rest of State	6,479,190	14.77	14.4	4.38

Table 3: Neonatal thyroid stimulating hormone values (TSH) per suspected exposure group, 1985-1996*.

Exposure Status	<u>Number of Screens</u>	Mean	Median	<u>Standard Deviation</u>
Exposed	1368	8.6	5	20.9
Unexposed	2105	8.99	6	21.1
Rest of State	799820	8.59	6	17.3

* TSH values are not routinely obtained on every newborn child, but are determined from a second phase of testing on those neonates with borderline-low initial levels of thyroid hormone.

Table 4: Hospitalizations listing agranulocytosis as one of the top five diagnoses for individuals residing in 95670 zip code, 1991-1995.

Year Diagnosed	Number of Cases	Rate/100K individuals*
1991	15	35.3
1992	20	47.1
1993	13	30.6
1994	10	23.6
1995	18	42.4
<hr/>		
Total	76	35.8

* Rate = number of cases per year / 1990 census population of 42,457 x 100,000.

Table 5: Hospitalizations listing aplastic anemia as one of the top five diagnoses for individuals residing in 95670 zip code, 1991-1995.

Year Diagnosed	Number of Cases	Rate/100K individuals*
1991	4	9.4
1992	3	7.1
1993	0	0
1994	0	0
1995	1	2.4
<hr/>		
Total	8	3.8

* Rate = number of cases per year / 1990 census population of 42,457 x 100,000.

Table 6: Expected and observed numbers of cancer cases, all sites combined, by census tract and gender, Rancho Cordova, Sacramento County, California, 1988-94.

<u>Census Tract Number</u>	<u>Expected #</u>	<u>Observed #</u>	<u>99% Confidence Interval</u>
8700			
Males	65	63	44.2 - 86.2
Females	55	62	43.3 - 85.1
8903			
Males	103	108	82.9 - 137.6
Females	99	82	60.3 - 108.1
8904			
Males	80	88	65.5 - 115.0
Females	85	111	85.5 - 140.9
8905			
Males	74	90	67.2 - 117.2
Females	78	71	51.0 - 95.5
8907			
Males	53	65	45.9 - 88.6
Females	57	61	42.5 - 83.9
8908			

Males	92	103	78.5 - 131.9
Females	93	108	82.9 - 137.6

9003

Males	53	60	41.7 - 82.8
Females	53	69	49.3 - 93.2

Table 7: Expected and observed numbers of thyroid cancer cases, by census tract and gender, Rancho Cordova, Sacramento County, California, 1988-94.

<u>Census Tract Number</u>	<u>Expected #</u>	<u>Observed #</u>	<u>99% Confidence Interval</u>
8700			
Males	0.7	2	0 - 9.1
Females	1.4	2	0 - 9.1
8903			
Males	0.7	3	0.2 - 10.8
Females	2.1	4	0.5 - 12.4
8904			
Males	0.7	2	0 - 9.1
Females	2.1	7	1.8 - 16.9
8905			
Males	0.7	0	-----
Females	1.4	0	-----
8907			
Males	0.7	2	0 - 9.1
Females	1.4	1	0 - 7.3
8908			
Males	0.7	0	-----
Females	1.4	0	-----

9003

Males	0.7	0	-----
Females	1.4	3	0.2 - 10.8

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CERTIFICATION

The Preliminary Health Reviews in Rancho Cordova, Aerojet-General Corporation Health Consultation was prepared by the California Department of Health Services under a cooperative agreement with the Agency for Toxic Substances and Disease Registry (ATSDR). It is in accordance with approved methodology and procedures existing at the time the health consultation was begun.

William Greim
Technical Project Officer, SPS, SSAB, DHAC

The Division of Health Assessment and Consultation, ATSDR, has reviewed this health consultation and concurs with its findings.

Richard Gillig
Chief, SPS, SSAB, DHAC, ATSDR

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HEALTH OUTCOMES

Preliminary reviews of the scientific literature were conducted by CDHS personnel located in the Environmental Health Investigations Branch looking for known health effects from exposure to perchlorate. Searches of the pertinent human and animal data bases found that the primary organ which is affected by perchlorate is the thyroid gland. However, there is a very small amount of information available related to perchlorate ingestion in healthy, human subjects; most of the information was found in studies of patients with Graves' Disease (hyperthyroidism), where perchlorate was used as an antagonist to decrease circulating thyroid hormone levels. Aside from producing hypothyroidism, perchlorate ingestion may also have produced goiter and hematologic abnormalities.

Several statewide databases were surveyed for these possible perchlorate-related health outcomes during the suspected years of contamination and limited to the likely areas of exposure (by zip code). Corresponding specific exposure information was not available at this time, so exposure was broadly defined as residing in a suspected contaminated zip code during the period from 1985 to 1996. Additionally, we have included in this health consultation, data analyses performed at the request of concerned citizens from Rancho Cordova regarding cancer incidence in suspected exposed areas.

Neonatal Thyroid Hormone Levels

Little medical information is available on perchlorate's developmental toxicity; however, it is believed that perchlorate acts in a fashion similar to other anti-thyroid medications (propyl thiouracil and methimazole) by crossing the placenta and inhibiting fetal thyroid synthesis, thus producing hypothyroidism in the newborn (9). Neonatal hypothyroidism can have tragic health consequences including mental retardation and cretinism, but can be treated, if problems are ascertained early. In California, thyroid hormone levels (T4) are drawn and maintained on file with the Genetic Disease Branch of the CDHS for all newborn infants. In a preliminary survey, thyroid hormone levels were obtained for all children born to mothers believed to have been exposed to perchlorate by residing in the following zip codes: 95670, 95742, 95655 and 95827. Additionally, data were abstracted for those children born to mothers residing in neighboring areas not believed to have been exposed to perchlorate from zip codes 95628, 95608, 95864 and 95662, as well as data from the remainder of California. The time period for this abstracted information was from 1985 through 1996.

There were 11,814 thyroid hormone screens in the potentially-exposed area with 4 cases of hypothyroidism observed. 3.76 cases would have been expected based on the statewide rate of 3.18 cases per 10,000 live births during this period. The non-exposed area found 6 cases of hypothyroidism out of

20,135 routine blood screens (6.41 cases were expected). [Table 1](#) shows these figures for exposed and unexposed zip codes as well as for the remainder of the state. These data do not show strong evidence of an association between residence in the potentially-exposed zip codes and neonatal hypothyroidism. Additionally, using residence as a proxy for exposure places limitations on the validity of any findings of this preliminary survey as there is no well-documented exposure information for the birth mothers. In addition, there are numerous other causes for neonatal hypothyroidism which instead may be responsible, including: deficiencies of Thyrotropin Releasing Factor and Thyroid Stimulating Hormone, aplasia or hypoplasia of the thyroid gland and iodine deficiency ([9](#)).

In addition to the above preliminary analysis, values of thyroid hormone (T4) and thyroid stimulating hormone (TSH) were obtained for each group, looking for differences in mean and median values between the exposure groups ([Tables 2](#) and [3](#), respectively). It should be noted that TSH levels are not routinely obtained in the initial screen of all live births, but are ascertained secondarily from neonates with low initial T4 levels (below 10 Iu/dl) who are then re-screened.

The mean neonatal thyroid hormone value in the potentially-exposed zip codes was statistically significantly lower than the non-exposed population ($p=0.0001$), yet statistically significantly higher than the population from the rest of the state ($p=0.0001$). If neonatal thyroid hormone levels were affected by maternal perchlorate ingestion, then one would expect the group levels in the exposed population to be lower than both populations. In addition, since exposures were not more accurately determined through dose-reconstruction analyses, it is not possible to more accurately assess whether perchlorate was responsible for the levels of T4 observed in the exposed group. For TSH values, the mean level observed in the suspected exposed group was not statistically significantly different from either the unexposed group ($p=0.49$) or the values found throughout the rest of the state ($p=0.99$).

Finally, it was also noted that from 1985 through 1996 there were only four cases of clinically significant neonatal hypothyroidism in the suspected exposure zip code area ([Table 1](#)). One case was born in 1985 and the birth mother resided in zip code 95827. This case's mother may not have regularly ingested contaminated water as the zip code location is the furthest west from the Aerojet facility and the time period may be before the drinking water wells in the Arden Cordova service area were affected by perchlorate contamination. The other three cases occurred from 1990 through 1996 and were all located in zip code 95670, which is the approximate area where perchlorate contamination of the drinking water wells is located. However, further information was unavailable to better define exposure status, without interviewing the family or reviewing the child's medical record.

Goiter

Perchlorate competitively binds to receptors on the surface of the thyroid and limits the uptake of iodide by the thyroid gland, with the subsequent inhibition of thyroid hormone release. Decreased circulating thyroid hormone exerts a feedback effect on the pituitary gland producing a compensatory increase in TSH. TSH stimulates the thyroid gland and may produce hypertrophy and thyroid gland enlargement ([10](#)). The OSHPD hospital discharge data base was reviewed, searching for the diagnosis of goiter among the first five reported diagnoses for each hospitalized individual residing in zip code 95670 from 1991 through 1995 ([11](#)). [The information obtained in this and the remaining surveys searched only in the 95670 zip code because this area was viewed as the most likely area of possible perchlorate contamination of the drinking water supply.] There were approximately 3-5 cases per year of goiter listed in the top 5 diagnoses. There are however, several problems with this approach. First, there are many

diseases or conditions which can produce a goiter other than perchlorate ingestion and the data base cannot differentiate this aspect well. Also, not all patients with goiter are admitted and treated in a hospital setting and so the OSHPD count is probably an undercount of the actual number of people with goiter. Because of these reasons, it was concluded that OSHPD data would not be helpful in determining the prevalence of thyroid enlargement in the affected water district.

Agranulocytosis/Aplastic Anemia

Aplastic anemia is a condition affecting the development of early blood cell precursors in the bone marrow which results in pancytopenia (reduced red and white blood cells and platelets). Agranulocytosis is the reduction of one particular blood cell line (white blood cells). Both aplastic anemia and agranulocytosis have occurred in individuals with Graves' Disease treated with perchlorate, documented in a series of papers in the early 1960s, which ultimately led to the discontinuation of perchlorate for the treatment of this condition (10). However, it is thought that the aplastic anemia seen in the Graves' Disease patients may have been a hypersensitivity reaction and unrelated to the dose of perchlorate ingested. Also, there is no information which would suggest that individuals without Graves' Disease would react in a similar fashion to perchlorate. Finally, aplastic anemia and agranulocytosis both may be caused by exposure to a variety of drugs or conditions including: cytotoxic medicines used in cancer chemotherapy, anticonvulsants, antibiotics, benzene, radiation, viral infections and genetic syndromes (11).

The OSHPD data was reviewed from 1991-95 for individuals residing in zip code 95670, searching for agranulocytosis or aplastic anemia as one of the top five diagnoses. This zip code was chosen because it was presumed to be the most likely area possibly receiving perchlorate-contaminated drinking water. [Table 4](#) displays OSHPD data for hospitalizations for agranulocytosis for individuals residing in zip code 95670 during this time. There were 76 total cases diagnosed with agranulocytosis who resided in this zip code from 1991 through 1995 for a rate of 35.8 cases/100,000 individuals per year. This figure is less than the statewide rate of 41.6 hospitalizations per 100,000 individuals per year generated from OSHPD data during 1994 and 1995. Because the data does not suggest any increase in risk of agranulocytosis for individuals residing in the suspected perchlorate-exposed area and there are other more likely causes for agranulocytosis, a further search of this data was not conducted.

[Table 5](#) lists the number of cases of aplastic anemia diagnosed in individuals who resided in the 95670 zip code from 1991 through 1995. For the five year time period, there were eight hospitalizations for 95670 zip code residents for a rate of 3.8 hospitalizations per 100,000 individuals per year, which is higher than the statewide rate of 2.2 hospitalizations per 100,000 individuals per year. However, all but one of the eight hospitalizations also had an additional diagnosis of cancer or chemotherapy or radiation which would seem to be the likely explanation for aplastic anemia, as chemotherapeutic agents and radiation treatments have been shown to produce bone marrow aplasia. It was not felt that reviewing the medical records of these individuals would provide meaningful information on the possible role of perchlorate.

Cancer

Reviews of the medical literature suggest that long-term interference of the thyroid-pituitary axis can lead to thyroid follicular cell neoplasia. Perchlorate may cause similar changes in thyroid cells by decreasing the amount of circulating thyroid hormones, thereby increasing stimulation of the thyroid

gland by TSH, with a concomitant hyperplasia of thyroid cells. Ultimately, with continued TSH stimulation, the diffuse hyperplasia may progress to nodular proliferation of the follicular cells and eventually to benign and malignant tumors (10). These changes have been observed in animal testing studies, primarily in rats, who appear to be a more sensitive species for these effects; it is not clear whether humans are similarly affected.

Concerned citizens of Rancho Cordova contacted the CCR and requested data reviewing the incidence of all types of cancer, thyroid cancer and cancer of the blood in the potentially-affected area. This area was confined to zip code 95670 during the years 1988 through 1994. The analysis was further stratified by gender (male and female) and the zip code was deconstructed into its corresponding 1990 census tracts (Figure 2). It should be noted that there is not an exact 1:1 correspondance for each census tract and the entire zip code, but this estimation is fairly close. Analysis of the data for cancer cases, all sites combined, failed to demonstrate evidence of a statistically significant increase in the observed number of cancer cases for any of the census tracts relative to the number of cases of cancer that would be expected, based on the statewide rate for cancer (Table 4). Also, cases of thyroid cancer were analyzed (Table 5) and no statistically significant elevations of observed numbers of thyroid cancer cases were detected compared to the numbers of cases which would be expected, based on corresponding statewide thyroid cancer rates. It is interesting to note that higher numbers of observed cancer cases and thyroid cancer cases were seen in census tract 8904 among women, however it is not possible to infer a relationship to perchlorate exposure from this limited data.

Childhood Leukemia

Leukemia is cancer of the white blood cell lines. Acute Lymphoblastic Leukemia (ALL) is the most common malignancy among children less than 15 years of age (12). Acute Myeloblastic Leukemia (AML) is the second most common childhood malignancy with about 400 new cases occurring annually in the United States (13). It has been postulated that risk factors for childhood leukemia include maternal exposures during pregnancy to radiation, infectious agents, pesticides, and genetic factors (12,13). No information concerning perchlorate's relationship with leukemia was found in the medical literature, however information concerning all leukemias and childhood leukemia in particular was readily available in the Cancer Registry data base and was another cancer which concerned residents from Rancho Cordova requested information on from CCR. The CCR, Region 3, provided information on all childhood leukemia cases from their data files for individuals residing in zip code 95670 from 1987 through 1996. (2) During that time, there were four cases in children aged less than 14 years, consisting of three cases of ALL and one case of AML. Since the total child population of this zip code was 9,648 individuals by the 1990 Census, the crude rate of childhood leukemia was calculated to be 4.2 cases per 100,000 children per year [4 cases/(9,648 people X 10 years)]. This rate is less than the corresponding childhood leukemia rate for California from 1988 through 1992 of 4.68 cases per 100,000 children per year.

In addition, after reviewing the data on all cases of leukemia, the CCR found no evidence of a statistically significant increase in the observed number of leukemia cases in the affected census tracts in Rancho Cordova from 1988 through 1994, when compared to the number of cases expected, based on statewide rates of leukemia.

Based on this information and the fact that additional factors may be responsible for adult and childhood leukemia, it was not recommended that further study be performed reviewing leukemia statistics at this

time.

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