Perchlorate (ClO₄⁻) has been detected in groundwater sources in numerous communities in California and other parts of the United States, raising concerns about potential impacts on health. For California communities where ClO₄⁻ was tested in 1997 and 1998, we evaluated the prevalence of primary congenital hypothyroidism (PCH) and high thyroid-stimulating hormone (TSH) levels among the 342,257 California newborns screened in 1998. We compared thyroid function results among newborns from 24 communities with average ClO₄⁻ concentrations in drinking water > 5 µg/L (n = 50,326) to newborns from 287 communities with average concentrations ≤ 5 µg/L (n = 291,931). ClO₄⁻ concentrations obtained from the California Drinking Water Program provided source-specific data for estimating weighted average concentrations in community water. Fifteen cases of PCH from communities with average concentration > 5 µg/L were observed, with 20.4 expected [adjusted prevalence odds ratio (POR) = 0.71; 95% confidence interval (CI), 0.40–1.19]. Although only 36% of all California newborns were screened before 24 hr of age in 1998, nearly 80% of newborns with high TSH were screened before 24 hr of age. Because of the physiologic postnatal surge of TSH, the results for newborns screened before 24 hr were uninformative for assessing an environmental impact. For newborns screened ≥ 24 hr, the adjusted POR for high TSH was 0.73 (95% CI, 0.40–1.23). All adjusted odds ratios (ORs) were controlled for sex, ethnicity, birth weight, and multiple birth status. Using an assessment of ClO₄⁻ in drinking water based on available data, we did not observe an association between estimated average ClO₄⁻ concentrations > 5 µg/L in drinking water supplies and the prevalence of clinically diagnosed PCH or high TSH concentrations. Key words: drinking water, newborn screening, perchlorate, primary congenital hypothyroidism, thyroid-stimulating hormone.

Published epidemiologic studies have not shown a consistent association between ClO₄⁻ in drinking water and congenital hypothyroidism or altered thyroid function. One study of Arizona newborns reported an association between ClO₄⁻ in drinking water and thyroid function (Brechner et al. 2000), whereas five other studies in California, Nevada, and Chile did not provide evidence supporting this association (Crump et al. 2000; Kelsh et al. 2003; Lamm and Doemland 1999; Li et al. 2000a, 2000b). Interestingly, no association was noted between exposure to ClO₄⁻ in drinking water and TSH in two studies with more quantitative exposure information (Crump et al. 2000; Li et al. 2000a). Thus, it is possible that the inconsistent results regarding exposure to ClO₄⁻ in drinking water and TSH concentrations in newborns may be the result of methodologic issues (Kelsh et al. 2003; Lamm et al. 2002; Lamm and Doemland 1999; Li et al. 2000a, 2000b).
The objectives of this investigation were to assess whether there was epidemiologic evidence of higher rates of PCH or high TSH levels among newborns in California communities with and without detectable ClO$_4^-$ in their drinking water supplies, and to evaluate the extent to which inconsistent results could be the result of the methodologic differences noted (Kelsh et al. 2003; Lamm 2003). This study expanded our earlier investigation of PCH and TSH concentrations in a southern California community where ClO$_4^-$ had been detected (Kelsh et al. 2003). The present study used data from the California Newborn Screening (NBS) Program for 1998 to examine the prevalence of PCH and TSH levels for all California newborns whose mothers resided in communities where water supplies were tested for ClO$_4^-$ in 1997 and 1998.

Until late 1997, California used a two-tiered T$_4$-TSH screening program to screen for PCH. In this program, all newborns were screened for T$_4$, and only those with a low T$_4$ (e.g., < 10 µg/dL) had their TSH measured. Beginning in December 1997, the California Department of Health Services (DHS) NBS Program replaced the two-stage screening procedures with TSH-only testing for PCH. Thus, since late 1997, TSH has been measured for all California newborns tested under the new program. TSH concentration is considered a more sensitive biomarker for thyroid function, whereas PCH is a specific clinical end point. TSH is a biomarker for thyroid function, whereas PCH is a specific clinical end point. The newborn’s physician is responsible for informing the parents of the newborn about the results of the screening tests and summary of the findings.

Study variables. Information abstracted from the NBS Program records for 1998 was used to construct variables for this analysis. Some missing or erroneous values were imputed or corrected. Details of the data editing and management process have been described elsewhere (Kelsh et al. 2003). The health or biomarkers outcomes investigated were diagnosis of PCH and high TSH level (defined by GDB as > 25 µU/mL). Elevated TSH is a biomarker for thyroid function, whereas PCH is a specific clinical end point. The newborn’s physician is responsible for reporting confirmed diagnosis of PCH to the screening program. Once physicians are alerted to a newborn with high TSH concentration, diagnosis of PCH is generally based on confirmatory tests of serum free T$_4$ and TSH levels and a detailed physical examination and neonatal history. Assessment may also include thyroid scanning and testing of serum-binding proteins and serum triiodothyronine levels.

Covariate data available from the newborn screening records included age (in hours of life) at time of specimen collection, sex, race/ethnicity, birth weight, and multiple birth status. The exposure variable derived from the California DWP was average ClO$_4^-$ concentration categorized as < 5 µg/L and ≤ 5 µg/L. In addition, a Colorado River indicator variable was assigned to each record if the mother’s residence received drinking water from the Colorado River.

California DWP. The DWP of the California DHS was established to monitor water sources of public water systems. Approximately 80 chemical and six radiological contaminants for which maximum contaminant levels (MCLs) have been established are monitored (California DHS 2003a). The DWP also monitors concentrations of other chemicals for which no MCL has been established. In 1997 and 1998, ClO$_4^-$ was one of the unregulated chemicals monitored by DHS.

The DWP initiated ClO$_4^-$ testing of drinking water wells in February 1997 (California DHS 2003b). These data are organized by water system (water company, distributor, or private entity such as a mobile home park); data for each water system may include testing data from multiple sources or wells, and each source may have been tested on multiple occasions. ClO$_4^-$ exposure estimates were based on samples from wells tested for ClO$_4^-$ from February 1997 through December 1998. We selected 1997 and 1998 water data, assuming these years would span the gestation periods for the 1998 newborns. Because testing data after 1998 may not accurately characterize concentrations in water sources in the 1997 and 1998 period, post-1998 ClO$_4^-$ testing data were not used. Analysis of post-1998 water quality data showed that about 90% of the groundwater sources tested in 1997–1998 were tested again sometime after 1998 and before March 2003. The median number of additional tests performed after 1998 was four (range 1–202). The concentrations in 1997–1998 and subsequent tests were below the nominal detection limit of 5 µg/L for 79% of the water sources with post-1998 testing. Of the remaining sources tested, 15% showed no statistically significant difference in ClO$_4^-$ concentration from samples tested in the two time periods, 3.4% showed a significant increase, and 2.6% had a significant decrease in ClO$_4^-$ concentration. Thus, most groundwater sources remained below-detection concentration level or showed no significant change in concentration after 1998.

DWP measurements for ClO$_4^-$ concentrations below the test detection limits were recorded inconsistently. Sample concentrations where ClO$_4^-$ was not detected were recorded either as 0.0, < 4, or < 5 µg/L. Most measurements that yielded concentrations too low to quantify were recorded as < 4 or < 5 µg/L based on the lower detection limit at the time of 4.5 µg/L. From 1997 and 1998, 48 water systems had one or more samples with detectable ClO$_4^-$, and 151 water systems had no detectable ClO$_4^-$ in any of their samples. We selected the cutoff point of 5 µg/L to represent concentrations at or below 5 µg/L.

Information for cities or towns served by each water system tested by the DWP was collected either from the DWP file or through Internet searches or telephone interviews conducted by research staff. In addition to relying on local groundwater wells, water
systems frequently purchase water from other distributors and wholesalers. Many southern California communities also receive a portion of their water from the Metropolitan Water District (MWD) of Southern California. The MWD distributes northern California and Colorado River surface water to 26 water systems that provide drinking water to nearly 18 million southern California residents (MWD 2003a). Information on Colorado River water allocations was collected through Internet searches and telephone inquiries to major southern California water wholesalers and the Colorado River Water Users Association (Colorado River Water Users Association 2003; MWD 2003b). This information was used to determine whether each city received Colorado River water.

Six samples from four MWD sources were tested in 1997 and 1998. The highest ClO₄⁻ concentration for these years was 9.0 µg/L, with an average of 4.1 µg/L. No public data source was available to identify the amount of water provided by the MWD to its affiliated water systems. Thus, after blending and mixing with other sources, the proportion of MWD-supplied water reaching consumers in a particular community at a particular time could not be determined.

In the absence of detailed and complete information on water distribution practices for each California water system, the following methods were adopted to estimate average ClO₄⁻ concentrations for each water system and city. The average water system ClO₄⁻ concentration was the arithmetic mean of median concentrations from each contributing water source or well. The average ClO₄⁻ concentration for a given city was then calculated as the weighted average of concentrations from the different water systems that provided drinking water to the city, weighted by the number of water sources, counting the MWD as one source. Thus, the ClO₄⁻ concentration for a community was estimated as

$$\bar{C} = \frac{\sum_{i} n_i C_i}{N},$$

where $n_i$ is the number of drinking water sources contributed by the $i$th water system, $C_i$ is the ClO₄⁻ average concentration for the $i$th water system, and $N$ is the total number of sources from all contributing water systems.

**Statistical analysis.** Primary congenital hypothyroidism. We examined the relationship between PCH occurrence and potential ClO₄⁻ exposure using logistic regression models to estimate adjusted prevalence odds ratios (PORs). In addition to the drinking water ClO₄⁻ classification of ≤ 5 µg/L or > 5 µg/L, covariates in the logistic regression analyses for PCH included birth weight, ethnicity, sex, and indication of multiple births. Only the first newborn in a multiple birth was retained for analysis, as characteristics of the subsequent newborns were unlikely to be independent.

**Thyroid-stimulating hormone.** The potential relationship between high TSH level and residence in communities with detectable ClO₄⁻ in drinking water was examined using logistic regression models to estimate adjusted PORs. The continuous TSH variable was dichotomized into “high” or “normal” based on the 1998 DHS GDB cutoff value of 25 µU/mL.

Covariates were those used in the PCH analyses as well as age at time of blood sample collection. Given the documented physiologic postnatal surge of TSH before 24 hr of age, we restricted the TSH analyses to those newborns with an age at specimen collection ≥ 24 hr. In our analyses, we also examined the subgroup of newborns with normal birth weights. Two-way interactions were examined and found to have minimal effect on the POR and thus were not included in the final model.

**Results**

**Newborn screening data.** Of the initial 515,476 records for California newborns whose screening data had accession dates (date the specimen arrived at the laboratory) from January to December 1998, 6,325 (1.23%) could not be included because of incomplete or inadequate data. The remaining birth records totaled 509,151 in the final data file included 201 diagnosed with PCH and 989 infants with TSH level > 25 µU/mL. Of the 509,151 California newborns with complete data, 342,257 newborns were identified as residing in communities where groundwells were tested for ClO₄⁻. Of these records, 50,326 newborns from 24 communities resided in areas with average ClO₄⁻ concentrations in drinking water sources > 5 µg/L and 291,931 newborns from 287 communities resided in areas with average ClO₄⁻ concentrations ≤ 5 µg/L. No apparent biases were evident as a result of the 3,584 records deleted because of various missing demographic data or screening test characteristics. Overall, 0.95% of records were deleted from the communities with average ClO₄⁻ concentrations > 5 µg/L compared with 1.05% deleted from communities with average ClO₄⁻ concentrations ≤ 5 µg/L in drinking water (Appendix 1). In addition, a sensitivity analysis, in which newborns from cities and towns where groundwater was not tested were classified into the low concentration category, did not significantly change the study findings.

**DWP water survey.** Overall, communities from 20 California counties were tested for ClO₄⁻ (Appendix 2). Four southern California counties (Los Angeles, Orange, Riverside, and San Bernardino) and one northern California county (Sacramento) had a total of 24 communities with average ClO₄⁻ concentrations in drinking water > 5 µg/L, based on the California DWP data for 1997–1998. In the same five counties, there were 139 communities with average ClO₄⁻ concentrations ≤ 5 µg/L.

**Primary congenital hypothyroidism.** Of the 201 newborns diagnosed with PCH in California in 1998, 141 newborns were from communities receiving drinking water that had been tested for ClO₄⁻ (Table 1). Fifteen

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**Table 1.** Number of newborns tested, number with high TSH, and number of PCH cases by ClO₄⁻ exposure classification, California, 1998.

<table>
<thead>
<tr>
<th>Exposure classification</th>
<th>Population after data editing</th>
<th>PCH (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All newborns from California communities tested for ClO₄⁻</td>
<td>342,257</td>
<td>141 (0.40)</td>
</tr>
<tr>
<td>Newborns from communities with average ClO₄⁻ concentrations &gt; 5 µg/L</td>
<td>50,326</td>
<td>141 (0.28)</td>
</tr>
<tr>
<td>Newborns from communities with average ClO₄⁻ concentrations ≤ 5 µg/L</td>
<td>291,931</td>
<td>141 (0.05)</td>
</tr>
</tbody>
</table>

*aTesting results provided by California DHS DWP. Some records may have invalid or missing information for more than one variable.

---

**Table 2.** ORs and 95% CIs for PCH by ClO₄⁻ exposure classification, Colorado River water status, and birth weight, California newborns, 1998.

<table>
<thead>
<tr>
<th>Average ClO₄⁻ concentrations</th>
<th>No PCH</th>
<th>PCH</th>
<th>No PCH</th>
<th>PCH</th>
<th>POR* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 5 µg/L</td>
<td>287,754</td>
<td>122</td>
<td>49,622</td>
<td>15</td>
<td>0.71 (0.40–1.19)</td>
</tr>
<tr>
<td>&gt; 5 µg/L</td>
<td>241,275</td>
<td>100</td>
<td>41,615</td>
<td>11</td>
<td>0.64 (0.32–1.5)</td>
</tr>
</tbody>
</table>

*Only first born of multiple births were included in these analyses. **POR was adjusted for race, sex, birth weight, multiple birth, and Colorado River water use. *Newborns with normal birth weight (2,500–4,000 g).
cases (10.6%) were from areas with average ClO₄⁻ concentrations in drinking water > 5 µg/L (20.4 cases were expected), and 126 (89.4%) cases of PCH were from communities with average concentrations of ClO₄⁻ in drinking water ≤ 5 µg/L (20.4 cases were expected), and 126 (89.4%) cases of PCH were from communities with average ClO₄⁻ concentrations > 5 µg/L (POR = 0.71; 95% CI, 0.40–1.19) (Table 2). For newborns in the normal birth weight category (2,500–4,000 g), the POR was slightly lower for newborns from communities with average ClO₄⁻ concentration > 5 µg/L (POR = 0.64; 95% CI, 0.32–1.15) than the results for all birth weights (Table 2).

Among newborns from areas that did not receive Colorado River water but had average ClO₄⁻ concentrations > 5 µg/L, the POR for PCH was near 1 (POR = 1.14; 95% CI, 0.52–2.28). In this analysis of communities that did not receive Colorado River water, the OR for newborns in the normal birth weight category (POR = 1.01; 95% CI, 0.39–2.26) was slightly lower than the OR for all newborns. The POR among communities that received Colorado River water was not elevated (POR = 0.43; 95% CI, 0.15–0.96).

Similar to previous reports of California newborn data (Lorey and Cunningham 1992; Waller et al. 2000), female newborns had a higher risk for PCH (POR = 1.94; 95% CI, 1.37–2.78). Variation by race/ethnicity status was also observed with Asians (POR = 1.83; 95% CI, 0.94–3.50) and Hispanics (POR = 2.17; 95% CI, 1.36–3.63) having higher risks, and African Americans (POR = 0.29; 95% CI, 0.05–0.99) having lower risks compared with whites. Low birth weight status (< 2,500 grams) was also associated with PCH (POR = 1.90; 95% CI, 0.99–3.31).

**TSH.** There were 684 newborns identified as having high TSH levels among 342,257 newborns screened from communities where drinking water was tested for ClO₄⁻ (Table 1). Of these, 537 (78.5%) were from communities with average ClO₄⁻ concentrations in drinking water ≤ 5 µg/L, and 147 (21.5%) were from areas with average ClO₄⁻ concentrations > 5 µg/L.

TSH concentrations rose rapidly as expected in the first 12 hr of life, then declined, stabilized by 24 hr after birth, and continued to decline (Figure 1). Among newborns from communities with drinking water tested for ClO₄⁻, 123,583 (36.1%) had their blood sample collected for TSH screening at < 24 hr of age. The majority of newborns (79.7%) with high TSH were identified as having high TSH levels among the population receiving Colorado River water, and had water system groundwater wells tested for ClO₄⁻. 230 newborns were identified as having high TSH, and 188 (81.7%) of these newborns had blood specimens collected < 24 hr (Table 3).

The adjusted POR associated with high TSH among newborns screened ≥ 24 hr of age and whose mothers resided in communities with average ClO₄⁻ concentrations > 5 µg/L was 0.73 (95% CI, 0.40–1.23) (Table 4). For newborns of normal birth weight screened ≥ 24 hr of age, the OR for high TSH was also not elevated (POR = 0.74; 95% CI, 0.37–1.33).

For communities that did not receive Colorado River water, the POR for high TSH followed a similar pattern. The adjusted POR for high TSH in communities with average ClO₄⁻ concentrations > 5 µg/L was 0.87 (95% CI, 0.37–1.83). Among normal birth weight newborns, the POR for high TSH was also not increased (POR = 0.71; 95% CI, 0.24–1.77) (Table 4). Among southern California residents who received Colorado River water, the POR was not elevated (POR = 0.57; 95% CI, 0.22–1.20) (Table 4).

Of the demographic factors and birth characteristics examined in our multivariate models, females had a higher risk for high TSH (POR = 1.89; 95% CI, 1.33–2.71) compared with males. By race/ethnicity status, results for high TSH were similar to the findings for PCH, with modest elevations for Asians (POR = 1.37; 95% CI, 0.73–2.48) and Hispanics (POR = 1.40; 95% CI, 0.91–2.20) and a decrease for African Americans (POR = 0.40; 95% CI, 0.12–1.02) compared with whites. Birth weight and multiple birth status were not associated with high TSH (data not shown).

**Discussion**

This statewide study was initiated as a follow-up analysis to a previous study of a southern California community (Kelsh et al. 2003) to verify whether similar findings would be observed in a larger study population. In addition to the increased sample size, this study of 1998 California NBS Program data offered several other analytical advantages. First, 1998 was the first year that TSH testing was conducted for all California newborns. Second, ClO₄⁻ drinking water monitoring data for the period 1997–1998 were available for a large number of drinking water sources in California to link with the NBS Program data. We observed 15 cases of PCH in 1998 in areas of California where ClO₄⁻ was detected at average concentrations > 5 µg/L, while 20.4 cases were expected. When we compared PCH cases in communities with average ClO₄⁻ concentration > 5 µg/L that did not receive Colorado River water, we did not find an excess number of cases, nor was there an excess number of cases observed among the population receiving Colorado River water as a drinking source.

In addition, we did not find evidence of high TSH levels for California newborns whose mothers resided in communities with average ClO₄⁻ drinking water concentrations > 5 µg/L. When we compared California communities that did not receive Colorado River water but had average ClO₄⁻ concentrations > 5 µg/L, there was also no excess risk of high TSH levels.

![Figure 1. TSH concentrations at 25th, median, and 90th percentiles by specimen collection time, California newborns, 1998. Included only newborns from areas where water system groundwater was tested for ClO₄⁻ in 1997–1998.](image-url)
Although slightly more than one third of all newborns in the study population were screened within the first 24 hr of life, the majority of newborns (79.7%) with high TSH concentrations were screened within the first day. The strong effect of time of sample collection on TSH level dictated our focus on TSH results after 24 hr of age. Given the large number of newborns with high TSH screened within the first 24 hr of life, this approach was considered more appropriate than analyses including all newborns regardless of sampling age and attempting to control for this powerful confounding factor in the data analysis.

Limitations. The California DHS uses nine screening laboratories that serve various geographic regions of the state. Thus, it is possible that laboratory variation may affect the outcome of TSH screening as a result of slight variations in methods and procedures and changes in personnel. This possibility was evaluated and appears unlikely, because the GDB uses standardized protocols and rigorous quality control procedures for all laboratory procedures. In addition, laboratory variation would more likely occur across years rather than within 1 year, as we have analyzed here.

Because we were using data for drinking water at a community level, the exposure classification protocol that we adopted does not account for variation due to individual consumption patterns (e.g., bottled water) or migration into and out of communities resulting from residential mobility or travel to work sites outside of mothers’ residential communities. In addition, the very dynamic and complex water systems for many of the study communities rely on several water sources, which often contribute different proportions of water at different times of the year. Specific water allocation data were not available for many of the different water companies.

Our method of averaging ClO₄⁻ concentrations based on water testing assumed that each water source contributed an equal proportion of water to the communities it served. Because of the uncertainty of this assumption, we used this calculation only to group communities into categories of potentially exposed (estimated average ClO₄⁻ concentration > 5 µg/L) and likely not exposed (estimated average ClO₄⁻ concentration ≤ 5 µg/L). This method does not incorporate personal water consumption patterns or the mixing of multiple water sources by water companies. Given the limitation of this method, these calculations were not used to conduct potential dose–response analyses.

Comparison with previous epidemiologic studies of newborns. Previous published studies have evaluated potential associations between T₄, TSH, or PCH and ClO₄⁻ exposure in newborn populations in California, Nevada, Arizona, and Chile (Brechner et al. 2000; Crump et al. 2000; Kelsh et al. 2003; Lamm and Doemland 1999; Li et al. 2000a, 2000b). We focused our analysis on PCH as a significant disease and on TSH as a sensitive indicator of thyroid function. TSH is considered a more sensitive and specific indicator for assessing subclinical thyroid function than T₄ (Nordyke et al. 1998) and is the preferred screening test for PCH (American Academy of Pediatrics 1993).

The results of the current study were similar to those of previous studies with respect to risk factors for PCH and elevated TSH levels (Kelsh et al. 2003; Lorey and Cunningham 1992; Waller et al. 2000). We found that ethnicity, sex, and birth weight were consistent predictors of PCH, whereas specimen collection time had the most pronounced effect on TSH levels (Allen et al. 1990; Waller et al. 2000). Blood samples collected at < 24 hr of age had much higher TSH levels than those collected 1 day or more after birth. When age at specimen collection time was taken into account, no differences in TSH level were observed between newborns from communities with average ClO₄⁻ concentrations in drinking water ≤ 5 µg/L and > 5 µg/L.

In this analysis of California newborns, we studied a much larger number of newborns with TSH results compared with previous studies in Chile, Arizona, and Nevada (Brechner et al. 2000; Crump et al. 2000; Li et al. 2000a). However, in each of those smaller studies, exposure information was likely more precise because the communities studied relied solely on one water supply, whereas across California, communities often rely on multiple water sources.

Our findings are consistent with previously published analyses of exposure to ClO₄⁻ in drinking water and PCH and TSH, with the exception of the analysis of Arizona newborns by Brechner et al. (2000). No increase in the number of PCH cases was found in counties where ClO₄⁻ had been detected in California and Nevada well water supplies (Lamm and Doemland 1999). Likewise, there was no association between TSH concentrations and low-level ClO₄⁻ exposures in drinking water among newborns in a study of Las Vegas and Reno, Nevada (Li et al. 2000a). In a Chilean study of three regions with high, medium, and nondetectable ClO₄⁻ concentrations in drinking water (Crump et al. 2000), no associations between newborns’ TSH concentrations and ClO₄⁻ region or between childhood TSH concentrations and lifetime residence in the three regions were reported. Our results were also similar to the findings of a 15-year study of newborns in a

### Table 3. Distribution of high TSH [no. (%)] by ClO₄⁻ exposure classification, Colorado River water status, and specimen collection time, California newborns, 1998.

<table>
<thead>
<tr>
<th>ClO₄⁻ exposure</th>
<th>Specimen collection &lt; 24 hr</th>
<th>Specimen collection ≥ 24 hr</th>
<th>Total</th>
<th>California communities not receiving Colorado River water</th>
<th>Specimen collection 24 hr</th>
<th>Specimen collection &gt; 24 hr</th>
<th>Total</th>
<th>Colorado River water communities (California)</th>
<th>Specimen collection 24 hr</th>
<th>Specimen collection &gt; 24 hr</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 5 µg/L</td>
<td>413 (76.9)</td>
<td>124 (23.1)</td>
<td>537 (100)</td>
<td>124 (79.0)</td>
<td>33 (21.0)</td>
<td>157 (100)</td>
<td>380 (100)</td>
<td>289 (76.1)</td>
<td>91 (23.9)</td>
<td>380 (100)</td>
<td>545 (78.6)</td>
</tr>
<tr>
<td>&gt; 5 µg/L</td>
<td>132 (88.8)</td>
<td>15 (10.2)</td>
<td>147 (100)</td>
<td>64 (87.7)</td>
<td>9 (12.3)</td>
<td>73 (100)</td>
<td>147 (100)</td>
<td>60 (91.9)</td>
<td>6 (8.1)</td>
<td>66 (91.9)</td>
<td>126 (18.3)</td>
</tr>
</tbody>
</table>

### Table 4. ORs and 95% CIs for high TSH by ClO₄⁻ exposure classification, Colorado River water status, and birth weight, California newborns, a 1998.

<table>
<thead>
<tr>
<th>Average ClO₄⁻ concentrations</th>
<th>≤ 5 µg/L</th>
<th>&gt; 5 µg/L</th>
<th>All communities tested for ClO₄⁻</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal TSH</td>
<td>185,409</td>
<td>119</td>
<td>29,100 14 0.73 (0.40–1.23)</td>
</tr>
<tr>
<td>High TSH</td>
<td>152,286</td>
<td>94</td>
<td>23,679 11 0.74 (0.37–1.33)</td>
</tr>
<tr>
<td>Normal birth weight a</td>
<td>46,653</td>
<td>32</td>
<td>13,113 8 0.87 (0.37–1.83)</td>
</tr>
<tr>
<td>High birth weight</td>
<td>38,121</td>
<td>24</td>
<td>10,462 6 0.71 (0.24–1.77)</td>
</tr>
<tr>
<td>California communities not receiving Colorado River water</td>
<td>138,756</td>
<td>87</td>
<td>15,987 6 0.57 (0.22–1.20)</td>
</tr>
<tr>
<td>All births</td>
<td>114,145</td>
<td>70</td>
<td>13,217 6 0.70 (0.27–1.49)</td>
</tr>
</tbody>
</table>

aMultiple births represented once; specimen collection ≥ 24 hr for all newborns was analyzed and adjusted for ethnicity, sex, multiple birth status, and birth weight. bPOR was adjusted for race, sex, birth weight, multiple birth, and Colorado River water use. cNewborns with normal birth weight (1,500–4,000 g).
southern California community (Kelsh et al. 2003). However, our results differed from those reported among Arizona newborns (Brechner et al. 2000). Further investigation of this study population suggests that differences in medical procedures, hospital practices, or other regional or demographic factors provide a more likely explanation of the TSH concentration differences observed for newborns in Yuma and Flagstaff than drinking water exposure to ClO₄⁻ (Goodman 2001; Lamm 2003).

Despite use of the same California newborn screening data (although for different years), our results do not support the findings of an unpublished analysis of ClO₄⁻ and TSH of California newborns in 1996, when the two-stage screening for PCH was in place (Schwartz 2001). As previously described, methodological and analytic differences between the study presented here and that of Schwartz do not allow for direct comparison of findings (Kelsh et al. 2003). These differences include evaluation of TSH data as a continuous variable in the Schwartz analyses and a dichotomous variable in this study. Analysis of TSH as a continuous variable would have to address the issue that more than 50% of the newborns screened had a value of 5 µU/mL recorded, because any TSH concentration below the limit of detection was recorded or censored at 5 µU/mL. Although this truncation of the data would not pose a problem for a screening program, ignoring the censoring of the data would distort the results when they are analyzed as a continuous variable in analysis of variance models. In addition, results reported by Schwartz suggest that several variables, especially the newborn blood specimen collection hour, appear to have been processed incorrectly in the Schwartz analyses, leading to misclassification of a significant number of newborn data records. The exposure assignment procedures used by Schwartz were also different but were not adequately documented to permit a comparison with our protocol. Thus, the different time periods examined, the different statistical analyses applied, the different exposure assignment procedures implemented, and the data misclassification errors that we identified in the Schwartz analyses have led to different results and conclusions between the current investigation and the Schwartz unpublished analysis.

Other studies. In addition to the community studies of newborn thyroid function and ClO₄⁻ concentrations in drinking water, several adult studies of thyroid disease and cancer have not identified an association with ClO₄⁻ in drinking water or occupational ClO₄⁻ exposure (Gibbs et al. 1998; Lamm et al. 1999; Li et al. 2001; Morgan and Cassidy 2002).

In an early study of treatment for hyperthyroidism, 11 of 12 newborns of mothers taking potassium ClO₄⁻ at 600 mg or 1,000 mg daily exhibited no abnormalities, while one had a transiently enlarged thyroid (Crooks and Wayne 1960). A recent volunteer study suggested that ClO₄⁻ in drinking water at the equivalent of 180–220 µg/L daily results in no effect on thyroid function (Greer et al. 2002). Given that the ClO₄⁻ concentrations in California communities’ drinking water, where ClO₄⁻ was detected, had a median value of 12 µg/L with a range from 5 to 87 µg/L, most of the testing results were below the detection limit. These concentrations, along with the results of the studies by Crooks and Wayne (1960) and Greer et al. (2002), argue against adverse health effects among California newborns.

Conclusions

In the current study of potential ClO₄⁻ exposure in drinking water and PCH and high TSH concentrations, we found that PCH rates in California communities where ClO₄⁻ concentrations in drinking water average > 5 µg/L were equal to or lower than those in communities with average ClO₄⁻ concentrations ≤ 5 µg/L. We also found no statistically or biologically relevant differences between newborns in these communities with respect to TSH concentrations. These findings are consistent with the medical literature, which reports that most cases of PCH result from developmental defects of the thyroid. In addition, most epidemiologic studies to date have not associated PCH or newborn TSH levels with exposures to ClO₄⁻ in drinking water. Recently, the National Academies’ National Research Council Committee to Assess the Health Implications of Perchlorate Ingestion (2005) reviewed the available data from animal, human, and epidemiologic studies, with greater emphasis placed on controlled human studies such as Greer et al. (2002). The committee concluded that the data across animal, human volunteer, and epidemiologic studies were not consistent with a causal association between exposure to ClO₄⁻ in the drinking water systems. Despite the results of some epidemiologic studies, the committee suggested that more research is needed to elucidate the potential health effects of ClO₄⁻ exposure, with a focus on the development of methods to accurately measure ClO₄⁻ concentrations in drinking water and to identify potential exposure pathways and endpoints of injury, in order to better understand the environmental and public health implications of ClO₄⁻ exposure.
water and either congenital hypothyroidism or thyroid function in normal full-term newborns (National Research Council 2005). Our findings in this epidemiologic study were consistent with that conclusion. Despite the limitations of using aggregate-level exposure data and the relatively small number of cases of PCH and high TSH levels even in this full statewide analysis, these results suggest that exposure to ClO₄⁻ in drinking water supplies in California at the levels reported does not appear to be associated with either PCH or high TSH levels.

REFERENCES


