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At 202/333-2239 (Fax) **DRAFT** Cong Hypo Paper 8-9-98

Has Environmental Exposure (water) to Perchlorate increased the Rate of Congenital Hypothyroidism?

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Abstract: Perchlorate has been found in drinking water supplies, including Southern California and Southern Nevada, following the development in April 1997 of a laboratory method to measure perchlorate at 4 ppb in drinking water. Exposure levels have been in the 4-16 ppb range. Since perchlorate at therapeutic levels is known to inhibit the thyroid gland, the question has risen as to whether these environmental levels of perchlorate in the drinking water are associated with an increased risk of congenital hypothyroidism (a preventable ~~form~~ cause of mental retardation). The county-specific congenital hypothyroidism rates for California (1996) and Nevada (1996-7) have been determined. Comparison shows that the counties with perchlorated water have somewhat lower rates of congenital hypothyroidism than do the counties without perchlorated water. These data do not support an associative hypothesis.

Purpose: Congenital hypothyroidism is a preventable cause of mental retardation that can be detected at birth through neonatal screening programs. Perchlorate is known to block thyroid hormone formation by competitively inhibiting the uptake of iodine by the thyroid gland. Perchlorate has been recently detected in the water supplies of a number of counties in California and Nevada. An analysis has been conducted to determine whether the counties with perchlorated water have an increased rate of congenital hypothyroid or not. PERCHLORATE IN THE WATER

Exposure Surveillance: Perchlorate was found in the drinking water supply of a number of California counties after the detection limit was lowered in April 1997 from 0.4 ppm to 4 ppb. The sources were generally found to be industrial sites manufacturing or using perchlorate for missiles, rockets, or fireworks. An industrial site in Nevada lead to contamination of Lake Mead ~~which lead~~ which led to contamination of the Colorado River water supply for Southern California and the water supply for Las Vegas (Clark County) Nevada at levels of 5-8 ppb and up to 16 ppb, respectively. The US Environmental Protection Agency (EPA Region 9 – Kevin Mayer) has identified the counties with perchlorated water supplies in California (n = 7) [Figure 1] and Nevada (n = 1).

Outcome Surveillance: The health departments of both California and Nevada have conducted neonatal screening programs for congenital hypothyroidism for over ten years. The neonatal screening program uses a heel-stick blood sample of the newborn to assess ~~for~~ the presence of a variety of congenital metabolic diseases. Participation is mandatory and covers all hospitals with birthing units. The county-specific congenital hypothyroidism case counts and live birth counts have been obtained for both California (1996) and for Nevada (1996-7) from their health departments.

California – Cases of congenital hypothyroidism were detected in 30 of the 59 counties of California in 1996. These data were supplied by George Cunningham, MD, MPH, Chief of the Genetic Disease Branch, Primary Care & Family Health Division,

California Department of Health Services. The congenital hypothyroidism birth prevalence rates were calculated for each county [Table 1] and the counties were ~~grouped~~ DICHOTOMIZED into the fifteen with higher rates (> 4.5/10,000 live births) [Figure 2] and the fifteen with lower (< 4.5/10,000 live births) [Figure 3]. Adjustment for hispanic ethnicity has affected the ranking little.

Nevada – Cases of congenital hypothyroidism were detected in 3 of the 17 counties of Nevada in 1996-7. These data were supplied by the Bureau of Family Health Services, Nevada State Health Division. The congenital hypothyroidism birth prevalence rates were calculated for each county [Table 2]. Clark County is the only county to receive perchlorated water as its water source is from the contaminated part of Lake Mead. The counties have been grouped into those counties without perchlorated water and the county with perchlorated water. The congenital hypothyroidism birth prevalence rates for these two groups (1996-7) have been calculated and compared with the rate for the state [Figure 5].

Analysis:

All seven of the California counties with perchlorated waters are in the group of counties have the lower rates of congenital hypothyroidism [Figure 4]. The Nevada county with perchlorated water appears to have a lower congenital hypothyroidism birth prevalence rate than do the other counties in the state [Figure 5].

Thus, both in California and in Nevada, the counties with perchlorated water appear to have lower birth prevalence rates for congenital hypothyroidism than do the counties without perchlorated water. Nearly the entire water supply for Clark County, Nevada comes from the source with perchlorate contamination. The California counties have more spotty and intermittent exposure.

These data, derived from public health sources, seem to indicate that current or recent levels of perchlorate in the drinking water do not increase the risk of congenital hypothyroidism.

Discussion:

Levels of perchlorate were detected in the drinking waters in California and Nevada in 1997, mainly in the range of 4-10 ppb (ug/l). At an assumed water intake of two liters per day, they would provide a daily dosage of up to 20 ug per day. Until April 1997, these levels would have been undetectable. In April 1997, the California Department of Health Services refined the methodology for measuring perchlorate in drinking water and reduced the level of detection from 0.4 ppm to 4 ppb.

A daily intake rate of perchlorate at 20 ug/day can be compared with the minimum effective dose of 200 mg/day (200,000 ug/day) that has been used medically to suppress the thyroid in treatment of hyperthyroidosis. Data from the 1950s showed that the thyroid uptake of iodide was not blocked by a dosage of 10 mg perchlorate (Stanbury

and Wyngarten, 1953), which suggests a no adverse effect level at 10 mg/day for the adult.

Congenital hypothyroidism occurs when both the maternal thyroid and the fetal thyroid are unable to supply adequate thyroid hormone to the fetus. This usually occurs only in the presence of severe iodine deficiency, a condition rarely ~~known~~ seen in the United States. Children born without a thyroid have normal intellect if thyroid treatment starts early (Burrow et al., 1994), because the maternal thyroxine that crosses the placenta is usually sufficient to sustain the fetus (Vulsma et al., 1989; Larsen PR, 1989). During intrauterine development.

If the maternal thyroid is not blocked at an exposure of 10 mg/day, it is not surprising that an exposure of 20 ug/day is not associated with an increased rate of congenital hypothyroidism.

Conclusion:

Analysis of the county-specific rates of congenital hypothyroidism in California and Nevada reveal that the counties with perchlorated waters to not have higher rates of congenital hypothyroidism. These data appear to indicate that the levels of perchlorate found in the drinking waters of California and Nevada are not associated with an increased rate of congenital hypothyroidism.

Table 1
California Counties with Congenital Hypothyroidism Case, 1996

County	Live Births	CH Case Count	Rate/10,000	Group	Group (Hisp Adj)
Colusa	211	1	47.39	H	H
Mendocino	1,019	1	9.81	H	H
Madera	1,294	1	7.73	H	H
El Dorado	1,322	1	7.56	H	H
Monterey	6,072	4	6.59	H	H
Santa Cruz	3,500	2	5.71	H	H
Yolo	1,845	1	5.42	H	H
Marin	1,850	1	5.41	H	H
Kern	11,175	6	5.37	H	H
Stanislaus	7,864	4	5.09	H	H
Shasta	2,079	1	4.81	H	H
Tulare	6,349	3	4.73	H	H
Santa Monica	6,354	3	4.72	H	H
Sutter	2,182	1	4.58	H	H
Ventura	10,923	5	4.58	H	L
Placer	2,237	1	4.47	L	H
Imperial*	2,353	1	4.25	L	L
San Bernardino	26,336	11	4.18	L	L
Orange	50,407	21	4.17	L	L
Los Angeles	172,115	65	3.78	L	L
Sonoma	5,693	2	3.51	L	L
Santa Barbara	6,109	2	3.27	L	L
Fremont	15,621	5	3.20	L	L
Merced	3,139	1	3.19	L	L
San Diego	41,117	13	3.16	L	L
Santa Clara	30,726	9	2.93	L	L
Alameda	21,690	6	2.77	L	L
Sacramento	19,839	4	2.02	L	L
Contra Costa	10,577	2	1.89	L	L
Riverside	21,861	1	0.46	L	L
Sum of Above	493,859	179	3.62		

* Unbolded = Counties with perchlorated water

Table 2

Congenital Hypothyroidism in Nevada (1996 and 1997) by Water Source

County	Live Births	CH Cases	CH Case Rate	95% LCL	95% UCL
None-Lake Mead Sources					
Carson City	1368	1			
Churchill	739	0			
Douglas	522	0			
Elko	1491	0			
Esmeralda	15	0			
Eureka	40	0			
Humboldt	618	0			
Lander	282	0			
Lincoln	83	0			
Lyon	660	0			
Mineral	137	0			
Nye	542	0			
Pershing	154	0			
Storey	17	0			
Washoe	9381	4			
White Pine	247	0			
Sub-total	16296	5	3.07	1.00	7.17
Lake Mead Source					
Clark	36016	7	1.94	0.73	4.00
Total	52312	12	2.29	1.19	3.76

Data received from the Nevada State Health Division, Bureau of Family Health Services (May 1998)

Figure 1

California Counties with Perchlorate Detected in Water Supply

Figure 2

Counties with High Rates of Congenital Hypothyroidism, 1996

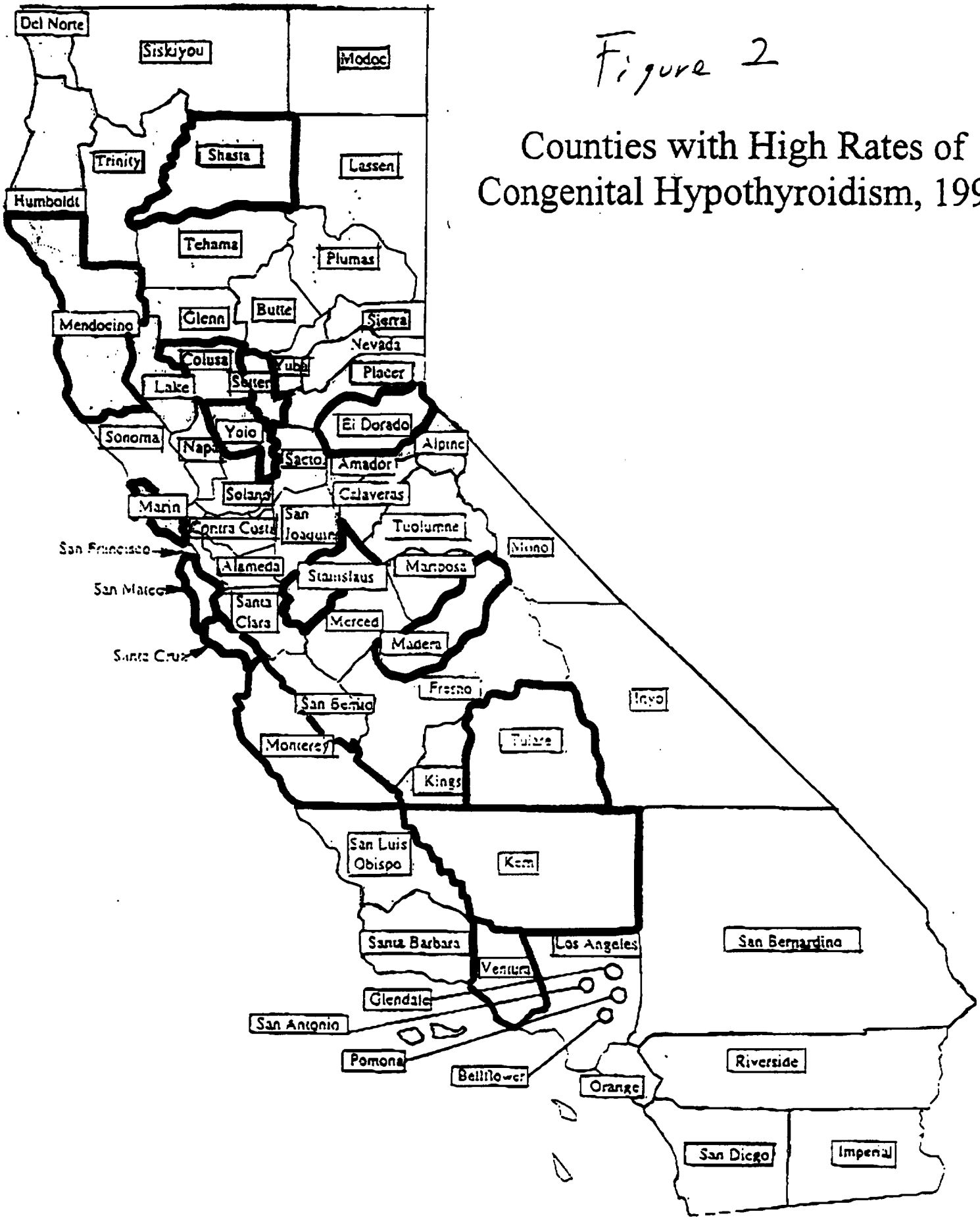
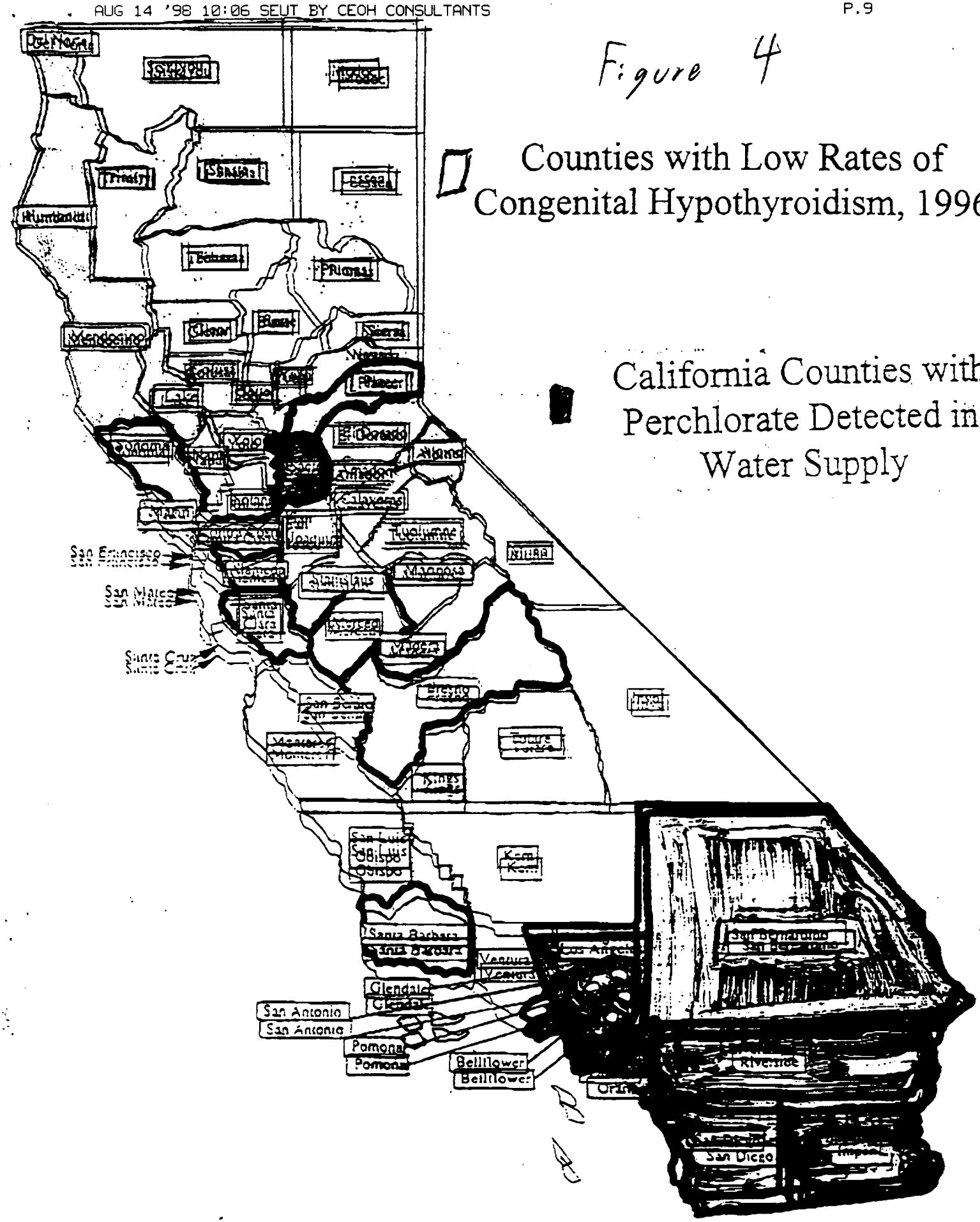


Figure 3

Counties with Low Rates of Congenital Hypothyroidism, 1996

Figure 4


Counties with Low Rates of Congenital Hypothyroidism, 1996
California Counties with Perchlorate Detected in Water Supply
San Francisco
San Mateo
Santa Cruz
San Antonio
Pomona
Bellflower
Glendale
Riverside
San Diego

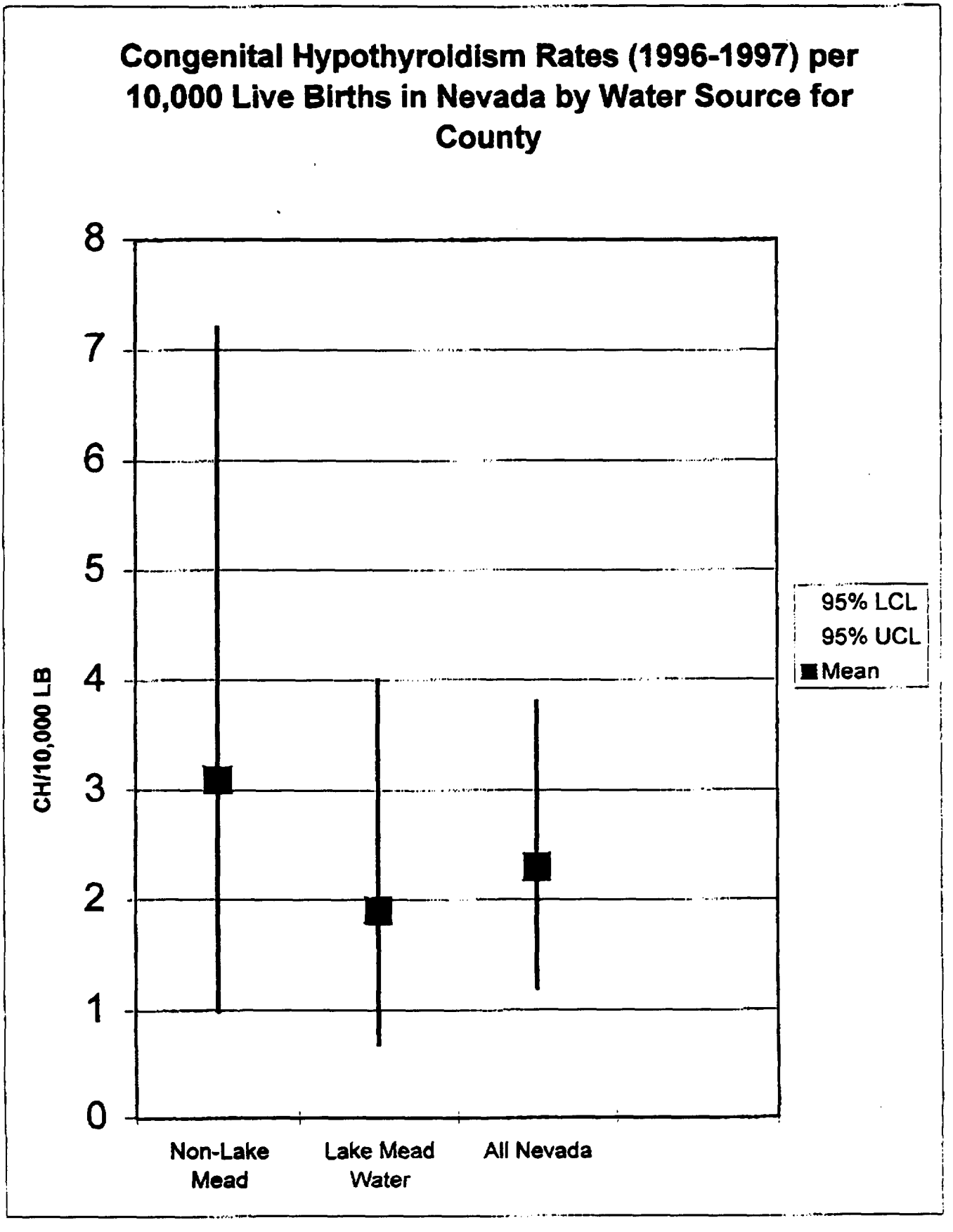



Figure 5
Congenital Hypothyroidism Rates in Nevada by water Source