

Perchlorate

Perchlorate is a naturally occurring and man-made chemical that is used to manufacture fireworks, explosives, flares, and rocket fuel.^{1,2} It is found naturally in groundwater and soils throughout many regions in the United States and other arid regions of the world.^{3,4} Perchlorate is presumed to migrate into groundwater during the process of irrigation,⁵ and has also been found in groundwater supplies near military and industrial facilities where perchlorate was used.⁶ Perchlorate has been detected in surface water; dairy products; and in some food crops, including lettuce, spinach, grapes, carrots, tomatoes, and other fruits and vegetables, produced in the United States and internationally.^{5,7-12} Perchlorate has been detected in some fertilizers produced in Chile; however, fertilizers appear to be a negligible source of perchlorate in the United States.^{1,13-17} The numerous sources of perchlorate located across the United States result in widespread exposures of perchlorate to the U.S. population.^{3,4}

Perchlorate has been detected in human breast milk, urine, blood, amniotic fluid, and saliva.¹⁸⁻²³ A national study representative of the U.S. population ages 6 years and older found perchlorate in the urine of 100% of the more than 5,000 people sampled; children had higher median urinary levels compared with those of adults, including women of child-bearing age.^{3,24} Infants are exposed to perchlorate through both breast milk and formula, but those who are fed breast milk may have higher exposures to perchlorate compared with those who are fed cow- or soy-based formula.²⁵ When comparing perchlorate doses (daily intakes per kilogram of body weight, estimated from urine samples), infants less than 2 months of age experience higher perchlorate doses compared with older infants, and estimated doses of perchlorate in infants are more than twice as high as estimated doses for adults.^{3,25,26} A study conducted in China found that blood samples of infants less than 1 year of age have higher mean perchlorate values than blood samples of both older children and adults.^{27,28}

Children might be directly exposed to perchlorate through perchlorate-contaminated water and foods containing perchlorate. Surveys conducted by the U.S. Food and Drug Administration have detected varying levels of perchlorate in many foods that may be consumed by both women and young children. The surveys, conducted in 22 states, tested 27 different types of food products and found the highest levels of perchlorate in spinach and tomatoes.¹² Some infant formulas have also been found to contain perchlorate, and the perchlorate content of the formula is increased if it is prepared with perchlorate-contaminated water.²⁹⁻³² However, computer modeling studies have concluded that exposure to perchlorate from food consumption is much greater than exposure from drinking water in the United States.^{33,34} These modeled predictions are consistent with empirical studies that attribute the majority of perchlorate intake dose in U.S. residents to food consumption.^{8,35-37}

Exposure to high doses of perchlorate has been shown to block the uptake of iodide into the thyroid gland.^{38,39} Exposure to perchlorate and other thyroid-disrupting chemicals is of particular concern for women of child-bearing age, because thyroid hormones are important

for growth and development of the central nervous system in fetuses and infants.^{1,40-42} The transfer of iodide from blood into the thyroid gland is an essential step in the synthesis of thyroid hormones that regulate how the body uses energy; influence bone growth; and influence the development of the brain, reproductive, and cardiovascular systems.⁴³ When this transfer of iodide into the thyroid gland is blocked, the thyroid may not have enough iodide to make thyroid hormones. Reduction in a woman's thyroid hormone levels during the first and second trimester puts the fetus at risk for impaired physical and mental development, with the severity of the impairment depending upon the degree of hormone deficiency.^{40,41} Moderate deficits in maternal thyroid hormone levels during early pregnancy have been linked to reduced childhood IQ scores and other neurodevelopmental effects, as well as unsuccessful or complicated pregnancies.⁴⁴ Prenatal and newborn hypothyroidism (low thyroid hormone levels) is a risk factor for intellectual disability (mental retardation) and other forms of impaired neurodevelopment.⁴⁵ In 2005–2008, approximately 38% of women ages 15 to 44 years in the United States had insufficient iodine intake,⁴⁶ potentially increasing the risk for effects on fetal development from exposure to perchlorate.¹

Associations between perchlorate exposure and thyroid hormones have been based on both epidemiological and animal-based studies. Animal studies have shown that exposure to high doses of perchlorate result in decreased thyroid hormone levels and physical alterations to the thyroid gland,¹ and have also found that these effects of perchlorate can be enhanced with exposure to other chemicals that block uptake of iodide.⁴⁷ In 2005, the National Research Council (NRC) concluded that the available epidemiological evidence concerning non-medical exposure to perchlorate did not indicate an association with thyroid disorders in adults or infants, and was inadequate for assessing the potential for adverse associations between prenatal perchlorate exposure and adverse neurodevelopmental outcomes in children.¹ The NRC also indicated that there was a lack of studies to evaluate potential effects of prenatal perchlorate exposures in infants and children, particularly in vulnerable populations.¹

Some further epidemiological research has been conducted since the NRC report was completed. A study of urinary perchlorate and thyroid hormone levels in more than 11,000 U.S. females ages 12 years and older in 2001–2002 found that increasing levels of perchlorate in urine were associated with decreased thyroid hormone levels.²⁶ Further analysis of this data set found that tobacco smoke and perchlorate may interact to affect thyroid function at commonly occurring perchlorate levels.⁴⁸ In contrast, a study of first-trimester pregnant women identified as iodine-deficient, and a long-term exposure study of women in early pregnancy and late pregnancy in Chile, found that exposure to low levels of perchlorate did not result in decreased levels of thyroid hormones.^{49,50}

Other studies have evaluated relationships between drinking water perchlorate levels and thyroid hormone levels in newborns. A study of California infants born in 1998 reported that babies born to mothers in communities with higher drinking water perchlorate levels were more likely to have elevated levels of thyroid stimulating hormone, which is an indication of reduced thyroid hormone levels.⁵¹ An earlier study of the same population and other studies

have not found associations between drinking water perchlorate levels and neonatal thyroid hormone function.^{50,52-56}

In January 2009, EPA issued an interim health advisory level to help state and local officials manage local perchlorate contamination issues in a health-protective manner, in advance of a final EPA regulatory determination.^{2,57} In February 2011, EPA decided to develop a federal drinking water standard for perchlorate, based on the concern for effects on thyroid hormones and the development and growth of fetuses, infants, and children.^{2,58} The process for developing the standard will include receiving input from key stakeholders as well as submitting any formal rule to a public comment process. California and Massachusetts have both set their own standards for perchlorate in drinking water.⁵⁹ No standards exist for perchlorate in food.

The indicator that follows uses the best nationally representative data currently available on urine perchlorate levels over time for women of child-bearing age. Indicator B13 presents median and 95th percentile urinary perchlorate levels for women ages 16 to 49 years. The indicator has been updated since the publication of *America's Children and the Environment, Third Edition* (January 2013) to include data from 2009–2014.

Indicator B13: Perchlorate in women ages 16 to 49 years: Median and 95th percentile concentrations in urine, 2001–2014

About the Indicators: Indicator B13 presents concentrations of perchlorate in urine of U.S. women ages 16 to 49 years. The data are from a national survey that collects urine specimens from a representative sample of the population every two years, and then measures the concentration of perchlorate in the urine. The indicator presents concentrations of perchlorate in urine over time. The focus on women of child-bearing age is based on concern for potential adverse effects in children born to women who have been exposed to perchlorate.

NHANES

The National Health and Nutrition Examination Survey (NHANES) provides nationally representative biomonitoring data for perchlorate. NHANES is designed to assess the health and nutritional status of the civilian noninstitutionalized U.S. population and is conducted by the National Center for Health Statistics, part of the Centers for Disease Control and Prevention (CDC). Interviews and physical examinations are conducted with approximately 10,000 people in each two-year cycle. CDC's National Center for Environmental Health measures concentrations of environmental chemicals in blood and urine samples collected from NHANES participants. Summaries of the measured values for more than 200 chemicals are provided in the *Fourth National Report on Human Exposure to Environmental Chemicals*.²⁴

Perchlorate

Indicator B13 presents urinary levels of perchlorate in women of child-bearing age. Perchlorate passes quickly through the body unchanged and is excreted in urine, with an elimination half-life on the order of hours.³ Therefore, perchlorate measured in humans is indicative of recent exposures. All values are reported as micrograms of perchlorate per liter of urine ($\mu\text{g/L}$).

Concentrations of perchlorate in urine have been measured in a representative subset of NHANES participants ages 6 years and older in 2001–2002, 2003–2004, 2009–2010, 2011–2012, and 2013–2014 and in all NHANES participants ages 6 years and older in 2005–2006 and 2007–2008.¹⁹

For 2013–2014, NHANES collected perchlorate biomonitoring data for 2,644 individuals ages 6 years and older, including 610 women ages 16 to 49 years. Perchlorate was detected in 100% of the individuals sampled in NHANES 2013–2014. The median and 95th percentile of urinary perchlorate levels for all NHANES participants in 2013–2014 were 3 $\mu\text{g/L}$ and 11 $\mu\text{g/L}$, respectively. The widespread detection of perchlorate, combined with the fact that perchlorate has a short half-life, indicates that perchlorate exposure is widespread and relatively continuous.

Individual Variability in Urinary Measurements

NHANES data for perchlorate are based on measurements made using a single urine sample for each person surveyed. Due to normal changes in an individual's urinary output throughout the day, this variability in urinary volume, among other factors related to the measurement of chemicals that do not accumulate in the body,⁶⁰ may mask differences between individuals in levels of perchlorate. Since perchlorate does not appear to accumulate in bodily tissues, the distribution of NHANES urinary perchlorate levels may over estimate high-end exposures (e.g., at the 95th percentile) as a result of collecting one-time urine samples.^{34,61,62} Many studies account for differences in hydration levels by reporting the chemical concentration per gram of creatinine. Creatinine is a byproduct of muscle metabolism that is excreted in urine at a relatively constant rate, independent of the volume of urine, and can in some circumstances partially account for the measurement variability due to changes in urinary output.⁶³ However, urinary creatinine concentrations differ significantly among different demographic groups, and are strongly associated with an individual's muscle mass, age, sex, diet, health status (specifically renal function), body mass index, and pregnancy status.^{64,65} Thus, this indicator presents the unadjusted perchlorate concentrations so that any observed differences in concentrations between demographic groups are not due to differences in creatinine excretion rates. These unadjusted urinary levels from a single sample may either over- or underestimate urinary levels for a sampled individual. However, for a representative group, it can be expected that a median value based on single samples taken throughout the day will provide a good approximation of the median for that group. Furthermore, due to the large number of subjects surveyed, we expect that differences in the concentrations of perchlorate that might be attributed to the volume of the urine sample would average out within and across the various comparison groups.

Birth Rate Adjustment

Indicator B13 uses measurements of perchlorate in urine of women ages 16 to 49 years to reflect the potential distribution of perchlorate exposures to women who are pregnant or may become pregnant. However, women of different ages have a different likelihood of giving birth. For example, in 2003–2004, women aged 27 years had a 12% annual probability of giving birth, and women aged 37 years had a 4% annual probability of giving birth.⁶⁶ A birth rate-adjusted distribution of women's perchlorate levels is used in calculating this indicator,ⁱ meaning that the data are weighted using the age-specific probability of a woman giving birth.⁶⁷

ⁱ There may be multiple ways to implement an adjustment to the data that accounts for birth rates by age. The National Center for Health Statistics has not fully evaluated the method used in ACE, or any other method intended to accomplish the same purpose, and has not used any such method in its publications. NCHS and EPA are working together to further evaluate the birth rate adjustment method used in ACE and alternative methods.

Data Presented in the Indicator

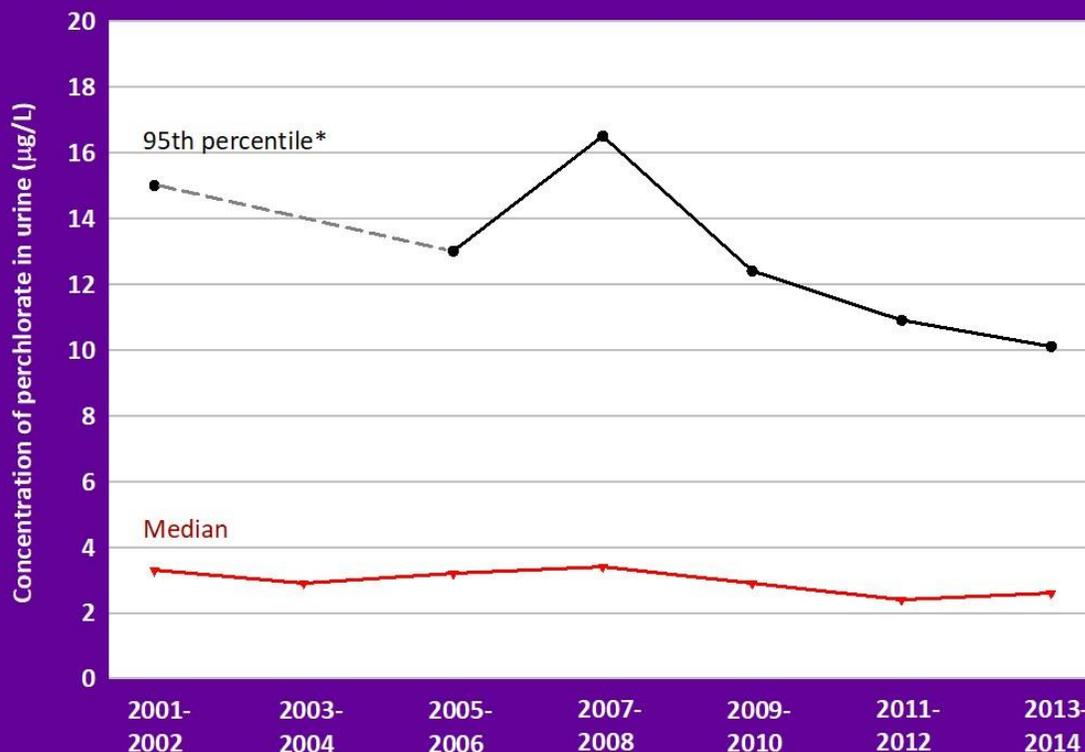
Indicator B13 presents median and 95th percentile concentrations of perchlorate in urine over time for women ages 16 to 49 years, using NHANES data from 2001–2014.

Additional information showing how the median and 95th percentile levels of perchlorate in urine vary by race/ethnicity and family income for women ages 16 to 49 years is presented in supplemental data tables for these indicators. Data tables also display information on the median and 95th percentile levels of perchlorate in urine for children ages 6 to 17 years, including how levels vary by race/ethnicity, family income, and age.

NHANES does not collect urine samples from children less than 6 years of age, and thus cannot assess the exposure of infants, who may be exposed to unhealthy levels of perchlorate due to the presence of perchlorate in breast milk and some infant formula.^{18,20,21,31,32}

Please see the Introduction to the Biomonitoring section for an explanation of the terms “median” and “95th percentile,” a description of the race/ethnicity and income groups used in the ACE3 biomonitoring indicators, and information on the statistical significance testing applied to these indicators.

Perchlorate in women ages 16 to 49 years: Median and 95th percentile concentrations in urine, 2001-2014



Data: Centers for Disease Control and Prevention, National Center for Health Statistics and National Center for Environmental Health, National Health and Nutrition Examination Survey
Note: To reflect exposures to women who are pregnant or may become pregnant, the estimates are adjusted for the probability (by age and race/ethnicity) that a woman gives birth.
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*The 95th percentile concentration for 2003-2004 is not reported because it has large uncertainty: the relative standard error, RSE, is 40% or greater (RSE = standard error divided by the estimate).

Data characterization

- Data for this indicator are obtained from an ongoing continuous survey conducted by the National Center for Health Statistics.
- Survey data are representative of the U.S. civilian noninstitutionalized population.
- Perchlorate is measured in urine samples obtained from individual survey participants.

- From 2001–2002 to 2007–2008, the median level of perchlorate in urine among women ages 16 to 49 years was 3 µg/L with little variation over time. From 2008–2008 to 2013–2014, the median level decreased from 3.4 to 2.6 µg/L.
 - The decreasing trend from 2001–2002 to 2013–2014 was statistically significant.

- From 2001–2002 to 2007–2008, the 95th percentile perchlorate levels among women ages 16 to 49 years varied between 13 and 17 µg/L. From 2007–2008 to 2013–2014, the 95th percentile level decreased from 17 to 10 µg/L.
 - The decreasing trend from 2001–2002 to 2013–2014 was statistically significant.
- In 2011–2014, there was little variation in median or 95th percentile perchlorate levels by race/ethnicity or income among women ages 16 to 49 years. (See Tables B13a and B13b.)
- From 2001–2002 to 2007–2008, the median level of perchlorate among children ages 6 to 17 years was 5 µg/L with little variation over time. From 2007–2008 to 2013–2014, the median level decreased from 5 to 3 µg/L. (See Table B13c.)
 - The decreasing trend from 2001–2002 to 2013–2014 was statistically significant.
- The 95th percentile perchlorate level among children increased from 15 µg/L in 2001–2002 to 19 µg/L in 2007–2008. From 2007–2008 to 2013–2014, the median level decreased from 5 to 3 µg/L. (See Table B13c.)
 - The decreasing trend from 2001–2002 to 2013–2014 was statistically significant after accounting for differences in sex, race/ethnicity, and income.
- The median perchlorate level among children ages 6 to 17 years was about 46% higher than the level found in women of childbearing age in 2011–2014, while the 95th percentile level among children ages 6 to 17 years was about 21% higher than in women of childbearing age. (See Tables B13a, B13b, B13d, and B13e.)
- Differences in urinary perchlorate levels by race/ethnicity and income among children ages 6 to 17 years were relatively limited. (See Tables B13d and B13e.)
- The median and 95th percentile urinary perchlorate levels were highest for young children ages 6 to 10 years and lowest for older children ages 16 to 17 years. (See Table B13f.)
 - The age group differences were statistically significant for the median, and were statistically significant for the 95th percentile after accounting for differences in sex, race/ethnicity, and income.

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