

Foetal growth and duration of gestation relative to water chlorination

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Abstract

Objective—To assess the effect of exposure to chlorination byproducts during pregnancy on foetal growth and duration of pregnancy.

Methods—A population based study was conducted of 137 145 Norwegian children born alive in 1993–5. Information was obtained from the Norwegian medical birth registry, waterwork registry, and social science data service. The outcomes of interest were birth weight, low birth weight (<2500 g), small for gestational age, and preterm delivery (gestational age <37 weeks). The exposure assessment was based on quality of drinking water in the municipality where the mother lived during pregnancy. Municipal exposure was calculated with information on chlorination and the amount of natural organic matter in raw water measured as colour in mg precipitate/l. The main exposure category was high colour and chlorination, which was contrasted with the reference category of low colour and no chlorination.

Results—In logistic regression analysis adjusting for confounding, the risks of low birth weight (odds ratio (OR) 0.97, 95% confidence interval (95% CI) 0.89 to 1.06) and small for gestational age (OR 1.00, 95% CI 0.91 to 1.10) were not related to exposure. Contrary to the hypothesis, the risk of preterm delivery was slightly lower among the exposed than the reference category (OR 0.91, 95% CI 0.84 to 0.99). The risks of the studied outcomes were similar in newborn infants exposed to high colour drinking water without chlorination and chlorinated drinking water with low colour compared with the reference category.

Conclusions—The present study did not provide evidence that prenatal exposure to chlorination byproducts at the relatively low concentrations encountered in Norwegian drinking water increases the risk of the studied outcomes.

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Keywords: water chlorination; foetal growth; gestational age

Chlorination is the oldest and most widely used method of water disinfection, and the practice of chlorination has had a tremendous impact in reducing water borne infections. It has been known since the 1970s that chlorination of raw water containing natural organic matter produces organochlorine byproducts—such as chloroform—several of which are

experimental carcinogens.^{1,2} Epidemiological studies have provided increasing evidence of carcinogenic effects of chlorinated water.^{2,3} The main cancer sites have been the bladder, colon, and kidney.^{3,4} Reproductive outcomes have received less attention.⁵⁻¹⁴ Six previous studies assessed the effect of chlorination byproducts on the risk of low birth weight and preterm delivery,^{5,7,8,10,11,14} and three studied the effect on the risk of being small for gestational age.^{5,7,11} Nieuwenhuijsen *et al*¹⁵ concluded in their recent review that toxicological and epidemiological evidence point towards an association between trihalomethanes, as an indicator of total disinfection byproduct load, and low birth weight, although the evidence is not conclusive. They found no evidence for an association between trihalomethanes and preterm delivery.

We conducted a registry based study in Norway to assess measures of foetal growth and preterm delivery relative to the content of natural organic matter in water and to chlorination in municipal waterworks in the mother's place of residence, applying a similar approach as in our recent study of birth defects as outcomes of interest.¹³

Methods

STUDY POPULATION

The source population comprised all 181 361 newborn infants registered by the Norwegian birth registry 1993–5. This registry has collected complete information on practically all the births in Norway and it maintains careful quality control procedures.¹⁶ We applied the following exclusion criteria: (a) no information on chlorination or natural organic matter content of water from any of the municipal waterworks at the mother's place of residence (40 284 newborn infants excluded); (b) one or more congenital birth defects (2608 excluded); and (c) no information on birth weight in the birth registry (1324 excluded). The study population comprised 137 145 live newborn infants. Gestational age was available for 123 747 (90.2% of the study population).

HEALTH OUTCOMES

The primary health outcomes were foetal growth and preterm delivery. We obtained information on birth weight, gestational age, and some potential confounders from The Norwegian medical birth registry, which is based on forms filled in during the child's first week of life, after examination of the child by a physician, most often a paediatrician. The gestational age is assessed by ultrasound examination on the 12–16th gestational week in most of the pregnancies. We used three different measures of foetal growth: birth weight (g),

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Table 1 Characteristics of the study population (n=137145) according to the categories of exposure, Norway, 1993–5

Characteristic	Exposure category				Total n (%)
	No chlorination low colour n (%)	No chlorination high colour n (%)	Chlorination low colour n (%)	Chlorination high colour n (%)	
Total	19480 (100)	11836 (100)	34063 (100)	71766 (100)	137145 (100)
Maternal age:					
<20	575 (3.0)	415 (3.5)	774 (2.3)	1470 (2.0)	3234 (2.4)
20–34	16371 (84.0)	9989 (84.4)	28731 (84.3)	60486 (84.3)	115577 (84.3)
≥35	2534 (13.0)	1432 (12.1)	4558 (13.4)	9810 (13.7)	18334 (13.4)
Parity:*					
0	7232 (37.5)	4164 (35.6)	13571 (40.1)	31033 (43.5)	56000 (41.1)
1	6746 (35.0)	4076 (34.8)	12655 (37.4)	25456 (35.7)	48933 (35.9)
2	3662 (19.0)	2467 (21.1)	5682 (16.8)	10846 (15.2)	22657 (16.6)
3–	1630 (8.5)	995 (8.5)	1921 (5.7)	4029 (5.6)	8575 (6.3)
Born in university clinic:					
No	19317 (99.2)	11146 (94.2)	32143 (94.4)	51711 (72.1)	114317 (83.4)
Yes	163 (0.8)	690 (5.8)	1920 (5.6)	20055 (27.9)	22828 (16.6)
Centrality:					
Low	14734 (75.6)	7547 (63.8)	11386 (33.4)	11732 (16.3)	45399 (33.1)
Medium	3922 (20.1)	958 (8.1)	10240 (30.1)	17497 (24.4)	32617 (23.8)
High	824 (4.2)	3331 (28.2)	12437 (36.5)	42537 (59.3)	59129 (43.1)
Population density (urban/total population(%)):					
<20	2557 (13.1)	2193 (18.5)	682 (2.0)	1702 (2.4)	7134 (5.2)
20–39.9	3783 (19.4)	3249 (27.5)	1778 (5.2)	3911 (5.4)	12721 (9.3)
40–59.9	5456 (28.0)	2994 (25.3)	5923 (17.4)	5481 (7.6)	19854 (14.5)
60–79.9	6081 (31.2)	2359 (19.9)	7050 (20.7)	13869 (19.3)	29359 (21.4)
80–	1603 (8.2)	1041 (8.8)	18630 (54.7)	46803 (65.2)	68077 (49.6)
Industrial profile:					
Low	494 (2.5)	610 (5.2)	108 (0.3)	421 (0.6)	1633 (1.2)
Medium	2025 (10.4)	985 (8.3)	2061 (6.1)	768 (1.1)	5839 (4.3)
High	16961 (87.1)	10241 (86.5)	31894 (93.6)	70577 (98.3)	129673 (94.6)

*Missing information 980.

low birth weight (<2500 g), and small for gestational age. Small for gestational age was defined as birth weight equal to or less than the 10th percentile, which was calculated from the present study population using 10 day intervals of gestational age. The preterm delivery was defined as gestational age less than 37 weeks.

EXPOSURE ASSESSMENT

Assessment of exposure was based on municipal water quality information on chlorination and natural organic matter content of raw water, and mothers' place of residence during pregnancy. A total of 233 waterworks in Norway, serving about 2.7 million people chlorinate their waters, and 1084 waterworks serving about 1.0 million people do not use chlorination. Exposure to chlorination byproducts through tap water takes place in areas where the waterworks chlorinate water with high levels of natural organic matter. Accordingly, we divided waterworks by the use of chlorination disinfection and used water colour in mg precipitate/l as a quantitative measure of the dissolved organic carbon. Water colour is highly correlated with the content of dissolved organic carbon ($r=0.82$, $n=634$).¹⁷ The colour number is recorded routinely in most of the waterworks. We calculated the weighted mean colour for each municipality with the fraction of population served by each waterwork as the weighting factor. We constructed four exposure categories on the basis of chlorination in the municipality (no or yes in one or more of the waterworks) and weighted mean colour (low <10 mg precipitate/l; high ≥10 mg precipitate/l). Chlorination combined with high colour represented the hypothesised exposure to chlorination byproducts and no chlorination combined with low colour represented the reference category. The mean colour for waterworks

that use surface water sources is 15 mg precipitate/l and 18% of the population served by such waterworks receive water with mean colour value below the cut off point of 10 mg precipitate/l used in the analyses.

COVARIATES

Information on maternal age, parity, and the place of birth were obtained from the routine birth registry data. We received municipal data from the Norwegian social science data services, which were used to construct three covariates. "Centrality" indicates the municipality's urbanity and geographical placement relative to a regional centre. In the present analyses, we used this variable divided into three categories, low (municipalities with urban centres up to 15 000 inhabitants), medium (urban areas up to 50 000 inhabitants), and high (includes a regional centre). "Population density" is a measure of the proportion of urban population in the municipality. We used the following categories: <20%; 20%–39.9%; 40%–59.9%, 60%–79.9% and 80% or more. "Industrial profile" describes the relative distribution of trades in the municipality.

STATISTICAL METHODS

We estimated the prevalence (%) of the dichotomous reproductive outcomes with 95% confidence intervals (95% CIs) based on the binomial distribution, and the mean of birth weight with 95% CIs based on the normal distribution. We compared the risks of adverse birth outcomes and mean birth weight between three exposure categories (chlorination and high colour; chlorination and low colour; no chlorination and high colour) and the reference category (no chlorination and low colour). We carried out bivariate analyses of the relations

Table 2 Measures of birth weight and gestational age by population chlorination proportion, color, maternal age, parity, place of birth, centrality, population density and industrial profile in Norway 1993–95

Determinant	n	Birth weight (g) mean (95% CI)	Low birth weight (<2500 g) prevalence (95% CI)	Small for gestational age prevalence (95% CI)	Preterm delivery (<37 weeks) prevalence (95% CI)
Total	137145	3537 (3534 to 3540)			
Exposure category:					
No chlorination, low colour	19480	3544 (3535 to 3552)	4.5 (4.24 to 4.83)	4.5 (4.18 to 4.76)	6.7 (6.37 to 7.11)
No chlorination, high colour	11836	3573 (3562 to 3584)	4.4 (4.02 to 4.75)	4.3 (3.89 to 4.61)	6.0 (5.58 to 6.50)
Chlorination, low colour	34063	3546 (3540 to 3552)	4.5 (4.32 to 4.76)	4.5 (4.24 to 4.68)	6.4 (6.17 to 6.72)
Chlorination, high colour	71766	3525 (3521 to 3530)	4.7 (4.52 to 4.83)	4.6 (4.41 to 4.72)	6.4 (6.19 to 6.56)
Maternal age:					
<20	3234	3437 (3417 to 3458)	5.8 (5.00 to 6.59)	5.7 (4.86 to 6.46)	8.8 (7.70 to 9.82)
20–34	115577	3540 (3536 to 3543)	4.4 (4.25 to 4.49)	4.3 (4.16 to 4.39)	6.1 (5.96 to 6.25)
≥35	18334	3540 (3530 to 3549)	5.8 (5.49 to 6.16)	5.7 (5.39 to 6.06)	7.9 (7.53 to 8.35)
Parity*					
0	56000	3447 (3442 to 3452)	5.8 (5.64 to 6.03)	5.7 (5.52 to 5.90)	7.5 (7.24 to 7.70)
1	48933	3590 (3585 to 3596)	3.6 (3.40 to 3.73)	3.5 (3.34 to 3.66)	5.4 (5.20 to 5.61)
2	22657	3622 (3614 to 3630)	3.7 (3.44 to 3.94)	3.6 (3.35 to 3.84)	5.8 (5.47 to 6.11)
≥3	8575	3600 (3586 to 3614)	4.7 (4.22 to 5.11)	4.6 (4.15 to 5.04)	7.0 (6.37 to 7.51)
Born in university clinic:					
No	114317	3546 (3543 to 3550)	4.5 (4.33 to 4.57)	4.4 (4.24 to 4.48)	6.3 (6.15 to 6.44)
Yes	22828	3492 (3484 to 3500)	5.3 (5.03 to 5.61)	5.2 (4.90 to 5.47)	7.0 (6.66 to 7.35)
Centrality:					
Low	45399	3548 (3543 to 3554)	4.4 (4.26 to 4.64)	4.4 (4.17 to 4.55)	6.4 (6.14 to 6.62)
Medium	32617	3539 (3533 to 3546)	4.7 (4.50 to 4.96)	4.6 (4.41 to 4.86)	6.4 (6.16 to 6.73)
High	59129	3528 (3523 to 3532)	4.6 (4.46 to 4.80)	4.5 (4.36 to 4.70)	6.4 (6.22 to 6.63)
Population density (urban/total population (%)):					
<20	7134	3567 (3552 to 3581)	4.5 (4.01 to 5.00)	4.4 (3.93 to 4.88)	6.6 (5.94 to 7.16)
20–39.9	12721	3571 (3561 to 3582)	4.1 (3.77 to 4.47)	4.1 (3.73 to 4.42)	5.7 (5.26 to 6.11)
40–59.9	19854	3557 (3548 to 3565)	4.4 (4.11 to 4.68)	4.3 (4.01 to 4.58)	6.6 (6.23 to 6.96)
60–79.9	29359	3540 (3532 to 3546)	4.7 (4.41 to 4.89)	4.6 (4.32 to 4.80)	6.4 (6.12 to 6.72)
≥80	68077	3521 (3517 to 3526)	4.7 (4.57 to 4.89)	4.6 (4.46 to 4.78)	6.5 (6.29 to 6.68)
Industrial profile:					
Low	1633	3565 (3536 to 3594)	4.0 (3.03 to 4.93)	3.8 (2.87 to 4.73)	7.5 (6.21 to 8.89)
Medium	5839	3552 (3536 to 3568)	4.4 (3.88 to 4.93)	4.3 (3.80 to 4.80)	6.1 (5.42 to 6.71)
High	129673	3536 (3533 to 3540)	4.6 (4.50 to 4.73)	4.5 (4.40 to 4.63)	6.4 (6.28 to 6.56)

*Missing information 980.

between the outcomes and exposures of interest. We used logistic regression to estimate adjusted odds ratios (ORs) for dichotomous outcomes, and linear regression to estimate the relations between exposure and birth weight. We included in the model all the potential determinants of the outcomes including maternal characteristics such as age and parity, the child's place of birth in the three university clinics located in the three largest cities in Norway (yes or no), and municipal indicators of socioeconomic level—such as centrality, population density, and industrial profile—of the municipality where the mother lived during pregnancy. To elaborate residual confounding, we studied the impact of each covariate by comparing measures of effect from models with and without the covariate of interest. We fitted models with different combinations of covariates. We also compared the measures of effect within different categories to show residual confounding and to elaborate effect modification. In the results section, we present systematically the risk estimates from the full model, because they provide the most valid or least confounded estimates.

Results

COMPARISON OF EXPOSED AND UNEXPOSED

Table 1 shows the study population according to the exposure categories. The municipalities with chlorination and high colour were more central, had a higher population density, and a larger proportion of mothers using the three university clinics compared with the reference category. The mean birth weight and the prevalence for low birth weight, small for gestational age, and preterm delivery are

presented in the main categories of water quality and covariates in table 2.

LOW BIRTH WEIGHT

Among the total of 137 145 newborn infants, we identified 6249 (4.6%) with birth weight below 2500 g. Table 2 shows the mean birth weight and the prevalence of the other outcomes by exposure and the other covariates. The mean birth weight in the chlorination and high colour exposure category (3525 g) was slightly lower than in the reference category (3544 g). We estimated the effect of exposure to chlorinated humic water on birth weight in linear regression analysis controlling for maternal age, parity, place of birth, centrality, industrial profile, and population density. The birth weight in the chlorination and high colour category was estimated as 4 g (95% CI -7.7 to 14.6) greater than in the reference category. The corresponding differences were 20 g (95% CI 6.2 to 34.2) for the no chlorination and high colour category, and 12 g (95% CI 0.3 to 33.3) for the chlorination and low colour category.

The adjusted OR of low birth weight contrasting chlorination and high colour with the reference category was 0.97 (0.89 to 1.06). The risk of low birth weight was related to neither the high chlorination nor high colour alone (table 3).

SMALL FOR GESTATIONAL AGE

Both birth weight and gestational age, needed for the calculation of being small for gestational age, were available for 123 747 newborn infants. As shown in table 3, the risk of small for gestational age was not related to exposure to chlorinated humic water (adjusted OR 1.00, 95% CI 0.91 to 1.10), unchlorinated water

Table 3 Water chlorination and risk of adverse reproductive outcomes in Norway 1993–5

Exposure category	Low birth weight (<2500 g) n=137145 OR* (95% CI)	Small for gestational age n=123747 OR* (95% CI)	Preterm delivery (<37 weeks) n=123747 OR* (95% CI)
No chlorination, low colour	1.00	1.00	1.00
No chlorination, high colour	1.02 (0.91 to 1.14)	1.02 (0.89 to 1.14)	0.92 (0.83 to 1.03)
Chlorination, low colour	0.99 (0.90 to 1.09)	1.00 (0.91 to 1.11)	0.95 (0.88 to 1.03)
Chlorination, high colour	0.97 (0.89 to 1.06)	1.00 (0.91 to 1.10)	0.91 (0.84 to 0.99)

*Logistic regression analysis adjusting for maternal age and parity, the child's place of birth, centrality, population density, and industrial profile of the municipality where the mother lived during pregnancy.

with high colour (OR 1.02, 95% CI 0.89 to 1.14) or chlorinated water with low colour (OR 1.00, 95% CI 0.91 to 1.11).

PRETERM DELIVERY

There were 7886 (6.4%) preterm deliveries in the study population. In the logistic regression models, we found no increase in the risk of preterm delivery related to exposure to chlorinated high colour tap water (table 3). Contrary to our hypothesis, the risk of preterm delivery was lower among the exposed population than in the reference category (adjusted OR 0.91, 95% CI 0.84 to 0.99). The risks were slightly reduced also in no chlorination high colour (OR 0.92, 95% CI 0.83 to 1.03) and chlorination, low colour categories (OR 0.95, 95% CI 0.88 to 1.03), although upper confidence limits were above unity.

Discussion

In this Norwegian study, we found no association between foetal growth and exposure to chlorinated surface water containing natural organic matter during pregnancy. The risk of preterm delivery was slightly lower in the exposed than in the reference group, which was contrary to our initial hypothesis.

VALIDITY OF RESULTS

Definition of relevant disinfection byproducts and assessment of exposure to these compounds represents a challenge for studies on effects on health, as recently discussed by Swan and Waller.¹⁸ Exposure to chlorinated water containing natural organic matter may result in complex mixtures with many potential causes of adverse reproductive effects. Exposure to a single component may be a contributor to adverse pregnancy outcomes, but at the same time it is likely to be an indicator of exposure to several other causal agents. A substantial variation in concentrations of byproducts over time adds another dimension of complexity.

Five of the six previous studies based their exposure assessment on measured concentrations of trihalomethane in municipal water and maternal residential address.^{5 7 8 10 11 14} Also, Gallagher *et al*¹⁰ applied hydraulic modelling and Dodds *et al*¹¹ modelled information from three sources to estimate residential specific concentrations. Savitz *et al*⁸ incorporated information on consumption of tap water during pregnancy to improve the individual exposure estimates.

We were not able to use concentrations of trihalomethane, which limits the comparability of the present and previous results. Although

total trihalomethanes are commonly used in monitoring disinfection byproducts, they may not be the main causes of the studied outcomes. Animal toxicological studies suggest that several different disinfection byproducts may cause reproductive effects including dichloroacetic acid,¹⁹ trichloroacetic acid,²⁰ dichloroacetonitrile,²¹ and trichloroacetonitrile.^{20 22} With total trihalomethanes as an indicator of exposure, it is difficult to separate the effects of chlorination byproducts from the effects of organic substances with higher molecular weight, because concentrations of organic compounds, some of which serve as precursors of chlorination byproducts, are likely to be related to concentrations of total trihalomethanes. Presence of natural organic matter may also be related to other chemical compounds with teratogenic effects, such as methylmercury and polychlorinated biphenyls. Control of this potential confounding would require information on many different chemicals. The concentrations of these potential confounders may vary according to geographic region and time. Assessment of time specific and individual exposure would not resolve this problem. A more feasible solution would be a study design, in which a comparison is made between exposure to chlorinated surface water and similar (preferably identical) unchlorinated surface waters. Unlike previous study areas in the United States and Canada, Norwegian waterworks commonly distribute unchlorinated surface water with a relatively high content of natural organic matter and at the same time some municipalities chlorinate source water with a low content of organic matter. This unusual setting made it possible to assess the effect of organic matter independent from the effect of chlorination as well as to assess the effect of chlorination in waters with both high and low content of organic matter.

We had no information on the individual amounts or sources of water consumed by women, which decreased the accuracy of exposure assessment. Alcohol consumption and cigarette smoking, particularly after the 28th week of gestation, are well established causes of reduction in foetal growth. We were not able to take into account these important determinants of reproductive outcomes. However, we do not have any reason to think that on an individual level chlorination and natural organic matter were associated with either smoking or drinking. Adjustment for centrality, population density, and industrial profile adjusted indirectly for regional differences in these behavioural factors. Registry linkage provided information on several potential municipal confounders, which were taken into account in the data analysis.

SYNTHESIS WITH PREVIOUS KNOWLEDGE

The observed lower risk of preterm delivery in the exposed groups was contrary to our original hypothesis. A possible explanation for this finding is that residual chlorine in chlorinated water lowers the risk of preterm delivery by preventing maternal infections during pregnancy. However, the five previous studies

Table 4 Summary of the results from the previous and present study

	Iowa	New Jersey	North Carolina	Colorado	Nova Scotia	Taiwan	Norway
Type of study	Case control, population based	Cross sectional, population based, 80938 infants	Case control, population based	Cross sectional, population based, 1244 infants	Cross sectional, population based, 50755 infants	Cross sectional, population based, 18025 infants	Cross sectional, population based, 137145 infants
Study population	159 Low birth weight 795 Controls 187 Small for gestational age 935 Controls 342 Preterm 1710 Controls	1853 Low birth weight 4082 Small for gestational age 7167 Preterm	178 Low birth weight 244 Preterm	72 Low birth weight 68 Preterm 333 Controls	2382 Low birth weight 4673 Small for gestational age 2659 Preterm	456 Low birth weight 719 Preterm	6249 Low birth weight 5372 Small for gestational age 7886 Preterm
Exposure-outcome relations (OR (95% CI)):							
Low birth weight	1.3 (0.8-2.2)	1.42 (0.90-2.20)	1.3 (0.8-2.1)*	2.1 (1.0-4.8) 1.5 (0.8-3.0)*	1.04 (0.92-1.18)*	0.90 (0.75-1.09)†	0.97 (0.89-1.06)
Small for gestational age	1.8 (1.1-2.9)	1.50 (1.14-1.94)	NA	5.9 (2.0-17.0)*†	1.08 (0.99-1.18)*	NA	1.00 (0.91-1.10)
Preterm delivery	1.1 (0.7-1.6)	NS	0.9 (0.6-1.5)*	1.0 (0.3-2.8)	0.97 (0.87-1.09)	1.34 (1.11-1.62)	0.91 (0.84-0.99)

*Contrast between the highest exposure and reference category.

†Only term births included.

provided inconsistent results (table 4). Studies from Iowa,⁵ North Carolina,⁸ Colorado,¹⁰ and Nova Scotia¹¹ reported risk estimates close to unity. The most recent study, from Taiwan, reported an increased risk (OR (95% CI) 1.31 (1.11 to 1.62)) related to maternal place of residence in a community with chlorinated drinking water.¹⁴ The present evidence is controversial and therefore epidemiological studies should elaborate further the relation between exposure to chlorination byproducts and duration of gestation.

The present study indicated no effect of chlorination byproducts on foetal growth, on the risk of low birth weight, or being small for gestational age. The previous risk estimates for low birth weight are heterogeneous, as shown in table 4. Population based case-control studies from Iowa⁵ and North Carolina⁸ and the two cross sectional studies from New Jersey⁷ and Colorado¹⁰ reported an increased risk, whereas the risk estimate from a study conducted in Taiwan¹⁴ indicated a decreased risk. All the four previous studies on gestational age reported increased ORs varying from 1.08 to 5.9.

The inconsistency of the findings could be related to both qualitative and quantitative differences in exposure between the compared studies. Although chlorination was the common method of disinfection, the proportion of individual chlorination byproducts may vary between the geographic regions due to differences in the raw water quality including the character of the organic compounds in the source water, which are important precursors of the chlorination byproducts. In the Iowa study, concentrations of four trihalomethanes—chloroform, bromodichloromethane, dibromochloromethane, and bromoform—from a municipal water quality survey were used as measures of exposure.⁵ Intrauterine growth retardation was related to chloroform concentrations above 10 µg/l. The relation was consistent both in shallow and deep sources of water, which was thought to argue against confounding due to pesticides or other contaminants known to vary by the depth of the water source. In the New Jersey, Colorado, and Nova Scotia studies concentrations of total trihalomethane were used as a measure of exposure and the effects of rather similar exposures were inconsistent. This points towards qualitative differences in the complex mixture. A study of 21 waterworks that use chlorination describes the levels of exposure in Norway.²³ The mean concentration of total trihalomethanes was 9.4 µg/l and the mean for halogenated acetic acids was 14.6 µg/l, clearly lower than concentrations reported in the United States.^{5-10 18} and Canadian¹¹ drinking water sources, although the average colour was 22 mg precipitate/l for these selected Norwegian waterworks.

Conclusion

In summary, our study indicates that the present practices of chlorination of Norwegian surface waters does not increase the risk of low birth weight, small for gestational age, or preterm delivery. The current body of evidence

including the present and five previous studies indicates little effect on the risk of preterm delivery. The studies of foetal growth are inconsistent, probably partly due to qualitative geographic differences in natural organic matter and lower concentrations of chlorination byproducts in Norwegian drinking waters compared with the United States and Canadian drinking waters.

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Vancouver style

All manuscripts submitted to *Occup Environ Med* should conform to the uniform requirements for manuscripts submitted to biomedical journals (known as the Vancouver style.)

Occup Environ Med, together with many other international biomedical journals, has agreed to accept articles prepared in accordance with the Vancouver style. The style (described in full in the *JAMA*[1]) is intended to standardise requirements for authors, and is the same as in this issue.

References should be numbered consecutively in the order in which they are first mentioned in the text by Arabic numerals on the line in square brackets on each occasion the reference is cited (Manson[1] confirmed other reports[2][3][4][5]). In future references to papers submitted to *Occup Environ Med* should include: the names of all

authors if there are three or less or, if there are more, the first three followed by *et al*; the title of journal articles or book chapters; the titles of journals abbreviated according to the style of *Index Medicus*; and the first and final page numbers of the article or chapter. Titles not in *Index Medicus* should be given in full.

Examples of common forms of references are:

- 1 International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomed journals. *JAMA* 1993;269:2282-6.
- 2 Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *N Engl J Med* 1976;294:687-90.
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