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**Low propotion of male births and low birthweight of sons of flour mill
worker fathers**

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Review

ABSTRACT

BACKGROUND: The Washington State Department of Health has collected and coded parental occupation information on birth certificates since 1980. We used these data to search for possible effects of parental occupational exposures on birth outcomes.

METHODS: We tabulated sex ratio, birth weight, and proportions of multiple births, still births, and malformations by mothers' and fathers' occupations.

RESULTS: There were 59 births (22 boys and 37 girls) where the father's occupation was specified as flour mill worker. The sex ratio of 0.373 (95% confidence interval (CI): 0.261-0.500) was lower than the mean sex ratio of 0.512. The mean birth weight for flour mill workers' boy babies was 3,180 grams (95% CI: 2,971-3,389), compared to an overall mean of 3,511 grams for all boy babies. The mean birth weight of flour mill workers' girl babies was 3,602 (95% CI: 3,380-3,824), compared to an overall mean of 3,389 for all girl babies.

CONCLUSION: The low prevalence of male infants born to fathers of flour mill workers in Washington State suggests that fumigants that they are exposed to are causing testicular dysfunction. The lower birth weight seen in the male infants of flour mill fathers is unprecedented and may be another genotoxic endpoint.

KEY WORDS: Sex ratio, birth weight, flour mill workers, fumigants genotoxicity

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2 INTRODUCTION: : Since the reappearance of the parental occupation item on the
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4 Washington State birth record in 1980, mothers' and fathers' occupation as stated on the
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6 birth certificate have been coded using a modification of the US Census Bureau code (1).
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8 The file now includes 1,731,590 live births and 10,219 stillbirths occurring to
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10 Washington residents during the years 1980-2002. An analysis of this file was done in
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12 1987 and a report submitted to the US National Institute for Occupational Safety and
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14 Health in fulfillment of a contract (Order Number 87-12500). The report has never been
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16 published, but a low sex ratio in births to carbon setter fathers who worked in aluminum
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18 reduction plants (2) and a low prevalence of twin births in fathers working in occupations
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20 with known carcinogenic exposures (3) have been reported. Fathers who are divers and
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22 high-performance pilots have been shown to sire more girls than boys (4).
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25 The objective of the current study is to exploit routinely collected vital statistics
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27 data to search for possible genotoxic occupations and agents.
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31 METHODS: The parental occupational and industry statements on the birth record and
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33 the decedents' occupation and industry statements on the death record are keyed and
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35 coded with a computer program (1). At present, about 97% of death record and about
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37 96% of birth record occupational statements are coded automatically. The occupational
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39 code scheme used is available on line at <http://www3.doh.wa.gov/occmort/>.

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41 The analyses of sex ratio and birth weight included only the live births, not the fetal
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43 deaths. We computed sex ratios for each occupational class, separately for mothers'
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45 occupations and fathers' occupations. We excluded from this analysis 19 births where the
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47 sex of the baby was not recorded. We computed 95% confidence intervals (CIs) for the
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2 sex ratios by the score method (5,6). We computed the mean birth weight for each sex
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4 separately for mothers' and fathers' occupations, and computed 95% CIs with the *t*
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6 distribution (7). We also computed the proportions of malformations, multiple births, and
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8 fetal deaths for each occupation. We performed multivariate regression analysis to assess
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10 the relationship between birth weights of boy babies and father's occupation as a flour
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12 mill worker, while controlling for potential confounders.
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16 RESULTS: There were 22 sons and 37 daughters of fathers who were flour mill workers.
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18 The sex ratio of 0.373 (95% CI: 0.261-0.500) was significantly lower than the ratio of
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20 0.512 among all live births. The mean birth weight for sons of fathers who were flour
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22 mill workers was 3,180 grams (95% CI: 2,971-3,389), significantly lower than the mean
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24 of 3,511 grams for all boy babies. The mean birth weight of daughters of fathers who
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26 were flour mill workers was 3,602 (95% CI: 3,380-3,824), compared to the mean of
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28 3,389 grams for all girl babies. Nearly one quarter of the female births (9 of 37) weighed
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30 above 4,000 grams while none of the 22 males weighed above 4,000 grams (see Table 1).
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32 In the years 1980-1989 there were 46 births (15 boys and 31 girls) to flour mill worker
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34 fathers compared to 13 births (7 boys and 6 girls in the years 1990-2000).
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36 There were only three births where the mother was classified as a flour mill worker, not
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38 enough to allow for meaningful analysis. We did not see unusual rates of malformations,
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40 fetal deaths or multiple births among children whose fathers were flour mill workers.
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43 Controlling for father's social class, mother's social class, mother's smoking
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45 history, parity, gestational age, and mother's age did not appreciably affect these results.
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DISCUSSION: Flour mill workers are exposed to a number of fumigants used to kill insects in stored grain and flour. A large number of very toxic agents have been used as fumigants. These include acrylonitrile, aluminum phosphide, calcium cyanide, carbon disulfide, carbon tetrachloride, chloroform, chloropicrin., cyanogen bromide, cyanogen chloride, 1,2-dibromo-3-chloropropane, 1,3-dichloropropene, dichlorvos, ethylene dibromide, ethylene dichloride, ethylene oxide, hydrogen cyanide, magnesium phosphide, methylbromide, methylene chloride, naphthalene, para-dichlorobenzene, phosphine, propylene dichloride, propylene oxide, sulfur dioxide, sulfuryl fluoride, and 1,1,1-trichloroethane. (see: American National Standard for respiratory protection during fumigation, ANSI Z88.3-1983). Methyl bromide, one of the most commonly used flour mill fumigants is currently being phased out by EPA because of atmospheric ozone depletion. (<http://www.epa.gov/ozone/mbr/>). Phosphine, a very common flour mill fumigant, has been shown to be genotoxic in humans (8). 1,2-dibromo-3-chloropropane (DBCP) has been banned for causing testicular dysfunction, sterility, and a low prevalence of male infants (9). The low prevalence of male infants born to fathers of flour mill workers in Washington State suggests that other fumigants may be acting like DBCP. The lower birth weight seen in the male infants of flour mill fathers is unprecedented and may be another genotoxic endpoint. The low number of births in the second half of the study period may reflect mill closure, aging of a stable worker cohort, or increasing sterility. Detailed study of the exposures and reproductive performance of flour mill workers should be able to explain these findings.

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We were able to conduct the study because of the large number of birth records coded to parental occupation which are available for analysis in Washington State.

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2 Working in a flour mill is an uncommon occupation, and this analysis could not have
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4 been done without a very large file of births coded to parental occupation. Even so, there
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6 were only 59 flour mill babies in our analysis.
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For Peer Review

Table 1

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Births Reported to Flour Mill Worker Fathers by Sex and Birth Weight, Washington State Birth Records, 1980-2002.

Birth Weight (Grams)	Males		Females	
	Number	Percent	Number	Percent
< 2000	1	4.5	1	2.7
2000-2499	1	4.5	0	0
2500-2999	6	27.3	7	18.9
3000-3499	8	36.4	9	24.3
3500-3999	6	27.3	11	29.7
4000-4499	0	0	5	13.5
4500+	0	0	4	10.8
TOTAL	22	100.0	37	100.0