Consumption of Contaminated Sport Fish from Lake Ontario and Time-to-Pregnancy

New York State Angler Cohort

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Sport fish from the Great Lakes are contaminated with halogenated organics, heavy metals, and pesticides, thus serving as a route of exposure for fish-consuming populations. These contaminants are recognized reproductive toxicants in animals; few human studies are available. The purpose of this study was to assess consumption of contaminated fish in relation to time-to-pregnancy (TTP) among women in the New York State Angler Cohort. In 1993, structured telephone interviews were conducted with 2,445 of 2,977 (82%) female cohort members aged 18–40 years who stated upon enrollment in the cohort in 1991 that they were considering pregnancy over the next 3 years. Among the 1,234 women who reported being pregnant, 874 (71%) had a known TTP and comprise the study sample. After descriptive analyses, log transformations of the number of years of fish consumption (duration) and TTP were performed and entered into multiple regression models that also included other covariates. Duration of fish consumption and maternal age accounted for only a small percentage of the explained variance in TTP ($R^2 = 0.005$), even after the analysis was restricted to women who reported eating fish ($R^2 = 0.006$). All beta coefficients were positive. These preliminary findings do not support an adverse effect of contaminated fish consumption on TTP. Am J Epidemiol 1997;146:949–54.

The Great Lakes comprise 20 percent of the earth’s surface freshwater supply (1). The International Joint Commission has identified various persistent toxic substances in the Great Lakes, including organochlorines (e.g., polychlorinated biphenyls), heavy metals (e.g., methylmercury), and benzo[a]pyrene (2). Contamination of the Great Lakes with these compounds has important implications for the aquatic ecosystems and the 38 million inhabitants of the Great Lakes Basin (3).

Great Lakes fish have become contaminated with toxic substances, largely through bioaccumulation (4). This is especially true for many organochlorine compounds because of their lipophilic nature (5). Previous studies have suggested that, for humans, food is the major source of exposure to organochlorine compounds (6, 7), with fish consumption as one of the most important dietary sources (8–10).

Colburn and Clement (11) have summarized the various adverse reproductive and developmental effects observed among wildlife that inhabit the Great Lakes Basin, e.g., enhanced embryo mortality, decreased mating behaviors, and congenital anomalies. Although various environmental contaminants have been isolated in both follicular and seminal fluid of humans (12–15), little is known about the effects, if any, of these substances on reproductive processes. To date, the effect(s) of chronic, low-level exposure of environmental contaminants such as organochlorines on human fecundity and fertility remains unknown, serving as the impetus for this study. Time-to-pregnancy (TTP) was chosen as the focus of the investigation because its utility as a measure of fecundability has been demonstrated. Previous authors have used TTP both as a continuous variable to estimate fecundability (16–19) and as a dichotomous variable to assess conception delay or subfecundity (20–23). For study purposes, TTP is used in its continuous form to assess the relation of contaminated fish consumption and female fecundity.
MATERIALS AND METHODS

New York State Angler Cohort

The New York State Angler Cohort (n = 18,082) is the referent study population. Briefly, this cohort comprises 10,518 male anglers, 913 female anglers, and 6,651 spouses/partners of male anglers who responded to a mailed survey in 1991. Fishing licenses maintained by the Department of Environmental Conservation were used as the sampling frame. To be eligible for inclusion in the study, anglers had to have a fishing license, be between ages 18 and 40 years, and be residents of one of the 16 counties surrounding Lake Ontario. Lake Ontario was of particular interest since it is reported to be the most polluted of the Great Lakes (24).

Structured, self-administered questionnaires were used to elicit information on fish consumption. The questionnaire was eight pages in length and asked anglers to quantify fish consumption by species, meal frequency and amount, methods of meal preparation and cooking, and body of water where the fish were caught. Respondents were asked to check each year from 1955 to 1991 in which they consumed fish caught in Lake Ontario. Total years of fish consumption referred to the summation of all individual years. Included on the questionnaire were questions about knowledge of and beliefs about fishing advisories and a variety of other variables, such as sociodemographic characteristics, cigarette smoking, alcohol consumption, and health and reproductive histories. Male anglers were instructed to have their female partners or spouses complete the reproductive history section, which also asked about fish consumption during pregnancy. (A copy of the questionnaire is available upon request.) Anglers and their respective partners were enrolled into the cohort upon receipt of completed questionnaires. A more complete description of the cohort is provided elsewhere (25).

Study design and sample

A cross-sectional design was used to query 2,977 (40 percent) female members (anglers and spouses/partners of male anglers) of the cohort who stated upon enrollment in 1991 that they were planning a pregnancy or were undecided about becoming pregnant in the next 3 years. Eighty-two percent (n = 2,445) of the eligible women were successfully located and interviewed in 1993.

Data collection

Information regarding species-specific Lake Ontario fish consumption was obtained from the detailed baseline questionnaire completed in 1991 by all women. Fish consumption was quantified by duration (in years) and recent frequency (number of fish meals per month in 1991). A standardized telephone interview was designed to elicit additional information on women's gynecologic health status and to update reproductive histories from the time of enrollment into the angler cohort. TTP was asked in 1993 in a manner similar to the short questionnaire method proposed by Baird et al. (26). Women with more than one pregnancy in the time period of interest were asked about their most recent pregnancy. Specifically, women were asked: Did you stop using birth control to become pregnant (yes/no)? Were you doing anything (at all) to prevent pregnancy at the time you most recently got pregnant (yes/no)? If the answer was no, they were asked: Did you get pregnant during the first menstrual cycle of unprotected intercourse (yes/no)? If the answer was no, they were then asked: during the second (yes/no)? If that answer was no, they were asked: Can you tell me during which cycle you became pregnant?

Of the 1,234 women who were pregnant at least once in the interval between 1991 and 1993, 874 (71 percent) reported a "known" TTP. Women who reported trying to prevent pregnancy (n = 188; 15 percent) were not asked TTP. The remaining 172 women (14 percent) could not provide a TTP because their pregnancies were "unplanned" or they did not know. Thirty of 874 women (3 percent) with a known TTP did not provide any information on fish consumption upon enrollment into the angler cohort and were excluded from analyses. Newly collected telephone interview data were systematically reviewed for accuracy by inspecting skip patterns and internal consistency prior to being appended to the baseline data file.

Data analysis

The data were analyzed in two phases. Frequency distributions and plots were computed for visual inspection of the data. Log transformation of TTP was performed to normalize the variable. Log transformation of fish consumption was performed to linearize the relation. Prior to log transformation, 0.5 years was uniformly added to the duration measure for all women, including those who reported no fish consumption. The test for the normality assumption was not significant. Cross-tabulations were performed to assess relevant covariates. The chi-square statistic was used to assess statistical significance for all categorical variables; the t test was used for continuous variables. A correlation matrix of all variables reflected the absence of collinearity, i.e., r ≤ 0.14. Missing data for study variables were minimal and ranged from 0.5 to 1.8 percent. Women with missing data were uniformly excluded in a casewise fashion from analyses.

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Multiple regression analysis was used to assess the linear relation between the log-years eating fish and log-TTP. Adjusted regression models included the covariates cigarette smoking, gynecologic pathology (e.g., endometriosis), and history of sexually transmitted disease(s), in addition to the log-years eating fish. These binary variables were added, given their role as potential confounders. Stratified analyses were performed for fish consumers and for all subjects by parity status (nulliparous/parous). Beta coefficients and corresponding standard errors were calculated to reflect the unit change in log-TTP for every unit change in log-years eating fish. The statistical significance of beta coefficients was assessed using t values (≤0.05). Multiple $R^2$ refers to the proportion of variance in log-TTP explained by the regression model. Statistical significance was determined based on the $F$ test ($p < 0.05$).

RESULTS

A description of the study sample is provided in table 1. The study sample comprises mostly white, parous spouses/partners of male anglers. Forty-five percent of the women reported ever having smoked. Only 9 percent reported that a doctor ever told them they had polycystic ovaries, endometriosis, or pelvic inflammatory disease. Seven percent reported a history of one or more sexually transmitted disease(s).

Approximately 42 percent of the women reported having eaten contaminated fish from Lake Ontario, despite highly publicized advisories warning against consumption of any fish from Lake Ontario by women of reproductive age. The mean duration of fish consumption was 2.2 (4.5) years for all women and 5.2 (5.6) years when the analysis was restricted to women who reported any fish consumption. Although not shown, no differences were observed between women who did and those who did not become pregnant during 1991–1993 with respect to any of the contaminated fish consumption variables. No differences were observed for fish consumption between women with known and those with unknown TTP. In addition, the age distributions for women with and those without a pregnancy between 1991 and 1993 were essentially the same.

Table 2 presents the results of multiple regression analyses for all women ($n = 844$) and for fish consumers ($n = 360$). Small, but positive, beta coefficients were observed for age ($\beta = 0.0165 \log\text{-}TTP$) and log-years eating fish ($\beta = 0.0352 \log\text{-}TTP$) for all women ($R^2 = 0.005$). A very slight increase in the beta coefficients was observed for the log-years eating fish ($\beta = 0.0666 \log\text{-}TTP$) when the analysis was restricted to fish consumers only. $R^2$ increased slightly ($R^2 = 0.006$) and may not represent a meaningful difference. The positive slope of the $\beta$ indicates that TTP was longer among exposed fish-consuming women, but not significantly so.

Table 3 presents the multiple regression results stratified by parity. A slightly, larger positive beta coefficient was observed for log-years eating fish ($\beta = 0.1314 \log\text{-}TTP$) among nulliparous women in comparison with parous women ($\beta = 0.0475 \log\text{-}TTP$). The larger positive beta coefficient observed suggests that the effect of duration of fish consumption on TTP may have been greater among nulliparous women than among parous women. Little change in $R^2$ was observed when models were stratified by parity ($R^2 = 0.02$ and $R^2 = 0.01$, respectively).

Table 4 presents multiple regression results for log-years eating fish by parity after smoking, gynecologic pathology, and sexually transmitted diseases were included in multiple regression models. Similar to the age-adjusted results, a larger positive beta coefficient was observed for log-years eating fish ($\beta = 0.1030 \log\text{-}TTP$) for nulliparous women in comparison with parous women ($\beta = 0.0095 \log\text{-}TTP$) in the adjusted multiple regression model. Among the 210 nulliparous women, a significant beta coefficient was observed for a history of gynecologic pathology. Among parous women, significant beta coefficients were observed for history of sexually transmitted disease, gynecologic pathology, smoking, and age. $R^2$ was slightly larger for nulliparous than for parous women ($R^2 = 0.04$ and $R^2 = 0.03$, respectively).

DISCUSSION

The results of this cross-sectional study do not support a significant adverse association between consumption of contaminated sport fish from Lake Ontario and time-to-pregnancy in this sample of women. Specifically, duration of fish consumption measured as the log-years of eating fish explained virtually none (0.5 percent) of the variation in TTP among all women with a known TTP. A slight increase in $R^2$ (2 percent) was observed when the analysis was restricted to nulliparous women. Log-years eating fish yielded a small, but positive, beta coefficient that was more pronounced for nulliparous than for parous women. However, neither coefficient achieved statistical significance. In addition, measurement error may account in part for the low $R^2$, given our use of (unvalidated) self-reported exposure data.

For several reasons, the results of this study need to be interpreted cautiously. First, this study comprises mostly fertile women with a known time to clinically recognized pregnancy. Approximately three quarters...
of women had a known (TTP) outcome. As such, potential bias associated with the intention to become pregnant or to plan a pregnancy cannot be ruled out (27). This study is not readily generalizable to women with unplanned pregnancies. This is an important limitation, given that 40–50 percent of pregnancies in the United States are reported to be unplanned (28). A seasonal effect of fish consumption on TTP is plausible, given that more fish are caught and (presumably) eaten during summer months than during winter months. Previous authors have noted that pregnancy planning is not evenly distributed and that summer months may be preferred (29). Other sources of potential bias for cross-sectional studies of TTP include information and selec-
Fish Consumption and Time-to-Pregnancy

TABLE 2. Time to pregnancy* in relation to duration of Lake Ontario fish consumption, multiple linear regression analysis, New York State Angler Cohort, 1993†

<table>
<thead>
<tr>
<th>Variable</th>
<th>All women (n = 844)</th>
<th>Fish consumers (n = 360)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.0165 ± 0.0096</td>
<td>0.0158 ± 0.0148</td>
</tr>
<tr>
<td>Log-years eating fish§</td>
<td>0.0352 ± 0.0316</td>
<td>0.0666 ± 0.0701</td>
</tr>
<tr>
<td>R² = 0.005</td>
<td>R² = 0.006</td>
<td></td>
</tr>
</tbody>
</table>

* Time to pregnancy (months) was log-transformed.
† None of the results were statistically significant.
§ Duration (years) was log-transformed.

TABLE 3. Time to pregnancy* in relation to duration of Lake Ontario fish consumption by parity, multiple linear regression analysis, New York State Angler Cohort, 1993

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nulliparous (n = 218)</th>
<th>Parous (n = 622)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.0331 ± 0.0240</td>
<td>0.0269 ± 0.0105*</td>
</tr>
<tr>
<td>Log-years eating fish§</td>
<td>0.1314 ± 0.0703</td>
<td>2.475E-05 ± 0.0345</td>
</tr>
<tr>
<td>R² = 0.02</td>
<td>R² = 0.01</td>
<td></td>
</tr>
</tbody>
</table>

* p = 0.01.
† Time to pregnancy (months) was log-transformed.
§ Duration (years) was log-transformed.

TABLE 4. Time to pregnancy* in relation to duration of Lake Ontario fish consumption by parity, multiple linear regression analysis, New York State Angler Cohort, 1993

<table>
<thead>
<tr>
<th>Variable</th>
<th>Nulliparous (n = 210)</th>
<th>Parous (n = 604)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>-0.0066</td>
<td>0.0215*</td>
</tr>
<tr>
<td>Log-years eating fish§</td>
<td>0.1030</td>
<td>0.0095</td>
</tr>
<tr>
<td>Ever smoke</td>
<td>0.0092</td>
<td>0.2287*</td>
</tr>
<tr>
<td>Gynecologic pathology</td>
<td>0.9561*</td>
<td>0.3140*</td>
</tr>
<tr>
<td>STDs§</td>
<td>0.0054</td>
<td>-0.4574*</td>
</tr>
<tr>
<td>R²§</td>
<td>0.04</td>
<td>R² = 0.03</td>
</tr>
</tbody>
</table>

* p < 0.05.
† Time to pregnancy (months) was log-transformed.
§ Duration (years) was log-transformed.
§§ STDs, sexually transmitted diseases; R², adjusted R-square.

Fish advisories warn women of reproductive age not to eat any fish from Lake Ontario. Despite such advisories, almost half of our sample reported having eaten sport fish from Lake Ontario. Thus, a large percentage of women in this populated geographic area are potentially exposed to chronic low levels of contaminants found in sport fish from the lake. Of particular concern is the subset (10 percent) of women who reported eating fish for a minimum of 7 years or when levels of contaminants in fish were considerably higher than in more recent years.

The low participation rate (39 percent for men and 49 percent for women) encountered in recruiting subjects for enrollment into the New York State Angler Cohort is of concern and prompted the investigators to assess nonresponse bias in a random sample of 100 of 110 (91 percent response) nonrespondents. Overall, nonrespondents were more likely to be single and to have lower educational attainments and household incomes than did respondents (25). Frequency of species-specific fish consumption, however, did not differ between the two groups (data not shown).

A second substudy attempted to assess the reliability of self-reported fish consumption among 104 randomly selected cohort members. Specifically, the percent of exact agreement for frequency of eating species-specific fish from Lake Ontario ranged from 85 to 89 percent (Pearson r = 0.4–0.7) (data not shown) (25). Nevertheless, fish consumption was entirely self-reported and may be subject to reporting errors.

Similar results for the TTP analyses were found when exposure was estimated based on the frequency of fish consumption (number of meals per month in 1991) or the estimated polychlorinated biphenyl (PCB) exposure based on the amount, duration, and type(s) of fish consumed. Duration (years) of fish consumption was found to be the most robust measure and therefore was selected for regression analyses.

This study represents one of the first attempts to assess the relation between consumption of contaminated fish and TTP by using methods that are applicable for large, population-based environmental studies. Previous authors have addressed the validity and reliability of a short questionnaire for TTP and have reported it to be reliable and free of systematic errors (26, 34, 35). The utility of using TTP to assess conception delays across the continuum of biologic fertility has been addressed recently (36). The applicability of using TTP to study environmental exposures has also been demonstrated (30).
Cohort. The beta coefficients were positive, as might be expected on the basis of evidence from experimental animals and wildlife populations. A prospective pregnancy study currently is under way that should address many of the limitations inherent in this cross-sectional study.

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REFERENCES