Short Communication

Ovarian Cancer, Cholesterol, and Eggs: A Case-Control Analysis

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The relation between diet and the risk of developing ovarian cancer is unclear. An interesting but unexplored finding is an increased risk of ovarian cancer with increasing egg consumption: we have aimed to explore this relationship more fully than has been done previously. Using a case-control study design, 716 histologically confirmed ovarian cancer cases from major gynecological-oncology treatment centers in three Australian states were enrolled. A total of 806 controls were selected from the electoral roll. All women provided dietary data via a validated self-completed food frequency questionnaire. There was a strong and significant dose-response relation between cholesterol from eggs and risk of ovarian cancer (odds ratio = 2.17 for highest intake of eggs; \( P_{\text{trend}} < 0.001 \)). However, there was no such positive relation with cholesterol from nonegg sources. The lack of a relation between nonegg cholesterol and ovarian cancer implies that the observed association between egg consumption and ovarian cancer risk is not due to the cholesterol in eggs. For now, alternative causal mechanisms, including environmental contaminants such as DDE, remain speculative.

Introduction

The nutritional epidemiology of ovarian cancer is unclear, other than for a possible role of dietary fat (1–3). While exploring this in an Australian case-control study, we noted an apparently increased risk of cancer related to eating eggs. This increased risk has been observed previously (3, 4) without receiving particular emphasis, other than from Risch et al. (3), who considered recent change in cases’ diet a likely explanation. Consequently, the biology of possible causal links remains relatively unexplored. Our analyses aimed to determine clearly whether an “egg effect” existed separately from a “cholesterol/fat effect” and, if so, to explore the possibility of environmental contamination (especially by xenoestrogens) of eggs as a basis for any carcinogenic connection.

Materials and Methods

The study methods have been described in detail elsewhere (5). In brief, we ascertained all histologically confirmed incident cases of primary epithelial ovarian cancer registered in all major gynecological-oncology treatment centers in three Australian states. With consent from the attending doctor, eligible cases (those aged between 18 and 79 years and competent to complete a questionnaire) were invited to participate either before discharge or while attending for follow-up. Controls were selected from the electoral roll by a random procedure yielding an age and regional distribution similar to that of cases. Cases not on the electoral roll were excluded from these analyses. A total of 716 cases (90%) and 806 controls (94%) provided dietary data via a self-completed food frequency questionnaire adapted from the instrument developed and validated by Willett et al. (6).

In the dietary analysis, women were classified into four groups, based on their reported frequency of whole egg consumption: (a) <1 per fortnight; (b) from 1 per fortnight to <1 per week; (c) 1–2 per week; and (d) ≥2 per week. Women were classified into approximate fifths based on the combined distribution of cholesterol intake. Analyses were conducted for total cholesterol and then conducted for cholesterol from eggs alone contrasted with that from other foods. ORs2 and 95% CIs were derived from multiple logistic regression models to control for potential confounding factors (see Table 1), with nutrients adjusted for total energy intake using the residual method (7). Polytomous logistic regression was used to estimate the risk of the various histological subtypes of ovarian cancer versus controls.

Results

Egg consumption among the women was relatively low overall, with fewer than 30% of cases and controls consuming 2 eggs or more per week. Cases reported eating more eggs than did controls, leading to a positive dose-response relation \( (P_{\text{trend}} < 0.001, \text{Table 1}) \). A lesser and nonsignificant positive association was also seen for increasing intake of total cholesterol (Table 1). After partitioning the cholesterol by food source, there was a strong and significant dose-response relation between cholesterol from eggs and risk of ovarian cancer \( (P_{\text{trend}} < 0.001; \text{Table 1}) \), but there was no such positive relation with cholesterol from nonegg sources. These findings were consistent across the major histological tumor types. The lack of a relation between nonegg cholesterol (about 80% of the total) and ovarian cancer implies that the observed association between egg consumption and ovarian cancer risk is not due to the cholesterol in eggs. The data of Risch et al. (3) support this contention. Furthermore, the association held regardless of the method of cooking the eggs (boiled, fried, scrambled, or poached), which suggests that fat and other additives used in the preparation of the eggs were not implicated. Nor did our data reveal any overall connection with poultry or bacon consumption. Earlier findings (3) that egg

1 The abbreviations used are: OR, odds ratio; CI, confidence interval; DDT, 1,1,1-trichloro-2,2-bis(4′-chlorophenyl)ethane; DDE, 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene; DDD, 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene.

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cholesterol intake was higher only among women with invasive tumors suggested this may have resulted from disease-related changes in diet rather than from a causal effect. Our data do not support this assertion because similar relations for high versus low egg consumption were observed for borderline (OR, 1.77; 95% CI, 0.93–3.39) and invasive tumors (OR, 1.79; 95% CI, 1.25–2.58) as well as for different disease stages. Whereas it is always possible that residual confounding may be present, extensive adjustments for other nondietary and dietary variables, including various forms of fat as well as vegetables (data not shown), did not explain the increased risk.

### Discussion

Of the two case-control studies that have examined the relationship between egg consumption and ovarian cancer, one showed a significant positive association (3), whereas the other (2), which used hospital controls, did not. However, two cohort studies have also found results similar to ours. In the Seventh Day Adventist cohort study (8), consumption of at least 3 eggs per week was associated with a threefold increased risk of ovarian cancer mortality (compared with less than 1 egg per week), and in the Iowa Women’s Health Study (4), eating eggs several time per week was linked to a twofold excess risk of ovarian cancer.

One possible explanation for an association between eggs and ovarian cancer is the presence in eggs of highly lipophilic organochlorine residues: dieldrin and DDT and its metabolites, DDE and DDD, which were the most common residues detected in commercially produced eggs in the 1996 Australian National Residue Survey (9). “Backyard” (homegrown) eggs, consumed by 24% of Australians (9), are even more likely to contain residues than commercially produced eggs. A 1997 survey of South Australian backyard eggs detected DDT and its metabolites in 68% of samples, with 5% exceeding the allowable maximum residue level (9). Whereas the residues themselves are only weakly estrogenic, prolonged exposure and hence bioaccumulation in adipose tissue may be harmful. In addition, in vitro assays using MCF-7 cells showed that o.p.-DDT and o.p.-DDE stimulate the formation of the genotoxic 16α-hydroxyestrone from estradiol (10).

We found no epidemiological studies that have examined the relationship between organochlorines and ovarian cancer risk, although the relationship with other cancers has been reported. Breast cancer has been most extensively studied, but overall, the results have been inconsistent. Several researchers found no association between exposure to organochlorines and the risk of breast cancer (11, 12), whereas others have observed possible effects on both the risk of developing breast cancer (13, 14), and subsequent survival (15). Although a recent pooled analysis (16) did not support a relationship between organochlorines and breast cancer, the relationship may be a complex one that is potentially modifiable by a number of factors, including estrogen receptor status (17), menopausal status (13), and body mass index (18). In addition, a negative association with endometrial cancer (19), and a positive one with pancreatic cancer (20) have been reported.

Thus it seems possible that eating eggs regularly is causally linked to the occurrence of a proportion of cancers of the ovary, perhaps as many as 40%, among women who eat at least 1 egg a week. Whereas the effects are modest, and the biological basis for this causal link is speculative, similar findings have been reported elsewhere (3, 4, 8). Historically, it has proved difficult to ascribe a definite causal role to environmental contaminants, but the possibility here warrants further attention, unless a plausible alternative explanation emerges. This could be either a different biological mechanism or a consequence of better understanding of other “risky” behaviors in which egg-eaters indulge.

### References


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**Table 1** Distribution and associations of eggs and cholesterol in relation to ovarian cancer

<table>
<thead>
<tr>
<th>Food/Nutrient group</th>
<th>Cases % (n = 717)</th>
<th>Controls % (n = 806)</th>
<th>OR</th>
<th>95% CI</th>
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</thead>
<tbody>
<tr>
<td>Eggs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1/fin</td>
<td>18.6</td>
<td>27.2</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>1/fin to &lt;1/wk</td>
<td>18.7</td>
<td>21.6</td>
<td>1.40</td>
<td>0.99–1.98</td>
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<tr>
<td>≥1/wk</td>
<td>32.8</td>
<td>29.5</td>
<td>1.71</td>
<td>1.25–2.35</td>
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<tr>
<td>≥2/wk</td>
<td>30.0</td>
<td>21.7</td>
<td>1.82</td>
<td>1.30–2.55</td>
</tr>
<tr>
<td>Total cholesterol group [median (in mg)]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (172)</td>
<td>17.7</td>
<td>22.2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2 (230)</td>
<td>20.1</td>
<td>19.7</td>
<td>1.29</td>
<td>0.90–1.84</td>
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<tr>
<td>3 (257)</td>
<td>19.0</td>
<td>21.2</td>
<td>1.07</td>
<td>0.74–1.54</td>
</tr>
<tr>
<td>4 (303)</td>
<td>20.7</td>
<td>19.2</td>
<td>1.37</td>
<td>0.95–1.98</td>
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<td>5 (387)</td>
<td>22.5</td>
<td>17.6</td>
<td>1.32</td>
<td>0.91–1.93</td>
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<td>Cholesterol from eggs group [median (in mg)]</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (5)</td>
<td>16.9</td>
<td>24.0</td>
<td>1.98</td>
<td></td>
</tr>
<tr>
<td>2 (25)</td>
<td>19.8</td>
<td>20.9</td>
<td>1.42</td>
<td>1.00–2.02</td>
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<td>3 (38)</td>
<td>20.3</td>
<td>21.0</td>
<td>1.48</td>
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<td>4 (56)</td>
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<td>19.0</td>
<td>1.55</td>
<td>1.08–2.22</td>
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<td>5 (124)</td>
<td>22.8</td>
<td>15.2</td>
<td>1.51</td>
<td>1.31–3.13</td>
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<tr>
<td>Cholesterol from other food groups [median (in mg)]</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>1 (123)</td>
<td>19.4</td>
<td>21.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2 (177)</td>
<td>22.7</td>
<td>19.8</td>
<td>1.02</td>
<td>0.71–1.45</td>
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<td>3 (205)</td>
<td>19.2</td>
<td>21.1</td>
<td>0.82</td>
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<tr>
<td>4 (239)</td>
<td>19.8</td>
<td>18.9</td>
<td>0.80</td>
<td>0.55–1.18</td>
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<tr>
<td>5 (292)</td>
<td>18.9</td>
<td>19.2</td>
<td>0.75</td>
<td>0.49–1.09</td>
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</tbody>
</table>

*a Adjusted for total fat and energy + all standard risk factors and matching factors (age, geographic location, education, parity, duration of oral contraceptive use, body mass index, smoking history, ever use of perineal talc, tubal sterilization, hysterectomy, and history of breast or ovarian cancer in a first-degree relative.
*b fn, fortnight.
*c Reference category.
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