Cancer risks among long-standing spouses

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We estimated risks for concordant and discordant cancers in spouses in order to quantify cancer risks from the shared environment. The study was restricted to spouses who had one or more children in common and who lived together for at least 15 years after the first child's birth. The nation-wide Family-Cancer Database was used as the source of family and cancer data. Standardised incidence ratios were calculated for concordant and discordant cancers in spouses after 50 years of age. Among the 18 cancer sites considered, only three sites, stomach, lung and bladder, showed concordant increases of cancer among spouses, standardised incidence ratios ranging only from 1.19 to 1.38. Additionally, gastric and pancreatic cancer were associated among spouses, as did many cancers which were related to tobacco smoking or human papilloma virus infection. By contrast, standardised incidence ratios of colon, rectal, renal and skin cancers showed no increases among spouses. Shared lifestyle among family members seems to explain only a small proportion of familial cancer susceptibility. Because lifestyles are likely to differ more between parents and offspring than between spouses, familial cancer risks between parents and offspring are even more likely to be due to heritable than environmental effects.

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Many lines of epidemiological evidence indicate that cancer is mainly an environmental disease (Doll and Peto, 1981; IARC, 1990; Lichtenstein et al, 2000; Peto, 2001). During the past decade it has become increasingly clear that overweight and lack of physical activity convey a risk of cancer, which may account for 5% of all cancers in Europe (Bergstrom et al, 2001; IARC, 2002). Moreover, the risks at the population level caused by various infections have become better understood, and the known infections have been estimated to account for 15% of cancer worldwide, though less in Europe (Pisani et al, 1997; Zur Hausen, 1999). In spite of the enormous research effort on diet and cancer, the proportion of cancer attributable to diet or to any specific dietary component remains speculative. It has been estimated that at least 50%, and probably as much as 70% of cancer deaths are unavoidable among non-smokers mainly because their aetiology remains unknown (Peto, 2001).

Decades long cohabitation by spouses should tend to result in many habits and carcinogenic exposures being similar. Interest in disease among spouses earlier focused on sexually transmitted diseases and the effects of passive smoking (IARC, 1995; Hackshaw, 1998; Hemminki et al, 2000a; Hemminki and Dong, 2000a). Besides assessing life-style factors and cancer risks, they can point to the environmental contribution to the familial aggregation of cancer, and they thus help to apportion heritable effects (Hemminki et al, 2001a,d). The studies from the Swedish Family-Cancer Database have shown limited spouse concordance, affecting mainly the sites of known environmental carcinogens (Hemminki and Dong, 2000b; Hemminki et al, 2001a). However, in the previous studies the length of cohabitation between the spouses was not considered, nor were any adjustments for socio-economic status carried out. We address these shortcomings here in a study of the 2001 update of the Family-Cancer Database, covering 10.2 million individuals and over one million tumours (Hemminki et al, 2001c). In addition to concordant cancers in spouses, a systematic analysis of discordant cancers was also carried out.

METHODS

The Swedish Family-Cancer Database includes persons born after 1932 with their biological parents (Hemminki et al, 2001c) together with cancers retrieved from the nationwide Swedish Cancer Registry for the years 1938 to 1998. Additionally, residential and socio-economic data were included from national censuses, carried out in 1960, 1970, 1980 and 1990. A four-digit diagnostic code according to a modified version of the seventh revision of the International Classification of Diseases (ICD-7) was used. The following sites were examined collectively: ‘upper aerodigestive tract’, lip, mouth and pharynx (codes 140, 141, 143 – 148) and leukemia (204 – 207), polycythemia vera (208) and myelofibrosis (209). Skin cancer only included squamous cell carcinoma; basal cell carcinoma is not registered in the Cancer Registry.

Spouses were defined as the parents of the woman’s first child, and they had to live in a shared address in at least two subsequent decennial censuses; thus the minimal cohabitation was 15 years by average. Even though data were available on the marital status, the above definition was preferable because many couples live together without being married. Follow-up was started at the age of 50 years, to allow latency time from the start of cohabitation. Standardized incidence ratios (SIRs) were calculated as the ratio of observed (O) to expected (E) number of cases. The expected numbers were calculated from site-, age-, period (10-year bands), area (three areas, three large cities, south Sweden and the rest), socio-economic status (manual workers, ‘intermediate’ workers, professionals and others) – and sex-standardized rates (Esteve et
RESULTS

A total of 71,020 couples presented with a concordant or discordant cancer after age 50 years, who fulfilled the entrance criteria for the study of being parents to the first child of the women and residing in a shared address at least through two consecutive censuses after the first childbirth. In Table 1, we show usefulness of the approach, by comparing cancer sites among spouses where increased risks should be expected due to shared smoking and sexual habits. When wives were probands and presented with lung cancer, husbands had increased risks of oesophageal (SIR 1.47), pancreatic (1.30), laryngeal (1.74) and lung (1.38) cancers. Cervical cancer was associated with pancreatic (1.28), laryngeal (1.53), lung (1.44) and penile (1.88) cancers in the husband. When husbands presented with a larynx cancer, their wives had an excess of lung (1.58) and cervical cancer (1.45). Lung cancer in husbands was associated with lung (1.32), cervical (1.31) and bladder (1.16) cancer in wives. Penile cancer was associated with cervical cancer in the wife (1.84).

Risks for spouses for concordant cancers are shown in Table 2 for sites where more than five pairs were recorded. Cancer at three sites was increased for husbands by cancer in wives: gastric (SIR 1.22). A few other significant associations between cancer sites were observed but because they were not confirmed in analysis when the sites were reversed (see last paragraph of Subjects and Methods), the data are not shown.

Table 1 Aggregation of tobacco- and sexual-behaviour-related cancers among spouses

| Proband: Wife | Cancer in husband | O  | SIR  | 95% CI |
|---------------|-------------------|----|------|--------|
| Lung          | Oesophagus        | 48 | 1.47 | 1.08–1.92 |
|               | Pancreas          | 114| 1.30 | 1.07–1.55 |
|               | Larynx            | 49 | 1.74 | 1.30–2.26 |
|               | Lung              | 406| 1.38 | 1.25–1.52 |
| Cervix        | Pancreas          | 115| 1.28 | 1.05–1.52 |
|               | Larynx            | 51 | 1.53 | 1.13–1.99 |
|               | Lung              | 458| 1.44 | 1.31–1.58 |
|               | Penis             | 19 | 1.88 | 1.13–2.86 |

| Proband: Husband | Cancer in wife | O  | SIR  | 95% CI |
|-------------------|----------------|----|------|--------|
| Larynx            | Lung           | 49 | 1.58 | 1.17–2.06 |
|                   | Cervix         | 51 | 1.45 | 1.08–1.88 |
| Lung              | Lung           | 406| 1.32 | 1.20–1.46 |
|                   | Cervix         | 458| 1.31 | 1.20–1.44 |
|                   | Bladder        | 194| 1.16 | 1.00–1.33 |
| Penis             | Cervix         | 19 | 1.84 | 1.11–2.76 |

Reference category was a spouse without cancer. The data were adjusted for site, age, period, residence and socio-economic level; female data additionally for parity and age at first childbirth.
between gastric and pancreatic cancers in spouses. Among the known or suggested environmental causes of pancreatic cancer, tobacco smoking, obesity and the resulting diabetes, high caloric intake and alcohol consumption are likely to be shared to some extent. However, for other cancers, such as lung cancer, the difference in lifestyle between spouses may be more pronounced, and the hereditary component is likely to be more important in spouses than between spouses, familial cancer risks between parents and offspring are more likely to be due to heritable rather than environmental effects. As a reservation, it needs to be considered that childhood and youth may be the most vulnerable period for carcinogenesis. Yet the present results suggest that, with the possible exception of lung cancer, the reported familial risks in cancer that occur in both genders are mainly due to heritable factors, many of which are yet unknown (Hemminki et al., 2001a).

In summary, the present analysis on cancer risks among spouses showed no significant deviation from the expected risks, with the exception of the association between gastric and pancreatic cancers. The present results suggest that, with the possible exception of lung cancer, the reported familial risks in cancer that occur in both genders are mainly due to heritable factors, many of which are yet unknown (Hemminki et al., 2001a). In summary, the present analysis on cancer risks among spouses showed no associations, which could not be explained by known risk factors, with the exception of the association between gastric and pancreatic cancers.

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