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INCIDENCE OF TESTICULAR GERM-CELL MALIGNANCIES IN ENGLAND AND WALES: TRENDS IN CHILDREN COMPARED WITH ADULTS

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The incidence of testicular cancer has been increasing markedly in most industrialised countries, and it is now the most common malignancy in young men (Swerdlow et al., 1998). Most testicular cancers are of germ-cell origin (Pike et al., 1987), which comprises 2 distinct groups: seminomas and non-seminomas. This latter group comprises several different cell types named differently according to various classification systems (Teppo, 1973); it is mainly equivalent to teratomas in the British system. In the England and Wales National Cancer Registry files, which cover a large population of about 50 × 106, testicular tumours are coded according to both site and histology, but the histological data appear not to have been analysed previously. We used data from these files to examine recent trends in these tumours and, in particular, to assess whether the incidence of testicular cancer at young adult ages has affected similarly its 2 major histological groups.

The rise in the incidence of germ-cell malignancies is known to have affected young adults, but it is less clear whether it has affected other age groups, particularly children. We used data from the National Cancer Registry file at the Office of National Statistics (ONS) and the National Registry of Childhood-Tumours to examine trends in testicular germ-cell malignancies overall in England and Wales from 1962 to 1990 and in children from 1962 to 1995. The incidence of testicular cancer at all ages rose by 3.4% (95% CI 3.3–3.6%) per annum from 1962 to 1990. A similar rise in the incidence of germ-cell malignancies occurred during the years for which histological information was available in the ONS files, 1971–1989 (3.4%; 3.1–3.6%), to which both seminomas and non-seminomas contributed equally. The incidence of non-seminomas in adults rose in men under age 55 years and declined in older men, whereas there were increases in the incidence of seminomas in both young and older men. Cohort analysis at young ages showed a marked rise in the risk of germ-cell malignancies up to the cohort born in 1955–1959 but no further rise for those born subsequently. The rise in the incidence of these tumours in young adults was paralleled by a similar trend, although less marked, in children aged under 15 years (1.3% per annum; 0.2–2.5%). The increase in risk for children in this very large data set alongside the rise in young adults is compatible with the hypothesis that childhood and adult testicular germ-cell malignancies may have some common risk factors, presumably pre-natal. Int. J. Cancer 83:630–634, 1999.

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by members of the UK Children’s Cancer Study Group (UKCCSG). The registry also receives death certificates of all deaths occurring in Britain under the age of 20 and with a neoplasm coded as the underlying cause. As a result, the Group’s register is particularly complete. We extracted from its files data on all testicular germ-cell malignancies incident in England and Wales during 1962–1995.

**Analysis of time trends**

Direct age-standardised incidence rates by single year of age were calculated using the 1971 mid-year male population of England and Wales as the standard. To assess secular trends, a Poisson regression model was fitted (Breslow and Day, 1987). For the ONS data adjusted for incompleteness of histological information, the estimated numbers of incident cases were truncated to whole numbers before the model was fitted.

To examine risks according to birth cohort, standardised cohort incidence ratios (SCIRs) were calculated by the indirect method, using the average age-specific rates for the entire period to derive the expected values for each cohort. These analyses were carried out by 5-year periods of birth. Since the cancer registry files contained information on the exact year of birth of the cancer cases, we also conducted more detailed analyses by single year of birth to examine possible sudden cohort changes in risk due to short-term changes in exposure levels (e.g., changes in maternal diet during World War II).

**RESULTS**

A total of 23,393 testicular cancers were included in the ONS cancer registry files for 1962–1990. For the years for which histological information was available (1971–1989), there were 17,215 testicular tumours after exclusion of 49 lymphoma and Hodgkin’s disease registrations that were erroneously coded as testicular cancers (WHO, 1977). Germ-cell tumours represented 97% (n = 15,763) of all testicular cancers of known morphology: 55.2% (n = 8,703) of these germ-cell tumours were seminomas and 44.8% (n = 7,060) non-seminomas.

Ninety-four percent of testicular cancers in the ONS data set were of known histology. However, this percentage varied by age: it was 95% at ages under 65 years but only 76% at ages 65 and over. There was little change in the overall percentage of histologically confirmed testicular cancers over time.

Age distributions by single year for the 2 major types of germ-cell tumour in adults are shown in Figure 1. Non-seminomas started to rise at age 13 and peaked around age 27, whereas seminomas began to increase and peaked some years later (at ages 16 and 34, respectively). As a result, non-seminoma was the most common histology at ages under 30 and seminoma at older ages.

A total of 298 testicular malignant germ-cell tumours in England and Wales were incident in children under age 15 during 1962–1995. The large majority of these were non-seminomas, with 76% (n = 225) being of yolk-sac origin and 21% (n = 62) teratomas. There were only 9 seminomas at these ages and 2 cases of unspecified germ-cell origin. Analysis by single year of age showed a peak at ages under 3, which differed for yolk-sac tumours and teratomas. For yolk-sac tumours, rates peaked in the second year of life and decreased thereafter, whereas for teratomas the maximum occurred in the first year of life with rates falling thereafter until they started to rise again at age 13 (the very beginning of the steep rise through adolescence and young adulthood).

There was a statistically significant increase in the risk of testicular cancer overall from 1962 to 1990 [mean annual percent change in rates = 3.4%, 95% confidence interval (CI) 3.3–3.6%; p < 0.001; Fig. 2]. This increase was much more marked at ages under 55 years (3.7%, 3.5–3.9%; p < 0.001) than at ages 55 years and above (1.2%, 0.7–1.7%; p < 0.001). Analyses of testicular cancer trends by histology were possible only for 1971–1989 (see ‘Material and Methods’). For these years, there was an increase in the overall incidence of germ-cell tumours, to which both seminomas and non-seminomas contributed equally (Table I). Similar results were obtained after adjusting for tumours of unknown histology. However, analyses by age showed diverging time trends in the incidence of non-seminomas for young and older men (Table I): at ages 0–54 there was a significant increase in the incidence of these tumours, whereas at older ages there was a decline. In contrast, the incidence of seminomas increased in both age groups, though more markedly at young than at older ages (Table I). Overall, the incidence of germ-cell tumours increased in young, but not in older, men (Table I). These analyses were unadjusted for cases of unknown histology, but adjusting for this gave similar results.

Further breakdown by 5-year age group showed mean annual percent increases in the incidence of non-seminomas in all age groups from 15 to 54 years but annual declines at older ages. For seminomas, the increase affected all age groups from 15 to 74 years; there was little change in risk at ages 75 and older, but this was based on a smaller number of cases. The mean annual percent increases in the incidence of germ-cell tumours at ages 15–19, 20–24 and 25–34 years were 2.1% (0.6–3.7%), 2.8% (2.0–3.7%), and 2.9% (2.4–3.4%), respectively. There were no statistically significant changes in risk at ages under 15 years, but the 95% CI were wide because of small numbers. At age 0–4, when the large majority of childhood germ-cell tumours occurred, there was a near significant increase (2.6%, −0.29–5.6%; p = 0.08).

Cohort analyses showed that the risk of testicular cancer at ages under 55 years remained relatively constant for men born from
1911 to 1935, increased for those born from 1935 to 1957 but stabilized again for those born subsequently (the SCIRs for all germ-cell malignancies combined for cohorts born in 1955–1959 and 1965–1969 were 114 (95% CI 109–118) and 106 (97–106), respectively) (Fig. 3). The rise was relative steady, with no obvious dips or peaks (apart from small random fluctuations) (Fig. 3a). In particular, there was no decrease in risk for men born during World War II. At older ages (not shown), the risk remained relatively constant for successive generations except for a slight increase for the last generations in these analyses (born 1920–1930). The cohort increase at young ages was similar for non-seminomas and seminomas (Fig. 3b). At ages 55 and over (not shown), there was a marked decline in the risk of developing a non-seminoma for successive generations of men born since the turn of the century but no clear trend for seminoma except for an increase in risk for the 2 most recent generations in these analyses. Similar results were obtained with the data adjusted for cases of unknown histology.

Analyses of secular trends in children under 15 years of age revealed an overall increase in the incidence of malignant germ-cell tumours during the years 1962–1995, entirely due to a rise in yolk-sac tumours (Table II). The 5-year age-specific trends were more difficult to interpret because of the small number of cases, particularly at ages 5–9. At ages 0–4, there was a rise in risk, but it was not statistically significant; however, the trends diverged by cell type, with a statistically significant rise in yolk-sac tumours and a significant decline in teratomas (Table II). At ages 10–14, the data were consistent with a rise in incidence but the 95% CIs were wide (Table II).

Table I – Trends in incidence of germ-cell malignancy of the testis by age and histology: England and Wales, 1971–1989

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Histological type</th>
<th>Rate 1971–1975</th>
<th>Mean annual percent change in rate (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–54</td>
<td>Seminomas</td>
<td>16.0</td>
<td>25.1</td>
<td>3.7 (3.3–4.1)</td>
</tr>
<tr>
<td></td>
<td>Non-seminomas</td>
<td>14.6</td>
<td>22.2</td>
<td>3.6 (3.1–3.9)</td>
</tr>
<tr>
<td></td>
<td>All germ cell tumours</td>
<td>30.6</td>
<td>47.2</td>
<td>3.7 (3.5–3.9)</td>
</tr>
<tr>
<td></td>
<td>Seminomas</td>
<td>10.3</td>
<td>12.0</td>
<td>1.6 (0.5–2.7)</td>
</tr>
<tr>
<td></td>
<td>Non-seminomas</td>
<td>3.6</td>
<td>2.1</td>
<td>-2.9 (-5.0 to -0.9)</td>
</tr>
<tr>
<td>55+</td>
<td>All germ cell tumours</td>
<td>13.9</td>
<td>14.1</td>
<td>0.6 (-0.3–1.6)</td>
</tr>
<tr>
<td></td>
<td>Seminomas</td>
<td>14.8</td>
<td>22.2</td>
<td>3.4 (3.0–3.8)</td>
</tr>
<tr>
<td></td>
<td>Non-seminomas</td>
<td>12.1</td>
<td>17.7</td>
<td>3.4 (2.9–3.8)</td>
</tr>
<tr>
<td></td>
<td>All germ cell tumours</td>
<td>26.9</td>
<td>39.9</td>
<td>3.4 (3.1–3.6)</td>
</tr>
</tbody>
</table>

1 Rates (per 10^5) age-standardised by single year to the 1971 England and Wales male population.

**DISCUSSION**

Our results show that the incidence of testicular cancer overall has increased markedly since 1962. The trends were different for the 2 main adult age groups, however, resulting from differences by age for non-seminoma: a rise in incidence in young men and a decline in older men. Analysis by birth cohort also implied an increasing risk of non-seminomas for successive generations of men at ages under 55 and a decline at older ages. In contrast, there were increases in the incidence of seminomas in young and older men. Similar increases in testicular cancer incidence at young ages with cohort effects underlying them have been shown in other studies (e.g., Schottenfeld et al., 1980; Brown et al., 1986; Østerlind, 1986; Bergström et al., 1996; Zheng et al., 1996; Weir et al., 1999). In those studies that presented analyses by cell type (e.g., Brown et al., 1986; Østerlind, 1986; Zheng et al., 1996; Weir et al., 1999), as in the present study, the rise in incidence at young ages affected seminomas and non-seminomas to the same degree, suggesting that they may be of similar aetiology. The cohort data presented here appear to indicate that risks have stabilised in the most recent cohorts, a trend seen also in Scotland (Swerdlow et al., 1998). In contrast, the rise in the incidence of testicular cancer at old ages observed in the present study, which was entirely due to seminomas, has not been shown in other studies (e.g., Brown et al., 1986; Østerlind, 1986; Zheng et al., 1996).

The completeness of the England and Wales national cancer registration scheme has probably not altered appreciably since 1971 (Swerdlow et al., 1993). Therefore, although improved completeness could have accounted, at least in part, for the rises of testicular cancer in the 1960s, it is unlikely to do so for more recent years. Potential late registrations, yet to be entered into the national cancer registry files, are likely to have been of negligible effect as the analyses were conducted only to 1990 using data extracted from ONS files several years later. Incompleteness of histological confirmation also is unlikely as an explanation for the findings as the proportion of cancers with unknown histology was small. This was particularly true at younger ages, when most of the tumours...
TRENDS IN THE INCIDENCE OF GERM CELL MALIGNANCIES OF THE TESTIS IN BOYS AGED UNDER 15 YEARS BY AGE AND HISTOLOGY, ENGLAND AND WALES, 1962–95

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Histological type (n)</th>
<th>Rate 1962–70 (9/100,000)</th>
<th>Rate 1986–95 (9/100,000)</th>
<th>Mean annual percent change in rate (95% CI), 1962–1995</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–4</td>
<td>Yolk sac (214)</td>
<td>2.32</td>
<td>3.66</td>
<td>1.7 (0.4–3.1)</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Teratoma (31)</td>
<td>0.89</td>
<td>0.45</td>
<td>–4.0 (–7.6 to –0.4)</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>All germ cell (247)</td>
<td>3.26</td>
<td>4.56</td>
<td>1.0 (–0.3–2.2)</td>
<td>0.13</td>
</tr>
<tr>
<td>5–9</td>
<td>All germ cell (13)</td>
<td>0.12</td>
<td>0.12</td>
<td>–1.3 (–6.1–3.6)</td>
<td>0.56</td>
</tr>
<tr>
<td>10–14</td>
<td>All germ cell (38)</td>
<td>0.31</td>
<td>1.01</td>
<td>4.1 (1.2–9.6)</td>
<td>0.13</td>
</tr>
<tr>
<td></td>
<td>Yolk sac (225)</td>
<td>0.81</td>
<td>1.30</td>
<td>1.7 (0.4–3.0)</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Teratoma (62)</td>
<td>0.04</td>
<td>0.05</td>
<td>–0.3 (–2.8–2.2)</td>
<td>0.80</td>
</tr>
<tr>
<td></td>
<td>All germ cell (298)</td>
<td>1.24</td>
<td>1.77</td>
<td>1.3 (0.2–2.5)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

1Rates (per 100,000) age-standardised by single year to the 1971 England and Wales male population. 2Analyses by cell type were not carried out because of the small number of cases in these age groups.
1989; Gallagher et al., 1995), have found an association with an early age of puberty. Another analysis found reduced risk for late puberty but not raised risk for early puberty (Møller and Skakkebæk, 1996). The increased risk of testicular cancer in tall men found in some studies (Gallagher et al., 1995; Swerdlow et al., 1989) suggests that nutrition and growth before puberty may also be important aetiological factors. Adult height has been increasing through the century (Floud et al., 1990), and this trend could potentially be related to the rise in the incidence of testicular cancer in young adults. The finding of Møller et al. (1995) that the secular increase in the incidence of testicular cancer was particularly marked in boys aged 15–19 years would be consistent with a possible role of peri-pubertal factors on the aetiology of this cancer. No similar finding was observed in our present study.

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