

Month of birth of men with malignant germ cell tumours of the testis

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SUMMARY A recent paper has suggested that there is a temporal cycle in birth rates of men with testis cancer with a peak in April/May. We have investigated the suggestion using data from the South Thames and Los Angeles cancer registries. There is some slight evidence of a peak in August, which is confined to teratomas. The effects demonstrated are, however, too small and inconsistent to provide any real clue to the aetiology of testis cancer.

In their recent analysis of birth dates of British men with cancer of the testis, Knox and Cummins¹ reported that "there was strong evidence of a temporal cycle... The cycle has a four-month period analogous with a school-term-related cyclical component". We have investigated this suggestion using data from the Thames Cancer Registry for the period 1968–83 and data from the cancer registry for Los Angeles County for the period 1972–84.

Materials and methods

The Thames Cancer Registry has collected cancer registration data for the South Thames Region since 1958, and data are reasonably complete for the period 1968–83. Germ cell tumours of the testis were classified as either seminomas ("pure" seminomas with no evidence of other elements) or teratomas (all others). Choriocarcinoma is included with teratoma.²

The University of Southern California Cancer Surveillance Program (CSP) is the population-based cancer registry for Los Angeles County, California.³ We analysed data on non-Hispanic white men diagnosed with germ cell tumours of the testis between 1972 and 1984, years for which the CSP has essentially complete ascertainment of all cancers diagnosed in Los Angeles County residents. Choriocarcinomas were included with teratomas so that the US and UK data are comparable.^{2,4}

Month-of-birth-specific "expected" numbers of testis cancer cases were calculated based on the month of birth distribution of all other male cancer cases in the relevant registry (non-Hispanic whites only in the CSP) as this distribution is likely to reflect the month of birth distribution of individuals surviving infancy.

These expected numbers were obtained by summing the individual year-of-birth-specific numbers of expected cases, calculated by multiplying the proportion of other cancer cases born in a particular month of a given year by the total number of testis cancer cases born in that year. In the South Thames computerised data system which we used, there are few instances where month of birth has been coded as June when in fact it was unknown: this would tend to slightly inflate both the observed and expected numbers for June.

Our method of calculating expected numbers differs from that of Knox and Cummins¹ who used "national birth data for 1950". They analysed testis cancer mortality data for England and Wales for 1978–82 and incidence data from the West Midlands and North Western Regional Cancer Registries for the years 1965–76 and 1974–9 respectively.

Three statistical tests were performed on each set of observed and expected numbers: (i) χ^2_{11} —standard Chi-squared test for heterogeneity by month on 11 degrees of freedom (Knox and Cummins¹ Annual Cycle test); (ii) χ^2_3 —Chi-squared test on 3 degrees of freedom, where observed and expected numbers are summed over every fourth month (January + May + September, etc.) (Knox and Cummins¹ One-third Annual Cycle test); (iii) χ^2_2 —Chi-squared test for seasonality on two degrees of freedom (Walter and Elwood's⁵ modification of Edwards' test for seasonal variation).

Results

The distributions of observed and expected numbers of testicular cancer cases by month of birth are shown

Table 1 Testicular cancer by month of birth: observed and expected numbers of cases and deaths*

Registry		Month of birth											Total	
		Jan	Feb	Mar	Apr	May	June	July	Aug	Sept	Oct	Nov		Dec
WM + NW†	Obs	78	95	91	113	115	76	93	85	101	87	74	92	1100
	Exp†	94.1	90.6	100.3	95.5	97.4	92.5	90.1	89.5	90.5	88.9	83.3	87.3	1100.0
	O/E	0.83	1.05	0.91	1.18	1.18	0.82	1.03	0.95	1.12	0.98	0.89	1.05	1.00
		$\chi^2_{11} = 16.02$ (p=0.14), $\chi^2_3 = 3.28$ (p=0.35), $\chi^2_2 = 1.01$ (p=0.61)												
ST	Obs	122	113	144	138	125	126	130	166	121	140	120	110	1555
	Exp	137.1	126.5	140.4	138.4	138.6	131.1	133.8	126.7	129.0	120.2	112.5	120.7	1555.0
	O/E	0.89	0.89	1.03	1.00	0.90	0.96	0.97	1.31	0.94	1.17	1.07	0.91	1.00
		$\chi^2_{11} = 22.29$ (p=0.02), $\chi^2_3 = 5.54$ (p=0.14), $\chi^2_2 = 5.98$ (p=0.05)												
LA	Obs	103	98	117	104	112	92	109	124	104	113	114	115	1305
	Exp	109.3	98.0	115.9	105.3	115.0	110.4	111.2	110.8	109.5	106.7	106.7	106.5	1305.0
	O/E	0.94	1.00	1.01	0.99	0.97	0.83	0.98	1.12	0.95	1.06	1.07	1.08	1.00
		$\chi^2_{11} = 6.98$ (p=0.80), $\chi^2_3 = 2.53$ (p=0.47), $\chi^2_2 = 1.92$ (p=0.38)												
E & W Deaths	Obs	75	45	66	75	75	67	57	89	78	67	54	79	827
	Exp†	70.8	68.1	75.4	71.8	73.2	69.6	67.8	67.3	68.1	66.8	62.6	65.6	827.0
	O/E	1.06	0.66	0.88	1.04	1.02	0.96	0.84	1.32	1.15	1.00	0.86	1.20	1.00
		$\chi^2_{11} = 23.62$ (p=0.01), $\chi^2_3 = 15.56$ (p=0.001), $\chi^2_2 = 4.56$ (p=0.10)												

* Statistical tests: see text.

† Expected values taken from Knox and Cummins!

‡ Abbreviations: WM + NW—West Midlands + North West; ST—South Thames; LA—Los Angeles; E & W—England and Wales.

in table 1. Knox and Cummins¹ reported a significant seasonal variation in observed to expected ratios for the West Midlands plus North Western Regions' incidence data and the England and Wales mortality data combined, and a significant one-third annual cycle. They found an excess of births in April/May and August/September. Table 1 shows, however, that when the incidence and mortality data used by Knox and Cummins¹ are disaggregated, only the mortality data show the significant annual cycle and one-third annual cycle previously reported.

The South Thames data show a significant annual cycle with a distinct peak in August and significant seasonality. The Los Angeles data also show a peak in August, but otherwise the observed numbers of cases by month of birth are close to those expected. The rank correlations between the observed to expected ratios in the four sets of data are shown in table 2. The South Thames and Los Angeles data show a significant correlation, and both have a prominent peak in August. The England and Wales mortality data also show a peak in August but otherwise do not agree with the South Thames and Los Angeles data.

Tables 3 and 4 subdivide the data from table 1 into seminomas and teratomas. There is no evidence of an annual cycle, a one-third annual cycle or a seasonality effect in month of birth of men with seminomas in any of the sets of data (table 3). There are no significant correlations between the three sets of data (table 2). The teratoma data from South Thames have a

Table 2 Rank correlation between observed: expected ratios by month in different areas

(a) Testicular cancer			
	WM + NW	ST	LA
ST	-0.20		
LA	0.04	0.59*	
E & W deaths	0.25	0.02	0.14
(b) Seminoma			
	WM + NW	ST	
ST	0.17		
LA	0.00	0.42	
(c) Teratoma			
	WM + NW	ST	
ST	-0.61		
LA	-0.06	0.27	

*p < 0.05

Abbreviations: see table 1.

significant annual cycle and seasonality, the most striking observation being the observed to expected ratio of 1.49 in August (table 4). The Los Angeles data also show a peak in August but none of the tests approaches statistical significance. The West Midlands plus North Western data show no evidence of seasonal differences. None of the data sets shows any correlation with each other (table 2).

Discussion

Knox and Cummins¹ "speculate upon possible mechanisms" for their finding of a significant seasonal

Table 3 *Seminomas by month of birth: observed and expected numbers of cases**

Registry	Month of birth												Total	
	Jan	Feb	Mar	Apr	May	June	July	Aug	Sept	Oct	Nov	Dec		
WM + NW†	Obs	43	43	46	59	57	43	50	44	50	49	38	38	560
	Exp	47.9	46.1	51.1	48.6	49.6	47.1	45.9	45.6	46.1	45.2	42.4	44.4	560.0
	O/E	0.90	0.93	0.90	1.21	1.15	0.91	1.09	0.97	1.08	1.08	0.90	0.86	1.00
		$\chi^2_{11} = 7.35$ (p=0.77), $\chi^2_3 = 0.62$ (p=0.89), $\chi^2_2 = 2.17$ (p=0.34)												
ST	Obs	60	57	73	72	67	59	64	70	62	69	60	59	772
	Exp	68.9	62.9	70.3	68.3	66.8	64.9	66.2	62.2	64.6	59.8	56.5	60.7	772.0
	O/E	0.87	0.91	1.04	1.05	1.00	0.91	0.97	1.13	0.96	1.15	1.06	0.97	1.00
		$\chi^2_{11} = 5.40$ (p=0.91), $\chi^2_3 = 1.26$ (p=0.74), $\chi^2_2 = 0.76$ (p=0.68)												
LA	Obs	53	47	58	52	55	43	59	52	53	61	52	57	642
	Exp	55.0	48.7	56.5	50.8	55.0	53.9	55.3	55.0	55.4	52.8	51.7	51.9	642.0
	O/E	0.96	0.97	1.03	1.02	1.00	0.80	1.07	0.95	0.96	1.16	1.01	1.10	1.00
		$\chi^2_{11} = 4.70$ (p=0.95), $\chi^2_3 = 0.50$ (p=0.92), $\chi^2_2 = 0.85$ (p=0.66)												

* Statistical tests: see text.
† Abbreviations: see table 1.

Table 4 *Teratomas by month of birth: observed and expected number of cases**

Registry	Month of birth												Total	
	Jan	Feb	Mar	Apr	May	June	July	Aug	Sept	Oct	Nov	Dec		
WM + NW†	Obs	30	43	34	42	47	31	38	34	45	34	22	39	439
	Exp	37.6	36.2	40.0	38.1	38.9	36.9	36.0	35.7	36.1	35.5	33.2	34.8	439.0
	O/E	0.80	1.19	0.85	1.10	1.21	0.84	1.06	0.95	1.25	0.96	0.66	1.12	1.00
		$\chi^2_{11} = 13.50$ (p=0.26), $\chi^2_3 = 3.28$ (p=0.35), $\chi^2_2 = 0.99$ (p=0.61)												
ST	Obs	62	56	71	66	58	67	66	96	59	71	60	51	783
	Exp	68.2	63.7	70.0	70.1	71.9	66.2	67.7	64.5	64.4	60.4	56.0	60.0	783.0
	O/E	0.91	0.88	1.01	0.94	0.81	1.01	0.98	1.49	0.92	1.18	1.07	0.85	1.00
		$\chi^2_{11} = 23.81$ (p=0.01), $\chi^2_3 = 5.03$ (p=0.17), $\chi^2_2 = 6.50$ (p=0.04)												
LA	Obs	50	51	59	52	57	49	50	72	51	52	62	58	663
	Exp	54.3	49.3	59.4	54.5	60.0	56.5	55.9	55.8	54.1	53.9	55.0	54.6	663.0
	O/E	0.92	1.03	0.99	0.95	0.95	0.87	0.89	1.29	0.94	0.97	1.13	1.06	1.00
		$\chi^2_{11} = 8.34$ (p=0.68), $\chi^2_3 = 2.79$ (p=0.43), $\chi^2_2 = 1.19$ (p=0.55)												

* Statistical tests: see text.
† Abbreviations: see table 1.

element in month of birth of men with testis cancer “pending confirmation of this finding through reference to additional data.” We have assembled two sets of such additional data from the South Thames and Los Angeles County cancer registries which offer little support to their results. Knox and Cummins¹ reported a peak in April/May with secondary peak in August/September. The major feature of the South Thames and Los Angeles data is a peak in births in August. Paradoxically, however, when we re-analysed the data presented in Knox and Cummins’ table 3 we found that their seasonality effect was confined to the

mortality data; these data also had a peak in August births.

The teratoma data from Los Angeles were subdivided into teratoma, embryonal carcinoma, and choriocarcinoma using the ICD-O classification for germ cell and trophoblastic neoplasms.⁶ Choriocarcinomas in the Los Angeles data (60 cases) comprised 5.9% of the group that we have combined under the heading “teratoma”. The tumours classified as choriocarcinomas by the US pathologists exhibited the greatest ratio of observed to expected cases for August births (O=13, E=4.7, O/E=2.74). The Los

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Angeles teratoma data excluding choriocarcinoma had a less prominent peak in August (O = 59, E = 50.8, O/E = 1.16). No comparable histological breakdown of the teratomas is available in South Thames.

The effects demonstrated here are small, not found in all the sets of data examined, and confined to teratomas. Little is known about the aetiology of germ-cell tumours of the testis apart from the strong relationship with undescended testis.⁷ This relationship applies to both seminomas and teratomas.⁸ A common aetiology for testicular cancer and undescended testis has been postulated⁹, but a recent analysis suggests that if there is a peak in month of birth of boys with undescended testis it is in March.¹⁰ If anything, our data may be consistent with the mother experiencing a first trimester infection which peaks during the winter months and which has some effect on the developing fetus (and testis differentiation). However, the effects demonstrated here are probably too small and inconsistent to provide us with any real clue to the aetiology of testicular cancer.

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