

# Occupation and Risk for Testicular Cancer: A Case-Control Study

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A case-control study of 271 testicular cancer cases aged 18-42, including 60 seminomas and 206 other germinal cell tumours, and 259 controls was carried out to study the association between occupation and testicular cancer risk. Study subjects were identified at three medical centres, two of which treat military personnel. Controls were men diagnosed with a cancer other than of the genital tract. Associations were identified between professional employment (administrators, teachers and other professionals) and risk for testicular seminoma, OR = 2.8 (95% CI: 1.4-5.4) and between employment in production work and risk for other germinal cell tumours, OR = 1.8 (95% CI: 1.1-2.7). No specific occupations within these broad groups were responsible for the observed increases. Self-reported exposure to microwaves and other radio waves was associated with an excess risk for both seminomas and other germinal cell tumours. However, an assessment of radio wave exposure based on job title did not support this finding. Although testicular cancer has been increasing in recent decades among young males, occupational factors did not appear to account for a substantial proportion of testicular cancer occurrence in the population studied.

Although testicular cancer is a rare disease, accounting for approximately 1% of all cancers among males in the US, it is the most common neoplasm found in white men aged 15 to 34.<sup>1</sup> Descriptive studies of the occurrence of testis cancer in the US and other countries<sup>2-4</sup> have shown that the incidence of this disease is increasing, particularly in younger men. Over the past 35 years, there has been a 25% increase in the incidence of this tumour in young males. The best documented risk factor for testicular cancer is cryptorchidism.<sup>5-9</sup> Other suggested risk factors are inguinal hernia,<sup>6,5,10</sup> testicular trauma,<sup>10,11</sup> low birthweight and other prenatal factors<sup>7,12</sup> and occupation.<sup>13-14</sup> It is unclear to what extent these factors account for the time trend of increasing risk among young men.

To investigate the reasons for this increase, we conducted a large study of young men referred to three

medical centres in the Washington DC area. Methods of study and non-occupational risk factors are described in detail in previous publications.<sup>9,11</sup> This paper reports on an investigation of the association between occupation and testicular cancer risk in young men identified at these centres.

## MATERIALS AND METHODS

### Study Population

Selected for study were all testicular cancer cases aged 18-42 who were newly diagnosed between 1 January 1976 and 30 June 1981 and referred to one of three collaborating medical institutions in the Washington DC area: the Uniformed Services University Navy Hospital (USUNH), The Uniformed Services University Walter Reed Army Medical Centre (WRAMC), and the National Institutes of Health Clinical Center (NIHCC). Because two of the three study hospitals were military hospitals, a large number of the subjects selected for study were active duty military personnel. Cases diagnosed prior to 1979 were ascertained from tumour registry, hospital admission, urology, and pathology records at the three centres and were interviewed over the telephone. In-person interviews were conducted in the hospital for the cases seen on the

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oncology, surgical, and urology wards during 1979–1981. In addition, telephone interviews were conducted with the mothers of cases and controls.

Controls were patients at the same hospital as the cases, diagnosed with a cancer other than cancer of the genital tract (ICD-8: 185–187). Controls diagnosed between 1976 and 1978 were identified from the computerized discharge logs at NIHCC and WRAMC and from tumour registry records at USUNH and were interviewed over the telephone. Controls diagnosed during 1979–1981 were identified on the oncology, surgical, and medical wards and were interviewed in the hospital in the same manner as the cases. Controls were diagnosed during the same time period and frequency matched to the cases by age ( $\pm 2$  years of age). To assess the possibility of biased results due to the use of cancer controls, some analyses were carried out limiting the control series either to subjects with lymphatic and haematopoietic malignancies or to subjects with other cancers. A total of 335 cases of testicular cancer were identified at the three institutions. Medical records were reviewed to confirm the date of diagnosis. Of the 308 living cases, interviews were completed for 271, yielding a response rate of 88%. Of the 288 selected controls, 259 were interviewed for a response rate of 90% (Table 1). Sixty-nine per cent of the cases and 71% of the controls were interviewed in person in the hospital and the remainder were interviewed at home over the telephone. The study population was 98% white with a mean age at diagnosis of 27 years for both cases and controls. Forty-eight per cent of the study subjects were seen at the NIHCC, 30% at WRAMC, and 22% at USUNH.

Histological type of testicular cancer was determined from review of pathology reports. Among the interviewed cases, 266 (98%) were germinal cell carcinomas. For this analysis, germinal cell carcinomas were grouped as seminomas ( $n = 60$ ) and all other germinal cell tumours ( $n = 206$ ). Major histological groups among the other germinal cell tumours were embryonal carcinoma ( $n = 69$ ) and teratocarcinoma

( $n = 67$ ). Three subjects with non-germinal cell tumours (Leydig cell) and two with testicular tumours of unknown type were excluded from the analysis.

The diagnoses among the controls were as follows: Hodgkin's disease (29%); non-Hodgkin's lymphoma (18%); melanoma (17%); soft tissue sarcoma, bone tumours, and leukaemia (7% each); nervous system tumours (4%), and other cancers (11%).

#### Interviews

Interviews of the study subjects were conducted during the years 1979–1981 and obtained detailed information on the study subjects' demographic characteristics, occupational history, and other variables of interest. For the occupational history, a job was defined as any type of employment which was held for six months or longer. Each position with a particular set of duties or job title was identified as a separate job. Also, time spent in a vocational training school was considered a job. Time spent as a student in an academic programme was recorded to account for gaps in the work history.

Information obtained for each job included the following: job title, activities and duties, materials handled, full or part-time status, name of company, type of business, site of employment (city, county, state/ship, base, station), year started, and year ended. The study subjects were asked if they had ever been exposed to or handled: (1) radioisotopes, radioactive materials, or nuclear materials, (2) radar equipment, (3) microwaves, microwave ovens or other radio waves, (4) pesticides, or (5) polycyclic aromatic hydrocarbons, for example, in the manufacture, combustion, or drilling of fossil fuels such as coal, natural gas, or oil. Specific questions about exposure to electromagnetic waves were included to investigate an *a priori* clinical impression that radar and other microwave exposure were common among military testicular cancer cases. Occupations were coded in accordance with the Standard Occupational Classification Manual.<sup>15</sup>

TABLE 1 The number and per cent of interviewed testicular cancer cases and controls, by age at diagnosis and referral hospital

Age	NIHCC (1)		USUNH (2)		WRAMC (3)		Total	
	Case No. (%)	Control No. (%)						
16–21	22 (18)	23 (18)	12 (20)	13 (22)	17 (20)	15 (21)	51 (19)	51 (20)
22–25	26 (20)	33 (26)	15 (25)	10 (17)	14 (16)	13 (18)	55 (20)	56 (22)
26–29	41 (32)	35 (27)	19 (32)	17 (29)	32 (38)	18 (25)	92 (34)	70 (27)
30–43	38 (30)	37 (29)	13 (23)	19 (32)	22 (26)	26 (36)	73 (27)	82 (31)
Total	127	128	59	59	85	72	271	259

The measure of statistical association used in this study is the odds ratio. This measure was adjusted by stratification for age and, where specified, for other potential confounders. The odds ratio, tests of statistical significance ( $P < 0.05$ , two-sided) and confidence intervals were derived by the maximum likelihood method.<sup>16</sup>

## RESULTS

In Table 2, a significant elevation in risk is found for seminoma among the broad occupational group of professionals, OR = 2.8. Two- to three-fold increases in risk are seen for all subcategories of professionals, with the risk for teachers and administrators being significantly elevated. Adjustment for education, cryptorchidism, and low birthweight did not change the risk for professionals. The association for seminoma among professionals remained statistically significant when the control groups were divided into subjects with lymphatic and haematopoietic malignancies (OR = 2.5; 95% CI: 1.2-5.1) and those with other cancers (OR = 3.1; 95% CI: 1.4-6.6). The median duration of employment among controls for all professional jobs

was only three years. When risk for seminoma is restricted to those with employment for three years or more, significantly elevated risks are found among the broad group of professionals (31 cases, 56 controls), OR = 4.0 (95% CI: 1.8-8.9) and among the subgroups of teachers (10 cases, 15 controls), OR = 3.2 (95% CI: 1.2-8.8) and 'other' professionals (11 cases, 15 controls), OR = 2.9 (95% CI: 1.1-7.6).

A non-significant excess risk for seminoma is seen among those ever employed in the broad occupational group of other white collar jobs. Specifically, there is a non-significantly elevated risk among health-related non-professionals and a significantly elevated risk among those who have ever held jobs as sales or service personnel. No excess risk of seminoma was associated with employment in the broad occupational group of blue collar workers. For agricultural, forestry and fishery workers and for construction workers, the associated risks were statistically significantly decreased.

In contrast, the other germinal cell tumours do not appear to be associated with employment in professional or other white collar occupations. However, the risk for these tumours is marginally elevated among

TABLE 2 Odds ratios (OR)\* for testicular cancer by occupation (ever employed) and histological type

Occupation	No. of controls	All testicular cancer (No. = 271)		Germinal cell carcinoma					
		OR	(95% CI)†	Seminoma (No. = 60)		Other (No. = 206)			
				OR	(95% CI)	No.	OR	(95% CI)	No.
Professionals	91	1.0	(0.7-1.6)	2.8	(1.4-5.4)	38	0.7	(0.5-1.2)	56
Administrator	53	1.0	(0.6-1.6)	2.1	(1.1-4.2)	23	0.7	(0.6-1.2)	28
Teacher	28	1.5	(0.9-2.8)	3.0	(1.4-6.7)	17	1.1	(0.6-2.2)	21
Physician/ veterinarian	3	1.1	(0.2-6.6)	3.3	(0.5-21.8)	3	0.4	(0.0-4.3)	1
Other professionals	35	0.9	(0.5-1.5)	1.6	(0.7-3.4)	14	0.7	(0.3-1.3)	19
Other white collar	188	1.1	(0.7-1.6)	1.4	(0.7-3.1)	48	1.0	(0.6-1.5)	148
Health related	18	1.4	(0.7-2.6)	1.9	(0.7-5.0)	8	1.2	(0.6-2.5)	17
Engineer/science	32	0.7	(0.4-1.2)	0.8	(0.3-2.1)	7	0.6	(0.3-1.2)	16
Other technician	41	0.5	(0.3-0.8)	0.7	(0.3-1.7)	7	0.4	(0.2-0.8)	14
Sales/service	118	1.3	(0.9-1.9)	1.9	(1.0-3.5)	36	1.2	(0.8-1.7)	103
Clerk	77	1.0	(0.6-1.4)	1.0	(0.5-1.9)	19	0.9	(0.6-1.4)	56
Blue collar	210	1.0	(0.6-1.6)	0.6	(0.3-1.2)	44	1.4	(0.8-2.3)	174
Agricultural/F/F	68	0.9	(0.6-1.4)	0.4	(0.2-0.9)	7	1.1	(0.7-1.8)	60
Construction	81	0.8	(0.6-1.2)	0.4	(0.2-0.9)	10	1.0	(0.7-1.5)	63
Mining	2	2.0	(0.3-15.8)	—	—	0	2.8	(0.4-22.7)	4
Transportation	33	1.1	(0.6-2.0)	0.7	(0.2-1.9)	6	1.3	(0.8-2.4)	31
Mechanics/repair	41	0.6	(0.4-1.1)	0.6	(0.2-1.6)	6	0.7	(0.4-1.2)	23
Garage Service	30	0.6	(0.3-1.2)	0.1	(0.0-0.8)	1	0.8	(0.4-1.5)	19
Electrical/repair	13	1.4	(0.6-3.0)	1.7	(0.5-5.5)	5	1.3	(0.5-3.0)	13
Other repair	21	0.5	(0.2-1.1)	0.5	(0.1-2.0)	3	0.5	(0.2-1.1)	8
Production	60	1.4	(0.9-2.1)	0.7	(0.3-1.6)	12	1.8	(1.1-2.7)	68
Other manual	61	1.3	(0.9-1.6)	1.0	(0.5-2.0)	14	1.4	(0.9-2.2)	63
Ship employment	42	0.7	(0.4-1.2)	1.9	(0.9-3.8)	17	0.4	(0.2-0.8)	14
Aircraft maintenance	22	0.8	(0.4-1.6)	1.3	(0.5-3.4)	7	0.6	(0.3-1.4)	11

\* Odds ratio, adjusted for age (16-21, 22-25, 26-29, 30-43).

† 95% CI = 95% confidence interval.

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51 (20)  
56 (22)  
70 (27)  
82 (31)  
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those who ever held blue collar jobs (OR = 1.4) and is significantly elevated among production workers (OR = 1.8). Adjustment for education (some or no college), cryptorchidism, and for low birthweight (<5 lbs), each separately, did not substantially alter the risk for production workers.

The median duration of employment among controls for all blue collar jobs was six years. For those employed three years or more in production work (34 cases, 25 controls), the associated risk was OR = 2.3 (95% CI: 1.2-4.3). Among production workers, the risk for other germinal cell tumours was consistently elevated for all subcategories: metal and plastic, OR = 1.6 (95% CI: 0.8-3.1), wood, OR = 3.0 (95% CI: 0.7-28.4), printing, OR = 2.4 (95% CI: 0.5-12.9), textile, OR = 1.8 (95% CI: 0.3-10.4), and other production workers, OR = 1.7 (95% CI: 0.7-3.9). The risk for embryonal carcinoma associated with production work (18 cases, 51 controls) was OR = 1.4 (95% CI: 0.7-2.7) and for teratocarcinoma (16 cases, 51 controls) was OR = 2.3 (95% CI: 1.2-4.4).

When the control group was limited to subjects with lymphatic and haematopoietic malignancies, the risk for the combined group of other germinal cell tumours associated with production work was OR = 2.4 (95% CI: 1.4-4.3), while it was only OR = 1.3 (95% CI: 0.8-2.3) when subjects with other cancers were considered as controls.

No significant associations were noted for the seminomas or other germinal cell tumours associated with employment in farming, aircraft maintenance, or employment on a ship; although, for the latter a moderate increase in risk, OR = 1.9, was found for the seminomas. When the analysis was restricted to cases and controls identified from the two military hospitals, no major changes in any of the ORs were noted.

In Table 3, the risks associated with reported occupational exposures are shown. The OR for exposure to microwaves or other radio waves is significantly elevated for all testicular tumours combined, OR = 3.1, and for the other germinal cell tumours, OR = 3.2, and is non-significantly elevated for the seminomas, OR = 2.8. When restricted to subjects identified in military hospitals, the risk for exposure to microwaves and other radio waves was OR = 3.5 (95% CI: 1.3-10.2). For other germinal cell tumours, non-significant elevations in risk of 1.5 or greater were seen for hydrocarbon and insecticide/pesticide exposure.

Based on job title, an industrial hygienist (MG) classified subjects' exposure to radar or other microwaves as high (e.g. electronic technicians and repairmen, power generator operators, and microwave system operators), medium (e.g. communications

operators and signal officers), or low level (e.g. airplane flight crews). In general, there was poor agreement (Spearman rank correlation = 0.4 (ns)) between self-reports of exposure to microwaves and other radio waves and exposure as assessed from the job title. Of those classified from the job title as having none, low, medium, and high exposure, 4%, 7%, 17% and 54%, respectively, had a reported history of exposure to microwaves and other radio waves. Among those classified as highly exposed according to the industrial hygienist's assessment, 3 of 12 cases and 9 of 14 controls did not report exposure. Based on the assessment by job title, risk increased non-significantly among subjects with low level exposure (OR = 2.3). However, risk was not increased for subjects with medium (OR = 1.0) or high (OR = 0.8) exposure (Table 4).

## DISCUSSION

In general, cancer caused by occupational exposures may be expected to increase in frequency with age, following the accumulation of exposure and the passage of sufficient time for disease development. Germinal cell cancers of the testis exhibit a sharp rise in incidence at about 10-15 years of age, peak in incidence at about 30-34 years of age, and then show a consistent decline in incidence into the fifth and sixth decades. Although this age pattern may not be typical of tumours with a large environmental or occupational component, the dramatic increase in testicular cancer incidence over the last several decades, and the importance of this tumour in young men make exploration of potential occupational risk factors worthwhile.

The strongest finding in the present investigation was the association between employment in professional occupations and the risk for testicular seminoma. The risk was elevated in all occupational subgroups of professionals and was greater among those employed longer in these occupations. The elevation of risk in a number of professions suggests that the association with testicular cancer is probably not directly related to occupational duties or specific occupation-related exposures. In this regard, the elevated risks among other white collar workers employed in health-related jobs and sales and services occupations are also noteworthy. For white collar employees, no association was noted for the other germinal cell tumours. Others<sup>17-18,14,19</sup> have noted an excess risk for testicular cancer among professionals. In the studies which examined this association by histological cell type, neither Ross et al.<sup>19</sup> nor Graham et al.<sup>18</sup> found that risk was restricted to the seminomas. Among Army men, Morrison found an increased risk associated with duration of schooling for seminomas only.

TABLE 3 Odds ratio (OR)\* for testicular cancer by self-reported exposure and histological type

Exposure	No. of controls	All cancer (No. = 271)		Germinal cell carcinoma					
		OR	(95% CI)†	Seminoma (No. = 60)			Other (No. = 206)		
				OR	(95% CI)	No.	OR	(95% CI)	No.
Radioactive material	23	1.2	(0.6-2.3)	1.3	(0.5-3.3)	8	1.2	(0.6-2.4)	20
Radar equipment	38	1.1	(0.7-1.9)	1.3	(0.6-2.8)	12	1.1	(0.6-1.9)	30
Microwave/other radiowaves	10	3.1	(1.4-6.9)	2.8	(0.9-8.6)	7	3.2	(1.4-7.4)	24
Hydrocarbons	12	1.5	(0.7-3.4)	1.0	(0.2-3.9)	3	1.7	(0.7-4.0)	15
Pesticides	29	1.2	(0.4-1.2)	0.1	(0.0-1.0)	1	1.5	(0.9-2.7)	32

\* Odds ratio, adjusted for age (16-21, 22-25, 26-29, 30-43).

† 95% CI = 95% confidence interval.

In the present study, there was a weak association with all blue collar jobs for the other germinal cell tumours. Among blue collar workers the excess risk was largely restricted to production workers. The risk among production workers was elevated among longer-term workers and was seen for all types of production work investigated. This latter observation again suggests that no specific exposure is involved.

Statistical adjustment for educational status, cryptorchidism and low birthweight could not account for either the association of seminomas with professional occupations or of the other cell types with production-related occupations. When the control group was divided into two groups for comparison with the case series, the association of seminoma with professional occupations remained. For the other germinal cell tumours, the association with production work, although in the same direction, was stronger in comparison to subjects with lymphatic and haematopoietic malignancies than in comparison with subjects with other cancers. This discrepancy may be due to random variation or to a bias in the control group selection.

When enquiries were made about specific exposures, a statistically significant association was found for reported exposure to microwaves and the other radio waves. The finding held for both seminomas and the other tumour types. However, an independent assessment by job title did not support this finding. Only the group defined as having low exposure showed any increase in risk. The poor agreement between self-reports of exposure and the exposure assessment by job title may be due in part to the limitations in both of these approaches.

There is currently a great deal of uncertainty about the role, if any, of low-frequency radiation in human carcinogenesis.<sup>21-23</sup> The assessment of the potential association of low-frequency electromagnetic radiation and cancer risk is hampered by uncertainties

about effective electromagnetic frequency ranges, the lack of a clear biological mechanism, as well as by difficulties of exposure assessment. The inconsistent results of the present study do not provide a firm indication of an associated risk for testicular cancer.

Dubrow and Wegman,<sup>24</sup> in a compilation of results from 12 large studies of occupation and cancer, found that the strongest association for testes cancer and employment is with the armed forces. Excesses of testicular cancer have also been reported from Great Britain<sup>25</sup> and Denmark<sup>26</sup> for members of the armed forces. Garland et al.<sup>27</sup> found no overall excess of testicular cancer in US Navy personnel, but did find excess risks among aviation support equipment technicians, enginemen and similar workers. We found no association for workers involved in aircraft maintenance. Among civilians engaged in repair of F4 Phantom Jets<sup>28</sup> and among leather tannery workers,<sup>29</sup> cases of testicular cancer have been found in excess among those possibly exposed to dimethylformamide. This interesting finding could not be assessed in the present study, as military personnel engaged in aircraft maintenance are not thought to have dimethylformamide exposure (AM Ducatman, personal communication). Although farming has been associated with excess risk

TABLE 4 Odds ratio (OR)\* risk for testicular cancer among military personnel by exposure to microwaves and other radiowaves, as determined by assessment from job titles.

	Exposure				
	None	Low	Medium	High	Any
Cases	116	10	6	12	28
Controls	107	4	6	14	24
OR	1.0	2.3	1.0	0.8	1.1
95% CI†	—	(0.6-9.4)	(0.3-3.8)	(0.3-2.0)	(0.6-2.1)

\* Odds ratio, adjusted for age (16-21, 22-25, 26-29, 30-43).

† 95% CI = 95% confidence interval.

for testes cancer,<sup>13,30</sup> this association has not been found consistently in other studies,<sup>31-34</sup> including a prior analysis of this study.<sup>35</sup>

Although this study was largely negative with regard to occupation and risk for testicular cancer, some aspects of the study design may have reduced our ability to identify such associations. A study of occupational exposure in young men will be concerned generally with employment of short duration. We examined risk separately for those employed three years or more, but even this exposure period is short. Further, the study subjects were generally at risk for development of disease for a relatively short period of time after initial employment. We did not examine risk for testicular cancer among subjects older than 42 years of age.

The power of this study was limited for the detection of small relative risks. With 10% of subjects employed in an occupation, the power was about 75% to detect risks less than 2.5 for the seminomas and 2.0 for the other germinal cell tumours. A considerably larger study would be needed to have sufficient power to detect lower risks.

Because the cases in this study were identified at referral hospitals, the population base from which they derived could not be well defined. Primarily for this reason, cancer controls were selected from the same hospitals. This choice may have reduced recall and interviewer bias.<sup>36</sup> Although we had no compelling *a priori* hypotheses about this, a positive association between risk factors examined and the diseases included in the control series would have biased observed excess risks toward the null. We carried out analyses limiting the control series either to subjects with lymphatic and haematopoietic malignancies or to subjects with other cancers, without finding any such bias.

In summary, this study demonstrates associations between professional employment and risk for testicular seminoma, and between production-related employment and risk for other germinal cell tumours. However, these findings were not related to specific occupations within these broad groups. A suggested association, based on self-reports, of microwaves and other radio waves with testicular cancer risk was not supported by an exposure assessment by job title.

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