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Adenocarcinoma of the nose and paranasal sinuses in shoemakers and woodworkers in the province of Florence, Italy (1963-77)

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ABSTRACT Adenocarcinoma of the nose and paranasal sinuses has been associated with occupational exposure to wood and leather dust. Strong evidence has been found for such an association in Florence, Italy, from 1963 to 1977. Sixty-nine cases of primary cancer of the nose and paranasal sinuses were identified from hospital records. There were 13 cases of adenocarcinoma, 11 of which were successfully traced and interviewed (patient or relative). Of the 11 cases, three were woodworkers with substantial exposure to wood dust (17 years' average employment) and seven were shoemakers, mostly trimmers. When matched to either of two separate sets of controls (non-cancer hospital patients, and non-adenocarcinoma nose or paranasal sinus cancer patients), the association with occupation was statistically significant. Smoking was ruled out as a source of bias.

Cancer of the nose and paranasal sinuses is rare in the general population. In the past decade reports from England,[1-7] France,[8-13] the United States,[14-17] Denmark,[18] and Australia[19] have shown an association between these cancers, particularly adenocarcinoma of the nose and paranasal sinuses, and exposure to wood dust. Both Acheson[6] and Hadfield[3] have reported a significantly high incidence of adenocarcinoma of the nasal cavity and paranasal sinuses among workers in the furniture and shoe industries in England exposed to wood or leather dust, or both. We present evidence for an association between leather and woodworking and mortality from adenocarcinoma of the nose and paranasal sinuses in Florence.

The province of Florence (population 1 150 000 in 1971) has a diverse economy with little heavy industry. Almost 1% (10 174 in 1971) of the population is engaged in shoe manufacturing, an industry entirely separate from the handbag manufacturing industry. Much of the shoe manufacturing is done in small establishments and home work shops. As the home work is often not reported to the government the census certainly underestimates the size of the work force. Between 1961 and 1971 the size of the reported work force in the shoe industry increased by 25%. A previous paper identified polyneuropathies among these leather workers from heavy solvent exposure in poorly ventilated workshops.[20]

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Materials and methods

As no cancer registry yet covers the province of Florence, records of the otorhinolaryngology clinic and the Radiology Institute of the University of Florence for 1963-77 were searched, and 69 patients (47 male, 22 female) with primary cancer of the nasal cavity and paranasal sinuses identified.

Three of the 69 were excluded because biopsy results were missing. For each of the remaining 66 an interview was attempted with the patient or a relative if the patient had died. The interview was conducted by a specially trained social worker, and data on occupational history, smoking habits, and other relevant issues were collected. Four patients (including two with adenocarcinoma) could not be located.

To determine the accuracy of the type of tumour given in the hospital record, 47 (76%) of the 62 cases with complete biopsy and interview data were reviewed by an independent pathologist, and classified by type of tumour.

A control group for the cases of adenocarcinoma was constructed from patients without malignant disease admitted to the department of internal medicine in the University Hospital. Controls were matched to patients by sex, age (± 5 years), place of residence (strongly associated with socioeconomic status), smoking habits, and year of hospital admission (± 5 years). The controls received the same interview as the cases.

A standard chi-square analysis was used to compare cases to controls.

Results

Table 1 summarises the 66 cases for whom biopsy data were available. Sex and median age by histological type are also shown. The results of an independent review of histological type are shown in table 2. Overall, 85% of the classifications listed in the hospital records were correct according to the independent review. For adenocarcinoma 89% (7/8) of the original classifications were confirmed. One case of adenocarcinoma was reclassified as mucoepidermoid tumour, but one epidermoid carcinoma was termed adenocarcinoma after review, so the overall number was unchanged. Because not all the cases could be reviewed for histological type, and because the results of this review of a large sample indicated overall accuracy in histological classification, the type listed in the hospital record was used in this study.

A preliminary analysis indicated that leather and wood work were often reported by the patients with adenocarcinomas, so these were matched to controls as has already been described. Table 3 summarises the relevant data for the 13 patients with adenocarcinoma (two could not be located for interview), and table 4 gives the distribution of patients with

Table 1 *Histological type, sex, and median age of all 66 patients with biopsy performed*

	Men		*Women*		*Total*	
	No of cases	*Median age*	*No of cases*	*Median age*	*No of cases*	*Median age*
Adenocarcinomas	12	58	1	72	13	58
Epidermoid and anaplastic carcinomas	23	59	15	64	38	61
Other primary cancers	11	56	4	58	15	56
Total	46		20		66	

Table 2 *Comparison of histological classifications by original diagnosis and by an independent pathologist for 47 patients*

Histological type in original diagnosis	*Histological type established by independent review*				
	Adenocarcinomas	*Epidermoid carcinomas*	*Anaplastic carcinomas*	*Other primary cancers*	*Total*
Adenocarcinomas	7	0	0	1	8
Epidermoid carcinomas	1	16	0	1	18
Anaplastic carcinomas	0	4	4	0	8
Other primary cancers	0	0	0	13	13
Total	8	20	4	15	47

Table 3 *Relevant data on patients with adenocarcinoma*

Case No	*Sex*	*Age at diagnosis*	*Occupation*	*Length of employment (years)*	*Latent period (years)*
1	M	64	Woodworker	13	31
2	M	47	Shoemaker (trimming)	7	32
3	M	60	Woodworker	30	40
4	M	73	Shoemaker and repairer	55	53
5	M	61	Shoemaker*	20	35
6	M	66	Shoemaker (trimming)	40	40
7	M	44	Woodcutter	?	?
8	M	58	Shoemaker (trimming)	?	?
9	M	53	Shoemaker (trimming)	30	30
10	M	62	Woodworker†	10	30
11	M	44	Shoemaker (trimming)	7	35
12	M	63	?	?	?
13	F	72	?	?	?
					median: 36

*Also exposure to wood dust.
†Also home work as a shoemaker (10 years).

Table 4 *Distribution of patients with adenocarcinoma and controls by occupation*

	Shoemakers	*Woodworkers*	*Others*	*Total*
Adenocarcinomas	7	3	1	11
Controls	0	2	20	22
Total	7	5	21	33

$\chi^2 = 23{\cdot}31$.
$p(\chi^2) = < 0{\cdot}0001$.

adenocarcinoma and controls by occupation. Sixty-four % (7/11) of the patients with adenocarcinoma had occupational experience as shoemakers, whereas none of the controls followed that occupation. Twenty-seven per cent of cases (3/11) and 9% of controls (2/22) had occupations exposed to wood dust.* These differences were statistically significant ($p < 0{\cdot}001$) (table 4). When the occupations of patients with adenocarcinoma were compared with those of patients with carcinoma and also other primary cancer of the nose and paranasal sinuses (table 5), the patients with adenocarcinoma were again more often shoemakers and woodworkers than were the other groups, and this difference was also statistically significant ($p < 0{\cdot}001$). Among these patients without malignant disease no occupational associations were observed. In the analysis of patients with adenocarcinoma only men aged 45-75 were included, because nearly all (9/11 with occupation known) the patients with adenocarcinoma are clustered in this older cohort.

Table 5 *Distribution of patients with adenocarcinoma and other cancer by occupation (men aged 45-75)*

	Shoemakers	*Woodworkers*	*Others*	*Total*
Adenocarcinomas	6	3	0	9
Epidermoid and anaplastic carcinomas	2	0	17	19
Other primary cancers	0	0	5	5
Total	8	3	22	33

$\chi^2 = 25{\cdot}68$.
$p(\chi^2) = < 0{\cdot}0001$.

A potentially confounding factor in this study is smoking habit. As shown in table 6, smoking does not appear to be associated differentially with cancer of any histological type studied.† Furthermore, the chi-square analysis of the data in table 6 was not statistically significant ($p = 0{\cdot}62$). Smoking habits are thus unlikely to be a source of bias in this population.

Table 6 *Comparison of smoking habits of patients with adenocarcinoma and patients with cancer of other histological types (men aged 45-75)*

	Adenocarcinomas	*Epidermoid and anaplastic carcinomas*	*Other primary cancers*	*Total*
Smokers	7	15	4	25
Non-smokers	4	4	1	9
Total	11	19	5	34

$\chi^2 = 0{\cdot}95$.
$p(\chi^2) = 0{\cdot}62$.

Discussion

Adenocarcinoma of the nasal cavity and paranasal sinuses is a rare cancer in Florence, as elsewhere, with only 13 cases reported in 15 years. Our data show, however, that this cancer occurs predominantly among men (male/female ratio = 12) heavily exposed to wood or leather dust. Among the seven shoemakers with adenocarcinoma, five worked in industry, mainly in trimming operations. The interviews indicated that they were heavily exposed to leather dust. The two other shoemakers were primarily shoe-repairers. This suggests a direct link between adenocarcinoma and exposure to leather dust.

Of the three woodworkers, one also repaired shoes at home for 10 years and so was exposed to both leather and wood dust. The others had small woodworking shops, and it was not possible to determine the extent of their exposure to wood dust.

The average latent period between the start of exposure and diagnosis of the disease was 36 years (33 for woodworkers, 37 for leather workers). This is a short latent period for this type of cancer, but may be due to the intensity of exposure (probably not less than ten hours a day, six days a week) and the poor ventilation of the work rooms.

A definite carcinogenic agent has not been identified in leather or wood, although chromate salts and tannic acid used in leather tanning are suspected carcinogens.[21] If they or some other common leather ingredients are responsible for nasal adenocarcinoma, then a large population is still at risk of this disease.

*The case listed as "wood cutter" cut wood with an axe, and the interview did not identify significant exposure to wood dust. He was not considered to have been exposed to wood dust.

†Again the analysis was restricted to the only sizable cohort, men aged 45 to 75 years at diagnosis.

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[1] International Steering Committee of Medical Editors. Uniform requirements for manuscripts submitted to biomedical journals. *Br Med J* 1979;**1**:532-5.
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