Papers and Originals

Nasal Cancer in the Northamptonshire Boot and Shoe Industry

E. D. ACHESON,* D.M., F.R.C.P. ; R. H. COWDELL,† D.M., F.R.C.PATH. ; B. JOLLES,‡ M.D., D.M.R.E., D.M.R.

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Summary: A survey of the incidence of nasal cancer in Northamptonshire during the period 1953 to 1967 is reported. Of the 46 patients with nasal cancer ascertained during the 15-year period 21 (19 males and 2 females) had been employed at some time in the boot and shoe industry. Five other cases diagnosed either before 1953 or after 1967 in persons who had worked in the boot and shoe industry in Northamptonshire were ascertained from various sources.

The incidence of nasal cancer (all histological types considered together) was significantly higher in male boot and shoe operatives in Northamptonshire than in males of all occupational classes in the Cancer Register areas selected for comparison and in males working in other occupations in Northamptonshire. The excess incidence has recently given rise to the occurrence of between 1 and 2 new cases per annum in the Northamptonshire boot and shoe industry.

The cases within the Northamptonshire industry occurred almost entirely in the relatively small number of workers who are exposed to the dust of the materials used in the manufacture of footwear.

Possibly there are two carcinogenic factors in the industry—one related to the production of nasal adenocarcinoma, and the other to squamous and possibly other types of carcinoma in the nasal cavity and sinuses. This requires further study. Our best estimate of the latent period for the adenocarcinoma cases was 54.6 years, which is substantially longer than for the patients with squamous, transitional, and anaplastic tumours (41.7 years). We have no evidence to answer the question whether the facts are still present in the industrial environment, though undoubtedly the standards of hygiene in the industry has improved substantially since these men were first exposed.

There is probably an increased risk of nasal adenocarcinoma in the footwear repairing industry, but this requires further study. Our evidence suggests that snuff taking should be considered as a possible contributory factor in both industrial and non-industrial nasal cancer.

A survey of the footwear manufacturing and repairing industry is recommended regarding cancer of the respiratory tract. Further attempts should be made to minimize the inhalation of dust. The case for the prescription of nasal cancer in the footwear industry should be considered.

Introduction

In the course of an analysis of nasal cancer, as it has affected workers in the furniture industry in the Oxford Regional Hospital Board area in recent years, an aggregation of cases was noted in Northamptonshire. This paper reports a detailed survey of nasal cancer in Northamptonshire and gives evidence which suggests that there may be an association between cancer of this site and work in the boot and shoe industry.

Material and Method

Means of Ascertainment

The material consists principally of two groups of cases of carcinoma of the nasal cavity and accessory sinuses occurring in persons resident in Northamptonshire. Group 1 consists of 46 patients in whom the diagnosis was made during the years 1953-67. As the degree of ascertainment of cases during these years is thought to have been high this material is used in the computation of incidence rates, using the 1961 census as the denominator. Group 2 consists of all other patients ascertained in the same area who were diagnosed either before 1 January 1953 or after 31 December 1967. The means of ascertainment used were different in the two groups. In addition to these two groups of cases brief mention is made of nine present or past workers in the footwear industry and two other persons in industrial contact with leather who have developed nasal cancer and whose cases have been ascertained from other parts of England.

The source of the cases in group 1 was the Oxford Cancer register, which was established in 1951. The high standard of ascertainment of this register has been remarked on elsewhere (Acheson, Cowdell, Hadfield, and Macbeth, 1968).

The cases in group 2 were obtained in the following ways: five (three occurred in 1968 and two in 1952) from the Cancer Register in the same way as those in group 1, three (two dating from 1950 and one from 1952) from a systematic search of the death benefit records of the National Union of Boot and Shoe Operatives, and seven were found in the Registers of Death Certificates of Northampton County Borough, which were searched systematically from 1900 to 1968. In all but two of these, confirmatory pathological evidence was found in the local hospitals and it was possible to determine the histological type of tumour.

Area Studied

The population of Northamptonshire at the 1961 census was almost exactly 400,000. About one-quarter lived within the

* Medical Director, Oxford Record Linkage Study.

† Consultant Pathologist, United Oxford Hospitals.

‡ Consultant Radiotherapist and Director of the Department of Radiotherapy, Northampton General Hospital.

boundary of the County Borough of Northampton. According to the census there were 16,030 male and 12,970 female leatherworkers actively employed in Northamptonshire in 1961. Most of these were workers in the boot and shoe manufacturing industry, about one-third of the national manpower of which is situated in Northamptonshire.

The estimated numbers of economically active and retired male leatherworkers in Northamptonshire in 1961 by age are given in Table I. We are grateful to Dr. G. Hill, senior medical statistician at the General Register Office, for these estimates, which are used in the calculation of incidence rates.

TABLE I.—Estimated Numbers of Economically Active and Retired Male Leatherworkers Aged 15 or over. Northamptonshire A.C. and C.B. 1961

	15-64	65 or over	15 or over
Tanners, etc. (090)*	1,940	230	2,170
Shoemakers (091)	200	40	240
Cutters, lasters, and other footwear operatives (092)	13,830	1,830	15,660
Leather product makers (093)	120	20	140
All leatherworkers (order IX)	16,090	2,120	18,210
All males	126,880	19,753	146,633

*Registrar General's classification of occupations.

Occupational Histories

Information was sought about the occupational histories of all the ascertained cases. Where possible the patient himself or a relative was sent a standard questionnaire or interviewed by a social worker. Other sources of information included hospital records, death certificates, and trades union records. Though the quality and quantity of the data varied it was possible to obtain some information in all but nine persons, of whom six were married women. The available information is summarized in the Appendix.

Verification of the Histological Material

As in the previous paper, an attempt was made to obtain and review all the histological material. Slides for 39 (64%) of the 61 cases finally accepted were located and examined. In group 1 30 of the 46 accepted cases were reviewed; in group 2 9 of the 15 accepted cases were reviewed. In addition, six other cases previously classified as carcinomas of this site were rejected following the review.

It should be stressed that the material was reviewed without knowledge of the patient's occupation. If two instances where the original material was unclassified are excluded, the reviewer agreed with the original classification in 27 (73%) of the 37 cases compared. This proportion is slightly lower than that found in the previous paper (82%). The proportion of agreements varies with the histological type of tumour. The term "adenocarcinoma" was used to describe the appearances on one or more occasions in 15 patients, and there was agreement between the observers in 11. The term "squamous" was used to describe the appearances once or more in 17 of the patients whose material was examined twice, with agreement in 14. Both these terms therefore seem relatively reliable. On the other hand, the term "transitional" was used once or more regarding nine patients, but there was agreement on only two occasions.

The principal difference between the classifications lies, therefore, in the use of the term "transitional." This term was used on four occasions in the material as it was originally ascertained, but according to the reviewer's reclassification there were 10 instances of this tumour, including two previously unclassified.

In view of the differences between the two classifications the question arose of which should be used for the purposes of the analysis. The second classification has been chosen because it is consistent with the previous paper, but the main conclusions can be shown with either.

Results

Histological Type and Sex

The cases are classified according to histological type in Table II. For comparison a breakdown is shown of all registered cases of carcinoma of the nasal cavity and sinuses in the South Metropolitan, South Western, and Birmingham Cancer Register areas (referred to collectively as the Southern Register areas) during the years 1961-5 inclusive. Material from these registers was used for comparison because a histological classification is recorded in a large proportion of their cases. The southern part of the Oxford Region is shown separately in Table II because the concentration of the furniture industry there leads to a disproportionate number of adenocarcinomas.

TABLE II.—Northamptonshire Cases (First and Second Classifications) by Histological Type Compared with Cases from Other Cancer Registers in England

Histological Type	Northamptonshire Cases				Oxon, Bucks, & Berks 1956-65		Southern England 1961-5	
	First Class		Second Class		No.	%	No.	%
	No.	%	No.	%				
Adenocarcinoma	17	25.4	17	27.9	23	27.7	39	8.3
Squamous carcinoma	31	46.2	29	47.5	36	43.4	328	70.1
Transitional carcinoma	4	6.0	10	16.4	5	6.0	19	4.1
Other and unclassified	15	22.4	5	8.2	19	22.9	82	17.5
Total	67	100.0	61	100.0	83	100.0	468	100.0

The first and second classifications of the Northamptonshire material are closely similar in the proportions of squamous and adenocarcinoma cases. The main difference lies in the proportions of transitional and other and unclassified cases. Both classifications differ in a striking manner from the distribution of cases in the Southern Register areas and resemble closely the distribution in the Oxford area. In Northamptonshire and the Oxford area less than half the cases were squamous carcinomas, but about a quarter were adenocarcinomas. In the other regions only 8% were adenocarcinomas while 70% were squamous carcinomas.

The material by sex and histological type is given in Table III. Overall there is an excess of males in the proportion of 1.8 to 1. The sex ratio for adenocarcinoma cases is marginally higher than for the other types but the difference is not significant. This contrasts with the situation in the southern part of the Oxford Region, where 33 of the 36 adenocarcinomas reported occurred in males (Acheson *et al.*, 1968).

TABLE III.—Distribution of Northamptonshire Cases by Sex and Histological Type of Tumour

Type of Tumour	Males	Females	Total	Male/Female Ratio
Group 1				
Adenocarcinoma	10	3	13	3.3
Squamous	15	7	22	2.1
Transitional	4	4	8	1.0
Other and unclassified	0	3	3	—
All	29	17	46	1.7
Group 2				
Adenocarcinoma	3	1	4	3.0
Squamous	5	2	7	2.5
Transitional	2	0	2	—
Other and unclassified	0	2	2	—
All	10	5	15	2.0
All Cases				
Adenocarcinoma	13	4	17	3.3
Squamous	20	9	29	2.2
Transitional	6	4	10	1.5
Other and unclassified	0	5	5	—
All	39	22	61	1.8

Age at Diagnosis and Histological Type

The histological type of tumour by age at diagnosis, in the Northamptonshire area for both sexes together, is shown in Table IV. There are no material differences in the age distributions of the various histological types. There is, however, an interesting difference between the age distribution of patients with adenocarcinoma in Northamptonshire and patients with the same type of tumour in the southern part of the Oxford Region. Thus in the Oxford material 6 of the 36 patients with adenocarcinoma (17%) were over the age of 65, while in Northamptonshire 11 out of 17 (65%) were over the age of 65. This difference is statistically significant ($\chi^2=12.2$, $P<0.001$, D.F.=1).

TABLE IV.—Histological Type of Tumour by Age, Both Sexes Together

Age at Diagnosis	Squamous	Adenocarcinoma	Transitional	Other and Unclassified	Total
		Group 1			
15-44 ..	1	—	—	—	1
45-64 ..	8	4	5	1	18
65+ ..	13	9	3	2	27
Total ..	22	13	8	3	46
		Group 2			
15-44 ..	1	1	—	—	2
45-64 ..	3	1	—	1	5
65+ ..	3	2	2	1	8
Total ..	7	4	2	2	15
		All Cases			
15-44 ..	2	1	—	—	3
45-64 ..	11	5	5	2	23
65+ ..	16	11	5	3	35
Total ..	29	17	10	5	61

Incidence Rates

The crude average annual incidence rates per million for carcinoma of nasal cavity and sinuses in Northamptonshire during the period 1953-67 were as follows. All histological types: males 9.9, females 5.5, both sexes 7.7; squamous carcinoma: males 5.1, females 2.3, both sexes 3.7; adenocarcinoma: males 3.4, females 1.0, both sexes 2.2. No material differences in incidence rate were found between Northampton County Borough and the Administrative County.

Occupation

Group 1 of the Northamptonshire cases (males only), which represents a collection of the material from the whole population over the period 1953-67, is displayed in Table V, according

TABLE V.—Occupation at Diagnosis or on Retirement by Histological Type (males only). The Original Classification is shown in Parentheses

Histological Type of Tumour	Boot and Shoe Trade	Other Trades	Not Known	Total
Squamous ..	7(7)	7 (7)	1(1)	15(15)
Adenocarcinoma ..	7(7)	3*(2)	—(0)	10 (9)
Transitional cell ..	3(1)	1 (0)	—(0)	4 (1)
Other ..	—(2)	— (2)	—(0)	— (4)
All ..	17(17)	11(11)	1(1)	29(29)

*2 ex-boot and shoe operatives.

to occupation at diagnosis or on retirement and histological type. The numbers in parentheses indicate the original histological classification for comparison.

It can be seen that 17 (59%) of the 29 male patients were or had been employed in the boot and shoe trade. In this table a man is classified as a boot and shoe worker if he was

employed as such at the time the tumour was diagnosed, or in the case of patients who were over 65 at diagnosis if they were employed as boot and shoe workers at the time they retired from full-time work. As only 17% of the male population aged 15 or over (see Table I) in Northamptonshire are active or retired boot and shoe workers* there is a *prima facie* case for an excess of cases in these trades.

The argument has been taken a step further in Table VI by estimating the expected number of cases which should have

TABLE VI.—Number of Cases Observed and Those Expected in Male Boot and Shoe Workers (092) According to the Incidence Rates Experienced in Parts of Southern England (1961-5). See Text For Further Details

Age Groups	Boot and Shoe Workers (092)								
	Adenocarcinoma			Squamous Carcinoma			All Types		
	Obs.	Exp.	O/E	Obs.	Exp.	O/E	Obs.	Exp.	O/E
15-64 ..	2	0.1	20	4	0.9	4	9	1.2	8
65+ ..	5	0.1	50	3	0.7	4	8	1.0	8
Total ..	7	0.2	35	7	1.6	4	17	2.2	8

occurred in boot and shoe workers* in Northamptonshire had the average rate for each histological type and all histological types together in males in the Southern Register areas applied. These incidence rates are shown in Table VII. It can be seen

TABLE VII.—Incidence Per Million Per Annum of Adenocarcinoma, Squamous Carcinoma, and all Types of Carcinoma (including Transitional Cell, Anaplastic, and Unclassified Cases) of the Nasal Cavity and Sinuses in Southern Register Areas of England (see text) 1961-5

Age Group	Population 1961 in Thousands	Adenocarcinoma		Squamous Carcinoma		All Carcinomas	
		Cases	Rate per 10 ⁶ per annum	Cases	Rate per 10 ⁶ per annum	Cases	Rate per 10 ⁶ per annum
Males							
15-64 ..	5,284.2	14	0.5	113	4.3	154	5.8
65+ ..	744.0	11	3.0	98	26.3	130	34.9
15+ ..	6,028.2	25	0.8	211	7.0	284	9.4
Females							
15-64 ..	5,375.3	4	0.2	52	1.9	83	3.1
65+ ..	1,230.7	10	1.6	65	10.6	102	16.6
15+ ..	6,606.0	14	0.4	117	3.5	184	5.6

that according to these calculations there was an eightfold excess of cases of nasal carcinoma (all histological types considered together) in boot and shoe workers during the period studied. The excess is more striking among adenocarcinomas than among squamous carcinomas.

Dr. A. S. Fairbairn, of the Oxford Record Linkage Study and Unit of Clinical Epidemiology, has kindly made formal tests of the significance of the differences in incidence rates (separately for adenocarcinoma and squamous carcinoma and for men aged 15-64 and 65 years or over) between (a) Northamptonshire boot and shoe workers (population 1) and other Northamptonshire men (population 2), and (b) Northamptonshire boot and shoe workers (population 1) and men in the Southern Register areas of England (population 3). The probabilities, using Fisher's exact test, are set out in Table VIII. All the differences are significant. In comparisons between populations 1 and 2 the probabilities are increased by the presence of ex-boot and shoe workers with nasal cancer in population 2 (see below).

The techniques used so far do not take account of the patients who had previously worked in the boot and shoe industry but who were working in another industry when their

* Occupational group 092.

TABLE VIII.—Probabilities of Differences in Incidence of Adenocarcinoma of Nasal Cavity and Sinuses, and of Squamous Carcinoma of Same Site Comparing Population 1 with Population 2 and 3 (see text)

Age Group	Adenocarcinoma		Squamous Carcinoma	
	Population 1 versus Population 2	Population 1 versus Population 3	Population 1 versus Population 2	Population 1 versus Population 3
15-64 ..	3×10^{-3}	6×10^{-3}	2×10^{-3}	1×10^{-2}
65+ ..	2×10^{-4}	6×10^{-8}	5×10^{-2}	5×10^{-2}

tumour was diagnosed or at the time they retired from active work. There were two such male patients in group 1, both of whom had adenocarcinomas (Cases 1010 and 1052). In addition, 2 of the 17 women in group 1 had been boot and shoe operatives before marriage (Cases 1008 and 1026). One had an adenocarcinoma and the other an anaplastic tumour. In addition there was one woman with an adenocarcinoma (Case 1001) and one woman with a transitional carcinoma (Case 1002), who were wives respectively of a boot and shoe factory foreman and a handbag manufacturer, but whose personal occupational history is unknown.

Secular Trend, Histological Type, and Occupation

The Northamptonshire cases are set out according to year of diagnosis and histological type in Table IX. Patients who

TABLE IX.—Northamptonshire Cases (Groups 1 and 2) Set Out by Year of Diagnosis and Histological Type

Year of Diagnosis	Adenocarcinoma		Squamous		Trans. & Anap.		All	
	B & S	Other	B & S	Other	B & S	Other	B & S	Other
1940-4 ..				1			1	1
1945-9 ..					1	3	6	10
1950-4 ..	3	2	2	5				6
1955-9 ..	3		3	4	3	2	8	11
1960-4 ..	2	3	3	6				6
1965- ..	4		1	4	1	2	6	
Total	12	5	9	20	5	10	26	35

worked in the boot and shoe industry are shown separately from the remainder. Within the limits set by the small numbers there is no evidence of either an increase or a decline in occurrence in any of the groups since 1950. A systematic search of the Death Registers of the County Borough of Northampton from 1900 until 1968 revealed no deaths attributed to nasal cancer in persons described as boot and shoe operatives before 1950.

Importance of Occupation within Industry

Valuable additional information was obtained by study of the occupational histories in the Appendix. With the help of Mr. L. P. Huggett and his colleagues of the Shoe and Allied Trades Research Association it was possible to assign 20 of the 26 patients who had worked in the boot and shoe industry to the department in which they had worked for the greater part of their time in the trade. It can be seen from the Appendix and Table X that no fewer than 17 of the 20 patients regarding whom a detailed classification was possible had worked in one or other of two of the six principal shoe factory departments—13 in the finishing-room and 4 in the areas concerned with sorting and cutting out the leather for soles and heels. It is interesting that almost exclusively it is the operatives in these two departments who are exposed to dust. Of the remaining six cases, one (Case 1048) was a general

maintenance worker and stoker in the trade, and another (Case 1006) had served his time in all departments. Both had almost certainly been exposed to dust. Another man (Case 1030) was engaged in assembling and finishing surgical boots. He is known to have been exposed to a great deal of leather and cork dust. In the remaining three cases the precise job description is unknown. It is noteworthy that no case has arisen in the shoe room which is the area where the finished shoe receives its sprays and lacquers. One patient (Case 1011) had been involved in inking as well as scouring soles and heels.

TABLE X.—Classification of Occupation of 26 Workers in Boot and Shoe Industry with Nasal Cancer (Groups 1 and 2)

Occupation	Adenocarcinoma	Squamous	Other	All
Preparation, bottom works, etc.	2	2		4
Closing			1	1
Closing			1	1
Lasting/making		1		1
Finishing	7	5	1	13
Shoe room				
Other, maintenance, etc. ..	1			1
Boot and shoe operatives, unspecified	2	1	2	5
All	12	9	5	26

No information is provided in the census about the numbers of workers in the various jobs within the boot and shoe industry. It was possible, however, to obtain approximate data from the Shoe and Allied Trades Research Association. The operatives working in the two departments particularly exposed to dust comprise a small minority of the total and probably contribute only about 20% of the skilled labour force. The fact that 85% of the classifiable cases occurred in this minority is strongly suggestive of a causal association with dust.

Cases Reported from Outside Northamptonshire

In the course of a survey in which an attempt is being made to ascertain all nasal adenocarcinomas diagnosed in England and Wales since 1961 (to be published), five cases have been found in the boot and shoe repairing industry (Cases 1080-1083, and 1086) and one in the boot and shoe manufacturing industry in Somerset (Case 1087).

Three cases of nasal squamous carcinoma have also been found in present or past boot and shoe operatives outside Northamptonshire. One occurred in a man who worked as a shoe finisher and a shoe factory cleaner in Norfolk (Case 1085), and another has been found (Case 1084) in a boot and shoe operative in Somerset who also worked for a time in a bakehouse (see Appendix). The third case of squamous carcinoma (Case 1088) has been ascertained in a man who worked for four years as a boot and shoe operative in East Anglia and spent the remainder of his working life as a tram and bus driver.

According to the Report of the Inspector of Factories (Ministry of Labour, 1966) there were about 10,000 boot and shoe repairers in England and Wales. This means that the crude average annual incidence of adenocarcinoma of the nasal cavity and sinuses in this group was about 0.08 per 1,000 over the period 1961-6. This is likely to be an underestimate, as no systematic survey of the footwear-repairing industry has yet been undertaken. When it is borne in mind that in the Southern Register areas the crude average annual incidence of nasal adenocarcinoma in males of all occupational groups is 0.0008 per 1,000 (Table VII) it appears that there is a prima facie case for an occupational risk of this tumour in the footwear-repairing industry in addition to the manufacturing industry. Men working in the footwear-repairing industry often work in small shops and dusty conditions.

The histories of two patients with occupations other than in the footwear industry involving contact with leather (Cases 1089 and 1090) are also reported briefly. The significance of these is at present uncertain.

Latent Period

In the absence of any information about the identity of the supposed carcinogenic factor or factors in the industrial environment of the boot and shoe manufacturing industry and the date of its introduction, the least arbitrary assumption in estimating the latent period is that exposure began on entry to the industry. The year of entry to the industry is known in 19 of the 26 Northamptonshire patients who were boot and shoe operatives. In the remaining seven it has been assumed that the patient entered the industry on leaving school at the age of 14, and the date is shown in parentheses in the Appendix.

The latent periods distributed by decade and histological type are shown in Table XI. The latent period for the patients with adenocarcinoma (mean 54.6 years) is substantially and significantly longer than for the patients with squamous, transitional, and anaplastic tumours (mean 41.7 years) ($P < 0.001$). Patients

Year of entry to industry and year of diagnosis in 26 cases of nasal cancer in workers in the Northamptonshire boot and shoe industry. The period of industrial exposure is shaded.

with adenocarcinoma tended to enter the industry before patients with the other types of tumour (Table XII). On the other hand, the distribution of year of diagnosis over the period studied (Table IX) is similar. These differences in the temporal pattern of the two groups of cases are shown in the Figure. They suggest that the aetiology of adenocarcinoma in the boot and shoe industry may differ from that of the other nasal tumours.

TABLE XI.—Interval Between Entry to Boot and Shoe Industry and Diagnosis, Including Six Cases from Outside Northamptonshire

Years between entry and Diagnosis	Adenocarcinoma	Squamous	Transitional and Anaplastic
30-39	1	4	4
40-49	5	3	1
50-59	5	2	—
60-69	4	1	—
70+	2	—	—
Total	17	10	5
Mean latent period	54.6 years	41.7 years	

TABLE XII.—Year of Entry to Boot and Shoe Industry by Histological Type of Tumour

Year of entry to B & S Industry	Adenocarcinoma	Squamous	Transitional and Anaplastic
1880-	2	—	—
1890-	3	2	—
1900-	5	1	—
1910-	4	2	1
1920-	3	3	3
1930-	—	2	1

Period of Exposure

Eight of the Northamptonshire adenocarcinoma patients (Cases 1048, 1010, 1003, 1012, 1011, 1049, 1052, and 1008) and two of the others (Cases 1070, squamous, and 1026, anaplastic) are known to have left the industry some years before the diagnosis of the tumour. In two of these the period of exposure was less than five years. If these cases are used and note is taken of the patients who entered the industry most recently and subsequently developed a tumour, it is possible to estimate minimum time limits for the presence of the carcinogen in the industrial environment. In the case of adenocarcinoma the factor may have been present in Northamptonshire at least as early as the last decade of the last century and was still present about 1920. One of the adenocarcinomas arising in the boot-repairing trade outside Northamptonshire occurred in a man entering the industry about 1928 (Case 1086). Tumours in the other histological group have arisen in men entering the industry in the 1930s.

Possible Aetiological Agents Outside the Industry

Two other trades appear more than once in the occupational histories. Three Northamptonshire patients—Case 1005 (adenocarcinoma) and Cases 1054 and 1032 (transitional cell carcinomas)—worked in the baking and confectionary business. Another boot and shoe worker from outside the area with a squamous carcinoma (Case 1084) worked in a bakehouse for an unknown period. The occupational histories of two other patients who worked in the bakery business have already been published (Acheson *et al.*, 1968). One of these (Case 008 in that series) was also a chairmaker and had an adenocarcinoma. The other (Case 205) worked as a baker's assistant for six years and later developed a transitional cell carcinoma. In addition we know of three further cases (not shown in the Appendix) of nasal adenocarcinoma, two in bakers' assistants and one in a miller, in persons exposed to flour. The possibility that the inhalation of flour may be associated with a risk of nasal cancer is being studied further.

Case 3002 (transitional cell carcinoma) was a cardboard box maker and Case 1058 (transitional cell carcinoma) was the wife of a commercial traveller in the cardboard box making industry.

Tobacco Snuff

In view of the finding in our previous survey that 3 out of 11 woodworkers with adenocarcinoma of the nasal cavity in whom the appropriate information could be obtained had been snuff takers, an attempt was made to obtain information on this habit in as many cases as possible. The results are set out in Table XIII. Of the 26 patients from whom information could be

TABLE XIII.—Tobacco-snuff Taking Habit in Nasal Cancer Patients in Northamptonshire

Tobacco-snuff Taking Status	Adenocarcinoma		Squamous		Transitional and Anaplastic	
	B & S	Other	B & S	Other	B & S	Other
Snuff	3	—	1	2	1	1
No snuff ..	5	1	2	5	2	3
Total	8	1	3	7	3	4
No information	3	5	6	13	2	6

obtained eight had been snuff takers. Three of these had been taking snuff occasionally but five were habitual or heavy snuff takers. The fact that the habit was not restricted to the boot and shoe operatives shows that its presence in cases of nasal cancer is not simply due to a tradition of snuff taking in the footwear

trade. Three of the adenocarcinoma patients from outside Northamptonshire were also habitual snuff takers (Cases 1082, 1084, and 1090). In the last case it is not certain whether the snuff contained tobacco. It seems therefore that snuff taking should be given further consideration as a contributory factor in the aetiology of nasal cancer.

Discussion

Two independent lines of evidence are described in this paper which suggest an association between cancer of the nasal cavity and sinuses and dust in the boot and shoe industry. The first involves a comparison between the incidence of nasal cancer in males in the Southern Register areas and the incidence in male boot and shoe workers in Northamptonshire. A second standard of comparison is the incidence of males employed in other occupations in Northamptonshire. In each comparison statistically significant differences in incidence rate were found between the boot and shoe operatives and the other groups in the 15-64 age group, the men over 65, and in men of all ages. It is only fair to point out, however, that there may be substantial errors (which might operate in either direction) in the estimates of the size and age structure of the population of boot and shoe operatives.

In theory the difference between the incidence in Northamptonshire boot and shoe operatives and the average male incidence in the Southern Register areas could be due to inadequate ascertainment of cases there. In fact, however, the average annual incidence per million for all age and occupational groups together in the two populations is very closely similar (Northamptonshire 1953-67: males 9.9, females 5.5; Southern Register areas 1961-5: males 8.5, females 5.1). Bias in case finding between the areas is unlikely, therefore, to account for the high incidence found in boot and shoe operatives.

The second line of evidence pointing to an association between an environmental hazard in the industry and nasal cancer lies in the distribution of the cases in the press and preparation rooms, where the materials are cut out and trimmed, and in the finishing room, where the bottom and heel of the shoes are scoured. On the whole, workers in the closing, making, and lasting rooms and in the shoe room are not exposed to dust. According to the Shoe and Allied Trades Research Association the operations which have been particularly dusty in the past have been as follows: sorting leather in the rough stuff room; revolution press operating; insole surface scouring, heel-building; heel and sole trimming and scouring. The fact that 17 of the 20 patients of whom there is information were engaged in one or other of these procedures, which together involve only about one-fifth of the workers, is very suggestive of a causal association with dust.

The appearance in a survey undertaken with different objectives, of a cluster of cases of nasal adenocarcinoma in shoe *repairers*, gives a further line of support for the hypothesis of a carcinogen present in the dust of material used in the manufacturing of footwear.

A precise estimate of incidence in the Northamptonshire industry is impossible in view of the small number of cases and other difficulties set out above. If the 17 male patients in group 1 with nasal cancer of all histological types who were boot and shoe operatives at the time of diagnosis or on retirement are taken, and related to the estimated population of 15,660 men in these categories (Table I), the average annual incidence is 0.07 (± 0.02) per 1,000. At least 11 of these men (including five with adenocarcinoma) worked in preparation or finishing departments. As we now have reason to believe that only a minority of the male workers have been engaged in these

operations the incidence of nasal cancer in this restricted group will be considerably higher. A survey of the industry to assess more precisely the numbers of workers exposed to dust seems desirable.

Significance of Histological Type of Tumour

The evidence suggests that there has been a relatively greater increase in the incidence of adenocarcinoma than in that of squamous carcinoma of the nasal cavity and sinuses (Table VI). Striking differences can also be shown between the latent periods of the adenocarcinomas on the one hand and squamous carcinomas on the other, the latter having a significantly shorter latent period than the former. These differences might point to the existence of two distinct carcinogens. That causing adenocarcinoma must have been present in Northamptonshire at least as early as the last decade of the last century, and it was still present about 1920. That causing squamous cancer (if different) was still present in the industry at least a decade later. Another possible explanation of the findings would be the existence of one carcinogen plus a co-carcinogen responsible for squamous and transitional metaplasia and for acceleration.

A further interesting feature is that the average latent period of adenocarcinoma in woodworkers in the furniture industry is significantly shorter than for adenocarcinoma in this industry (39.8 years as opposed to 54.6 years).

Nature of the Hazards

The composition of the dusts in boot and shoe factories has varied considerably with the materials used in the manufacture of footwear both from factory to factory and over the period studied. The principal materials used until the last decade were leather, rubber, shoe fibreboard (made of a mixture of wood and leather fibres, the former derived principally from waste paper), and to a lesser extent cork. In recent years plastic materials have been introduced. The presence of wood fibres in fibreboard used in building up soles and heels provides a possible link with adenocarcinoma in furniture workers. Another possible link lies in the vegetable infusions from wood, bark, fruit, leaves, galls, etc., used in tanning leather for soles and heels.

A number of dyes are used in the preparation of fibreboard and are therefore likely to have been present in small quantities in the dust of some shoe factories. Of these dyes, chrysoidine has been found to induce hepatomas in mice and is forbidden for use in foods (Malolepszy, 1963; Richter, 1963). It does not necessarily follow from the animal work that it is carcinogenic in man. It would seem advisable, however, to find a substitute for this dye if it is still in use, and to investigate the properties of the other dyes used in fibreboard.

Bronchial carcinoma is known to occur in some workers in the chromates-producing industry (Bidstrup and Case, 1956). Calcium chromate has been found to be a potent carcinogen for the subcutaneous tissues of the rat (Roe and Carter, 1969). Since the latter part of the nineteenth century chromate salts have been used in the tanning of leather mainly for the upper parts of boots and shoes. In general the operations involving leather for uppers are much less dusty than those involving heels and soles, and are unlikely to be a factor.

The association of dusts from organic materials (wood, leather, and possibly wheat) with nasal cancer, particularly nasal adenocarcinoma, also raises the possibility that carcinogenic metabolites of moulds or fungi might be relevant in this connexion, as they have been shown to be in hepatic and other cancers in animals (Schoental, 1967).

Literature

The only reference which we have found to nasal cancer in workers in the footwear trades is in the paper of Debois (1969) from Louvain. This reports 29 cases of nasal cancer, of which 15 were in woodworkers and 2 in shoemakers. Both of the shoemakers had adenocarcinomas. By the courtesy of Professor V. Desmet, of the Institute of Pathology at Louvain, a sample of the slides was examined by one of us (R.H.C.), who was in complete agreement with the histological classification.

According to the Registrar General (personal communication, 1969) the proportional mortality ratio for nasal cancer in leatherworkers in England and Wales calculated from death certificates was not raised for the years 1958-62.

Recommendations

It is important to point out that the environmental conditions which probably gave rise to the cases of nasal cancer reported in this paper existed in the industry many years ago, and we have no evidence to determine whether or not such conditions still exist. Over the past 30 years substantial im-

provements have taken place in exhaust ventilation in the larger boot and shoe factories, leading to a general reduction in the quantity of dust inhaled by workers. Improvements in hygiene in the smaller factories and in the repair shops have probably been less effective. There have also been changes in the composition of the dust since the workers studied here entered the industry.

Nevertheless as a matter of common prudence we recommend that further studies of the standard of hygiene and of the composition of the dusts in this industry should be made, along with measures to minimize the exposure of workers. While the substantial increase in incidence we have found in what is usually a very rare tumour indeed gives rise at present to only between one and two cases of the disease per annum in the Northamptonshire industry, the risk is not spread evenly and may be material in small groups of workers engaged in dusty operations.

We also recommend that a formal survey of the boot and shoe industry and of the shoe-repairing industry be made for nasal cancer and for other malignant disease of the respiratory tract. The question of prescription of nasal cancer in the footwear making and repairing trades should be considered.

Appendix

Occupational Histories of Northamptonshire Cases

Serial No.	Sex	Year of Birth	Year of Entry to Boot and Shoe Industry	Year of Departure	Year of Diagnosis	Site	Occupational History	History regarding Snuff	Type of dust exposure as stated by patient or relative
<i>Adenocarcinomas</i>									
1048	M	1894	1907	1965	1967	Maxillary antrum	Maintenance worker, stoker and boilerman at a boot and shoe factory	Snuff since 1920	Coke, rubber, and possibly leather
1005	M	1890	—	—	1962	Maxillary antrum	Worked in bakery 1904-14. After war service, 1914-19, worked as painter and decorator	Not known	Flour
1010	M	1891	1903	1923	1957	Ethmoid	Heel trimmer in finishing-room 1903-23. Served in Army 1916-18 and was gassed. Also worked as coke deliverer 1930-9; then gardener	Took snuff 1939-57	Leather dust
1003	M	1886	1900	1950	1960	Ethmoid	Worked all his life as a shoe finisher. 1900-1950	No	Leather dust
1004	M	1876	1890	—	1961	Antrum	Worked all his life at a shoe factory. Precise occupation unknown	No	Leather dust
1012	M	1888	1903	1952	1957	Nasal cavity	Worked all his life in the rough stuff room at a shoe factory. 1903-1952	No	Leather dust
1051	M	1905	1917	—	1966	Ethmoid	1917-20 Clicker. 1920-65 worked in finishing department at a shoe factory	Not known	Leather, rubber, and plastics
1011	M	1895	1908	1960	1965	Inferior turbinate	1908-1915 inking and bottom scouring. 1919-60 bottom making in finishing-room at a shoe factory	Not known	Leather
1049	M	1871	1885	1936	1950	Nasal cavity	Boot and shoe industry. Hand finisher of soles and heels 1885-1936	No. Smoked pipe moderately	(Trade Union case)
1052	M	1901	1915	1916	1953	Ethmoid	1915-16 six months in shoe industry; 1916-26 Army; 1926-1949 Engineer with a lift Company	Not known	
1079	M	1903	1917	—	1966	Ethmoid	Worked as a finisher in the boot and shoe industry all his life. A "very dusty job"	No. Non-smoker	Leather and rubber dust
1071	M	1885	1899	—	1952	Ethmoid	Boot pressman 1899-1952. Revolution press operator	Not known	(Trade Union case)
1069	M	1906	—	—	1951		Never in boot and shoe industry. Local government officer and policeman	Not known	(Death Register case)
1007	F	1896	—	—	1960	Ethmoid	Never employed in a dusty trade. Husband's occupation, lorry driver	Not known	
1008	F	1878	1896	1898	1957	Ethmoid	Worked sanding heels of shoes 1896-8	Heavy snuff taker	Leather dust
1001	F	1891	—	—	1960	Ethmoid	Worked for 12 years in a dressmaking firm. Husband was a boot and shoe factory foreman	No	Dust of various types of cloth
1050	F	1912	—	—	1950	L. antrum	Own occupation unknown. Husband a shoe stretcher	Not known	(Death Register case)

Serial No.	Sex	Year of Birth	Year of Entry to Boot and Shoe Industry	Year of Departure	Year of Diagnosis	Site	Occupational History	History regarding Snuff	Type of dust exposure as stated by patient or relative
1047	M	1894	—	—	1964	Nasal Septum	<i>Squamous Carcinomas</i> Worked as clerk in Brewery Company all his life	Heavy snuff taker	
1046	M	1892	—	—	1962	Antrum	Worked for Northamptonshire Gas Company all his life	Not known	Coal and coke dust
1065	M	1889	(1903)	—	1955	Antrum	Boot and shoe operator (laster)	Not known	
1070	M	1918	1932	1938	1968	Maxillary antrum	Heel scourer at a shoe factory 1932-8. After war service worked as a wood merchant 1946-8. Lorry driver 1948-52. Dye mixer 1952-60. Scrap merchant 1960	Not known	Leather dust
1042	M	1916	—	—	1960	Antrum	After being a farm labourer for a few years was an ironstone worker for the rest of his life	Not known	
3001	M	1895	—	—	1961	Nasal cavity	1908-14 motor engineer; 1914-19 Army service; 1920 to present time self-employed haulage contractor and general carrier	Not known	
1025	M	1910	1925	—	1958	Antrum	1925-41 heel scourer; 1946 to present time examiner and repairer for shoe factory	Occasionally before the war	Leather dust
1041	M	1885	—	—	1965	Ethmoid	Civil servant; other details unknown	Heavy snuff taker	
1068	M	1883	—	—	1952	Maxillary antrum	Worked as upholsterer all his life; never worked in boot and shoe industry	Not known	
1090	M	1894	—	—	1967	Maxillary antrum	Farmer	Not known	
1064	M	1903	—	—	1954	Antrum	Shop assistant	Not known	
1013	M	1916	(1930)	—	1963	Ethmoid	Shoe finisher	Not known	
1067	M	1885	(1899)	—	1954	Ethmoid	Boot and shoe operative	Not known	
1029	M	1902	(1916)	—	1960	Antrum	Boot and shoe operative in finishing-room	Not known	
1028	M	1881	(1895)	—	1957	Antrum	Boot and shoe finisher	Not known	
1098	M	1896	1910	—	1951	Ethmoid	Heel sorter and sole and heel cutter	Not known	(Death Register case)
1066	M	1871	—	—	1941	Ethmoid	Not known	Not known	(Death Register case)
1027	M	1913	1927	—	1964	Maxillary antrum	1927-39 worked as clicker in boot and shoe trade. After Army service worked 1946-64 as sorter leather trade	No	
1045	F	1913	—	—	1960	Maxillary antrum	A single woman who worked as a needlewoman and did other domestic work throughout her life	No Non-smoker	
1060	F	1889	—	—	1953	Antrum	Never worked in leather, woodworking, or other dusty trade	No	
1040	F	1877	—	—	1956	Ethmoid	Worked as children's nurse and a machinist in the clothing trade before marriage to a poultry farmer	No	
1044	F	1880	—	—	1960	Antrum	Postman's wife who never worked other than as a housewife	No	
1061	F	1875	—	—	1955	Antrum	Wife of a soldier. Other details unknown	Not known	
1062	F	1888	—	—	1952	Antrum	Occupation unknown	Not known	
1093	F	1887	—	—	1968	Antrum	Wife of a Brewer's Accountant. Never worked outside the home environment	No	
1059	F	1889	—	—	1955	Ethmoid	Occupation unknown	Not known	
1053	F	1896	—	—	1953	Antrum	Wife of an engineer. Further details unknown	Not known	
1094	M	1924	—	—	1968	Antrum	1938-40 apprentice joiner, 1940-48 apprentice engineer 1955-68 millwright	No	Wood dust, metal dust, flour dust
1063	M	1887	—	—	1955	Maxillary antrum	Occupation unknown	Not known	
3002	M	1873	—	—	1949	Antrum	<i>Transitional Cell Carcinomas</i> Cardboard box maker	Very occasionally	(Death Register case)
1006	M	1910	1927	—	1963	Antrum	Served his time in all departments of a shoe factory 1927-30; then became a representative	Not known	Leather dust
1014	M	1895	—	—	1958	Nasal mucosa	Dispatch clerk in steel industry. Never worked in boot and shoe trade	No Non-smoker	
1055	M	1914	1928	—	1966	Ethmoid	1928-9 a clicker, subsequently always in finishing-room of shoe trade as edge trimmer	Occasionally 30-40 years ago	Leather dust
1030	M	1908	(1922)	—	1962	Antrum	Boot and shoe operative making surgical boots	No	Leather and cork dust
1072	M	1897	(1911)	—	1950	Ethmoid	Boot and shoe clicker	Not known	(Trade Union case)
1054	F	1887	—	—	1955	Antrum	1897-1950 cake maker in confectioner's business	No	Flour
1032	F	1900	—	—	1960	Ethmoid	1914-28 packer of pork pies. Subsequently a barmaid	No	Flour
1058	F	1869	—	—	1954	Ethmoid	Wife of commercial traveller in cardboard boxes. Personal history unknown	Not known	
1002	F	1888	—	—	1965	Antrum	Wife of handbag manufacturer. Personal history unknown	Not known	

Serial No.	Sex	Year of Birth	Year of entry to Boot and Shoe Industry	Year of Departure	Year of Diagnosis	Site	Occupational History	History regarding Snuff	Type of dust exposure as stated by patient or relative
<i>Other and Unclassified Carcinomas</i>									
1026	F	1916	1930	1945	1963	Ethmoid (anapl.)	1930-7 worked in closing-room of shoe factory and from 1939 to 45 in canteen of same	No	Leather dust
1091	F	1873	—	—	1954*	Nasal sinus (not known)	Wife of shoe finisher	Not known	(Death Register case)
1092	F	1900	—	—	1950	Antrum (Not known)	Wife of art publisher	Not known	(Death Register case)
1024	F	1884	—	—	1965	Ethmoid (anapl.)	Unknown	Not known	
1043	F	1890	—	—	1961	Ethmoid (anapl.)	Wife of stock farmer and butcher. Never worked other than as a housewife	Not known	

Serial No.	Sex	Year of Birth	Year of entry to Boot and Shoe Industry	Year of Departure	Year of Diagnosis	Histology	Site	Occupational History	History regarding Snuff	Type of dust exposure as stated by patient or relative
1080	M	1873	1887	1945	1961	Adeno	Ethmoid	After a few years in his father's boot shop worked as a leather cutter in a very dusty boot repair shop until aged 58	No	
1081	M	1907	1921	—	1964	Adeno	Ethmoid	Boot and shoe repairer all his life	No	
1082	M	1908	1922	—	1965	Adeno	Nasal cavity	Benching and finishing in shoe repair shop	Took snuff	Exposed to leather and rubber dust
1083	M	1902	1919	—	1964	Adeno	Nasal cavity	Footwear repair workshop supervisor	No	Exposed to leather and rubber dust
1084	M	1910	1924	—	1964	Squamous	Maxillary sinus	1924 shoe factory worker in Somerset. Later worked in bakehouse and as hospital ward orderly	Regularly all life	
1085	M	1907	1922	—	1967	Squamous	Left nasal vestibule	1922-7 worked making shoes in boot and shoe industry. 1927 until present time has worked as finisher and cleaner of floors and dust extraction plant	No	Exposed to leather dust since 1922
1086	M	1914	1928	—	1966	Adeno	Ethmoid	Worked as shoemaker in Sunderland. Further details unknown	Not known	
1087	M	1879	—	—	—	Adeno	Ethmoid	Shoe factory worker. Further details unknown	Not known	
1088	M	1896	1910	1914	1964	Squamous	Maxillary antrum	1910-14 boot and shoe operative. After war service worked as a tram and bus driver for rest of life	No	
1089	F	1891	1914	1918	1961	Squamous	Exact site within nose unknown	1904-14 and 1918-46 worked as cleaner in offices, private homes, and hotels. 1914-18 worked at home making handbags	No	
1090	F	1908	—	—	1964	Adeno	Exact site within nose unknown	1923-4 worked in the Yeovil glove trade. 1924-5 worked in the horsehair, feather, and flax trade in Somerset. 1939-45 worked as an upholsterer in London	Yes: a snuff containing menthol and eucalyptus	

*Date of death; date of diagnosis not known

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