A STUDY OF ADENOCARCINOMA OF THE PARANASAL SINUSES IN WOODWORKERS IN THE FURNITURE INDUSTRY

Hunterian Lecture delivered at the Royal College of Surgeons of England on 4th December 1969 by

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Collection of material

I WILL BEGIN by putting before you the evidence to show that adenocarcinoma of the nasal sinuses is a particular hazard to woodworkers in the Furniture Industry. In order to do this I have made a study, over the last 15 years, of every established case of carcinoma of the sinuses occurring in the whole of Oxfordshire and in that part of Bucking-

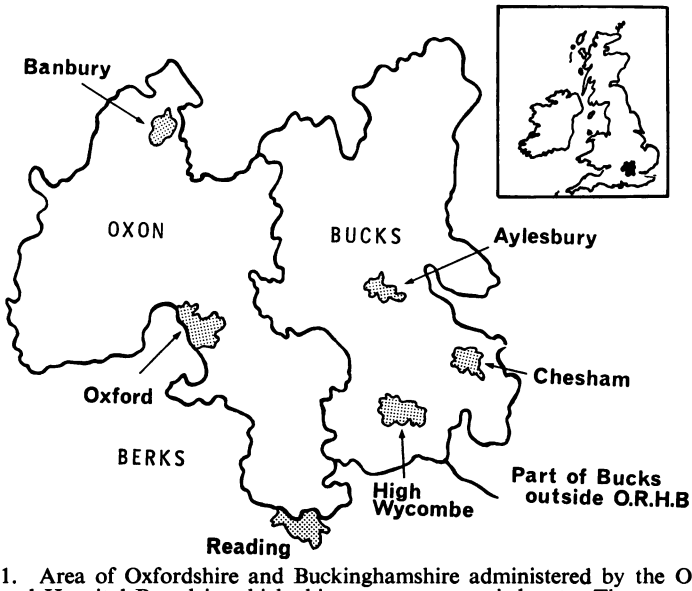


Fig. 1. Area of Oxfordshire and Buckinghamshire administered by the Oxford Regional Hospital Board in which this survey was carried out. The map of the British Isles is inset for comparative purposes.

hamshire which lies within the area administered by the Oxford Regional Hospital Board (Fig. 1).

The cases were collected with the help of the Oxford Regional Cancer Registry and the Oxford Record Linkage Study and it is reasonably certain that no established case has been overlooked. In any event this is a survey in which the incidence of various histological types of carcinoma

is compared, so if patients have been sent out of the Region for treatment the loss will be reflected in the absolute numbers and not in the relative numbers.

In 1960 the population of the Oxfordshire side of the area under survey was 306,000 and of the Buckinghamshire side 313,000. This rough equality makes comparison remarkably easy. It will be understood that there is some elasticity of county boundaries. This is particularly true in the case of Reading and Oxford, where a large hospital situated near the boundary is certain to draw cases from the adjacent part of the other county. Here, however, as we shall see later, the gains and losses are about even.

The High Wycombe Furniture Industry

The main concentration of the Furniture Industry in this region is centred on the town of High Wycombe and in the surrounding villages. In Banbury there is one old-established factory. In Oxford there were once half a dozen small factories, turning out specialized furniture. Chesham at one time supported a thriving wood-turning industry but, as in the case of Oxford, this has tended to die out with the exception of one or two larger concerns.

It is of some interest to look briefly at the development of the Furniture Industry in Buckinghamshire. It began some 200 years ago, not only in High Wycombe but also in the surrounding villages, on the beech-clad Chiltern Hills, where easy access to the local timber facilitated the manufacture of simple wooden chairs. About this time Chippendale and Sheraton, working in London, were making the fine furniture which decorated the great houses of the day. The Wycombe Chairmasters did not rival the great ones; their simple chairs, Windsors and splay-backs, found their way to the kitchens and servants' quarters, to lesser houses, schools, churches, and inns. These early Chairmasters each employed about a dozen men, some of them working in the factory, others in the very woods where the trees grew. Here some cut the timber into planks, while others, known locally as Bodgers, made chair legs and stretchers in the shelter of rough wooden huts. As the market for chairs increased a simple industry grew up, perhaps one of the last to be established before the Industrial Revolution. By 1875 there were 70 Chairmasters in the Wycombe area. They employed some 600 men and probably as many women and children. A lot of the work was subcontracted or done at home. It was the custom for children to help their parents, either at home or in the factory, when they had finished their schoolwork for the day. Up to the turn of the century the Wycombe Chairmasters continued to produce good, but inexpensive, simple wooden chairs. From 1900 onwards they developed the production of better quality chairs and began to make other furniture as well. At the present time High Wycombe makes 12% of all wooden furniture and 80% of all chairs in the United Kingdom.

A great deal of beech timber is still used in High Wycombe. However, the gradual depletion of native hardwoods combined with changes in taste and fashion have led to the increased use of imported timber. Yet the men still have a loyalty to the local beech. A number of cases of dermatitis, asthma and vasomotor rhinitis occur as the result of exposure to wood dust, and the sufferers invariably maintain that they are caused by ' foreign ' woods. In many cases they are right, but it was difficult to accept this assertion from one of the men with carcinoma of the ethmoid sinuses when it was found that, apart from a period of three weeks when he was using African cherry, he had worked with beech all his life.

According to the 1961 census there were 9,520 woodworkers in Oxfordshire and Buckinghamshire (Table I). About half of them, 4,270, were carpenters and joiners, the other half cabinet makers, chair makers, wood sawyers and wood machinists, were employed in the Furniture Industry, most of them in the High Wycombe area.

TABLE I

DISTRIBUTION OF WOODWORKERS IN OXFORDSHIRE AND BUCKINGHAMSHIRE
1961 *Census*

	Bucks	*Oxon*	*Total*
Carpenters and joiners ..	2,660	1,610	4,270
Cabinet and chair makers ..	1,580	240	1,820
Wood sawyers and machinists..	1,950	300	2,250
Unclassified wood workers ..	930	250	1,180

Histological types of carcinoma

Having defined the population on which the study was made we can now consider the histological types of carcinoma to be included. There can be no objection to putting them into three groups; the first being the squamous carcinomata, the second the adenocarcinomata, while in the third are put together the transitional cell, anaplastic and unclassified carcinomata. Some of the blocks from which the sections of the earlier cases were cut had been destroyed, but wherever possible the histological classification was reviewed by an independent pathologist.

In Table II we have the histological classification of all the 92 cases in the study, and the remarkable thing is that there are as many cases of adenocarcinoma as squamous carcinoma. In no other series (apart from the one which we published in the *British Medical Journal* in 1968, and which is in effect included in this study) is there such a large proportion of adenocarcinomata. In other published series the squamous carcinomata outnumber the adenocarcinomata by more than 10 to 1.

TABLE II

CARCINOMATA OF NASAL SINUSES
Oxon and Bucks, 1956–69

Squamous carcinoma	34
Adenocarcinoma	35
Anaplastic transitional unclassified	23
Total	92

Distribution of the cases

In Table III we have the division of these 92 cases between Oxfordshire and Buckinghamshire. It will be remembered that the populations of the two counties are about equal. It will be seen that while the first and third groups are equally divided there are four times as many adenocarcinomata in Buckinghamshire as in Oxfordshire.

Figure 2 gives the breakdown of the figures to show the incidence in males and females. Again the first and third groups correspond reasonably well, but when we look at the adenocarcinomata, the incidence in men in Buckinghamshire is seven times greater than in Oxfordshire.

In Figure 3 the Buckinghamshire figures are further broken down into cases occurring in High Wycombe and in the rest of the county. This shows the high incidence of adenocarcinoma in men in High Wycombe.

Or these figures can be converted into crude annual incidence rates per million, which give an incidence rate for men in High Wycombe 10 times greater than it is for men in the rest of Buckinghamshire (Fig. 4).

TABLE III

	Oxon	*Bucks*
Squamous carcinoma	18	16
Adenocarcinoma	7	28
Anaplastic transitional unclassified ..	12	11
Total	37	55
Population 1960	306,000	313,000

Occupational histories

Now we can consider the occupations, at the time of diagnosis, of the 35 patients with adenocarcinoma. All the 24 men above the line in Table IV were woodworkers in the Furniture Industry. Most of them

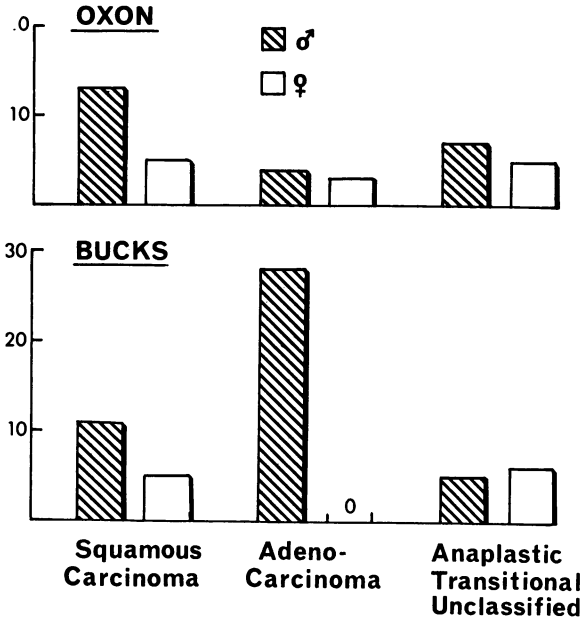


Fig. 2. Incidence of the three groups of histology showing male : female ratios (Oxford and Buckinghamshire).

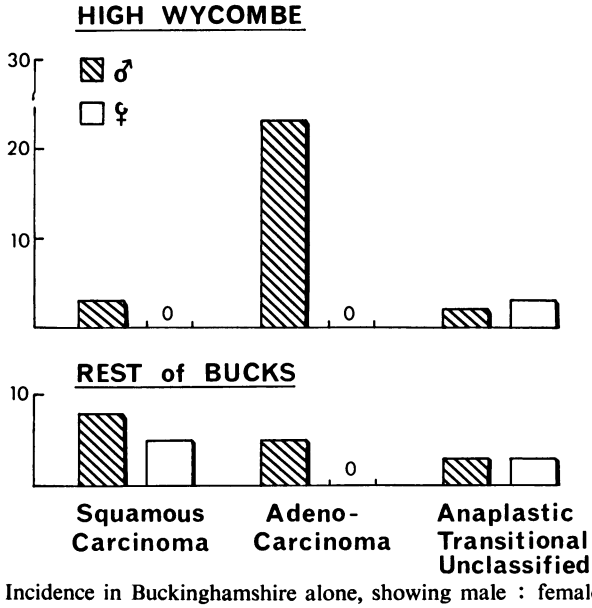


Fig. 3. Incidence in Buckinghamshire alone, showing male : female ratios.

worked in the Wycombe area, but two came from Banbury and two from Oxford. None of the men working in Oxfordshire had ever worked in the Wycombe Furniture Factories.

You may wonder why I have included polishers as woodworkers. Up to the last war all polishing was done by hand, the so-called ' French polishing ' method. At one stage in this procedure the polisher used to sandpaper the whole surface down to the bare wood and it was at this time that he was exposed to wood dust. Since the war, spray polishing has almost entirely replaced French polishing, so polishers no longer come in contact with wood dust. These two polishers are included because they had been French polishers in the past.

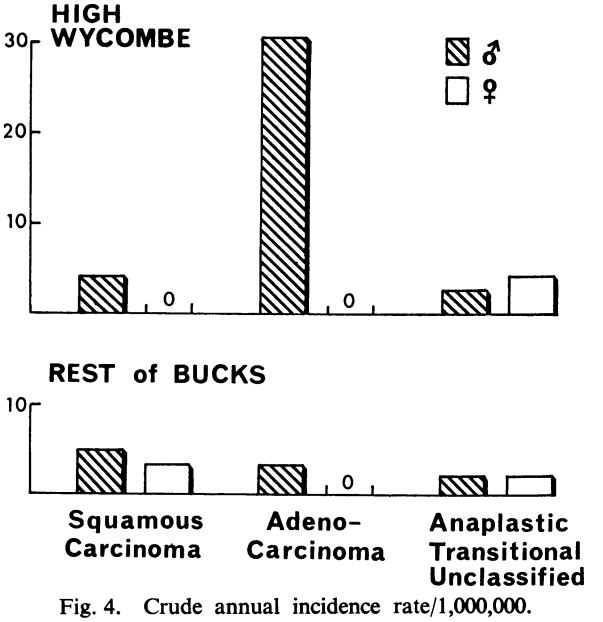


Fig. 4. Crude annual incidence rate/1,000,000.

If we examine the occupational histories of the 11 men and women below the line we find that five of them had been previously employed as woodworkers in the Furniture Industry. Of the three men in the Building Trade, one had been a cabinet maker, one a wood machinist and the third a wood-turner. Both the garage proprietor and the chimney sweep had previously been wood machinists. So if we add these five men to those who were still employed in the Furniture Industry at the time of diagnosis we find that out of 35 patients with adenocarcinoma 29 of them were or had been woodworkers in the Furniture Industry (Table V).

There can be no doubt that this evidence clearly shows that these men have been exposed to a carcinogenic agent which in a small but not

inconsiderable proportion causes adenocarcinoma of the sinuses. It seems likely that the carcinogen was, and probably still is, a constituent of the hardwood dust produced during the manufacture of furniture. One can go no further than this on the present evidence. The identification of the actual carcinogen now becomes a matter for the interested laboratory worker. However, satisfying as this would be from a purely personal point of view, it is extremely doubtful if its identification would contribute much to our present knowledge on carcinogenesis. The research worker in this field has passed beyond the identification of carcinogens, of which he already has an embarrassing number. He is now rightly concerned with the mechanisms of their action.

The figures that I have given you correspond well with those given in our previous survey, which was conducted over a wider area. Further-

TABLE IV

OCCUPATION AT TIME OF DIAGNOSIS

Wood machinist	10	
Cabinet maker	5	
Chair maker	5	
Polisher	2	24
Stoker/labourer in furniture factory	1	
Veneer worker	1	
Building trade	3	
Engineer	2	
Garage proprietor	1	
Cost accountant	1	11
Chimney sweep	1	
Housewife	2	
Bakery trade ♀	1	
		35

more we have had considerable corroborative evidence of these findings from correspondents in this country and from abroad.

Occupational cancer

I do not need to remind this audience that in 1785, Sir Percivall Pott, a past President of this College, described the first cases of occupational cancer, namely cancer of the scrotum in chimney sweeps. However, you may have forgotten that it was not until 122 years later that compensation was given to victims of this disease. By then chimney-sweeps cancer had practically disappeared, to be replaced by mule-spinners cancer; the carcinogen being contained in the crude mineral oil, which was used to lubricate the spinning mules in the cotton industry. In 1920, 135 years after the condition was first described, Industrial Skin Cancer became a notifiable disease. We published our preliminary report in the *Lancet* in 1967 and the full report in June 1968. In May of this year

(1969) adenocarcinoma of the nasal sinuses in woodworkers in the Furniture Industry became a prescribed disease under the 1959 National Insurance (Prescribed diseases) Regulations. This means that a man who is unable to work, is disabled by or dies from the disease is entitled to increased financial benefits. It is the patient, or his widow, who has to apply to the local office of the Department of Health and Social Security for the increased benefits, but it is the doctor's responsibility to tell the patient that he has a prescribed disease and to advise him of his rights in these circumstances. When a patient dies from a prescribed disease the coroner has to be informed in order that the cause of death can be proven: otherwise the widow will not receive the increased pension. I do not apologize for mentioning this because the majority of us are extraordinarily ill-informed of our responsibilities in these matters.

TABLE V

OCCUPATION/PREVIOUS OCCUPATION

Wood machinist	10	29
Ex-wood machinist	3	
Cabinet maker	5	
Ex-cabinet maker	1	
Chair maker	5	
French polisher	2	
Stoker/labourer in furniture factory	1	
Ex-wood turner	1	
Veneer worker	1	
Engineer	2	6
Cost accountant	1	
Housewife	2	
Bakery trade ♀	1	
		35

Other woodworkers

The question may be raised why this disease should affect woodworkers in the Furniture Industry and yet does not occur in carpenters and joiners. After all, in the whole area in the study there were as many men in the one group as in the other. There is no certain answer to this question but there are a number of theories. Carpenters use more softwoods and fewer hardwoods. Most of the timber they use has a high moisture content, having been air dried but not kiln dried; also their work is less well finished and in consequence the wood dust produced is much coarser. Again, much of a carpenter's work is done at least partly in the open air, for example in half-constructed houses, when the wind and moist air carry away the dust particles.

Dust extraction

Having established the fact that there is a carcinogen in the wood dust in Furniture Factories, let us turn for a moment to the question of

protecting the men exposed to it. There are at least three ways of tackling this problem.

1. It may be found that the carcinogen is only present in one particular wood, in which case men working on this wood could take special precautions.

2. Men doing particularly dusty jobs in the factory could wear masks. Some men do in fact wear them but, as will be appreciated, a man has to be very frightened of cancer to wear a mask for eight hours a day, five days a week.

3. Dust extraction methods can be expanded and improved. Dust extraction is already of a high standard in the larger factories but in the smaller ones is often rather inefficient.

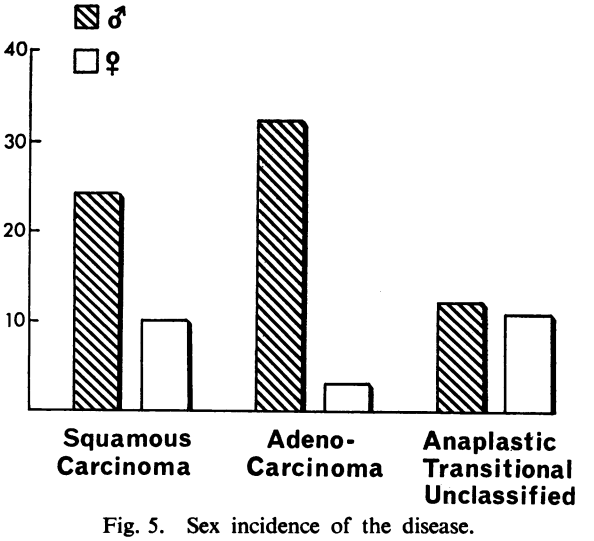


Fig. 5. Sex incidence of the disease.

Natural history

Now let us consider the natural history of the disease and see what differences there are between the various histological types (Fig. 5).

Sex incidence

We have already mentioned the incidence of the disease in males and females, but there are two further points. Squamous carcinoma occurs twice as often in males. I can offer no explanation for this, but it seems to follow the general trend of squamous carcinoma as it appears elsewhere in the upper respiratory tract. In the adenocarcinoma group the male-to-female incidence is 10 : 1. This is explained by the fact that only a tiny number of the women employed in the Wycombe Furniture Industry were, or are, regularly exposed to wood dust. In any event

some cases of adenocarcinoma do occur without exposure to a known carcinogen. In the anaplastic, transitional and unclassified groups the sex incidence is about equal. It is perhaps worth mentioning in passing that two out of the 11 women in this group had been exposed to wood dust in Wycombe Furniture Factories. One had been a French polisher, the other had worked for eight years doing sandpapering.

Infection

In case it should be thought that we are entirely absorbed in the carcinogenic properties of wood dust, it should be said at this stage that we did consider various other aetiological factors. Infection we think can be ruled out. None of the 92 patients gave a past history of sinusitis and none of them had had nasal polypi removed. We did find some benign nasal polypi at operation in relation to the tumour mass in a small number of the patients, but it seems likely that these polypi were a secondary phenomenon, due to surface infection of the tumour, and not a pre-existing condition.

Cigarette smoking

Many of the patients were or had been cigarette smokers. But this is unlikely to be a primary causal factor because of the commonness of the habit and the rarity of the tumour. However, there is no evidence one way or the other regarding its importance as a contributory factor.

Snuff

One is more interested in the use of snuff. This used to be a relatively common habit in the Wycombe Furniture Factories. The men are forbidden to smoke at work because of the danger of fire. Many of them say that a pinch of snuff clears the nose when the work is especially dusty, and some believe that it relieves the nasal congestion brought on by exposure to some particular dust. Our records are incomplete with regard to this habit. However, we were able to get definite information from 17 of the men with adenocarcinoma, and three of them had taken snuff regularly. In view of this, snuff-taking should be regarded with interest as a possible contributory factor in the causation of the disease.

Agents

It has also been suggested that the carcinogen is derived, not from the wood dust, but from glues, stains and varnishes to which some of the woodworkers are also exposed. Certainly glue is used by chairmakers, cabinet makers and veneer matchers, but wood machinists do not use it. Stains and varnishes were used by French polishers, but not by the other groups. In fact exposure to wood dust is the only thing that they all have in common.

Age

We should also consider the age of the patient at the time of diagnosis. In the squamous, transitional and anaplastic groups the disease manifested itself between the ages of 55 and 75 years. The majority of the adenocarcinoma patients were 10 years younger: that is to say they were in the 45–65 age group. Only four of the 35 patients with adenocarcinoma were over 65 at the time of diagnosis.

Site of origin

It is when we come to think about the site of origin of the tumour that we find the most striking difference (Fig. 6). In all the 35 patients with adenocarcinoma the tumour appeared to originate in the ethmoid sinuses. In six of these 35 patients the disease was extensive when they

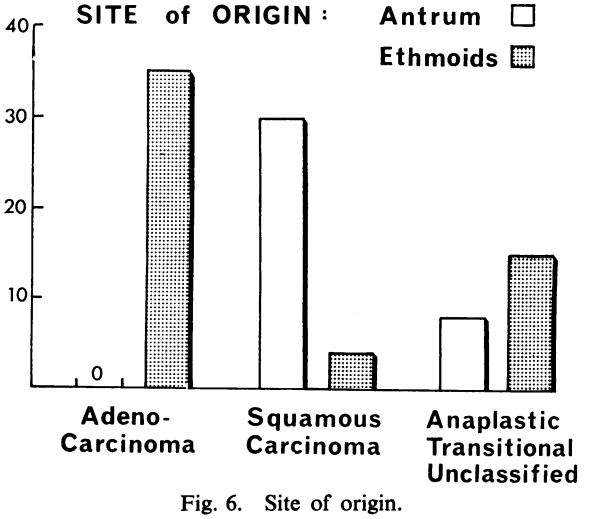


Fig. 6. Site of origin.

were first seen. Yet in none of these 35 patients, not even when they presented with extensive disease, was there any histological evidence of the tumour having trespassed into the antrum. The squamous carcinomata, on the other hand, seemed to have a predilection for the antrum. Of the 34 patients in the squamous group 30 were found to have a tumour originating in the antrum. In only four did it originate in the ethmoids. In the case of the tumours in the third group it was sometimes more difficult to decide the site of origin and the operation notes are less helpful. Eight of these tumours were certainly of antral origin, but several of the 15 which are designated as being of ethmoid origin did show evidence of antral invasion at operation. In this respect they differed from the adenocarcinomata. Or, to put it briefly, all the adenocarcinomata in this series originated in the ethmoid sinuses, the majority of the squamous carcinomata originated in the antra, the

transitional, anaplastic and unclassified tumours appeared twice as often in the ethmoids as in the antra. In none of the 92 patients was a primary tumour found in the frontal sinuses.

Symptoms

There is an obvious correlation between the site of origin of the tumour and the presenting symptoms of the disease. None of the tumours in this series could be considered as early cases. Because one sees relatively advanced cases one is perhaps less mindful of the early symptoms of the disease. In the majority of the ethmoid cases there were two early symptoms—namely, a unilateral blood-stained nasal discharge and unilateral nasal obstruction. Two of the ethmoid cases had intermittent nose bleeding from the same side for almost a year before the other symptoms appeared. In about half the ethmoid cases epiphora was also an early symptom. In most of the cases where the tumour originated in the antrum the first symptoms to be noticed were pain and paraesthesia in the distribution of the second division of the trigeminal nerve and an increased unilateral nasal discharge. To begin with, this discharge was thick and mucoid; later it became blood-stained. In four of the antral cases the first symptom was a swelling of the cheek or of the palate. This indicated, of course, that the tumour had broken out of the antrum and had invaded the adjacent soft tissues.

Lymph nodes

There is also a marked difference in behaviour between the adenocarcinomata and the other carcinomata regarding the involvement of the local lymph nodes. None of the patients with adenocarcinoma have had clinical evidence of cervical lymph node metastases at any time during the course of the disease. Nor was any found in the eight patients in this group who were examined post mortem. On the other hand the cervical nodes were found to be involved either during life or at post mortem in at least nine of the 58 patients in the other histological groups. You may wonder if the adenocarcinoma patients died before there was time to develop lymph node metastases, but in fact the survival times are about the same for all three groups. Two of the patients with squamous carcinoma had histologically proven cervical lymph node metastases when they were first seen, although they did not have particularly extensive primary tumours.

Blood-borne metastases were found post mortem in all the histological groups, but in none of them were they found often.

Exposure and latent period

Turning once more to carcinogenesis in relation to the development of adenocarcinoma there are two further questions to be answered. First, what is the shortest exposure necessary for the development of a

cancer? Secondly, how long is the latent period?—that is, the interval between exposure and appearance of tumour. In order to answer these questions one has to have a number of patients who were in the Industry for a known time and then got another job where they were not exposed to wood dust. We have certain information for six such patients. The length of exposure to wood dust ranged from 18 months to nine years. The latent period ranged from 28 to 45 years, the mean being 38 years. This being the case it might well be asked why we are including in the survey (about which I shall talk later) men who have been in the Industry for only five years. There are several reasons. We want to identify a premalignant change. The manufacturers want cases of the disease to be detected early. The men simply want to know that they have not got cancer.

Plan of treatment

The majority of these 92 patients received the same course of treatment. There were five exceptions, all of whom had advanced disease and obvious intracranial extension of the tumour when they were first seen. Two of this group were not treated at all, the other three were given palliative radiotherapy. The remaining 87 patients were treated in three stages. They started with a 28-day course of external irradiation, consisting of 12 treatments given three times a week to give a tumour dose of 4,000 to 4,500 rads. The earlier cases had High Voltage Therapy, the later cases were treated on the Cobalt unit. After this they had about 10 days rest and then surgical excision of the tumour. In most cases this was done intra-orally, through a fenestra made either in the hard palate or in the canine fossa. In seven of the ethmoid cases the tumour was approached through a lateral rhinotomy incision. This gives a more direct approach to the ethmoid air cells and is necessary in cases where the tumour has broken out of the ethmoids into the orbit, because the orbital contents can be cleared *en bloc* with the nasal part of the tumour. About two weeks after the excision of the tumour the antro-ethmoid cavities were packed with radium ovoids to give a surface dose of 5,000 equivalent rads to the walls of the cavity. The patients were then passed on to the dental surgeons and the prosthesis makers for completion of masks and obturators. A depressing number of these patients developed a local recurrence of the tumour. Where the recurrence was accessible a more extensive operative removal was carried out, followed, in some cases, by further local application of radium.

Cause of death

I think that the excellent masks that the prosthesis makers can now produce have encouraged even the most cautious of us to clear the orbit sooner rather than later. Yet no matter how radical an assault we make on the sinuses we are still losing patients from extension of the tumour into the anterior cranial fossa. In our experience of ethmoid tumours,

death is invariably associated with intracranial extension of growth, while antral tumours on the whole kill by blood-borne metastases.

Results of treatment

Turning now to the results of treatment, of the 92 patients in the series 31 are alive and 61 are dead. Of the patients who are alive only 13 have survived for longer than five years. In Figure 7 we have the overall survival rates according to histological type, and although the squamous group do not look quite as good as the other two groups the difference is not great enough to be of any real significance. The patients who have survived for more than five years are pretty equally divided between the three histological groups. Of the 61 patients who are dead, 39 died within the first two years. There is very little difference in the survival time between the three groups. Adenocarcinomata take about a year longer to kill the patient than the squamous and other histological varieties do. This is to be expected because they are well differentiated tumours, they grow relatively slowly and do not produce metastases.

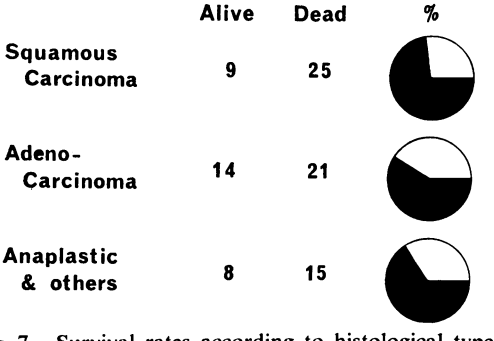


Fig. 7. Survival rates according to histological type.

Developments in treatment

There are two obvious ways of improving these results. One can make changes in the techniques of treatment and one can try to attract patients at an earlier stage in the disease. With regard to treatment, the most interesting possibilities seem to be in the use of intra-arterial cytotoxic drugs as an adjunct to irradiation. On the other hand, when we realized that there was a relatively high incidence of the disease in woodworkers in the Furniture Industry it seemed to us that this might be an opportunity to pick up early cases or perhaps to identify a pre-malignant lesion. With this in mind we approached the Furniture Manufacturers for their help.

Nasal survey in Furniture Industry

Early this year (1969), the High Wycombe branch of the Furniture Manufacturers Society (with the keen support of the Unions) decided to finance

a five-year survey of men employed in the woodworking side of the Furniture Industry in High Wycombe and the surrounding district. It was agreed that every man who was exposed to wood dust, and who had been in the Industry for longer than five years, should be given the opportunity of an annual examination by an ear, nose and throat surgeon. The men are being examined in the factories where they work. This is partly to save their working time but also because we are interested in the deposition of wood dust on the nasal mucosa. Approximately 3,000 men will be examined each year for the next five years. The men are first interviewed by a secretary, who obtains a complete occupational history. At the same time arrangements have been made for a register to be set up of all woodworkers in this Industry in the area.

Deposition of dust on nasal mucosa

The most interesting observation that has emerged so far is in relation to the deposition of wood dust on the nasal mucous membrane. The dust is fine and very little of it seems to be caught by the hairs in the nasal vestibules. However, we have found that in an overwhelming number of subjects the dust is deposited in two areas. First, on a small area, oval in shape, measuring 1 cm. by $\frac{1}{2}$ cm. low down on the anterior part of the nasal septum, just behind the mucocutaneous junction. (This, incidentally, is just where a chrome ulcer of the septum is normally located, and it has the same shape as a chrome ulcer with the long axis parallel with the floor of the nose.) Secondly, the dust is deposited on the anterior ends of the middle turbinates in a roughly circular pattern 1 cm. in diameter. We have noticed, not surprisingly, that there is a greater deposition of dust on that side of the nose where the airway is better. Only in the relatively few subjects who have an absolutely straight septum is the dust distributed equally on both sides. In the light of this observation one naturally reviewed the clinical findings in cases of adenocarcinoma of the ethmoids, expecting to find that there was a deviation of the septum to the opposite side on which the carcinoma was situated. In this one was disappointed. In only four of the cases was there any mention in the notes of the septum being deviated one way or the other. In these, as one expected, the tumour was located on the side of the better airway. In the majority of cases the surgeon had been so concerned with noting the appearance and extent of the tumour that the shape of the septum had not been mentioned. This is, of course, the sort of situation which faces one again and again when making a retrospective study.

Nasal physiology

It is essential at this stage to refer briefly to two important points in the physiology of the nose. These are the direction of the air currents on respiration and the mechanism of the mucociliary blanket. For the greater part of our knowledge of these matters we are indebted to Sir Victor Negus and Arthur Proetz.

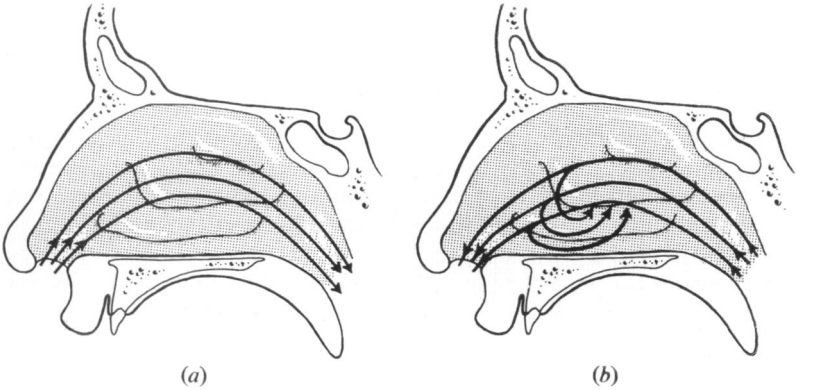
Air currents

Four factors determine the direction of the upper respiratory pathways. These are: the downward direction of the anterior nares, the relative sizes of the anterior nares and the posterior choanae, the streamlining of the turbinates and the shape of the nasal cavities. Figure 8 (*a*) shows the stream of inspired air, at first directed upwards to the level of the middle turbinate then downwards and backwards towards the posterior choana. The greater part of this air stream impinges on the anterior end of the middle turbinate. It then passes backwards between it and the septum. Very little, if any, of it reaches the orifices of the paranasal sinuses. It is therefore not surprising that we found considerable deposits of wood dust on the anterior ends of the middle turbinates. The remarkable thing was that it seemed to stay there. Figure 8 (*b*) shows the direction of the expired air streams. Here you see the eddy currents which carry some of the expired air in the direction of the sinus orifices. This is important because it means that the greater part of the air entering the sinuses by their natural orifices has already been filtered by its passage through the entire respiratory tract. It is therefore unlikely that this air contains any particulate matter and most improbable that the carcinogen enters the sinuses by this route. Or look at it the other way: if the carcinogen gains access to the sinuses via the natural ostia, why does it produce cancer only in the ethmoids and not in the other sinuses?

Mucociliary blanket

As is well known, the greater part of the nasal mucous membrane has a surface layer of respiratory epithelium of the pseudostratified columnar ciliated type. On the other hand the epithelium in the nasal vestibule is of the stratified squamous variety. It is generally accepted that in many people (and especially in the older subject) this squamous epithelium tends to spread a little on to the anterior part of the inferior turbinates. In the olfactory region the mucous membrane consists of a superficial layer of pseudostratified columnar cells, without cilia, interspersed by olfactory receptor cells. The healthy nasal mucosa is covered by a layer of mucus in which particulate matter in the inspired air is trapped. By the action of the cilia this contaminated mucus is continually being directed into the nasopharynx and is eventually swallowed. As I have mentioned already it seemed to us quite remarkable that this otherwise efficient mucociliary mechanism should fail to remove the dust deposits from the anterior parts of the middle turbinates. We then began taking smears from the noses of the men who had particularly heavy deposits of dust. It was found on cytological examination that in these people the nasal secretions contained unusually large numbers of squames. We had already observed in a certain number of these men that after removing the surface layer of dust and mucus the underlying mucosa covering the

anterior ends of the middle turbinates had a fine granular appearance on naked-eye examination. When we have biopsied the mucosa in this area we have been confronted over and over again with the report of squamous metaplasia. Clearly this explains the persistence of the dust deposits in these people, because where there is squamous epithelium and no cilia the mucociliary mechanism will break down. Particulate matter will be entrapped in the mucus but will not be carried away if there are no cilia to propel it. It seems logical that if the wood dust does contain a carcinogen, as we believe it does, then its prolonged contact with the mucous membrane covering the anterior end of the middle turbinate would provide it with an excellent port of entry to the anterior ethmoid air cells lying immediately behind. On the other hand, it is just as likely that the tumour originates on the anterior end of the middle turbinate, just where the dust is deposited, and then grows by direct extension into the anterior



(*a*) (*b*)

Fig. 8. (*a*) Direction of inspiratory pathways. (*b*) Direction of expiratory pathways.

ethmoidal air cells. In this case one would expect a squamous carcinoma rather than an adenocarcinoma because it would have originated from an area where we already know there is often squamous metaplasia. This, however, presupposes that the tumour is derived from surface epithelium: it may in fact derive from the glandular elements in the subepithelial connective tissue.

Site of origin of adenocarcinoma

Although we have insufficient evidence to decide on the exact point of origin of the tumour, I personally believe that it arises on the superficial part of the middle turbinate and involves the ethmoid air cells by direct extension. There is one recent case, not included in this study, where the clinical findings give some support to this theory. This man had a large tumour completely filling one nostril. The ethmoid air cells were a little cloudy on X-ray, but there was no apparent breakdown of

the cell walls. He was examined under anaesthetic and all the tumour visible in the nose was removed. It was growing along the entire length of the middle turbinate. The diagnosis was adenocarcinoma. Then he was treated on the Cobalt Unit giving a tumour dose to the ethmoid area of 4,750 rads. Following this he had a transpalatal ethmoid clearance. There was no histological evidence of tumour either in the antrum or ethmoids. As the adenocarcinomata are not particularly radiosensitive, one can only suppose that the tumour had been completely removed intranasally in the first instance. Obviously we must have a wider experience of early cases before we can decide on the site of origin of these tumours, but this one case may point the way.

One other point: the question may be asked, Why have we not found tumours on the nasal septum? because, as you will remember, dust was deposited there as well. I have no explanation for this apart from the observation that the septum, like the trachea, is an area of low cancer potential under all known conditions.

Normal histology of middle turbinate

Having become rather alarmingly involved in the pathological changes to be found in the mucosa covering the anterior part of the middle turbinate, it seemed sensible to start at the beginning and to review the normal histology of this area, All the authorities seemed to agree that the epithelium is of the pseudostratified columnar ciliated type interspersed by mucus-secreting goblet cells and lying on a fibro-elastic tunica propria which separates it from the subepithelial connective tissue. However, in spite of this unanimity of opinion in respect of the normal histological picture, we thought that it might be instructive to run a small control series taking biopsies from the anterior ends of the middle turbinates from 30 subjects who had no symptoms or signs of nasal disease. We did this in 20 young men and women and in 10 children, none of whom had been exposed to irritant dusts or fumes. We found that in 17 of the 20 adults and in 8 of the 10 children there were small areas of squamous epithelium surrounded by larger areas of the normal respiratory type. Further reference to the literature brought to light a paper by Oppikofer written in 1906. In it he described the normal histology of 200 turbinate bones. In 80% of them he found islands of squamous epithelium surrounded by areas of the pseudostratified columnar ciliated type. We will have to examine many more normal subjects, but the presence of squamous epithelium in this area in children and young adults seems to indicate that it is a normal histological finding and not a metaplastic change due to irritation of the mucosa.

We propose to continue this survey, at any rate for the first year, along the lines already indicated. In order to decide eventually on the best screening method we will need to learn a great deal more about the

correlation between histological and pathological findings and the changes in the nasal mucosa visible on naked-eye examination. At the same time we need to develop a better understanding of what is pathological and what is normal. This is a difficult enough task in relation to any epithelial surface. It is especially difficult in the upper respiratory tract where the signs of chronic disease and early neoplasia are so easily distorted by acute infections and allergic episodes.

It may be felt that undue importance is attached to the actual site of origin of the tumour. Yet this may be important when it comes to determining the best method of making an early diagnosis. If the tumour originates within the ethmoid air cells, then there may well be some radiological evidence of its presence before it makes its appearance in the nose. If, on the other hand, it originates on the surface of the middle turbinate, it should be visible on clinical examination, or its presence may be suspected on cytological examination of the nasal secretions.

In any event one is hopeful that, in the time allowed us to make this survey, some of these questions may be answered, and some of these early theories may become established matters of fact.

ACKNOWLEDGEMENTS

That elegant phrase, 'No man is an Island, entire of itself', is very applicable in the field of clinical research. There are many people here to-day, too many to mention, who know how great is my debt to them. Yet more especially do I want to remember those stout-hearted craftsmen of High Wycombe—who lived and died with this disease and on whose lives and deaths the foundations of this paper were laid.

SYMPOSIUM ON MEDICAL COMPUTING

A SYMPOSIUM ON 'Progress in Real-Time Medical Computing' will be held at the Royal College of Surgeons of England on Friday, 10th July 1970, under the Chairmanship of Professor Sir Hedley Atkins, K.B.E.

'A number of major medical computing projects sponsored by the Department of Health and Social Security are now under way in the United Kingdom aimed at exploring the possible uses of on-line computers and data-terminals in wards, clinics and general practitioners' consulting rooms. The influence of these experiments on the future shape and forms of medical practice is likely to be considerable.

'The purpose of this symposium is to bring together those with the medical responsibility for the more important projects, and to explain in clear terms to those as yet not directly affected what they are attempting to do and the likely outcomes of their activities on medical practice. It is not a forum for the experts to address each other.'

Application is by ticket only, obtainable from The Symposium Secretary, 13 Parkway Court, St. Albans, Herts. In view of the strictly limited number that can be accommodated, ticket allocation will be made strictly in order of application. Fee: £5 15s.