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Lung cancer and tobacco consumption

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The pronounced increase in lung cancer is a fact that has been established repeatedly in the years since 1920. The reason for this increase has been attributed to a range of circumstances by different authors. Most importantly, certain air pollutants have been investigated. Lung cancer due to occupational exposures is relevant in this context, which in the case of the Schneeberg lung cancer and cancer due to chromate or asbestos is recognized as an occupational disease. Exposure to exhaust fumes of motors, which are inhaled in many occupations but also by the general public in cities and on main roads, has also been examined. To this day it has not, however, been convincingly shown that increased inhalation of such fumes leads to an increase in carcinoma of the lung. Arguments against this notion include the experiments of Schmidtmann,[8] the fact that country and city dwellers contribute to the same extent to the increase in lung cancer, and that occupations dealing with combustion engines are not particularly frequent among the diseased. The observation that the male gender is much more frequently afflicted by carcinoma of the lung than the female does not exactly support the notion that this cancer is predominantly caused by exhaust fumes because both genders are exposed to almost the same degree. The marked predominance of the male gender in lung cancer (six times more men than women contracted the disease in our material) suggests important internal factors in the development of the disease. However, there is also an external factor, which is much more common in men than in women: smoking. It has indeed repeatedly been pointed out that a close association between the increase in tobacco consumption and carcinoma of the lung could exist. In the first instance this assumption is supported by the results from experimental cancer research.

Roffo *et al.*[6] have successfully induced cancer by applying tar extracted from tobacco. Roffo also showed that the same tar contained the strongly carcinogenic benzpyrene. Taking into account that the tobacco consumed by a heavy smoker in 10 years would yield 4 kilograms of tar, it follows that considerable damage could be done to the epithelium of the airways, in particular if the smoke is inhaled.

In clinical research attempts have also been undertaken to prove the association between tobacco consumption and carcinoma of the lung. Müller[5] ascertained the amount of tobacco consumed in 86 men diagnosed with lung cancer during a certain period of time and compared it to that consumed by 86 healthy men of the same age. His figures show that a much greater proportion of patients with lung cancer were heavy smokers than would be expected while, to the contrary, non-smokers and moderate smokers were more frequent among controls than among lung cancer patients. Müller therefore concluded that the increase in carcinoma of the lung is, at least to an important degree, due to the increase in tobacco consumption.

To us the data of Müller seemed to be very significant in relation to the lung cancer problem. We considered, however, that further investigations were necessary to show their general validity. In the material of the Pathological Institute in Jena we had, as had Berblinger[2] earlier, observed a substantial absolute and relative increase in carcinoma of the lung while, for example, stomach cancer did not show such an increase. Table 1 which shows the increase in lung cancer during the years 1910 to 1939 was taken from the dissertation of Wüstner.[10] This increase continued in the war years until 1941. The number of bronchial carcinomas as a proportion of the number of autopsies among patients older than 20 years was 3.61% in the year 1940 and 2.95% in the year 1941.

In line with the work of Müller we investigated tobacco consumption among our lung cancer material (the years 1930 to 1941, 195 cases). We sent a questionnaire, which was similar to the one designed by Müller, to the relatives, most of whom were resident in Thuringia. We asked whether or not the deceased had smoked, what his daily tobacco consumption was, and whether or not he may have cut down on the amounts smoked or stopped, particularly during the illness. Furthermore, we investigated his occupation and possible occupational damage due to air pollution. The same questionnaires were sent to the relatives of patients who died from cancers of the stomach, colon, prostate, oesophagus and tongue during the same time period. We thus intended to get material for comparison which was as complete as possible, allowing an assessment of the influence of smoking on other types of cancer. As shown in Table 2, about 50 to 60% of questionnaires were completed such that they could be analysed, for example 109 out of 195 in the case of lung cancer.

Furthermore, we sent questionnaires to 700 men aged 53 and 54 years (corresponding to the mean age of 53.9 years of our lung cancer deaths) in order to ascertain their tobacco consumption before the war and during the war. Only 270 men completed these questionnaires in a satisfactory manner.

The results from these surveys are listed in Table 2. The first column shows the total number of cases, the second column the number of usable responses, in the following columns the data are separated into men and women. One sees that for lung cancer there are six times as many usable responses for men as for women, corresponding to the six times greater number of cases. The same is observed for cancers of the oesophagus and tongue, whereas the gender ratio is about 2:1 for cancers of the stomach and colon.

Among women there were only two light and one moderate smokers (see last column of Table 2) and they were therefore

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Table 1 Increase of lung cancer in the autopsy material of the Institute of Pathology in Jena, 1910–1939 (adapted from Wüstner[10])

Period	Total no. of autopsies	No. of autopsies in patients >20 years of age	No. of cancers	No. of lung cancers	Proportions (%)		
					Total cancers as proportion of autopsies in patients >20 years of age	Lung cancers as a proportion of autopsies in patients >20 years of age	Lung cancers as a proportion of all cancers
1910–1914	2347	1725	363	8	21.05	0.46	2.2
1915–1919	3280	2400	337	10	14.05	0.42	2.9
1920–1924	2430	1629	341	24	21.80	1.53	7.0
1925–1929	3358	2368	443	31	18.74	1.31	7.0
1930–1934	3220	2462	439	46	17.82	1.87	10.5
1935–1939	4714	3462	734	88	21.87	2.77	12.0

Table 2 Smoking patterns among cancer patients and controls

Cancer site	No. of questionnaires sent out	No. of valid questionnaires	Gender distribution		Smoking patterns in men					Smoking patterns in women
			Men	Women	Non-smokers	Light smokers	Moderate smokers	Heavy smokers	Very heavy smokers	
1. Lung	195	109	93	16	3	11	31	19	29	0
2. Tongue	32	17	15	2	2	0	4	6	3	0
3. Oesophagus	35	14	10	4	0	2	3	1	4	0
4. Stomach	320	189	128	61	20	55	26	14	13	2 light smokers
5. Colon	108	65	40	25	3	14	6	8	8	1 moderate smoker
6. Prostate	60	33	33	–	6	8	7	6	6	–
7. Controls	700	270	270	–	43	98	57	47	25	–

excluded from further analyses. The men are stratified according to their tobacco consumption (before development of the disease) in four additional columns of Table 2. Here we used the categories of Lickint.[4] According to him, a light smoker smokes 1 cigar or up to 5 cigarettes per day; a moderate smoker 2 cigars or 6–10 cigarettes per day; a heavy smoker 3–4 cigars or 11–20 cigarettes daily; a very heavy smoker more than 4 cigars or more than 20 cigarettes daily.

It is already very clear from Table 2 that in comparison with patients with stomach cancer or normal controls, non-smokers are fairly rare whereas heavy smokers and, particularly, very heavy smokers are strongly represented among patients with carcinoma of the lung. An association similar to lung cancer is observed for tongue and oesophageal cancer. For these two cancers the number of cases are, however, too small to allow statistical analysis. The number of cancers of the colon and prostate is also quite small, we therefore combined those cancers for which an influence of smoking was not probable into one group in Table 3.

In Table 3 we give the number of non-smokers, light, moderate and heavy smokers (we combined the groups of heavy and very heavy smokers from Table 2) as percentages for each of the three main cancer groups (lung cancer, stomach cancer, colon and prostate cancer) to allow immediate comparison. The female cases were hereby not included because women, with the exemption of a tiny minority, were non-smokers. In the same manner, we present as a fourth group all male cancer cases examined by us, corresponding to about two thirds of the total number of male cancer cases in this time period, and as a fifth group the normal controls.

It is evident from Table 3 that the distribution of cases across the different smoking categories differs quite markedly between different types of cancer. Among lung cancer patients we find the fewest non-smokers and the highest proportion of heavy smokers, among stomach cancer patients, on the contrary, the highest proportion of non-smokers and light smokers and the fewest heavy smokers. The percentages in the group of colon and prostate cancer fall about mid way between the former two, as well, as expected, the percentages for all types of cancer combined. The results for the normal population are again to be found between those for stomach cancer and colon and prostate cancer. One thus gains the impression that lung cancer is much

Table 3 Prevalence of smoking in per cent among cancer cases and in a normal male population

Cancer site	Non-smokers	Light smokers	Moderate smokers	Heavy smokers
Lung cancer	3 ± 1.8	12 ± 3.7	33 ± 4.9	52 ± 4.7
Stomach cancer	16 ± 3.3	43 ± 4.5	20 ± 3.6	21 ± 3.5
Cancer of the colon or prostate	12 ± 3.8	32 ± 5.4	18 ± 4.6	38 ± 5.7
All examined cancers in males	10.7 ± 1.7	28.4 ± 2.6	24.2 ± 2.4	36.7 ± 2.7
Normal male population aged 53–54 years	15.9 ± 2.2	36.3 ± 2.9	21.1 ± 2.5	26.7 ± 2.7

Table 4 Comparison of tobacco consumption in per cent between lung cancer cases and normal controls. Data from Cologne (Müller 1940[5]) and Jena

	Lung cancer		Controls	
	Cologne	Jena	Cologne	Jena
Heavy smokers (heavy to extreme smokers of Müller)	65.12	52	36.04	26.7
Light and moderate smokers (moderate smokers of Müller)	31.19	45	47.68	57.4
Non-smokers	3.49	3	16.28	15.9

more frequent among heavy smokers, and much rarer among non-smokers, than colon and prostate cancer. Conversely, heavy smokers appear to be relatively rare among patients with stomach cancer, even in comparison with colon, prostate cancer or normal controls. The differences between lung cancer on the one hand, stomach cancer and normal population on the other are, as far as the groups of non-smokers and heavy smokers are concerned, statistically certain. Conversely, the differences between colon and prostate cancer on the one hand and lung or stomach cancer on the other are at best statistically probable.

As reported above, Müller[5] concluded that in his material from Cologne heavy smokers are more likely to contract lung cancer than non-smokers or light smokers. A comparison of our results with his results is fraught with difficulties in so far as Müller used different categories for smokers. His 'heavy to extreme' smokers correspond approximately to our 'heavy' and 'very heavy' smokers; his 'light' smokers to our 'light' and 'moderate' smokers. On this basis we made a comparison in Table 4, again giving percentages. One sees that the figures from Cologne and Jena essentially correspond to each other. Heavy smokers are, however, more frequent in the normal population in Cologne than in Jena, the same being evident among patients with lung cancer. The differences between the normal population and patients with carcinoma of the lung are statistically certain in Müller's material for the group of heavy smokers and non-smokers.

The relatively high proportion of non-smokers, 15% to 16% in the comparison groups of both Cologne and Jena is peculiar. The percentage of non-smokers has, for example by Lickint,[4] been estimated to be considerably lower (5–10%). One could imagine that the age groups considered here perhaps smoke not as much as younger people. The suspicion nevertheless arises that some interviewees did not report their tobacco consumption entirely honestly. This applies to the Cologne comparison group. Our comparison material also has some weaknesses. Out of 700 questionnaires only 270, not even half, were completed satisfactorily. It is to be feared that for some considerations related to the war played a part when completing the questionnaire. One could image that therefore more heavy smokers than non-smokers refrained from answering and that in this way an unbalanced selection occurred.

Such considerations should, however, not have played a role in our other comparison groups, stomach cancer and colon and prostate cancer. Here the surveys were conducted in exactly the same way as for lung cancer. A comparison of the material is therefore perfectly possible and admissible. As already mentioned, differences emerged in comparisons with lung cancer.

This applies in particular to the group with stomach cancer. The distribution across the various smoking categories corresponds almost to that among the 'normal male' population, although heavy smokers are even less frequent than among the latter. If we could assume that our surveys really represent an average of the normal population then we could conclude that no relationship exists between stomach cancer and smoking. We have, however, reasons to assume that among our 'normal population' there were too many non-smokers and too few heavy smokers. We must consider that among stomach cancer patients there were particularly few heavy smokers and particularly many non-smokers and light smokers. This may perhaps be explained by the fact that some of the patients with stomach cancer had suffered from a 'weak stomach' for some time and therefore refrained from heavy smoking.

The differences in tobacco consumption between patients with stomach cancer and lung cancer are, however, not explained by a more pronounced reduction in smoking during the course of the illness among stomach cancer patients. This is clearly evident from Table 5. The table shows, in percentages, how many refrained from consumption or reduced it during their last illness. One sees that this was the case in equal measure for the two types of cancer.

The group of colon and prostate cancer also shows, as is evident from Table 3, considerable differences compared to lung cancer. The distribution of the various categories of smoking in this group corresponds largely to the group which combines all examined male cancers. Any relationship between smoking and the development of colon and prostate cancer is, in our view, unlikely. We would therefore believe that the distribution of smoking in this group is most likely to correspond to the norm. Unfortunately, the number of cases is relatively small (73), such that the average error becomes relatively large. The difference compared to lung cancer, which seems substantial, is therefore statistically uncertain. The difference between lung cancer on the one hand and the group of all cancers on the other is also only likely (for the groups of heavy smokers and non-smokers).

When drawing conclusions from the material which is available so far (including Müller's material) we can say that there is a *high probability* in support of the contention that lung cancer develops much more frequently among heavy smokers and is

Table 5 Reduction of smoking in patients with lung cancer and stomach cancer

In the course of the illness smoking was	Lung cancer	Stomach cancer
Stopped	60%	56%
Reduced	20%	28%
Unchanged	11%	10%
Increased	5%	0%
No information	2%	6%

much rarer among non-smokers than expected in general. Unfortunately, it has not been possible so far to collect completely flawless material for comparison, or the sample was too small to allow statistically certain conclusions. The task, therefore, remains to study the relationship between smoking and lung cancer in a larger sample. The same applies to the entirely different relationship found for stomach cancer.

The question of how these differences in tobacco consumption may be generated deserves some brief comment. Concerning stomach cancer one can, as discussed above, only imagine that in many cases a 'sensitive' stomach leads to moderation in smoking as well as to the development of cancer. An inhibitory effect of heavy tobacco consumption on the development of stomach cancer is unlikely.

On the other hand it seems logical to consider that high tobacco consumption has a promoting effect in the case of lung cancer. This is supported by the concomitant increase in tobacco consumption and lung cancer in the past decades. Tar and carcinogenic substances contained in tobacco could hereby play an important part. The results of our survey, which are shown in Table 5, are clear evidence against the assumption that the increased tobacco consumption was a consequence of patients smoking more for palliation. According to our findings most patients stopped or reduced smoking during their illness and only a few smoked more.

We thus have to assume that heavy smoking is a cause of the increase in lung cancer. It cannot, however, be the sole cause of lung cancer as a few non-smokers are also afflicted by cancer. But we can assume that smoking is a very important cause leading an existing pre-disposition to proceed to the development of lung cancer. We are reminded here of the experiments which showed that in mice, which themselves have only a moderate pre-disposition for lung cancer, the additional application of tar or carcinogenic substances produced a much larger number of lung cancers (Anderfont[1]). There are numerous other examples, which show that in a terrain that is already prepared for it, additional stimuli can produce cancer. Rous and Friedländer,[7] for example, showed that treatment of virus-induced papillomata with methylcholanthrene provokes a rapid transformation to cancer in rabbits.

We attempted to assess other external causes of lung cancer, in particular pollution of ambient air, by designing our questionnaire correspondingly. Our material does not, however, provide any clues. Fifty-two of our patients with lung cancer had a dust-free occupation. Thirteen were occupationally exposed to stone dust, ten were exposed to metal dust. Further details are given by Wüstner[10] and Schöniger.[9] All occupations were represented in about the same proportion as in the normal population. An increase of workers who deal with lead, as found by Müller in his material, was not evident among our cases. A particular increase of lung cancer in silicosis (slate and porcelain workers) was not observed either. Lung cancer was associated with tuberculosis in 10 out of 189 cases (Wüstner), and once with actinomycosis of the lung. From these figures a causal association cannot be derived either. There was no evidence for a relationship with previous bouts of flu (Berblinger[2]) or with scars in the lungs (Friedrich[3]) to the presence of which we paid particular attention in recent times. Once a localized scar had been found it was never clear whether it should be seen as a consequence of the bronchial cancer (collapse and consolidation).

Summary

Following the studies of Müller (Cologne) an investigation into the consumption of tobacco was conducted among cancer cases of the Pathological Institute in Jena, and among a comparison group from the normal male population of the same age in Jena.

We could confirm the report of Müller that non-smokers rarely get lung cancer whereas heavy smokers get it more frequently than the average. Conversely, we found few heavy smokers and many non-smokers and light smokers among patients with stomach cancer.

Our comparison material was less than satisfactory and the association between heavy tobacco consumption and lung cancer is therefore statistically, and causally, only likely. In order to confirm this association, larger investigations are required which we hope to stimulate with the present investigation.

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