Published in final edited form as:

Prev Med. 2012 September ; 55(3): 171–177. doi:10.1016/j.ypmed.2012.05.008.

Quality, originality, and significance of the 1939 “Tobacco consumption and lung carcinoma” article by Mueller, including translation of a section of the paper

Alfredo Morabia^{*}

Center for the Biology of Natural Systems, Queens College, City University of New York, NY, USA

Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA

Abstract

Background—The 1939 article “Tobacco consumption and lung carcinoma” by Mueller has been praised for its quality and its originality but is still not available in English.

Methods—Summary of the 29-page long paper and translation of part of its investigative section. Re-analysis of the clinical and smoking characteristics of the lung cancer cases. Comparison with pre-1945 case–control studies and a similar but prior tobacco and cancer report.

Results—The article primarily consists of a detailed description of the smoking, clinical and occupational characteristics of 96, mostly dead, lung cancer cases. Occupation and the flu are discussed for the cases only. The paper makes unexplained assumptions about the smoking habits of 20 cases and is silent about the sampling, recruitment and interview modes of the “healthy” subjects, supposed to reflect “normal tobacco consumption.” The dearth of methodological information distinguishes this paper from case–control studies published before 1939. Major selection and differential misclassification cannot be ruled out.

Conclusion—Access to the 1939 Mueller article is provided for non-German speakers. The quality of the group comparison was modest and it did not add qualitatively new knowledge compared to a report published 8 years earlier.

Keywords

History; Smoking; Lung cancer; Epidemiology

Introduction

The establishment of a causal link between tobacco use and lung cancer has played an important role for science, medicine, and public health. It punctuated a large scale controversy about the health effects of a ubiquitous environmental exposure, which involved, in the US, governmental interventions and judicial battles (Brandt, 2007; Kluger, 1997; Miura et al., 2006; The Surgeon General's Advisory Committee, 1964).

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^{*}Center for the Biology of Natural Systems, Queens College, CUNY, 65-30 Kissena Boulevard, Flushing, NY 11367, USA. alfredo.morabia@qc.cuny.edu.

Conflict of interest statement

The author declares that there are no conflicts of interest.

Part of the material related to the historical process that led to the recognition of the tobacco-cancer link is still not available in English. This includes the 1939 German publication by Mueller (Mueller, 1939), which, for at least two reasons, needs to be made available for a non-German speaking public.

The first reason is that its quality has been praised in two influential books. It has been described as “an exquisite piece of scholarship” by Proctor in his *Nazi War on Cancer* (Proctor, 1999, p.194), and as “probably the best-informed and most persuasive scientific paper of the decade on the smoking and health question” by Kluger in his *Ashes To Ashes: America's Hundred-Year Cigarette War, The Public Health, And The Unabashed Triumph Of Philip Morris*. (Kluger, 1997, p.145)

The second reason is that Mueller's study has been claimed to be the first comparative study assessing the carcinogenic effect of tobacco in humans. According to Proctor, it was “the world's first case-control epidemiological study in the field of tobacco” (Proctor, 1999, p. 197). In Kluger's terms, it was “the first careful study of its kind,” “pathbreaking” (Kluger, 1997, p.145) and “seminal” (Kluger, 1997, p.780).

I therefore perform here a technical evaluation of the paper, describing its content and translating the sections about a series of lung cancer patients, and their comparison with a group of “healthy” men (Box 1). I also re-analyze for the first time Mueller's lung cancer case descriptions. And then I discuss the validity, originality and significance of the study, comparing it with case-control studies published before 1945.

Mueller's 1939 study

The study was submitted on December 24, 1938 and published in 1939, in German, in the *Zeitung fuer Krebsforschung* [Journal for Cancer Research] (Mueller, 1939). Its stated objective was to explain the increase in “primary lung cancer” incidence observed in the pathology reports of hospitals in Cologne between 1918 and 1937. The original paper is 29-pages long.

The paper has five sections. Section 1 (pp. 57–59) reviews the evolution of biopsy results in Cologne and in Germany. Section 2 (pp. 59–60) quantifies the evolution of tobacco sales in Germany, indicating a fivefold increase in cigarette sales since 1907, and points to the recent increased usage of tar-rich tobacco products as potentially related to greater lung cancer frequency. Section 3 (pp. 60–62) reviews animal studies supporting a carcinogenic effect of tobacco tar, in particular provoking skin cancer in the ears of rabbits exposed to condensed tobacco tar rich in polycyclic aromatic hydrocarbons. It then speculates that yearlong exposure of an organism to tobacco smoke “predisposes” it to cancer.

Case series

Section 4 (pp. 62–77) is entitled “Investigations.” Box 1 in Appendix A provides a translation of the paragraphs describing the recruitment of a series of 96 lung cancer patients, 86 men and 10 women, identified in various hospitals in Cologne, in the Western part of central Germany. Information was collected partly from the patient records, partly using in-person interviews of the sick, but “mainly” from a questionnaire (reproduced in Box 1) completed by relatives querying whether their late parent had been a current or a former smoker, their daily consumption of cigars, cigarettes, pipe tobacco, and recent changes therein.

I have not translated the 13 pages of Section 4 dedicated to the individual description of the 96 patients with lung cancer. But I coded the information and abstracted it into an electronic

database. For each case, numbered from 1 to 96, we are given, in the following order and if available: the medical chart number/year, initials, occupation, age, smoking habits, other respiratory exposures, history of respiratory diseases, the type of lung cancer and whether it was diagnosed clinically or anatomopathologically. For example, the data for case # 94 are: "94. 379/31, L.H., artist, 33 y, nonsmoker. *Other external exposures of the airway*: not known. *Previous diseases of the respiratory organ*: at age 21 y pneumonia. At age 26 y again pneumonia. At age 31 y again pneumonia with relapse. *Anatomical diagnosis*: bronchial carcinoma of the right lung" (Mueller, 1939).

The case list is subdivided into "A. Extreme smoker," "B. Heavy smoker," "C. Moderate smoker or non-smoker." The 10 female lung cancer patients (10% of the series) were non-smokers.

Results

Section 5 (pp. 77–84) is entitled "Results of our investigations." It is itself divided into 3 subsections: "a) Tobacco smoking" (pp. 77–79), "b) Other external exposures of the airways" (pp. 79–82), and "c) Flu" (pp. 83–84). There is finally a "Summary" (page 84) and a bibliography of 27 references.

The Subsection 5.a. (pp. 77–79) is translated in Box 1. It groups the lung cancer cases into five smoking categories defined on the basis of the consumption of cigarettes, cigars, and pipes: 3.5% had never smoked and 65.1% had been "heavy" smokers or more. It also compares the daily tobacco consumption of the lung cancer cases with that of "the same number of healthy men, of the same age." The comparison is tabulated in what was originally "Table 2" of the "healthy" men, 16.3% were non-smokers and about 36% were "heavy" smokers or more.

Mueller also transformed each smoking category into daily grams of tobacco smoked, multiplied them by the number of subjects in each group, and reported that "the 86 lung cancer cases had smoked more than twice the amount (2900 g of tobacco) compared to the same number of healthy people (1250 g)." This comparison is depicted as histograms in the original Fig. 2 (shown in Box 1).

Subsection 5.b (pp. 79–82) discusses the etiologic relevance of the occupational exposures of the cases to lead (17/86 lung cancer patients had been exposed to lead), metals (in particular, chromium), substances used in ammunition plants (in which three of the women with lung cancer had worked), and tobacco in cigarette production plants. It indicates that the presence of moderate smokers among the lung cancer patients might be explained by their occupational exposures. There is no comparison with the occupational exposures of the 86 "healthy" men.

Subsection 5.c discusses the role of the flu as an etiological factor of lung cancer in the literature and in this sample of lung cancer cases, and specifies that the topic warrants more research.

Mueller concluded that tobacco was "the most important factor [Moment]" of the rising incidence of lung cancer. The paper ended with the need for broad information about the dangers of tobacco smoke to prevent a further rise in primary lung cancer incidence. In particular, people with a family history of cancer and those with a "chronic catarrh of the respiratory airways" should be dissuaded from smoking.

Re-analysis

I have analyzed electronically the information given on the 86 male and 10 female lung cancer patients (Table 1). Their mean age was 57 y (range 32–87 y) for men and 51 y (range 26–65 y) for women. One of the 10 (current) housewives also worked as an ironer. Dates of the hospital charts were from 1928 to 1939. Cigarette smoking was more common in younger men, while pipe smoking was more common among older people (Table 2). Of the male cases, 55% were blue collar workers, and included many occupations (n = 21) such as electricians, metal workers, bookbinders, heat treaters, insulators, heated metal workers, and construction laborers which we know today are at high risk of lung cancer (Morabia et al., 1992). Mueller did not mention that at least 6 cases (2 boilermen, 1 insulator, 3 electrician/plumber/roofer) had been exposed to asbestos even though its association with lung cancer may have been known then (Nordmann, 1938).

Overall, I was able to classify only 66 out of 86 male lung cancer patients into the categories of smoking determined by Mueller. The relatives of 20 of the cancer patients had not specified the amounts smoked. Some patients had a qualitative description of tobacco exposure, such as “smoked all day long,” and some had no information on amounts smoked at all. Thus, Mueller allocated to smoking categories about 25% of the cases for whom he did not have the relevant information. There must have been a high level of misclassification, which prompts questions about the validity of the comparative analysis. Moreover, misclassification must have been differential as smoking habits were self-reported by “healthy” subjects and proxy-reported for cancer patients.

Table 3 shows that leaving out the 20 lung cancer patients for whom the amount of pipes, cigarettes, and cigars smoked was missing, leads to smaller percentages of “very heavy” and “extreme” smokers and a higher percentage of “heavy” smokers. Some smokers, for whom the smoking amount was available, were misclassified too, mostly among the “very heavy” and “extreme” smokers.

I could not reproduce exactly the estimates of the daily quantity smoked in grams for the lung cancer patients (2900 g/d) and the healthy subjects (1250 g/d). By imputing 50 g, 42.5 g, 28.5 g, 10 g and 0 g to the 5 smoking categories, and following the same approach that Mueller used, I calculated 2656 g and 1450 g using Mueller's numbers, vs. 1821 g and 1450 g using only the 66 subjects for whom the amount smoked was available. The difference is 371 g (20.4%) instead of Mueller's 1206 g (45.4%). In any case, Mueller does not seem to have been aware of the imprecision of these estimates. The weight of tobacco in a modern American cigarette can vary by as much as 50% (0.49–0.89 g) (Counts et al., 2004).

With respect to the comparative component of the study, the paper does not indicate how the “healthy” men had been sampled, where and how they were recruited, nor how they were interviewed.

Discussion

Mueller's paper consists primarily of a review of the ecological and laboratory evidence linking tobacco to lung cancer and of a detailed description of a series of 96 cases. The discussion of the results is largely dedicated to the occupational exposures of the cases. The comparison of the male lung cancer cases with “healthy” men is restricted to smoking habits and takes a small section of the paper. But it is this component of the paper that distinguishes it from the previous mass of work on tobacco and lung cancer, because there had been only one of these comparative studies before 1939 (Hoffman, 1931). It is also this comparison that gave the paper the notoriety it acquired later, when case-control studies and cohort studies on the same topic were conducted in Europe and North America.

I therefore focus this discussion on the quality (1. *Was the group comparison valid?*), originality (2. *Was this the first group comparison on tobacco and lung cancer?*) and significance (3. *What has been its impact on later epidemiologic work?*) of the group comparison described in Box 1.

Was the group comparison valid?

The paper does not provide the information needed to assess whether the comparison of the lung cancer cases with the “healthy” men was valid. There is no information in Box 1 about how the “healthy” sample was selected and recruited, and how information was obtained and analyzed. Was this a convenience or a random sample? Were they recruited from the population or were they colleagues and staff of Mueller's hospital? Nor is there any description of two key variables: age, which Mueller claimed was similar in the compared groups, and occupation, which Mueller considered as the main alternative cause of lung cancer. The author does not discuss either the implications of having obtained smoking histories from the relatives of the cases and, putatively, from the healthy subjects themselves.

We cannot rule out that more detail might have been found in Mueller's archives, but these may have been destroyed during the war (Proctor, 1999, p. 194). Nonetheless, there are at least two reasons for which it is extremely puzzling not to find in a 1939, 29 page-long paper, information about the comparison group. The first is that such information would have calmed concerns that the “healthy” smoking distribution was derived from subjects likely for any imaginable reason to underreport their true consumption or to belong to a low smoking subgroup of the population. The second reason for perplexity is that, given the age range (32–87 y), it must have been quite an endeavor to randomly select 86 age-matched “healthy” people. The memory of the hard work must have still been fresh in Mueller's mind when he wrote his manuscript.

The detailed description of the case series is a boon, because it allows us to explore their characteristics and repeat Mueller's computations. But the inconsistencies between Mueller's findings and those of the re-analysis plus the dearth of methodologic details dampen the quality and potential validity of the study, even with pre-World War II expectations.

Could it be that Mueller's failures were common practice around 1939 and would not have been apparent to his contemporaries? To the best of my knowledge, there is no evidence supporting this explanation. Of the six case-control studies I am aware of published before 1945 (English et al., 1940; Glendy et al., 1937; Johnson, 1929; Lane-Clayton, 1926; Lombard and Doering, 1928; Stocks and Karn, 1933), all provided sufficient detail about the ways their controls were ascertained and recruited for their design to be reproduced by others. They express the obvious intent to convince the reader that the design was sound, that the recruitment was independent of exposure, and that the controls could be legitimately compared to the cases. The case-control studies published by Johnson, in 1929, 10 y before Mueller's, in the *Journal of the American Medical Association* (Johnson, 1929), are striking examples of the wide-spread dissemination of these essential concepts of case-control studies long before Mueller published his report. Johnson, a clinician, presented two case-control comparisons he performed himself to evaluate the effect of smoking on blood pressure and on angina pectoris (Johnson, 1929). He provided abundant details about how he proceeded.

It is important to note that there is no hint that Mueller understood what a case-control study was or intended to perform one. Clearly, assembling and describing the exposures of a large (at that time) series of lung cancer cases were his primary intention. The information on the case series is so detailed that it would allow us to find the charts today if they still existed.

On the other hand, the smoking habits of the “healthy” men are given to confirm that extreme tobacco consumption was expectedly rare in the population, which is reminiscent of the way comparisons were made before the advent of case-control studies (Morabia, 2007; Morabia, 2010). Mueller did not even use a comparative approach in the sections about occupational exposures or about the flu.

Was this the first group comparison on tobacco and lung cancer?

As mentioned in the Introduction. Mueller's study has been claimed to be the “first” comparative work on tobacco and lung cancer ever. But was it? Had there been before Mueller's study another report of smoking habits in cases of lung cancer and some kind of referent group?

The answer is yes and it is unfortunate that more attention has not been given yet to the cancer epidemiology of Frederick L. Hoffman, who in 1931 had published results similar to those of Mueller (Hoffman, 1931). Hoffman had observed in his extended San Francisco Cancer Survey a prevalence of heavy smoking of 67% among 27 lung cancer patients, of 46% among 1356 cancer patients, and of 43.9% among 537 non-cancer patients. He also referred to a survey (Bogen, 1929) showing that 12.5% of industrial workers had smoked more than a pack of cigarettes a day. Hoffman concluded that “smoking habits unquestionably [italicized in original] increase[d] the liability to cancer of the mouth, throat, esophagus, larynx and lungs” (Hoffman, 1931). Mueller did not cite Hoffman.

Undoubtedly, Mueller's lung cancer case series was larger than Hoffman's and had more detailed tobacco consumption data. But Hoffman's report was based on more clearly defined sources of subjects free of lung cancer than Mueller's. Thus, Hoffman's works precedes Mueller's with evidence of the same type.

What has been the impact of Mueller's study?

An English summary, covering about a third of a page of the *Journal of the American Medical Association*, appeared in 1939 (Anonymous, 1939). It mentioned the literature review and the “statistical survey of 96 dead patients” (Anonymous, 1939). It briefly alluded to the comparison with the “healthy” subjects, but it is important to note that the main emphasis was put on the prevalence of moderate smokers and non-smokers among the cases: “the fact that about one third of the subjects [with lung cancer] surveyed smoked moderately or not indicates the presence of other carcinogenic factors besides smoking such as influenza and industrial working conditions” (Anonymous, 1939).

In 1943, Schairer and Schoeniger attempted to reproduce Mueller's finding (Schairer and Schoeniger, 1943). This other German study shared many of the same weaknesses as Mueller's. Otherwise, I know of no other citation of Mueller's paper before 1949, not even by Mertens from Munich in a discussion of the evidence on smoking and lung cancer published in 1941 in the same *Zeitung fuer Krebsforschung* (Mertens, 1941).

The association reported by Mueller was strong. The study was therefore bound to attract much attention after the war, when the epidemiologic research on the tobacco-lung cancer connection was suddenly boosted. Still, appreciation varied. In their comparison of 82 lung cancer cases with several cancer control groups, submitted in September 1949, Schrek et al. (1950) acknowledged the precedence of the comparative evidence by Hoffman, but qualified Mueller's findings as “striking” and concluded that “the uniformity of the findings obtained by Mueller and Wynder & Graham [of which they knew the data presented at a March 1949 conference of the American Cancer Society and National Cancer Institute in Memphis, TN, USA (Cameron, 1949)], and in the present study is impressive” (Schrek et al., 1950).

In 1950, Wynder, a medical student, and Graham, a thoracic surgeon, wrote: “Mueller (15) in 1939, from a careful but limited *clinical* statistical study, offered good evidence that heavy smoking is an important etiologic factor” ((Wynder and Graham, 1950), my emphasis).

In spring 1950 also, Levin, an epidemiologist at the Bureau of Cancer Control, Division of Medical Services, New York State Department of Health, and colleagues did not cite specific articles but indicated that “reviews of the literature for the past twenty years reveal that it is often conflicting and that it consists for the most part of studies which are inconclusive because of lack of adequate samples, lack of random selection, lack of proper controls or failure to age-standardize the data” (Levin et al., 1950).

Several months later, Doll and Hill also mentioned Mueller's study: “In Germany, Mueller (6) found that only 3 out of 86 male patients with cancer of the lung were nonsmokers, while 56 were heavy smokers, and, in contrast, among 86 “healthy men of the same age groups” there were 14 nonsmokers and only 31 heavy smokers” (Doll and Hill, 1950). Doll and Hill cited Schrek et al. (1950) and Jones (as a personal communication), and pointed out that: “Clearly, none of these small-scale inquiries can be accepted as conclusive, but they all point in the same direction. Their evidence has now been borne out by the results of a large-scale inquiry undertaken in the U.S.A. by Wynder and Graham (9)” (Doll and Hill, 1950).

Mueller's paper does not seem to have served as a model since all these post-war epidemiologic studies had hospital, not “healthy”, controls.

In 1950, clinicians remained quite divided about the issue: “for every expert who blames tobacco for cancer of the lung, there [was] another expert who says tobacco is not the cause” (Cameron, 1949). But the tobacco-lung cancer case-control studies published in 1950 (Doll and Hill, 1950; Levin et al., 1950; Wynder and Graham, 1950) were larger and better designed than all the pre-war studies. They paved the way for the design of cohort studies (Doll and Hill, 1954; Hammond and Horn, 1954) which were the really decisive pieces of evidence which led to the official recognition of the causal effects of tobacco smoke (Kluger, 1997; The Surgeon General's Advisory Committee, 1964).

Who was Mueller?—Franz H Mueller (1914-?) studied at the University of Cologne, where he defended his medical dissertation in 1939 (Proctor, 1999, p. 194). All we know is that he was Catholic, Aryan, and a member of the Nazi party and the army. Apart from his 1939 paper, there is no other known published scholarly work by him.

The Nazi Party membership of Mueller, combined with a superficial appraisal of his paper, is at the origin of the theory according to which a Nazi scientist first established the epidemiological link between tobacco and lung cancer (Proctor, 1999). I have tried to show here that these claims fall short of withstanding a technical scrutiny of the paper content and a thorough review of the historical literature, even from a pre-1945 perspective.

Conclusion

This paper provides for the first time access for non-German speakers to a 1939 published study of smoking and lung cancer. The study was of modest quality and evidence and did not add qualitatively new knowledge about the causal link of tobacco smoke and lung cancer compared to a report published 8 years earlier.

Acknowledgments

This work was supported by a grant from the National Library of Medicine 1G13LM010884-01A1. I thank Prof Sigrid Beer-Borst and one of the reviewers for checking the translation of Mueller's paper provided in Box 1. Most of the historical articles can be found on the website of the People's Epidemiology Library, for teaching or research purposes only.

Appendix A. Translation

Box 1

Franz H Mueller, Misuse of tobacco and cancer of the lung (Zeitung fuer Krebsforschung, 1939, 49:57–85).

[The full paper has 29 pages, 13 of which are dedicated to the description of the clinical characteristics of the 96 lung cancer cases. I have translated only the 4 pages dedicated to the sampling, interview, and comparison of 86 of these cases with 86 “healthy people.” AM] p.62

“4. Investigations

A relatively large number of patients with lung cancer have been treated in our Division of Internal Medicine at the municipal public hospital [staedtisches Buergerhospital] of the city of Cologne during the last years. A closer look at the lifestyle of these patients showed that a strikingly large number of them had been very heavy smokers. It was not rare for these patients to report having consumed 30–50 cigarettes per day or equivalent quantities of cigars or pipe tobacco.

This clinical observation has motivated the present work. It was performed using data, which were collected partly from the medical records, and partly using detailed in-person interviews of the sick, but the information was mainly obtained from answers to questions asked to the relatives of the deceased.

The wording of the questionnaire mailed to the relatives was the following:

1. *Was deceased Mr a smoker?*

Answer:

If yes, what was his daily consumption of cigars, cigarettes, pipe tobacco? (Please provide exact information, if possible in numbers!)

Answer:

The information in the medical records about smoking did not appear satisfactory, because they only indicated the current level of tobacco consumption, and often only contained the annotations “heavy smoker” or “moderate smoker” which does not tell anything about the true tobacco consumption. In very many cases the sick patients had reduced or even stopped their former heavy smoking habit during the course of the disease or at the time of hospital admission because of the worsening of the disease symptoms. We therefore asked specific questions about earlier tobacco consumption as well:

2. *Had the deceased smoked in the past and later quit smoking?*

Answer

Until which year of life?

Answer:

If yes, what was his daily consumption of cigars, cigarettes, pipe tobacco? (Please provide exact answers in numbers!)

Answer:

3. Had the deceased smoked more in the past but then reduced his smoking?

Answer

Until which year of life?

Answer:

What was in that case his daily consumption of tobacco products before and after? (Please, exact answers!)

Answer:

Besides smoking we also included other deleterious exposures of the airways, in particular the occupational ones, as part of this investigation about the etiology of primary lung cancer and added in our questionnaire:

4. Can you tell me if the deceased was, during his occupational activity or outside this activity exposed to the effect of polluted air for a longer period of time? Did the polluted air contain materials such as, e.g., smoke, soot, dust, tar, fumes, combustion products, exhaust gases, coal or metal dust, chemical compounds, vapor of cigarettes or analogous substances?

Answer:

By far the largest part of those who received the questionnaire responded positively to our requests. We collected the address of eligible persons from all larger hospitals of Cologne. Thus, we had access for our investigations to the autopsy reports of the Pathology Institute of the University and of the Pathology Institute of the municipal hospital of Cologne-Muelheim, as well as the medical records of the Division of Internal Medicine of the Lindenburg hospital, of the St. Elizabethan hospital of Cologne-Hohenlind, of the municipal hospital of Cologne-Muelheim besides the medical records of the Division of Internal Medicine of the public hospital and of the municipal hospital of Cologne-Deutz thanks to the kind mediation of the directors of these institutions. Closer details about the work conditions of a part of the craftsmen and workers in our patients were disclosed upon our request from the plants in which these sick people had been employed for longer periods of time.

That way, we have assembled the following 96 cases of disease."

[Pages 64 to 77 provide the list and clinical characteristics of these cases, e.g., "94. 379/31, L.H., artist, 33 y, nonsmoker. *Other external exposures of the airway*: not known. *Previous diseases of the respiratory organs*: at age 21 y pneumonia. At age 26 y again pneumonia. At age 31 y again pneumonia with relapse. *Anatomical diagnosis*: bronchial carcinoma of the right lung." This information has been coded and entered into a database — AM].

p.77

5. "5. Results of our investigations

- a. Tobacco smoking

The 86 male cases of lung cancer listed above were categorized as:

1. Extreme smoker: 25 = 29.07%
2. Very heavy smoker: 18 = 20.93%
3. Heavy smoker: 13 = 15.12%
4. Moderate smoker: 27 = 31.39%
5. Non smoker: 3 = 3.49%

A comparison with the daily tobacco consumption assessed from the same number of healthy men of the same age group, demonstrates a huge difference between these values and the normal tobacco consumption, as shown in the following table:

Distribution of daily tobacco consumption in 86 male lung cancer cases compared to 86 healthy men.

	Absolute number		Percent	
	Lung cancer patients	Healthy	Out of 86 lung cancer patients	Out of 86 healthy men
Extreme smoker (daily consumption of 10–15 cigars, more than 35 cigarettes, more than 50 g of pipe tobacco)	25	4	29.07	4.65
Very heavy smoker (7–9 cigars, 26–35 cigarettes, 36–50 g of pipe tobacco)	18	5	20.93	5.81
Heavy smoker (4–6 cigars, 16–25 cigarettes, 21–35 g of pipe tobacco)	13	22	15.12	25.58
Moderate smoker (1–3 cigars, 1–15 cigarettes, 1–20 g of pipe tobacco)	27	41	31.39	47.68
Non smoker	3	14	3.49	16.28
Altogether	86	86	100.00	100.00

Moreover, the computation of the total daily amount of tobacco smoked (1 cigar = 5 g, 1 cigarette = 0.8 g) provides an impressive comparison, as shown in Fig. 2. The 86 lung cancer cases had smoked more than twice the amount (2900 g of tobacco) compared to the same number of healthy people (1250 g)!

On the basis of the positive results of the animal experimental research and of the present investigations of a large patient population, which clearly shows the massive spread of tobacco abuse among the lung cancer cases, we have become convinced that *tobacco smoking is a major etiologic cause of the primary lung carcinoma. The huge increase in tobacco consumption over the last decades has to be made primarily responsible for the growth of primary carcinoma of the lung.*

The fact that there were moderate smokers and non-smokers among the lung cancer patients, for about one third of the cases, suggests the existence of other carcinogenic factors besides tobacco smoking. In line with this stands the fact that in our patient population, occupations such as civil servants and people who work in clean air environments, such as sales persons, clerks, restaurant owners, etc., find themselves almost without exception among the heavy smokers, while among the moderate smokers and non-smokers we observe other, mostly occupational airway exposures. We will now evaluate the degree to which these exposures need to be considered as causative factors of the disease.”

Fig. 2. Total amount of daily tobacco consumption in grams. A = by the 86 lung cancer patients; B = by 86 healthy persons.

[p. 79, end of translation]

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Table 1

Characteristics of male and female patients with lung cancer as derived from their individual descriptions in Mueller (1939).

Variables	Categories	Men		Women	
		n	%	n	%
Total		86	100	10	100
Age (y)	<35	9	10.4	3	30.0
	35–44	4	4.7	0	0
	45–54	25	29.1	2	20.0
	55–64	26	30.2	4	40.0
	65+	22	25.6	1	10.0
Occupation	Blue collar	52	55.2	1	10.0
	Else	34	44.8	9 ^a	90.0
Cancer diagnosis	Clinical	21	24.4	1	10.0
	Macroscopic	40	46.5	7	70
	Microscopic	25	29.1	2	20.0
Year of medical chart	Before 1930	8	9.3	1	10.0
	1930–1934	22	25.6	4	40.0
	1935–1939	56	65.1	5	50.0

^a All housewives.

Table 2

Distribution of (non-exclusive) tobacco use by age in Mueller (1939).

Age groups	N	Cigarettes	Pipes	Cigars
		%		
<44y	13	53.9	7.7	46.2
45–54 y	25	56.0	40.0	40.0
55–64 y	26	15.4	38.5	53.9
65+y	22	0	59.1	63.6
All	86	29.1	39.5	51.2

Distribution of daily tobacco use in lung cancer patients with and without data about amount smoked and percentages of miscategorization in Mueller (1939).

Table 3

	All		Amount smoked available		Miscategorization	
	N	%	n	%	(Percent point differences)	
Extreme smoker	25	29.1	16	24.2	+4.9	
Very heavy smoker	18	20.9	10	15.2	+5.7	
Heavy smoker	13	15.1	16	24.2	-9.1	
Moderate smoker	27	31.4	21	31.8	-0.4	
Non smoker	3	3.5	3	4.6	-1.1	
Altogether	86	100	66	100		