LUNG CANCER 1980

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Lung Cancer 1980

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Postgraduate Course

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Introduction

In connection with the II World Conference on Lung Cancer in Copenhagen 1980 under the auspices of I.A.S.L.C. a postgraduate course on lung cancer has been arranged. Outstanding authors who have contributed to the knowledge on the different aspects of lung cancer have accepted to give carefully up-dated reviews on their field, thus providing a modern overview of problems and facts. This booklet is a combination of these contributions.

The problem of lung cancer is indeed to-day one of the most challenging in medicine, both with regard to etiology, pathogenesis and treatment. The magnitude of the lung cancer problem with regard to morbidity and mortality makes research on causal factor mandatory in order to provide means for prevention of the disease. Cigarette smoking stands out as a major risk factor but also other exogene factors are emerging. The prognosis of patients with lung cancer continues to be poor, and while awaiting for better prevention, improvement of treatment is desperately needed. The general basis for rational treatment consists of proper classification, staging and evaluation of patients. Intensive coordination on these matters is of outmost importance for progress. As to the treatment strategies, it becomes increasingly clear that multimodality approaches including surgery, radiotherapy, chemotherapy and immunotherapy are needed. The improvement with regard to overall prognosis for lung cancer patients have not been impressing, but for certain groups e.g. patients with small cell anaplastic lung cancer, definitive therapeutic progress has been made during the latest years.

The aim of this booklet is to provide the participants in the postgraduate course and any other physicians or students who are interested in lung cancer with a comprehensive review on these different problems, and especially to emphasize the unanswered questions in the hope that research on these areas might be stimulated.

We greatfully acknowledge the financial support from Lundbeck Foundation Copenhagen to this publication.

Copenhagen, May 1980

HEINE H. HANSEN MIKAEL RØRTH

Introduction

Epidemiology and Etiology of Lung Cancer

A. B. Miller

Introduction and descriptive epidemiology

In most technically advanced countries lung cancer is acknowledged to be the most important cancer in men and to be rapidly approaching this position in women. One of the most useful compilations of incidence data has been derived by the International Union Against Cancer and subsequently by the International Agency for Research on Cancer from a number of cancer registries throughout the world.[1-3] In volume three, giving data from many registries from the early 1970's, the highest rates in males are reported from Liverpool in the United Kingdom, the lowest from Ibadan in Nigeria (Figure 1). In addition to registries in the United Kingdom, high rates are reported from Finland and from black in many registries in the United States. Many developing countries show low rates while low rates are also found in Japan and rural Norway. A moderately low rate is found from Utah in the United States where a high proportion of the population are Mormons who do not smoke.

A somewhat different pattern is seen in females (Figure 2). The highest rate is from the Maoris of New Zealand with oriental populations from a number of areas (Bay Area of the U. S., Hawaii and Singapore) showing high rates as well as white females in the Bay Area, Alameda California and Hawaii. Females in Liverpool show the highest rates for the U. K. but are 13th in the world while females in Finland show low rates (67th out of 80 rates recorded). When all rates are standardized to the world population for comparative purposes, it is found that the highest rate in males is 89.5 per 100,000 from Liverpool, the lowest 0.8 from Ibadan. Nineteen registries have rates between 60 and 79, another 21 between 40 and 59, 26 between 20 and 39 and only 12 below 20. In comparison in females three registries have rates above 20, 8 between 15 and 19, 21 between 10 and 14, 32 between 5 and 9 and 15 below 5. The range is from the high of 35.4 per 100,000 in Maoris in New Zealand to 0.8 in Ibadan, Nigeria.

When one compares changes in incidence in lung cancer in registries that contributed to the first and third volumes of Cancer Incidence in Five Continents (Table 1), it is found that one registry in males showed a more than 100% increase, 7 an increase between 50 and 74%, 3 between 25 and 49% and 13 less than 25%. Only one showed a decrease. In females 3 showed an increase greater than 100%, 2 between 75 and 99%, 6 between 50 and 74%, 8 between 35 and 49% and only 4 an increase of less than 25% while 2

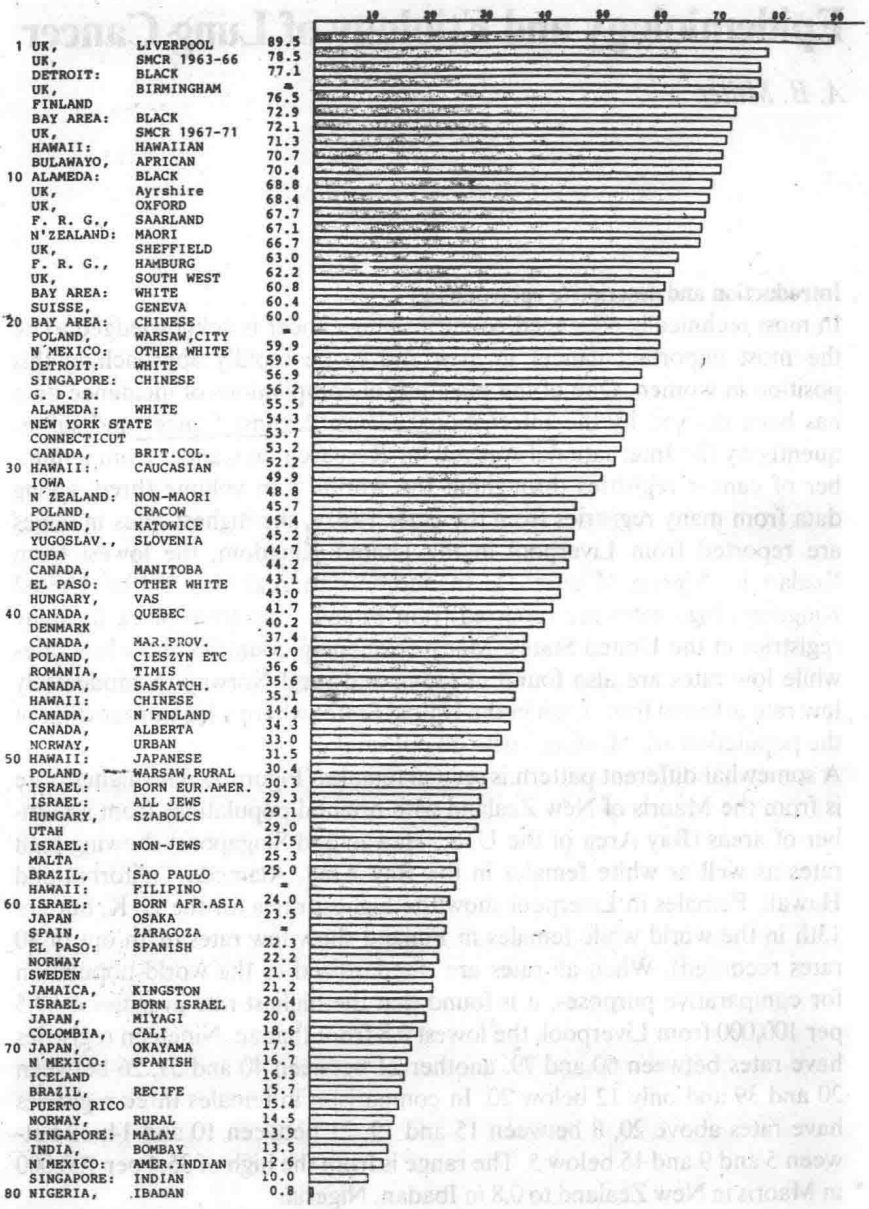

Fig. 1. Incidence of lung cancer in males, standardised to world population (Source, reference 3).

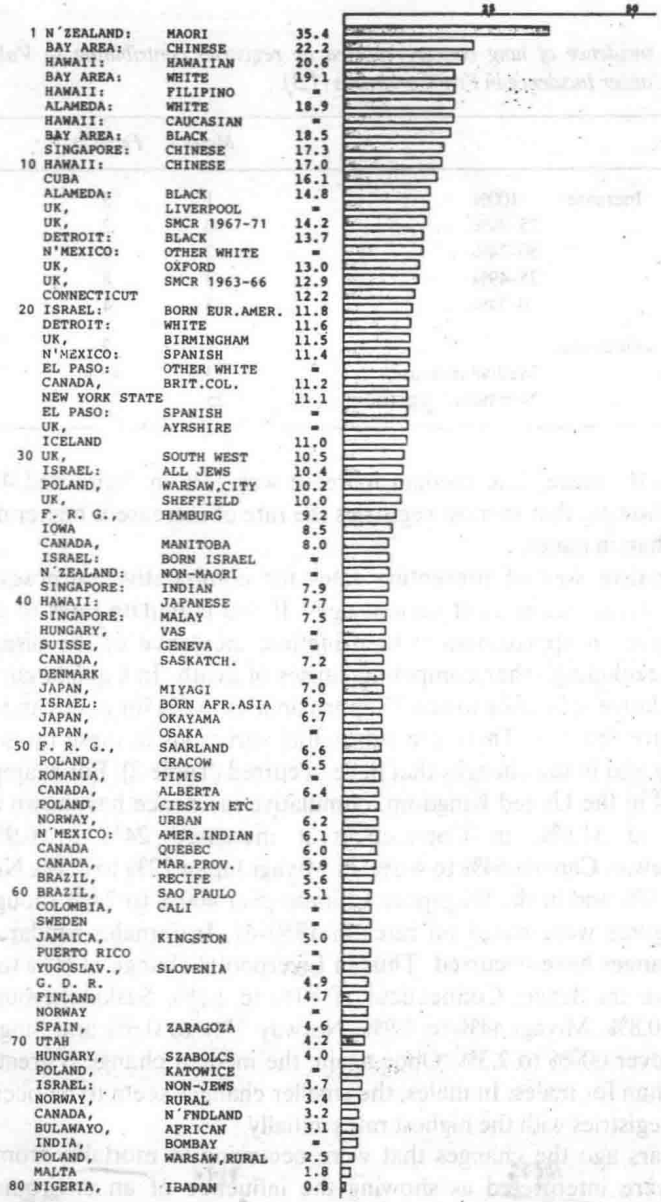

Fig. 2. Incidence of lung cancer in females, standardised to world population (Source, reference 3).

TABLE I

Change in incidence of lung cancer reported by registries contributing to Volumes I and III of Cancer Incidence in Five Continents (1,3).

		Males	*Females*
Increase:	100%	1	3
	75–99%	0	2
	50–74%	7	6
	25–49%	3	8
	0–24%	13	4
Decrease:		1	2
	Median increase	23%	43%
	Number of registries	25	25

showed a decrease. The median increase was 23% in males and 43% in females showing that in most registries the rate of increase is higher now in females than in males.

An alternative way of presenting rates for comparative purposes is to cumulate incidence rates at various ages. If you cumulate rates to age 75 you achieve an approximation to a lifetime incidence of the disease in question excluding other competing causes of death. In Canada currently the cumulative incidence to age 75 approximates to 6% for males and is just over 1% for females. There are substantial variations in these rates internationally and in the changes that have occurred (Table 2). For example, in Liverpool in the United Kingdom, cumulative incidence has shown a 14% increase to 11.6%, in Connecticut it increased 24% to 6.9%, in Saskatchewan Canada 64% to 4.6%, in Miyagi Japan 22% to 2.5%, Norway 67% to 3.0% and in the Singapore Chinese over 400% to 7.6% though the earlier figures were based on rates in 1950–61. In females similar if not larger changes have occurred. Thus in Liverpool a change of 60% to 1.8% cumulative incidence, Connecticut of 84% to 1.5%, Saskatchewan over 100% to 0.8%, Miyagi 44% to 0.9%, Norway 57% to 0.6% and Singapore Chinese over 600% to 2.3%. Once again, the median change is greater for females than for males. In males, the smaller changes seem to be occurring in those registries with the highest rates initially.

Many years ago the changes that were occurring in mortality from lung cancer were interpreted as showing the influence of an environmental factor. Clemmensen from Denmark was one of the first to identify these trends.[4] Changes are still continuing as is shown with the continued upward trend in mortality for lung cancer in Canada[5] though the rate of increase is less now in males than in females (Figure 3). The marked international variation confirms the importance of environmental factors as does the changes that have occurred in the rates of disease in groups of migrants. One interesting aspect of this has been the tendency for those who migrate

TABLE II

Change in cumulative incidence per 100 to age 75 in incidence of cancer of the lung reported by registries contributing to Volumes I and III of Cancer Incidence in Five Continents (1,3).

Registry	*Males*			*Females*		
	1959–62	*1968–72*	*% change*	*1959–62*	*1968–72*	*% change*
U. K. Liverpool	10.16	11.63	*14*	1.13	1.81	*60*
U. K. Birmingham	9.39	10.34	*10*	0.90	1.43	*59*
U. K. S. Metr.	9.20	9.54	*4*	1.22	1.79	*47*
Finland	8.48	10.07	*19*	0.50	0.54	*8*
FRG Hamburg	7.94	8.50	*7*	0.92	1.12	*22*
Hawaii Hawaiians	6.67	8.88	*33*	2.30	3.04	*32*
U. K. S. West.	6.67	8.34	*25*	0.85	1.33	*56*
USA Connecticut	5.61	6.94	*24*	0.79	1.45	*84*
Hawaii Caucasians	5.42	6.67	*23*	0.92	2.30	*150*
Canada Manitoba	5.16	5.63	*9*	0.74	0.95	*28*
USA N. York State	4.94	7.03	*42*	0.55	1.32	*140*
Yugoslavia Slovenia	3.95	6.10	*54*	0.53	0.61	*15*
Canada Alberta	2.98	4.74	*59*	0.58	0.79	*36*
Canada Saskatchewan	2.82	4.62	*64*	0.33	0.83	*152*
Hawaii Japanese	2.55	3.19	*25*	0.60	0.89	*48*
Canada Newfoundland	2.40	4.41	*84*	0.47	0.35	*26*
Sweden	2.14	2.85	*33*	0.49	0.60	*22*
Colombia Cali	2.07	2.09	*1*	0.51	0.60	*18*
Japan Miyagi	2.01	2.46	*22*	0.66	0.95	*44*
Jamaica K. & St. A.	1.87	2.81	*50*	0.32	0.64	*100*
Norway	1.78	2.98	*67*	0.35	0.55	*57*
Iceland	1.43	2.01	*41*	0.49	1.26	*157*
Singapore Chinese	1.37*	7.62	*456*	0.32*	2.28	*613*
Median Change	–	–	*25*	–	–	*48*

*Rates derived from 1950–61.

from Britain to places like Canada, Australia and South Africa to end up with rates intermediate between those they might have been expected to have encountered if they had remained in Britain and those that prevailed in the host country even when account is taken of differences in smoking intensity.[6–8] The older they were when they migrated, the nearer their rates corresponded to those of Britain. This would seem to sugggest that the British were carrying with them some sort of factor related to increased risk which seems unlikely to be of genetic origin, even though some studies have suggested familial associations of lung cancer,[9] but may well have been related to background exposure to possible causative factors when young, such as virus infections of the respiratory tract or maybe air pollution.

In some countries there has been an indication, particularly in males, of a down turn in mortality from lung cancer at certain ages.[10, 11] This has been

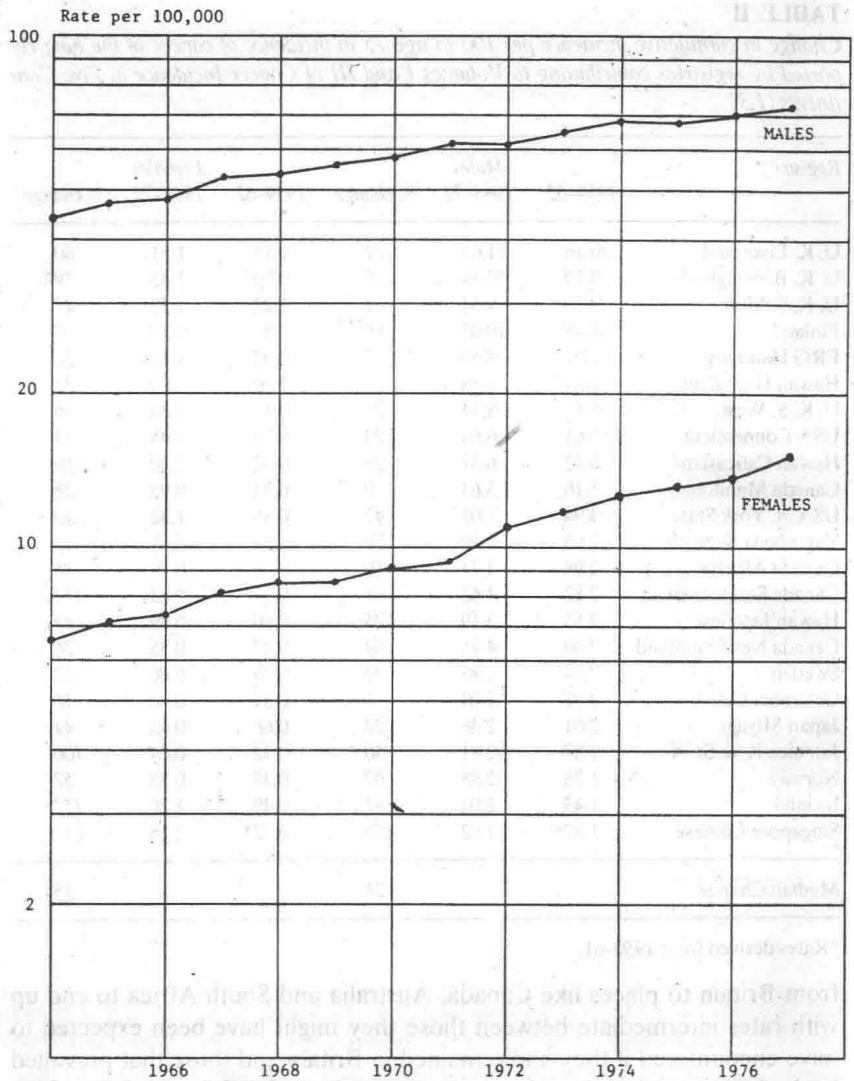

Fig. 3. Incidence of Lung Cancer in Canada Age Standardised rates ("European" population).

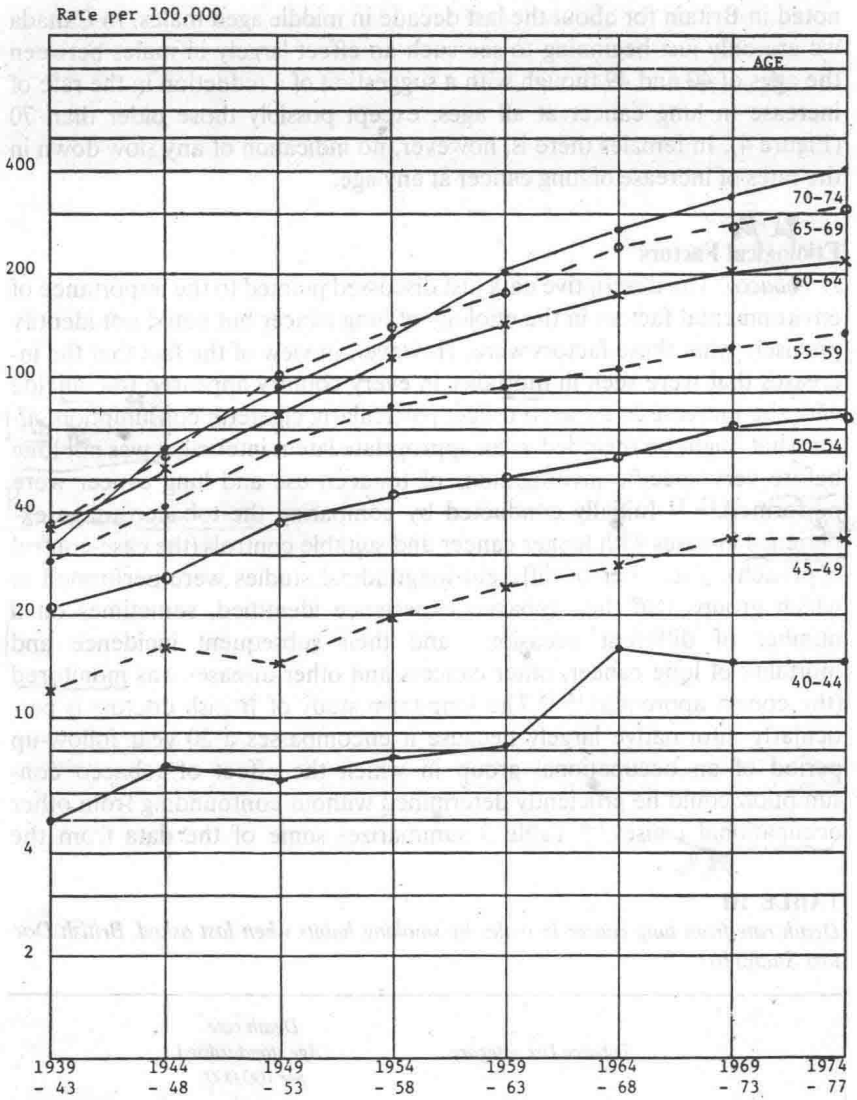

Fig. 4. Age specific rates for lung cancer mortality in males, Canada, 1939–77.

noted in Britain for about the last decade in middle aged males. In Canada we are only just beginning to see such an effect largely in males between the ages of 40 and 49 though with a suggestion of a reduction in the rate of increase in lung cancer at all ages, except possibly those older than 70 (Figure 4). In females there is, however, no indication of any slow down in the rates of increase of lung cancer at any age.

Etiological Factors

1. Tobacco: The descriptive data just discussed pointed to the importance of environmental factors in the etiology of lung cancer but could not identify precisely what these factors were. However, in view of the fact that the increases that were seen in mortality in every country appeared to coincide with the increase in tobacco usage, particularly cigarette consumption, after what might be regarded as an appropriate latent interval, it was not long before very specific investigations of tobacco use and lung cancer were performed.[12, 13] Initially conducted by comparing the tobacco usage experience in cases with lunger cancer and suitable controls (the case-control approach), a number of different longitudinal studies were performed in which groups had their tobacco experience identified, sometimes on a number of different occasions, and their subsequent incidence and mortality of lung cancer, other cancers and other diseases was monitored (the cohort approach).[14, 15] The long-term study of British doctors is particularly informative largely because it encompasses a 20 year follow-up period of an occupational group in which the effect of tobacco consumption could be efficiently determined without confounding from other occupational causes.[1-6] Table 3 summarizes some of the data from the

TABLE III

Death rate from lung cancer in males by smoking habits when last asked, British Doctors Study (16).

Tobacco Use category	*Death rate (Age standardised per 100,000)*
Non-smokers	10
Ex-smokers	43
Continuing smokers:	
Any tobacco	104
Pipe and/or cigar only	58
Mixed	82
Cigarette smokers only	140
Number smoked per day:	
1–14	78
15–24	127
25 or more	251