Death Rates from Cancer of the Respiratory and Oral Tracts in Different Countries, in Relation to the Types of Tobacco Smoked

L. A. ELSON*† and T. E. BETTS

Brompton Hospital, Fulham Road, London SW3, United Kingdom

Abstract—The differences in death rates from respiratory and oral tract cancers among smokers in different countries cannot be attributed entirely to variation in the number of cigarettes smoked, degree of inhalation, or tar and nicotine content of the smoke. The different types of tobacco must also be taken into account. Flue-cured tobacco cigarettes appear to be the most dangerous with regard to respiratory tract cancers. The smoking of air-cured or blended tobacco cigarettes is associated with a lower lung cancer death rate, but a relatively higher death rate from oral tract cancers. The smoking of cigars made from air-cured, fermented tobacco appears to constitute much less of a carcinogenic hazard for both oral and respiratory tract cancers, than does cigarette smoking.

INTRODUCTION

Although the relation between cigarette smoking and lung cancer has now been generally established, the wide differences in death rates from this cause in smokers from different countries has yet to be satisfactorily explained.

An approach to this aspect for the European countries of Scotland, England and Wales, Finland, The Netherlands, Denmark, West Germany, Italy, Switzerland and France, together with the white and non-white populations of the U.S.A., is now presented. The choice of these countries was determined by a number of factors among which were that reliable figures for cancer mortality were available from the publications of Segi [1] and the figures for cigarette consumption were presented in Tobacco Research Council papers [2].

We have covered the period 1930–1965, during which time cigarette consumption steadily increased, but the types of tobacco smoked remained fairly constant. Since that time there has been an increasing trend towards filter tipped cigarettes of various lengths and tobacco content, together with the introduc-

tion of numerous brands of low tar cigarettes, which would make the extension of these studies to the present day, complicated and less reliable.

MATERIALS AND METHODS

During the years 1967–1971 over 160 estimations of sugar content and smoke pH and 'buffering capacity', were made on popular cigarette brands smoked in the ten countries. The methods have been described in full by Elson, Betts and Passey [3], where the results were used to establish the relation between a tobacco's sugar content and the pH of its smoke [4].

RESULTS

Table 1 shows the annual cigarette consumption during the years 1930–1965 and the lung cancer death rates for men aged 60–64 for the year 1964–65. It also shows the range of sugar contents of the cigarettes and the smoke pH and 'buffering capacity'. Since separate figures for Scotland and England and Wales are not available, the cigarette consumption per adult is that for the United Kingdom as a whole; a similar position holds for the two populations of the U.S.A.

There appears to be no obvious relation between the number of cigarettes smoked and the lung cancer death rates in the different

Accepted 14 July 1980.

^{*}Emeritus Professor of Biochemistry of Drug Action, University of London.

[†]Present address; 20, Ruden Way, Epsom Downs, Surrey.

$\boldsymbol{\tau}$	- L	1. 1
- /	nn	e

Country		Annual cigarette consumption per adult		Lung cancer death rate*	Range of		
		Year 1965	Average over 35-yr period	males aged 60–64 for year 1964–65	sugar content of cigarettes (%)	Range of smoke pH (20 mm butt)	Range of smoke buffering capacity
Scotland				437			
	1380	2760	2139		15-20	4.3 - 4.6	1.7 - 0.9
England and Wales				371			
Finland	1570	1680	1580	322	10-13	4.5 - 4.7	1.1-0.8
Netherlands	680	1620	1150	286	8-15	4.3 - 4.8	1.7-0.7
W. Germany	680	2100	942	238	8–11	4.5 - 5.1	1.0-0.6
Denmark .	510	1510	900	214	8-16	4.5 - 4.7	1.1-0.8
Switzerland	540	2570	1370	200	1-11	4.5 - 6.4	0.9 - 0.1
U.S.A. (white)	1370 3770		0700	193	8-12	4.8-5.0	0.7.0.5
U.S.A. (non-white)	1370	3//0	2700	175	0-12	4.0-3.0	0.7–0.5
Italy	450	1480	852	175	3-10	4.7 - 6.4	0.7 - 0.1
France	570	1410	901	142	1 - 3	5.8 - 7.7	0.3 to -0.3 to -0.3

^{*}Per 100,00 population.

countries. Great Britain has the highest lung cancer death rate, and although the cigarette consumption is high it is considerably exceeded by that of the U.S.A., which has only half the lung cancer death rate. Again, France has a much lower lung cancer death rate than Denmark, although both countries have a similar cigarette consumption.

The best correlation with lung cancer death rates would appear to be with the sugar content of the tobacco and its related smoke pH and 'buffering capacity'. In general the lower the acid buffering capacity the lower the lung cancer death rate.

In considering oral tract cancers in relation to repiratory tract cancers, age adjusted death rates must be used. There is little doubt that smoking is an important factor in the induction of most cancers of the upper digestive tract, the respiratory tract and to a lesser extent the bladder. Cancer mortality in cigarette smokers relative to that of non-smokers of the same ages has been given as 12.1 for lung, 12.5 for pharynx, 4.1 for oral cavity, 6.2 for oesophagus and 10.0 for larynx. The ratio for bladder at 2.2 is less striking and that for stomach, 1.6, is not regarded as significant [5].

Table 2 gives the ratio of death rates from cancers of these sites to death rates from cancer of the lung, bronchus and trachea. Whereas there is a high ratio of lung to oral tract cancers in all six countries in the top half of the table, there is an abrupt fall in the

ratio of the remaining countries. This change is however scarcely obvious for bladder cancer and does not occur at all for cancer of the stomach. The demarcation between the two groups of countries is greatest in cancers of the buccal cavity and pharynx. It is less consistent in cancers of the oesophagus where factors other than smoking, such as alcohol consumption, also play a causative role [6].

Table 3 shows the ratios of deaths from respiratory tract cancers to the deaths from oral tract cancers in relation to the proportion of tobacco consumed as cigars or cigarettes.

Since cigar smokers generally have a lower lung cancer death rate than cigarette smokers [7, 8], and cigar smoke has an alkaline pH and 'buffering capacity', it might be supposed that those countries with a high proportion of cigar smokers would have a lower lung:oral tract cancer death ratio.

During the period 1950–1965 in The Netherlands, half the tobacco consumption was in the form of cigars, but in spite of its high proportion of cigar smokers the ratio of respiratory to oral tract cancers is the highest recorded in the table. The other cigar smoking countries in the top half of the table, i.e., Denmark and West Germany, also have high lung:oral tract cancer ratios. However, Switzerland and the U.S.A., where cigars also form a considerable proportion of the tobacco smoked, have low ratios. It would seem then that cigar smoking is a considerably less im-

Country	Ratio to lung, bronchus and trachea					
	Lung, bronchus and trachea*	Buccal cavity and pharynx	Larynx	Oesoph- agus	Bladder	Stomach
Scotland	75.55	21.0	38.1	13.9	11.0	3.0
England and Wales	67.72	21.5	36.8	15.6	9.2	2.9
Finland	60.72	22.0	16.4	11.0	14.4	1.5
Netherlands	51.12	28.0	32.4	16.9	8.2	1.8
West Germany	40.38	29.0	20.3	10.8		1.1
Denmark	35.84	19.0	29.4	13.0	4.9	1.6
Switzerland	33.39	4.8	10.5	3.5	6.9	1.3
U.S.A. (white)	36.86	8.3	18.0	11.2	7.4	3.9
U.S.A. (non-white)	37.72	6.7	14.7	4.1	9.2	2.1
Italy	27.57	5.1	5.1	6.4	5.2	0.8
France	25.55	2.8	2.5	1.9	5.2	1.1

Table 2. Age-adjusted death rates (males) from 1964-1965, after Segi.

portant factor than cigarette smoking in the development of oral tract and respiratory tract cancers.

DISCUSSION

Although it is generally accepted that the heavy smoker (40 + cigs/day) is at a higher risk than the moderate smoker (10–20 cigs/day), [5], a direct relation between the number of cigarettes smoked and deaths from respiratory and oral tract cancers cannot be the only explanation for the differences in death rates which occur in different countries.

Briefly, smoking tobacco falls into three main types; flue-cured, air-cured and cigar tobacco. These tobaccos vary in their chemical composition due to differences in their culturing, harvesting and curing. The reader is referred to Wynder and Hoffman [9] who fully explain the differences in tobacco types.

Some information on the preferential types of cigarettes smoked in different countries is obtainable from the publications of UCTAD-GATT [10]. In all countries represented in the top half of the tables, flue-cured tobacco has predominated in the composition of the most popular brands. In Great Britain, since at least 1930, the great majority of cigarettes have been made entirely of flue-cured (Virginia) tobacco. These have a high sugar content (15–20%) and evolve a smoke of high acid 'buffering capacity'. In West Germany, Denmark and The Netherlands, the cigarettes consist of blends of air-cured, flue-cured and oriental tobacco. Sugar contents range from

8 to 16% and the smoke is of a medium to high acid 'buffering capacity'.

Countries, like France, in the lower half of the table have consistently smoked air-cured tobacco. In the U.S.A. the commonest cigarettes are blends of air-cured and flue-cured tobaccos with the addition of some oriental tobaccos. Before 1939, the Swiss were essentially consumers of cigars and cheroots, but post war developments have strongly favoured the adoption of American type cigarettes. In all these countries the cigarettes contain a high proportion of air-cured tobaccos, the sugar contents ranging from 1–12%, the smokes having a low acid or low alkaline 'buffering capacity'.

With regard to tar and nicotine yields, it is probable that over the period 1930–1965 there was very little variation between the cigarettes smoked in the different countries. Certainly no marked national trends are discernable. Cigars and cigarillos, smoked mainly in The Netherlands, Denmark, U.S.A. and Switzerland, all have very high tar and nicotine yields. There appears to be no direct relation, internationally, between lung cancer mortality and tar and nicotine yields of cigarettes or cigars.

How then can we best account for the differences in death rates from cancer of the respiratory and oral tracts in the different countries? Obviously the number of cigarettes smoked must play a part; however, taking into account the total amount of tobacco smoked as cigarettes (Table 3) this still does not account for the national differences in cancer

^{*}Deaths per 100,000 population.

Table 3

	Age-adjusted cancer death rates (males) for 1964–1965			Average annual tobacco consumption per head of adult population 1930–1965		
Country	Respiratory tract* (A) ⁺	Oral tract (B)†	Ratio A/B	Cigarettes (lbs)	Cigars (lbs)	
Scotland	75.5	11.02	6.85	4.7	0.05	
England and Wales	67.72	9.32	7.26	4.7	0.05	
Finland	60.72	11.89	5.10	3 .5	0.04	
Netherlands	51.12	6.46	7.48	2.6	2.6	
W. Germany	40.38	7.48	5.39	2.1	1.5	
Denmark	35.84	5.88	6.09	2.0	2.0	
Switzerland	33.39	19.68	1.69	3.0	1.6	
U.S.A. (white)	36.86	9.75	3.78	5.0	1.2	
U.S.A. (non-white)	37.72	17.40	2.16	5.9		
Italy	27.57	15.05	1.83	1.9	0.2	
France	25.55	32.63	0.79	2.0	0.1	

^{*}Lung, bronchus and trachea.

death rates. The U.S.A. for instance smokes nearly three times the cigarette tobacco per head as France, but has only $l\frac{1}{2}$ times the male lung cancer death rate, whereas Great Britain, smoking 20% less tobacco than the U.S.A. has twice the male lung cancer death rate.

In addition to the quantitative aspects of tobacco consumption, and tar and nicotine inhalation it would seem that smoke pH or preferably 'buffering capacity' should also be considered. Until now it has been largely disregarded in the assessment of smoking risks. For example the addition of a filter tip to a cigarette in many cases decreases the 'buffering capacity' of the smoke [3] so that any effects of filter tips in the reduction of lung cancer risks may be due as much to this as to a reduction in tar and nicotine delivery.

From the ratios of respiratory to oral tract cancers (Table 3) in Denmark and The Netherlands, where cigar smoking accounts for a significant proportion of tobacco consumption, it appears that cigar smoke plays a very minor role relative to cigarette smoke in the incidence of all these cancers. Cigar smoke could thus be considered to present a less carcinogenic hazard than cigarette smoke. This concept is in accordance with laboratory investigations which have shown more severe pathological effects in rats exposed to the smoke of flue and air-cured tobaccos than the relatively mild effects of exposure to the

smoke of fully fermented cigar tobacco cigarettes [11–14].

It would appear that there may be some toxic factor present in the smoke of flue-cured and unfermented air-cured tobacco which is less evident in the smoke of cigar tobacco. Presumably such a factor, or more likely a precursor which would give rise to it in the combustion-pyrolysis process of smoking, is at least partially removed or modified in the fermentation process undergone by cigar tobacco. Such a factor is not likely to be distinguished from skin cancer producing hydrocarbons in the tobacco 'tar' by the normal mouse skin painting tests for carcinogenicity. Davies and Day found no significant difference in mouse skin carcinogenicity between smoke condensates of flue-cured and cigar tobaccos [15].

Research is needed, both on the chemical and epidemiological aspects of this hypothesis; however, one may perhaps speculate on the possible nature of such a toxic factor. For instance the content of organic acids decreases considerably during the fermentation process [16]. One that is particularly affected is malic acid, a beta-hydroxy acid which accounts for some 9–10% of the tobacco leaf. In the flue-curing process it remains virtually unchanged in quantity [17] but suffers considerable decrease during air-curing and particularly in the subsequent fermentation of cigar tobacco

[†]Buccal cavity and pharynx, larynx and oesophagus.

[‡]Deaths per 100,000 population.

[16]. It is possible that in the high temperature conditions within the burning cone of the cigarette the beta-hydroxy acid undergoes transformation to a lactone, such as beta-

propiolactone, which is known to be highly carcinonogenic.

Acknowledgements—We wish to thank Dr. J. Clemmesen, Director of the Cancer Registry, Copenhagen, for his very valuable help and advice.

REFERENCES

- 1. M. SEGI, M. KURIHARA and T. MATSUYAMA, Cancer Mortality for Selected Sites in 24 Countries. (No. 6, 1964/5) Department of Health. Sendai, Japan (1972).
- 2. G. F. Todd, Tobacco Consumption in Various Countries. Tobacco Research Council, Research Papers (6), London (1963).
- 3. L. A. Elson, T. E. Betts and R. D. Passey, The sugar content and the pH of the smoke of cigarette, cigar and pipe tobaccos in relation to lung cancer. *Int.* J. Cancer **9**, 666 (1972).
- 4. L. A. Elson and T. E. Betts, Buffering capacity of the smoke of different tobaccos in relation to lung cancer risks. *Cancer Lett.* 1, 285 (1976).
- 5. Sir RICHARD DOLL, Cancers Related to Smoking. The Second World Conference on Smoking and Health. Health Education Council, London (1972).
- 6. Sir Richard Doll, Strategy for detection of cancer hazards to man. *Nature* (*Lond.*) **265**, 589 (1977).
- 7. E. C. Hammond and D. J. Horn, Smoking and death rates—report on 44 months of follow up of 187,783 men. J. Amer. med. Ass. 166, 1294 (1958).
- 8. H. A. Kahn, The Dorn study of smoking and mortality among U.S. veterans. *Nat. Cancer Inst. Monogr.* **19**, 1 (1966).
- 9. E. L. Wynder and D. Hoffman, *Tobacco and Tobacco Smoke*. Academic Press, London and New York (1967).
- 10. UNCTAD-GATT, The Major Markets for Unmanufactured Tobacco. International Trade Centre Publications, Geneva (1968)
- 11. R. D. Passey, M. Blackmore, D. Warbrick-Smith and R. Jones, Smoking risks of different tobaccos. *Brit. med. J.* 4, 198 (1971).
- 12. T. E. Betts and L. A. Elson, The alpha-1-acute phase protein response in rats as a possible indicator of the relative smoking risks of different tobaccos. *Nature (Lond.)* **248**, 709 (1974).
- 13. T. E. Betts and L. A. Elson, Lung cancer risks in the smoking of different tobaccos. *Brit. J. Cancer* 38, 193 (1978).
- 14. T. E. Betts, Biological Effects of the Smoke of Different Tobaccos. Institute of Biology, London (1975).
- 15. R. F. Davies and T. D. Day, A study of the comparative carcinogenicity of cigarette and cigar smoke condensate on mouse skin. *Brit. J. Cancer* 23, 363 (1969).
- 16. W. G. Frankenburg, Chemical changes in the harvested tobacco leaf. *Advanc. Enzymol.* **10**, 325 (1950).
- 17. C. W. BACON, R. WENGER and J. F. BULLOCK, Chemical changes in tobacco during flue-curing. *Ind. Eng. Chem.* 44, 292 (1952).