Institute of Hygiene,
Karolinska Institute, Stockholm

Dept. of Environmental Hygiene,
National Institute of Public Health, Stockholm

Cancer in MZ and DZ Twins

R. Cederlöf, B. Floderus, L. Friberg

Important works on the question of hereditary influence on the occurrence of cancer with application of twin series are those by v. Verschuer and Kober (cf. Spranger and v. Verschuer, 1964), Jarvik and Falek (1961) and Harvald and Hauge (1963). Their findings are by and large consistent with most earlier reports (Schull et al, 1959) and indicate that hereditary factors do not seem to influence the development of cancer as such, but possibly play a role in the localization of the tumor. In view of the fact that (except for Harvald and Hauge's investigation) the twin series studied have been comparatively small and yielded statistically unreliable numbers of cancer of specific site, it seems to be of value to extend the data by reporting findings from the Swedish Twin Registry, comprising about 11000 unselected twin pairs.

The present paper reports mortality and morbidity in cancer of different site as well as concordance rates for MZ and DZ twins. In addition, the influence of smoking habits on cancer development has been analyzed, as this environmental factor is known to be associated with certain forms of cancer, particularly lung cancer (Smoking and Health, 1964).

Cancer data have been obtained from two sources, the Swedish Cancer Registry and the Registry of Causes of Death.

The Swedish Twin Registry in the present report comprises 10 945 twin pairs, and covers, in principle, all same-sexed twins born in Sweden in 1886-1925, and still living in the country as unbroken pairs at the time of compilation (1961). A detailed report of the compilation procedures and demographic data is given by Cederlöf (1966).

Information of cancer morbidity has been obtained from the Swedish Cancer Registry, operating since 1958. The material is based on compulsory reports from all physicians attending in- and outpatient departments in hospitals, asylums and other establishments for medical treatment, be they under public or private administration. The classification used is identical with the international system recommended by the WHO (1955). The diagnoses treated in this context are covered by the numbers 44-59 of the A-classification list.

The material is complete up to and including the year 1965, which means that morbidity data for the twin series are not complete for the last three years. Despite this fact, all records available, including the period 1966-1968, have been utilized.

Mortality data originate from certificates kept by the Central Bureau of Statistics. The classification follows the code given by the WHO, referred to above. Information on cancer

Acta Genet. Med. Gemellol. (1970), 19: 69-74

mortality covers the period 1961-1968. The criterion in question is " the underlying cause of death ", which also corresponds to the definition recommended by the WHO.

In this report analyses have been made both on cancer mortality and cancer morbidity, which include the total registration of cancer mortality.

Cancer Mortality

In order to assess the representativeness of the twin series, a comparison has been made between the twins and the general population in regard to cancer mortality. Expected values were calculated on the basis of Official Statistics of Sweden, taking differences in age distribution into account.

The observed and expected numbers of death for cancer in general *in relation to the total number of deaths*, by sex and year of birth, are shown in Tab. I.

Tab. I. Number of deaths and deaths due to cancer by sex and year of birth

Sex	Year of birth	Deaths observed	Deaths due to cancer	
			Observed	Expected
♂	1886-1895	222	40	44.6
	1896-1905	212	64	51.2
	1906-1915	141	26	31.9
	1916-1925	54	10	10.5
	1886-1925	629	140	138.2
♀	1886-1895	257	55	48.5
	1896-1905	180	60	58.4
	1906-1915	101	45	44.7
	1916-1925	35	21	15.4
	1886-1925	573	181	167.0
Total		1202	321	305.2

The correspondence between observed and expected number of individuals deceased for cancer is high for both males and females.

A more detailed tabulation, elucidating the mortality due to cancer of specific sites, has been performed. Tab. II shows the actual prevalence in comparison with age-standardized expectancies.

In this comparison, it is also apparent that the twin material is highly congruent to population statistics.

Cancer Morbidity

The number of individuals deceased in cancer amounted to 321. When adding the Cancer Registry material, the number of affected individuals is 703. As men-

Tab. II. Number of deaths due to cancer of specific sites by sex

Site of cancer	♂		♀	
	Observed	Expected	Observed	Expected
Pharynx	1	2.7	2	2.1
Oesophagus	2	2.8	2	1.6
Stomach	19	21.7	21	16.4
Intestine (excepting rectum)	10	10.9	19	14.3
Rectum	3	6.5	8	5.4
Larynx	—	0.7	—	0.2
Trachea, bronchus, lung	28	23.8	10	8.4
Breast		0.2	32	31.5
Uterus		—	18	14.0
Prostate	23	14.7	—	—
Skin	5	2.2	2	1.8
Bone and connective tissue	—	1.5	1	0.8
Unspecified	34	35.4	57	57.8
Leukemia and aleukemia	5	5.8	3	5.3
Lymphosarcoma and other neoplasms of lymph and hemapoietic system	10	9.2	6	7.0
Total	140	138.1	181	166.6

tioned above, morbidity data are complete only before 1966. Hence, the morbidity ratios are not quite comparable to the rates in the general population and are not presented. As there is no reason to believe, however, that the nonavailable records from the remaining period should not be distributed at random with regard to zygosity group, concordance rates for cancer morbidity will be given in the following paragraph.

Concordance Rates

The number of concordant pairs with regard to cancer morbidity is shown in Tab. III.

Tab. III. Number of concordant pairs as to cancer morbidity

Cancer morbidity	MZ	DZ
Both twins	11	19
One twin	216	399
No twin	3429	6432
Total	3656	6850
Exp. coincid.	5.33	9.24
Obs./exp. coincid.	2.06	2.06

https://doi.org/10.1017/S1120962300025051 Published online by Cambridge University Press

The table also shows an age-adjusted expectancy of coincidence, based on the square of the prevalence rate; i.e., the probability of a pair being concordant due to chance alone. The expected coincidence was 5.33 and 9.24 for MZ and DZ twins respectively. The actually observed number of concordant pairs in relation to the expected coincidence is also given. It appears that, for both zygosity groups, the observed numbers are significantly higher than the expected ones. There is, however, no appreciable difference between the zygosity groups.

As to site, the material is indeed limited. There are three concordant pairs in each zygosity group — one pair in each group being concordant as to cancer of the stomach, the remaining two pairs in the MZ group having the uterus affected, and two pairs in the DZ group having one the uterus and the other the prostate affected.

Occurrence of Cancer Among Smokers and Nonsmokers

The influence of smoking habits on the development of diseases, especially coronary heart diseases and respiratory symptoms, has been a main subject in utilizing the Swedish Twin Registry (Cederlöf et al, 1966). In the present report the association between tobacco consumption and cancer, as it appears in this material, will be reported.

The question has been approached in two ways. One approach utilizes the total twin material, being treated as an ordinary survey sample, divided into smokers and nonsmokers. In the other approach, smoking-discordant pairs have been selected. Data concerning tobacco consumption were collected mainly in 1961 by mailed questionnaires. The type of consumption as well as the quantity were registered. In this context, " nonsmokers " implies subjects who have never smoked, or have at least not smoked in their lifetime more than 5-10 packs of cigarettes, or 50-75 cigars, or 3-5 packs of pipe tobacco.

An analysis of different sites of relevance would have been valuable. As the material is too limited, detailed classifications have been omitted, with an exception for lung cancer.

Based on the first approach, association between smoking and cancer morbidity, lung cancer being separated, is shown by sex and year of birth in Tab. IV.

An increase in occurrence of cancer-all sites does appear among the smoking males in the older age group, but cannot be shown in any other group. For the older males the difference is statistically significant ($P < 0.01$).

With regard to lung cancer, increased frequencies among smokers are consistent in both male subgroups. The numbers in the female groups are too small to warrant conclusions. Lung cancer prevalence is high among the smoking males, which may have contributed to the significant difference between smokers and nonsmokers in gross cancer morbidity. The significance test for this group (lung cancer excluded) still remains significant, however, but on a lower level ($P < 0.05$). The figures for

Tab. IV. Cancer morbidity as to smoking group by sex and year of birth

		♂				♀			
		1886-1905		1906-1925		1886-1905		1906-1925	
		NSM	SM	NSM	SM	NSM	SM	NSM	SM
Total		1000	1713	2230	4663	3472	283	6258	2061
Cancer-all sites	N.	43	131	30	54	186	14	174	66
	%	4.3	7.6	1.3	1.1	5.3	4.9	2.8	3.2
Lung cancer	N.	0	25	1	7	5	1	3	1
	%	—	1.4	0.04	0.15	0.14	0.35	0.05	0.05
Cancer-remaining sites	N.	43	106	29	47	181	13	171	65
	%	4.3	6.2	1.3	1.0	5.2	4.6	2.7	3.1

lung cancer are generally too small to warrant statistical testing, but in the older male group where the difference is highly significant ($P < 0.001$).

When only smoking-discordant pairs are utilized for the analysis, the numbers become very small (Tab. V). No increased morbidity in cancer-all sites can be shown among the smokers in the pairs, neither among MZ nor among DZ. The lung cancer cases are only 3 in the total material of 1816 pairs, all occurring among smokers.

Tab. V. Cancer morbidity as to smoking-discordant MZ and DZ pairs by sex and year of birth

		♂				♀			
		1886-1905		1906-1925		1886-1905		1906-1925	
		NSM	SM	NSM	SM	NSM	SM	NSM	SM
MZ	Total	62		138		35		251	
	Cancer-all sites	3	5	1	1	4	2	4	7
	Lung cancer	0	0	0	0	0	0	0	0
DZ	Total	133		455		122		620	
	Cancer-all sites	7	6	9	4	8	2	26	20
	Lung cancer	0	1	0	1	0	0	0	1

Conclusion

The findings of the present report support the results of earlier investigations. According to the classical twin method, no hereditary influence could be shown as to development of cancer as such. With regard to specific sites, the material is too limited to give a result of statistical significance. The tendency is, however, the same

https://doi.org/10.1017/S1120962300025051 Published online by Cambridge University Press

as in earlier findings; i.e., the genetic influence seems to be of importance with regard to the localization of the tumour. A follow-up would permit an extended analysis on this question, and should be a most valuable future project.

The comparison between expected and observed coincidence of cancer showed that the actual within-pair coincidence highly exceeds the random expectancy. This family influence seems to be in agreement with the findings of several studies applying the proband method.

As to cancer occurrence in connection with smoking habits, the number of affected individuals was not higher among smokers with regard to cancer as such, except in one subgroup, i.e., among males 63-82 years of age. This difference was not consistent when smoking-discordant twins were analyzed.

The difference between smokers and nonsmokers becomes more apparent when separating lung cancer. In spite of small numbers, the association between smoking and lung cancer is evident.

References

Cederlöf R. (1966). The Twin Method in Epidemiological Studies on Chronic Disease. Doctoral Dissertation, Stockholm.

— et al (1966). Respiratory symptoms and « angina pectoris » among monozygotic and dizygotic twins with reference to smoking habits. Arch. Environ. Health (Chicago), **13:** 726-737.

Harvald B., Hauge M. (1963). Heredity of cancer elucidated by a study of unselected twins. J.A.M.A., **186:** 749-753.

Jarvik L. F., Falek A. (1961). Cancer rates in aging twins. Amer. J. Hum. Genet., **13:** 413-422.

Schull W. J., Morton N. E., Macklin M. T., Oliver C. P. (1959). Genetics and Cancer. The University of Texas M. D. Anderson Hospital and Tumor Institute, Austin.

Smoking and Health (1964). Report of the Advisory Committee to the Surgeon General of the Public Health Service. Public Health Service Publication.

Spranger J., Verschuer O. v. (1964). Studies on the problem of the hereditary nature of cancer. Follow-up studies on the unselected twin series of v. Verschuer and Kober. Z. Menschl. Vererb. u. Konstitutionsl., **37:** 549-571.

Sveriges officiella statistik (1961-1967). Statistiska Centralbyrån, Stockholm.

World Health organization (1955). Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death.

R. Cederlöf, Ph. D., Institute of Hygiene, Karolinska Institutet, Stockholm 60, Sweden.