

Mortality in Smoking Discordant Monozygotic and Dizygotic Twins

A Study on the Swedish Twin Registry

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Among 706 male, dizygotic, smoking discordant twin pairs born in 1901 to 1925, 13 deaths occurred among nonsmokers or less exposed partners against 34 among smokers or more exposed. In 246 corresponding monozygotic pairs the figures were 14 against 9. The excess mortality among male dizygotic smokers was not associated with any specific cause of death. Four cases of lung cancer among males occurred only in smokers. Accidents and suicides seemed to be associated with smoking, supporting the hypotheses regarding differences in personality type between smokers and nonsmokers. Only time will show whether trends found are stable. The data suggest, however, that part of the greater mortality in smokers is not due to smoking per se but to factors associated with smoking.

THE SWEDISH Twin Registry was set up in the years 1959 to 1961. It contains 10,000 twin pairs of the same sex born within the country between 1885 and 1925 and with both members living when the registry was formed. The main reason for establishing the registry was to study mortality in groups of twins with differing smoking experience. Even if a positive association exists between smoking and early death from several diseases,^{1,2} the excess mortality among smokers might not necessarily be caused by

smoking alone. Smokers and nonsmokers are not comparable in all respects, partly because of possible differences in genetic characteristics relevant to the occurrence of disease, and partly because of many other environmental exposure factors which may be correlated both with smoking and with the diseases.

The advantage of using twins has been discussed at a meeting arranged by the World Health Organization in Geneva in 1965,³ by Cederlöf in 1966,⁴ and at a meeting in San Juan, Puerto Rico in 1969.⁵ Since the establishment of the registry several studies on smoking and health have been carried out both on the Swedish registry and collaboratively with the US Twin Registry of the National Research Council.^{4,6-14} The Swedish contributions include questionnaire studies on the entire roster as well as clinical studies on subsamples. A questionnaire study was conducted using the US twins.

The present report presents data on mortality, including cause of death, in smoking discordant monozygotic and dizygotic twin pairs in the Swedish registry born in 1901 to 1925. Mortality data without cause of death are given for twin pairs born in 1886 to 1900. The report includes mortality from the forming of the registry until the fall of 1968.

Methods

General information about the twin registry is given in an earlier publication.⁴ Smoking habits were determined from questionnaire replies obtained in 1961. The subjects were asked whether they were smokers or nonsmokers,

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about the type of smoking, and whether their cigarette consumption was 1 to 10, 10 to 20, or more than 20 cigarettes.⁴

The mortality among the twins was established in the following way. Lists enumerating all twins registered were sent to the county boards which are obliged to keep records of the residents in their respective counties. This procedure gives time and place of death. The cause of death was obtained in the following way. The information from the county offices was matched against the Central Registry of Death Certificates at the Central Bureau of Statistics. In this way the name of the physician that signed the death certificate was obtained. If the deceased twin had been treated at a hospital the name of the hospital could be determined. Hospital records, information from general practitioners, and other pertinent information was then examined. The final evaluation was made without any knowledge of smoking status. When medical information was not available, the cause of death was obtained from death certificates.

For 95 deaths hospital records or autopsies or both were available, and for five deaths information was obtained from local physicians. In 14 cases only death certificates were used and in two cases there was no information. These two latter cases have been included under "other causes."

The evaluation of hypotheses about the effects of smoking has been carried out by comparing death data for cigarette smokers and nonsmokers in dizygotic and monozygotic pairs, respectively. Cigarette smokers include cigarette smokers who also smoke cigars or pipes or both.

The exposure to tobacco in these groups is presented in Table 1 for pairs born in 1901 to 1926. There is practically no difference between dizygotic and monozygotic pairs.

In order to increase the number at risk in the comparison using smoking discordant pairs, a "less exposed" group has been added to the nonsmokers and a "more exposed" group to the smokers. These two added groups have been operationally defined.

Less Exposed	More Exposed
1. Cigarettes only, <10/day (men: 144 DZ pairs, 69 MZ; women: 95 DZ, 49 MZ)	Cigarettes only, 10 to 20 per day; cigarettes, 10 to 20 per day and cigars or pipe or both
2. Cigarettes only, <10/day (men: 16 DZ, 6 MZ;	Cigarettes only, >20/day; cigarettes, >20/day and

women: 1 DZ, 0 MZ)	cigars or pipe or both
3. Cigarettes only, 10 to 20 per day (men: 25 DZ pairs, 10 MZ pairs; women: 1 DZ pair, 5 MZ pairs)	Cigarettes only, >20/day; cigarettes, >20/day and cigars or pipe or both

In all comparisons when not otherwise specified, smokers include former smokers.

The age distribution for dizygotic and monozygotic twin pairs born in 1901 to 1925 is shown in Table 2. For the men only minor differences between dizygotic and monozygotic pairs exist. A somewhat higher proportion of the dizygotic than of the monozygotic women was classified into the oldest age group in the less exposed-more exposed comparison but not in the smoker-nonsmoker comparison.

Results

Table 3 and 4 show the number of deaths among smoking discordant dizygotic and monozygotic pairs born in 1901 to 1925 for men and women, respectively. It is apparent in the male dizygotic pairs that the smokers have a higher mortality than the nonsmokers. This excess mortality is statistically significant using the χ^2 statistic ($P < 0.01$). The mortality of monozygotic smokers is not greater than that of the monozygotic nonsmokers, and it can be shown that, regardless of the nature of the association, the monozygotic and dizygotic samples did not come from populations with the same smoking effect ($P < 0.01$ one-sided test). For women of either zygosity, no consistent or statistically significant differences can be seen.

In the analysis carried out above, former smokers were included among the smokers. Table 5 shows data for nonsmokers compared to former cigarette smokers. The association with smoking among dizygotic males born in 1901 to 1925 is statistically significant using the χ^2 statistic ($P < 0.02$).

Table 6 shows mortality of the older age groups (born in 1886 to 1900) by smoking status, zygosity, and sex. No increased mortality associated with smoking is found.

Table 7 shows mortality data for pairs where one member is a nonsmoker and the partner smokes only cigars or pipe or both. There is no excess mortality among the smokers. In fact there are fewer deaths among the

Table 1.—Percent of Twins in Smoking Discordant Pairs (Nonsmokers-Smokers) Born in 1901 to 1925*

No. of cigarettes per day	Men				Women			
	DZ		MZ		DZ		MZ	
	Nonsmokers	Smokers	Nonsmokers	Smokers	Nonsmokers	Smokers	Nonsmokers	Smokers
Nonsmokers	100	...	100	...	100	...	100	...
<10	...	68	...	67	...	82	...	84
11-20	...	29	...	30	...	17	...	15
>20	...	3	...	3	...	1
Total	521		161		684		272	

* By number of cigarettes smoked, sex, and zygosity.

Table 2.—Age Distribution (Percent) in Smoking Discordant Pairs Born in 1901 to 1925 by Sex and Zygosity

Yr of Birth	Men				Women			
	Nonsmoker-Smoker		Less Exposed-More Exposed		Nonsmoker-Smoker		Less Exposed-More Exposed	
	DZ	MZ	DZ	MZ	DZ	MZ	DZ	MZ
1901-1905	13	14	10	12	9	8	8	0
1906-1910	17	14	16	15	16	14	11	9
1911-1915	20	19	17	22	19	24	14	22
1916-1920	25	24	27	25	24	24	24	28
1921-1925	25	28	30	26	32	31	42	41
Total	521	161	185	85	684	272	97	54

Table 3.—Number at Risk (Pairs) and Number of Deaths in Smoking Discordant Male Twin Pairs Born in 1901 to 1925*

Yr of Birth	Dizygotic			Monozygotic		
	Total No.	Deaths		Total No.	Deaths	
		Nonsmokers	Smokers†		Nonsmokers	Smokers†
1911-1925	364	6	10	115	2	2
1901-1910	157	3	13	46	2	3
1901-1925	521	9	23	161	4	5
		Less Exposed	More Exposed		Less Exposed	More Exposed
1911-1925	501	9	14	177	6	3
1901-1910	205	4	20	69	8	6
1901-1925	706	13	34	246	14	9

* By zygosity and smoking status; for explanation of smoking status, see Methods section of text.

† Former smokers included.

smokers than among the nonsmokers.

Apart from the groups discussed here there are several other groups discordant in smoking habits, namely groups discordant for cigarette smoking but concordant or discordant for cigar or pipe smoking or both in different ways. These groups have not been included in the above presentation, as it seemed unclear whether or not they should be considered discordant. Table 8 shows

mortality in those groups combined. They have been defined as less exposed and more exposed, according to cigarette consumption. The numbers are too small to allow conclusions. Data by smoking habits, sex, zygosity, and cause of death are given in Table 9 for twin pairs born in 1901 to 1925, corresponding to Table 3 and 4. The numbers are small and formal statistical testing has not been carried out.

Table 4.—Number at Risk (Pairs) and Number of Deaths in Smoking Discordant Female Twin Pairs Born in 1901 to 1925*

Yr of Birth	Dizygotic			Monozygotic		
	Total No.	Deaths		Total No.	Deaths	
		Nonsmokers	Smokerst		Nonsmokers	Smokerst
1911-1925	510	6	11	213	4	2
1901-1910	174	11	6	59	0	4
1901-1925	684	17	17	272	4	6
		Less Exposed	More Exposed		Less Exposed	More Exposed
1911-1925	588	6	12	262	4	2
1901-1910	193	12	8	64	0	4
1901-1925	781	18	20	326	4	6

* By zygosity and smoking status; for explanation of smoking status, see Methods section of text.
 † Former smokers included.

Table 5.—Number at Risk (Pairs) and Number of Deaths Among Nonsmokers and Former Cigarette Smokers*

Total No.	Dizygotic		Total No.	Monozygotic	
	Deaths			Deaths	
	Nonsmokers	Former Smokers		Nonsmokers	Former Smokers
Men 146	2	10	50	2	2
Women 122	3	3	57	1	3

* In smoking discordant twin pairs born in 1901 to 1925 by zygosity and sex.

Table 6.—Number at Risk (Pairs) and Number of Deaths in Smoking Discordant Twin Pairs Born in 1886 to 1900*

Total No.	Dizygotic		Total No.	Monozygotic	
	Deaths			Deaths	
	Nonsmokers	Smokerst		Nonsmokers	Smokerst
Men 67	22	17	39	5	4
Women 58	8	9	14	1	3
	Less Exposed	More Exposed		Less Exposed	More Exposed
Men 89	30	22	50	6	5
Women 58	8	9	18	2	5

* By sex, zygosity, and smoking status; for explanation of smoking status, see Methods section of text.
 † Former smokers included.

Table 7.—Number at Risk (Pairs) and Number of Deaths in Male Twin Pairs Born in 1901 to 1925*

Total No.	Deaths	
	Nonsmokers	Cigar and/or Pipe Smokers
Dizygotic 235	12	4
Monozygotic 66	3	2

* Discordant for cigar or pipe smoking or both.

Table 8.—Number at Risk (Pairs) and Number of Deaths in Male Twin Pairs Born 1901-1925*

Total No.	Deaths	
	Less Exposed	More Exposed
Dizygotic 112	3†	1‡
Monozygotic 65	1§	1

* Discordant for cigarette smoking, but concordant or discordant for cigar or pipe smoking or both in different combinations.

† Coronary heart disease, two cases; accident, one case.
 ‡ Suicide.
 § Cancer.
 || Coronary heart disease.

Table 9.—Cause of Death in Smoking Discordant Pairs Born in 1925 by Sex and Zygosity*

Cause of Death	Men				Women			
	Dizygotic		Monozygotic		Dizygotic		Monozygotic	
	Non-smokers Less Exposed	Smokers† More Exposed	Non-smokers Less Exposed	Smokers† More Exposed	Non-smokers Less Exposed	Smokers† More Exposed	Non-smokers Less Exposed	Smokers† More Exposed
Coronary heart disease	5	8	5	6	3	2	0	0
Cerebrovascular disease	0	3	1	1	1	3	0	1
Cancer of the lung	0	4	1	0	0	1	0	0
Cancer, other forms	3	8	0	1	8	7	3	3
Suicides	0	2	0	0	0	2	0	0
Accidents	1	4	2	1	0	2	0	1
Other causes	4	5	5	0	6	3	1	1
All causes	13	34	14	9	18	20	4	6

* For explanation of smoking status, see Methods section of text.

† Former smokers included.

The excess mortality of smokers in the male dizygotic group is due to several causes and it is not possible to associate it particularly with any specific disease. Of the total number of 21 excess deaths associated with smoking, three were caused by coronary heart disease. Four cases were due to cerebrovascular diseases, one due to lung cancer, five due to other forms of cancer, five due to suicides or accidents, and one due to other causes.

One case of lung cancer occurred in a male monozygotic twin belonging to the less exposed group. Four suicides or accidents occurred among female dizygotic smokers compared to none in nonsmokers.

Comment

The number of deceased twins in smoking discordant pairs is small. Only time will show whether the trends found in this study are stable. However, even now the data suggest that the differences found have a significant biological meaning. There is no indication in the present data that the different relationships seen in the dizygotic groups compared to the monozygotic groups were caused by differences in smoking habits or age distribution. For both variables very similar distributions were found for the two zygosity groups. It seems more reason-

able that the different results in the two groups of twins are the consequence of differences between smokers and nonsmokers in genetic and other factors associated with the twins' behavior and exposure to physical, chemical, and social environments. That such differences exist has been shown.¹²

In most of the analyses former smokers have been included among smokers. The separate analysis carried out on former smokers shows that this approach is justified at least for men born in 1901 to 1925.

The results for the women are inconclusive and to some extent contradictory. It is obvious that it will be necessary to obtain information from future follow-ups.

In this analysis it has not been possible to associate the excess mortality among male, dizygotic smokers with any specific cause of death. Several causes contributed to this excess mortality, but the numbers are still too small to allow conclusions. There are certain findings, though, which are intriguing and worth pointing out. The four cases of lung cancer among dizygotic men occurred only in smokers. Accidents and suicides taken as one group seemed to be associated with smoking in the dizygotic twins, particularly if the data for both men and women were combined. This finding is of interest since, considering the nature of these deaths, it supports the hypothesis that

smoking may be a symptom of a certain personality type.

Summing up all the evidence, the data suggest that part of the greater mortality in smokers is not due to smoking per se but to factors associated with smoking.

It will be valuable to follow the groups

under study and also to get new data on smoking and on socioeconomic and other environmental factors.

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MODERN LOSS OF VALUES

To become ill these days or otherwise to straggle in life's parade is perhaps a mite safer than for a baboon to fall behind the troop in the wilds of Africa. The metaphysics of natural inequality, be it physical or mental, serves the absolutist well. Our brash, noisy world is doing strange things to people as man takes something of a beating from man. The medical student and physician would not be expected to escape the modern alienation.

It would be remarkable if attitudes were not as debased as the environs, where the rapid pollution and deterioration of the biosphere, and the substitution of the "experience" for the artistic are orders of the day. Is it to be wondered that manners, dignity, service, morals, and ethics and initiative are at something of a discount? The times are conducive to ersatz, to vulgarity, and to the devaluation of honesty and mercy, of dignity, love, respect, and fair play.—Aring CD: The Physician's Constitution. *The Pharos of Alpha Omega Alpha* 32:3-5, 17, 1969.

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