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Hammond and Horn[1] presented evidence that the death rate due to diseases of the coronary arteries is significantly and appreciably higher in 50-to-69-year-old males who were regular cigarette smokers than in men who never smoked. It is a problem of major interest therefore to determine what mechanisms may underlie the excessive coronary heat disease mortality in cigarette smokers.

Elsewhere[2,3,4] we have presented evidence that the ultracentrifugally measured $S_f^o 0-12$, $S_f^o 12-20$, $S_f^o 20-100$, and $S_f^o 100-400$ serum lipoproteins are quantitatively related to the mortality rates due to coronary heart disease. Such features as the age trend in coronary disease mortality, the male-female difference, and the role of obesity are all quantitatively explainable on the basis of coronary heart disease considered as an accumulative process with a rate proportional to a value a $\left[a \text{ being defined} = 0.1 (S_f^o 0-12) + 0.16 (S_f^o 12-400) \right]$. The a value represents the discriminant function in segregating coronary-disease from noncoronary-disease populations.

To determine whether or not the association of cigarette smoking with coronary heart disease might operate via the lipoprotein mechanism, analyses have been made in a consecutive series of several hundred employed clinically healthy adult males. A questionnaire was filled out at the time of physical examination to indicate smoking habits in a quantitative manner. The analysis below is based upon two groups: (a) those who claim never to have smoked cigarettes, cigars, or pipes and (b) those who are currently smoking 10 or more cigarettes daily. At the present time these groups are the only ones where sufficient numbers of subjects are available to warrant serious statistical analysis of the findings. The data in the other smaller groups are presented in tabular form even though the series are small, including those who smoke cigars and pipes but who do not smoke cigarettes and those who smoke fewer than 10 cigarettes per day. The findings are presented in Table I.

Table I

Serum lipoprotein levels and serum cholesterol values in
smokers and nonsmokers

20-to-29-year Males

All lipoprotein and cholesterol values are in mg/100 ml

Category	No. of Subjects	Mean Age (years)	S_f^o 0-12	S.D.	S_f^o 12-20	S.D.	S_f^o 20-100	S.D.	S_f^o 100-400	S.D.	Chol.
Never smoked	48	25.9	309.5	77.0	32.6	17.1	54.3	29.5	18.0	19.7	211.3
Smoke fewer than 10 cigarettes/day	9	25.3	365.9	69.7	37.2	15.4	66.5	28.6	21.1	26.6	
Smoke more than 10 cigarettes/day	48	26.0	354.1	81.0	42.5	23.9	73.1	42.4	31.1	34.5	220.3
Smoke pipe or cigars only	6	27.7	302.4	----	38.2	----	55.9	----	21.7	----	

30-to-39 year Males

Category	No. of Subjects	Mean Age (years)	S_f^o 0-12	S.D.	S_f^o 12-20	S.D.	S_f^o 20-100	S.D.	S_f^o 100-400	S.D.	Chol.
Never smoked	51	33.4	349.9	70.4	42.0	21.4	76.6	64.0	38.5	58.5	222.4
Smoked fewer than 10/day	9	36.0	348.0	44.3	52.1	13.5	86.9	46.9	48.0	59.5	
Smoke more than 10 cigarettes/day	77	34.3	378.6	90.2	48.5	27.8	86.9	49.4	45.9	60.5	234.0
Smoke pipe or cigars only	16	34.3	351.8	----	51.6	----	100.4	----	56.3	----	

40-to-49 year Males

Category	No. of Subjects	Mean Age (years)	S_f^o 0-12	S.D.	S_f^o 12-20	S.D.	S_f^o 20-100	S.D.	S_f^o 100-400	S.D.	Chol.
Never smoked	9	43.4	403.2	65.9	51.3	18.3	96.0	37.5	38.3	40.9	
Smoked fewer than 10/day	3	44.0	421.6	----	42.6	----	88.9	----	51.9	----	
Smoked more than 10/day	44	43.1	379.4	101.1	51.1	25.1	110.3	95.9	58.4	75.6	
Smoke pipe or cigars only	6	44.1	411.8	----	63.3	----	95.0	----	55.8	----	

Individuals smoking 10 per day are included in the "more than 10 group". All values are mean values. S.D. values represent standard deviation of the distributions.

The analysis of the data indicate that in the 20-to-29-year age group of males there is an appreciable and significant elevation of each of the four lipoprotein classes in the regular cigarette smokers (10 or more per day) over those in the group that does not use tobacco in any form. These elevations and their statistical significance are presented as follows:

Males 20 to 29 years

Regular cigarette smokers versus nonsmokers

S_f^o 0–12 lipoprotein difference   45.0 mg/100 ml Significant, p 0.005

S_f^o 12–20 lipoprotein difference   9.9 mg/100 ml Significant, p 0.02

S_f^o 20–100 lipoprotein difference 18.8 mg/100 ml Significant, p 0.01

S_f^o 100–400 lipoprotein difference 13.1 mg/100 ml Significant, p 0.02

For the 30-to 39-year age group of males the differences observed are all in the same direction as for the 20-to-29-year-old group, but statistical significance within these data can be shown only for the S_f^o 0–12 lipoprotein class. These findings are as follows:

Males 30 to 39 years

Regular cigarette smokers versus nonsmokers

S_f^o 0–12 lipoprotein difference   28.7 mg/100 ml Significant, p 0.035

S_f^o 12–20 lipoprotein difference   6.5 mg/100 ml Not Significant, p 0.13

S_f^o 20–100 lipoprotein difference 10.3 mg/100 ml Not Significant, p 0.3

S_f^o 100–400 lipoprotein difference 7.4 mg/100 ml Not Significant, p 0.5

The series of 40-to-49-year-old nonsmokers currently available is too small to make statistical analyses worth while. One trend in the findings is suggestive, however, when compared with the younger age groups. In going from the 20-to-29-year age group toward the 40-to-49-year age group the difference in S_f^o 0–12 lipoprotein level between smokers and nonsmokers shows an unmistakable trend downward. The S_f^o 12–20 appears to behave similarly. Within these data, however, it appears that the S_f^o 20-100 and 100-400 classes do not necessarily show this trend in going from the younger to the older age group. Apparently by whatever mechanism cigarette smoking operates to alter lipoproteins, such mechanism has a large effect upon S_f^o 0–12 lipoproteins in the younger male and a decreasing effect with age.

For the S_f^o20-400 lipoproteins this age trend is not present, and indeed further data might reveal a trend in the opposite direction for these lipoproteins.

Utilizing the concept of accumulated coronary disease, we may determine the excessive mortality hazard of smokers of more than 10 cigarettes per day as follows. The mean value, from the above data, is approximately 10% higher (averaging the three decades studied) in the regular cigarette smoker than in the nonsmoker. If this elevation is assumed to operate throughout the distribution of alpha values, raising them all by 10%, and if the approximation is made that smokers start smoking at 20 years of age, it becomes possible to calculate the relative coronary disease mortality rate for smokers and nonsmokers in the 50-to-59- and 60-to-69-year age decades by application of the methods of Reference (4) for comparison with the observations of Hammond and Horn. This comparison is given below.

Age Group, Males	(Smokers/nonsmokers) Relative Coronary Mortality Calculated from ACD Concept	(Smokers/nonsmokers) Relative Coronary Mortality Observed by Hammond and Horn
50 to 59 years	1.4	2.1
60 to 69 years	1.5	1.7

(Relative coronary mortality values represent mortality rates for smokers divided by those for nonsmokers)

Consideration of the limitations of both sets of data suggests that the ACD predications are in reasonable quantitative agreement with the observations of Hammond and Horn. Therefore it is highly likely that the association of cigarette smoking with elevation of the serum lipoproteins accounts for a major share, at least, of the observed relationship of cigarette smoking with coronary artery disease mortality.

References

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