

indicate damage to the muscle and myoneural junction. Such changes do not occur in primary muscle disorders, denervation atrophy, or drug toxicity.² Similar changes at the myoneural junction have, however, been reported in Becker's type of progressive muscular dystrophy.³ In the absence of other factors known to precipitate muscle damage our data indicate that isotretinoin may induce reversible damage to skeletal muscle. Since there were no symptoms or signs of damage to the myoneural junction we refrained from performing a study of "jitter" or repetitive nerve stimulation.

We cannot offer an adequate explanation for our findings, although muscle pain and stiffness are features of chronic vitamin A toxicity.⁴ A recent experiment showed that retinoic acid given in large doses to pregnant mice modified the phenotype expression of developing muscles in the fetus and increased creatine kinase activity.⁵

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Fish consumption and mortality from coronary heart disease

An inverse relation between consumption of fish and mortality from coronary heart disease has been found in some recent studies¹⁻³ but not in others.^{4,5} In a 14 year follow up of 10 966 subjects in Sweden we studied the association between fish consumption and mortality from myocardial infarction and from coronary heart disease (including myocardial infarction).

Subjects, methods, and results

Information on current dietary habits, including fish consumption, was obtained by a self administered questionnaire in 1967-8 from 15 864 (75%) of the

21 152 subjects in the population based register of twins born in Sweden from 1886 to 1925. Each subject's average fish consumption in 1967 was related to his or her total intake of food and classified as high, moderate, low, or no fish consumption. Information on previous cardiovascular symptoms, including angina and myocardial infarction, was also obtained, and all subjects who reported such symptoms were excluded from the study. A link with the records of the Swedish National Cause of Death Register provided information on the year and cause of death for those among the remaining 10 966 subjects who died during 1969-82. The number of deaths from myocardial infarction and from coronary heart disease was related to the number of person years at risk during the period of observation. Relative risks for different levels of fish consumption were calculated using people who consumed little or no fish as the reference group. Differences in age and sex distribution were accounted for.⁶ The results in the table show a dose response relation, with the lowest risk for those who had high fish consumption. Sex specific relative risks showed a similar pattern for men and women. Further adjustment was made for smoking habits, relative weight, marital state, geographical region, and degree of urbanisation (information obtained from the previously mentioned questionnaire in 1967-8), and for a history of hypertension (information obtained from a questionnaire in 1963). These adjustments, however, had little or no effect on the relative risks shown in the table.

Comment

The classification into high, moderate, low, or no fish consumption was performed in 1967-8—that is, before the observation period. There were few subjects who never consumed fish, and we therefore had to include subjects with low fish consumption in the "unexposed" group. This may have led to an underestimation of the strength of the inverse relation between fish consumption and death from myocardial infarction and coronary heart disease. Similarly, the high levels of fish consumption in some earlier studies may account for the apparent lack of effect in these studies.

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Relative risks of death from coronary heart disease and myocardial infarction in relation to fish consumption of 10 966 subjects

Fish consumption	No of person years at risk	Coronary heart disease		Myocardial infarction	
		No of deaths	Relative risk* (90% confidence intervals)	No of deaths	Relative risk* (90% confidence intervals)
High	12 315	69	0.85 (0.69 to 1.06)	28	0.70 (0.50 to 0.98)
Moderate	70 848	373	0.94 (0.83 to 1.06)	184	0.91 (0.76 to 1.08)
Low	57 084	358	1.00	183	1.00

*Adjusted for age and sex.