2 Health Benefits From Eating Fish

2.1 Introduction

In addition to providing high quality protein, essential fatty acids, and other nutrients required daily in the human diet (discussed in Chapter 3: *Nutritional Benefits of Eating Fish Compared to Other Protein Food Sources*), fish consumption is also associated with certain health endpoints over the longer term. This chapter provides a brief overview of health endpoints that have been shown, or are hypothesized, to be associated with fish consumption. In some cases the weight of evidence supports the relationship between eating fish and a lowered risk of disease (e.g., coronary heart disease or CHD). For other health endpoints, the link is more controversial (e.g., arthritis) and more research studies are needed. This report refers to the changes in health endpoints associated with fish consumption as benefits, because they generally involve a reduction in the risk of chronic disease. The chapter begins with an overview of the major studies that have examined the association between fish consumption and CHD, both those studies that have found associations and those which have not. It then continues with a brief description of studies that have looked at fish consumption in relation to several other endpoints.

The concept that eating fish may reduce the risk of CHD apparently originated from reports on the small population of non-acculturated Eskimos in arctic Greenland, where high consumption of marine animals (e.g., seal, fish) was observed (Bang *et al*., 1971, 1980). It was claimed that coronary rates were low, but available data were B and remained B limited and tenuous. The inhabitants of the Japanese island of Okinawa were also observed to have low CHD mortality rates, and they too consume high amounts of fish (Kagawa *et al*., 1982). The "Seven Countries Study" (Keys, 1980) conducted by Dr. Keys found that rates of CHD and myocardial infarctions (MI) were lower in southern Italy, Spain and Greece than rates in the United States, the Netherlands, and other countries. This raised the question of whether the Mediterranean diet, which includes fish, red wine, olive oil, nuts and legumes, was partly responsible for the findings.

These observations prompted epidemiologic investigations -- the first from the Netherlands (Kromhout *et al*., 1985) -- on the relationship of fish consumption to CHD and MI. When the results of the long-term, prospective studies became available in the mid-1980s and 1990s, they provided strong evidence that higher levels of fish consumption among middle-aged men, free of CHD at baseline examination, were associated with a lower risk of mortality from CHD. Early hypotheses on the protective biological mechanism of fish consumption focused on the very long chain, polyunsaturated fatty acids of the omega-3 class (n-3 FA), since fish are one of the few good dietary sources of these types of fatty acids. It was thought that the n-3 FA of fish contributed to more healthful ratios of blood lipids (fats, including cholesterol), and this reduced one of the major risk factors for CHD: high blood levels of cholesterol and saturated fats. Later studies focused on the factors that cause blood platelets and other materials to clump together and deposit on the inside of artery walls, and specifically, the role that n-3 FA have in the synthesis of prostaglandins, which reduce platelet aggregation.

The American Heart Association has issued a statement regarding fish consumption, fish oil, lipids, and CHD. The primary focus of this statement, however, is on the evidence of health

benefits from n-3 FAs. It concludes that it is premature to recommend general usage of fish oil supplements at this time, but that the "inclusion of marine sources of the n-3 PUFA in the diet seems reasonable because they are good sources of protein without the accompanying high saturated fat seen in fatty meat products" (American Heart Association 1996). For reasons that will be discussed further in this section, it is unlikely that n-3 FA are the primary factor responsible for the observed association between fish consumption and lowered risk of CHD.

In addition to the relationship between fish consumption and sudden death from CHD and MI, other health endpoints have been examined. Scientists have investigated possible associations between eating fish and inflammation-related diseases such as rheumatoid arthritis, since the n-3 FA in fish oils are believed to have anti-inflammatory effects (reviewed by Simopoulos, 1991). Relatively few studies have been done, however, and their findings are still controversial. Other research has suggested that eating fish may be associated with reduced incidences or severity of asthma, psoriasis, gastrointestinal diseases, as well as lung damage caused by smoking. (Of course, even if fish consumption does protect against these diseases, it may exert its protective effect through mechanisms other than the reduction of inflammation by n-3 FA.) Recently, possible associations between fish consumption and other health endpoints for pregnant women, unborn babies and young infants have been reported. For example, there is evidence that consuming substantial amounts of fish during pregnancy may lengthen gestation (Olsen, Hansen & Sorensen, 1986), thereby resulting in higher birthweights. The n-3 fatty acids that fish provide have important roles in the development of the retina, brain and other central nervous system tissues in the unborn and infant (up until 12 months of age), as well.

The following sections briefly review available results of research on the association between fish consumption and several endpoints, and the possible health benefits of eating fish for adults, pregnant women, developing fetuses and infants. The nutritional contributions of fish to the diets of children are also highlighted.

2.2 Health Benefits Associated with Fish Consumption

2.2.1 Coronary Heart Disease (CHD) and Myocardial Infarction (MI)

Table 2-1 presents a summary of the samples, designs and main findings of 13 published reports examining the association between fish consumption and CHD. Studies 1 to 9 and study 13 are prospective studies, a strong epidemiological study design in which individuals who have no observable symptoms of CHD are categorized according to their level of fish consumption, and then followed for long periods of time to observe who later develops CHD and who does not. Studies 10 and 11 are case-control designs, whereby those who already have CHD are matched on important characteristics with those who do not, and retrospective information about their diets is collected. Study 12 is a randomized, controlled, clinical trial, the only study included here that contains an intervention. A brief summary of the findings of each of these 13 reports follows the table.

Table 2-1. Studies of Fish Consumption and Coronary Heart Disease (CHD)**{**PRIVATE **}**

Study, Country, Type of Study, Reference No.	**Year of Baseline & Follow-Up Duration**	**No. of Participants, Gender, Baseline Ages, Background**	**Diet Assessment Method**	**Stratification of Fish Intake (no. or % of persons, or person-years)**	**CHD End Points, Number of Events**	**Main Findings, Fish Intake and CHD**
1- Zutphen, The Netherlands, prospective epidemiologic (Kromhout *et al*, 1985)	1960 20 years	852 men ages 40-59; urban community general population	in-depth cross-check diet history	0 g/d (159), 1-14 (283), 15-29 (215), 30-44 (116), ≥45 (79), mean: 0, 8, 22, 36, 67 g/d, about 2/3 lean fish	CHD death; 78 deaths	significant independent inverse relationship; RR values for strata: 1.00, 0.60. 0.57, 0.46, 0.42, p for trend <0.05
2- Rotterdam, The Netherlands, prospective epidemiologic (Kromhout *et al*., 1995)	1971 17 years	292 men and women (137 & 135) ages 64-85; urban general practitioner's list	in-depth cross-check diet history	non-consumers (about 40%) and consumers; for latter, mean: 24 g/d (21.6 g/d lean fish)	CHD death; 58 deaths	significant independent inverse relationship; RR = 0.51, 0.41 for men, 0.64 for women; no relation of fish intake to all causes death (RR = 0.96)
3- Swedish Twins, prospective epidemiologic (Norell *et al*., 1986)	1967-68 14 years	10,966 men and women ages 40-70; nationwide population-based twin registry	self-administered questionnaire	none (few people) + low (12,315 p-y), moderate (70,848 p-y), high (57,084 p-y)	CHD and MI death; 800 and 395 deaths	CHD: age-sex adjusted RR (95% CI) -- 1.00, 0.94 (0.83-1.06), 0.85 (0.69-1.06); MI 1.00, 0.91 (0.76-1.08), 0.70 (0.50-0.98); results similar with multivariate adjustment, and for 2 sexes separately

Table 2-1. continued

Bergen, Norway, prospective epidemiologic (Norell *et al.*, 1986)	1967 14 years	11,000 men, 65% ages 55+, 30% ages 65+; urban community general population	postal questionnaire, including 3 questions on fish intake	Fish index approximating no. of times fish eaten/month; 0-4 (642), 5-9 (2242), 10-14 (4412), 15-19 (1726), 20-24 (1497), ≥25 (482)	CHD and MI death before age 80; 967 CHD deaths, 301 in healthy subcohort, 22 in men ages <45 at entry	CHD, MI (also all causes death): no relationship; for men ages <45 at entry, inverse relationship, fish and CHD death, p = 0.058
4- Honolulu Heart Program, Hawaii, U.S.A., prospective epidemiologic (Curb *et al.*, 1985)	1965-68 12 years	7,615 Japanese-American men ages 45-68; urban community general population	questionnaire on usual frequency of eating various foods; 24-hour dietary recall	from usual frequency questionnaire: almost never (32), <2 times/wk (4143), 2-4 times/wk (2884), almost daily (545), >once/day (10); from 24-h recall: 0 g/d (4232), 28-56 (1374), 84-112 (1092), 140-168 (505), >168 (412)	CHD incidence and CHD death; nos. of events not stated	no significant relationships

Table 2-1. continued

5- Adventist Health Study, California, U.S.A., prospective epidemiologic (Fraser *et al*., 1992)	1976 6 years	26,473 non-Hispanic white Californian Seventh-Day Adventists ages 25+, 10,003 men, mean age 51, 16,470 women, mean age 53	65-item semi-quantitative food frequency questionnaire mailed to cohort	never (43%), <1/wk (47%), ≥1/wk (10%)	Definite Nonfatal MI, 134 events; Definite Fatal CHD (clinical, autopsy-based), 260 deaths; Fatal CHD (death certificate), 463 deaths	multivariate adjusted RR: 1.00, 1.11 (0.75-1.66), 1.04 (0.55-1.96); 1.00, 1.01 (0.76-1.35), 0.74 (0.42-1.33); 1.00, 1.10 (0.89-1.37), 1.09 (0.73-1.61)
6- Physician's Health Study, U.S.A., prospective epidemiologic (Morris *et al*., 1995)	1982 4 years	21,185 U.S. male physicians nationwide, ages 40-84, free of history of major disease	self-administered semi-quantitative food frequency questionnaire	<1 meal/wk (4,501), 1 (8,156), 2-4 (7,455), ≥5 (1,073)	nonfatal MI and all MI; 259 and 281 events (i.e., 22 MI deaths)	multivariate adjusted RR, nonfatal MI: 1.0, 1.4, 1.2, 0.8; all MI 1.0, 1.5, 1.3, 0.9 -- nonsignificant; p for trend 0.78, 0.72

Table 2-1. continued

7- Physician's Health Study, U.S.A., (Albert *et al*., 1998)	12 years	20,551 U.S. male physicians from above cohort	same	<1 meal/month and 1+; also, <1, 1-3, 1-<2/wk, 2-<5/wk, 5+/wk	sudden death (within 1 hour of symptom onset); 115 deaths	<1 vs. 1+ meal/month: unadjusted RR 0.44 (0.22-0.91), p 0.03; multivariate adjusted RR 0.51 (0.25-1.05), p 0.07; age-adjusted RR for 5 strata: 1.00, 0.71 (0.29-1.77), 0.44 (0.20-0.94), 0.43 (0.15-0.98), 0.39 (0.15-0.98)
8- Health Professionals Follow-Up Study, U.S.A., prospective epidemiology (Ascherio *et al*., 1995)	1986 6 years	44,895 male health professionals nationwide, ages 40-75, free of known CVD	self-administered semi-quantitative food frequency questionnaire	servings of fish <1/month, 0 g/d (2,042); 1-3/month, 7 g/d (3,314); 1/wk, 18 g/d (12,296); 2-3/wk, 37 g/d (16,920); 4-5/wk, 69 g/d (6,271); ≥6/wk, 119 g/d (4,052)	fatal CHD (264), nonfatal MI (554), any MI (811), CABG (735), any CHD (including CABG) (1543)	for fatal CHD, multivariate adjusted RR 1.00, 0.74, 0.86, 0.71, 0.54, 0.77, all 95% CIs include 1.00; for RR 0.54, 95% CI 0.29-1.00; p for trend 0.14; for CABG, 1.0, 1.31, 1.43, 1.40, 1.71, 1.65; all 95% CIs include 1.00; p for trend 0.02; for other end points, no significant relationship

Table 2-1. continued

9- Northern Italy hospital-based case-control study (Gramenzi *et al*., 1990)	Jan. 1985-Feb. 1989	287 women ages 22-69 with MI identified in CCUs of 30 hospitals; 649 controls ages 21-69, in-hospital with acute disorders other than CHD	interview with use of structured questionnaire on frequency of consumption of individual foods and beverages	tertiles of portions consumed per week: <1, 1, >1-- for cases: 148, 81, 58; for controls: 270, 220, 159	nonfatal MI	age-adjusted odds ratio: 1.0, 0.7, 0.6, p <0.05
10- Seattle and suburban King Co., Washington case-control study (Siscovick *et al*., 1995)	Oct. 1988 to July 1994	334 men and women with primary cardiac arrest, ages 25-74, mean age 59, 80% men, 493 population-based controls, age-sex matched	quantitative food frequency questionnaire, including 25 fish and 10 shellfish, consumption during prior month; spouse as proxy respondent	no seafood intake, and quartiles of long-chain n-3 polyunsaturated fat intake, equivalent to 0 servings/month of fresh salmon (0 g/m), 0.6 (15g), 2.0 (45g), 3.7 (84g), 9.1 (207g)	primary cardiac arrest	multivariate adjusted odds ratio (OR): 1.0, 0.9 (0.8-1.0), 0.7 (0.6-0.9), 0.5 (0.4-0.8), 0.4 (0.2-0.7)

Table 2-1. continued

11-DART secondary prevention randomized controlled trial, Wales, U.K., factorial design (Burr *et al*., 1989)	2 years	2,033 men <70 years old, recovered from acute MI, diagnosed at 21 hospitals, randomly assigned to 1 of 8 groups, with no dietary advice, fat modification, increased fiber intake from cereals, increased intake of fatty fish	dietary counseling	1015 men, randomly assigned, asked to consume at least 2 portions per week (200-400 g) of fatty fish, plus advice on 2, 1, or no other dietary factors; intake of eicosapentanoic acid estimated for 2 groups to be 2.3 & 0.7 g/week	nonfatal + fatal CHD, fatal CHD	for CHD incidence end point, multivariate adjusted RR 0.84, 95% CI 0.66-1.07; for CHD death, unadjusted RR = 0.68, p <0.01; for all causes death, 0.71 (0.54-0.93), p <0.05
12- Chicago Western Electric Study, U.S.A. (Daviglus *et al*., 1997)	1957-58 30 years	1,822 men ages 40-55; urban workers	in-depth cross-check diet history	0 g/d (189), 1-17 (646), 18-34 (745), $\geq$ 35 (245)	Fatal CHD, (430), fatal MI (293), nonsudden death (> 12 hours of symptom onset)	significant independent inverse relationships; for fatal CHD, RR 1.00, 0.88, 0.84, 0.62, p for trend 0.040; for fatal MI, RR 1.00, 0.88, 0.76, 0.56 p for trend 0.017; for nonsudden MI, RR 1.00, 1.04, 0.76, 0.33, p for trend 0.007

2.2.1.1 Kromhout, Bosschieter and Coulander, 1985. "The Zutphen Study" (1)

This was the first prospective study to create great interest in the topic of fish consumption and CHD risk reduction. The investigators followed 852 men for 20 years; there were 78 CHD deaths with 100% follow-up. The results showed an inverse relationship between the amount of fish reported and the relative risk of death from CHD ($p<0.05$). This association held even for the group reporting the lowest fish consumption (at 1-14 grams of fish/day, RR=0.6, i.e., only 60% of the risk of death from CHD compared to the group which didn't eat fish.) A limitation of this study (and prospective cohort studies in general) is that it assumes the usual rate of fish consumption remains relatively unchanged over the period studied.

Up until this study was released, it was believed that the protective effects were associated with eating very large amounts of cold-water fatty fish and marine mammals, based on studies of Eskimo and Inuit populations. The Zutphen study was a landmark in three respects: it demonstrated that (1) eating as little as one or two meals of fish each week was associated with a lower risk of heart disease; (2) this was a dose-response relationship (the higher the usual fish consumption, the lower the risk of death from CHD); and (3) the effects could be obtained with lean fish (two-thirds of the fish eaten by this Dutch sample were lean fish such as cod) as well as fatty fish.

2.2.1.2 Kromhout, Feskens and Bowles, 1995. General practice patients in Rotterdam, the Netherlands. (2)

This study was undertaken in 1971 in an elderly population in Rotterdam, the Netherlands. Men and women (n=282) born before 1907 were recruited from a general practice, and followed for 17 years. Dietary information, body mass index (an indication of body fatness), blood pressure, serum lipids, and smoking were recorded at baseline. The status of the study population was checked in 1988, and for those who had died, both primary and secondary causes of death were used because they can be difficult to distinguish in an elderly population.

The prevalence of myocardial infarction (MI) was higher ($p<0.05$) among the group of men who ate no fish, compared to the group which consumed fish (OR=0.34). A similar association between fish consumption and risk of MI was seen in all female participants. The risk of dying from CHD was also less than half for the group who consumed fish compared to those who did not (RR=0.47). Survival analyses indicated that the difference in CHD mortality between fish eaters and non-fish eaters became evident after 5 years of follow-up. When men and women were separated in the analysis, the difference in RR was not significant. The results of this study showed an inverse relationship between fish intake and CHD mortality in an elderly population of men and women, an association previously reported with middle-aged men.

2.2.1.3 Norell, Ahlbom, Feychting, and Pedersen, 1986. "Swedish Twins" (3)

In this letter to the editor of the British Medical Journal, Norell and colleagues provided data on 10,966 Swedish men and women who had no angina, myocardial infarctions or other history of CHD in 1967, who had participated in a 14-year prospective study of twins. Information on fish consumption was collected using a self-administered questionnaire, and the subjects were then

classified as high, moderate or low fish consumers based on ratios of average amounts of fish eaten in relation to other foods. Individuals who reported that they did not eat fish were included in the "low consumption" group, a limitation of this study. By combining the "unexposed" subjects and "low exposure" subjects into one statistical group, this "may have led to an underestimation of the strength of the inverse relation between fish consumption and death from MI and CHD" (p.426).

The results showed that 800 people died of coronary heart disease, 395 of whom had fatal myocardial infarctions. When the relative risk of death from each was calculated, controlling for gender and age, there was a dose-response relationship: those in the highest category of fish consumption had a relative risk of .85 for CHD death, and .70 for MI death when compared to the low/no fish group. The investigators report that when the data were controlled using multivariate analysis techniques the results were similar.

2.2.1.4 Vollset, Heuch and Bjelke, 1985. "Norway Postal Dietary Survey" (4)

In a letter to the editor of the New England Journal of Medicine, Vollset and his colleagues reported findings from a subset of 11,000 middle-aged and older men from their Norwegian prospective study, who were followed for 14 years. These men reported their smoking and "selected cardiovascular symptoms" in 1964, and their fish consumption in 1967. The investigators used the latter information to construct "a fish index approximating the number of times fish was eaten per month" (p.820). Overall, there were 967 deaths, 301 of which were due to fatal myocardial infarctions. The distribution of deaths observed, according to six categories of number of fish meals per month, was not significantly different from the predicted distribution. When the analyses excluded men who had reported CHD symptoms (such as angina) in 1964 and used only data from the 301 who died from acute MIs, there was still no significant relation between fish consumption and CHD death. However, the analyses did not control for a number of possibly important confounding factors (e.g., level of physical activity level, body fatness, high blood pressure, parental history of early death from CHD, diabetes mellitus, etc.).

2.2.1.5 Curb and Reed, 1985. "Honolulu Heart Program" (5)

The NEJM letter by Vollset and colleagues was followed by another letter to the editor reporting the relationship between fish consumption and CHD. Curb and Reed provided the results of a 12-year study following 7,615 Japanese men participating in the Honolulu Heart Program. The ages of the men upon enrolment into the study were not given, but the men were "without prevalent atherosclerotic disease". The results showed few differences in the rates of CHD and of fatal CHD across the categories of frequency of fish meals and amounts eaten in the previous 24 hours, and there were no statistically significant trends. The authors did not mention if they controlled for other risk factors for CHD in their analyses. Given that this population had high mean levels of fish consumption (--44% reported eating fish during the previous 24 hrs, with portion sizes ranging from 28 to 476 grams--) with few subjects reporting that they never ate fish (n=32) compared to other similar studies, the authors wondered if "maximal benefit" from fish consumption was already being obtained.

2.2.1.6 Fraser, Sabate, Beeson, and Strahan, 1992. "The Adventist Health Study" (6)

A cohort of 26,473 non-Hispanic Caucasian Seventh Day Adventists aged 25 years or older in 1974, was followed for 6 years. The sample was well educated and concerned about health; participants tended to abstain from smoking and the use of alcohol, and follow lacto-ovo-vegetarian diets (i.e., diets that include dairy products and eggs, but exclude meat, fish and poultry). The criteria for participation in this study were stricter than most previously conducted: those with a known history of heart disease, or whose history for CHD had not been assessed, as well as individuals with diabetes, were excluded. Baseline data were collected using a mailed self-administered questionnaire in 1976, and unlike other prospective studies, yearly data on hospital admissions (with access to medical records) and the development of CHD symptoms were also collected. Death due to CHD was strictly defined and three end-points were used: definite nonfatal MI (134 events), definite fatal MI (260 cases), and confirmed fatal CHD (463 cases).

The adjusted relative risks from multivariate analyses for three levels of fish consumption (none, less than once/week, once a week or greater) suggested protective effects for those consumers eating fish once a week or more, only for death from MI (adjusted RR = 0.74; 95% C.I = 0.42-1.33). The group eating fish less than once a week had similar adjusted relative risks to the group eating no fish, for all 3 end-points. Given that only 10% of the largely vegetarian sample ate fish once a week or more, and that the sample was followed for only 6 years and was still relatively young (mean age of 51.3 years for men and 53.2 years for women), these effects may have been underestimated.

2.2.1.7 Morris, Manson, Rosner, Buring, Willett and Hennekens, 1995. " The US Physicians' Health Study: 4 years" (7)

This prospective study followed 21,185 U.S. physicians aged 40-84 years, with no history of MI or other cardiovascular disease, cancer, liver or renal disease, peptic ulcer, gout or use of certain drugs (including aspirin), from 1983 to 1987. As with the previous study, information on CHD symptoms was collected annually. What is different from other prospective studies, however, is that annual information was also collected on fish consumption, foods high in saturated fats, and parental MI events; as well, use of aspirin and beta-carotene were controlled for in analyses. Several CHD endpoints were used, along with all stroke events, and these were confirmed by ECG and enzyme test records, other patient records or autopsy. The relative risk values for all cardiovascular and stroke events (fatal and nonfatal) for subjects who ate 1 meal, 2-4 meals, and 5 or more fish meals per week were not significantly different from values for subjects who ate less than 1 meal of fish weekly, and there were no statistically significant trends across the four levels of fish consumption. The number of subjects at each level of fish consumption for each of the cardiovascular disease outcomes was relatively small, though (e.g., stroke and cardiovascular deaths each had only 7 subjects who consumed 5 or more fish meals per week), and some confidence intervals were wide (e.g., 95% CI = 0.8-5.9). As with the Swedish Twins Study above, grouping low consumers with consumers who never ate fish may have underestimated the benefits of eating modest amounts of fish (one or two meals weekly, such as in the Zutphen Study). As well, four years is a relatively short period of follow-up.

2.2.1.8 Albert, Hennekens, O'Donnell, Ajani, Carey, Willett, Ruskin and Manson, 1998. "The US Physicians' Health Study: 12 years" (8)

This was a continuation of the previous study, and examined the association between fish consumption and the risk of sudden cardiac death in men over an 11-year period. Eighty percent of the sample consumed fish between 1 and 4 times/week; the high fish consumers tended to be those who were at risk for cardiovascular disease (e.g. family history of CHD) and, being physicians, were aware of this risk. After controlling for age, and aspirin and beta carotene use, risk of sudden cardiac death was inversely related to fish consumption, and showed a significant decline ($p<.05$) across the five levels of fish consumption. Physicians who ate 1-2 fish meals/week had a significantly lower risk (RR=0.42, $p=0.02$) of sudden death compared to those who ate fish <1/month. The magnitude of difference in risk did not change significantly with higher consumption, suggesting a threshold effect. After adjusting for coronary risk factors and prior cardiovascular disease, the decline in risk was no longer significant across the five categories of fish consumption but remained significant across three of the categories (<1/month, 1-3/month, and $\geq$1/week). Although fish consumption was inversely associated with sudden cardiac death, it was not related to non-sudden cardiac death, risk of coronary heart disease or total cardiovascular death.

2.2.1.9 Ascherio, Rimm, Stampfer, Giovannucci and Willett, 1995. "The Health Professionals Follow-Up Survey" (9)

This six year prospective study followed a cohort of 44,895 male health professionals who were aged 40 to 75 in 1986. Men who reported MI, angina, stroke, transient ischemic attack, peripheral artery disease, coronary artery surgery, diabetes, high blood pressure, high blood cholesterol, or who knew their blood cholesterol at baseline (and thus may have altered their lifestyles or diets to reduce their `high risk'), were excluded from analyses, as were men who had CHD events during the first 4 years of follow-up. Questionnaires were sent every 2 years to ask for recent information on CHD events. Follow-up was complete for 94% of subjects. Endpoints were fatal CHD, nonfatal MI, coronary-artery bypass grafting (CABG) and angioplasty, and were confirmed using international criteria, patient records (ECG & cardiac enzyme results), and autopsy in addition to death certificates.

This study assessed the association of both fish intake and n-3 FA intake in relation to CHD endpoints. For analyses, fish intake was divided into 6 categories ranging from less than once per month (n=2,042) to 6 or more times weekly (n=4,052) with sufficient numbers of subjects in each category for multivariate analyses by CHD endpoints. No association was found between n-3 FA intake or fish oil supplements and risk of CHD disease. Compared with men who ate little or no fish (less than 1 serving per month), the relative risk of fatal CHD (after adjusting for many potential confounders) for men who ate fish 1 to 3 times a month was 0.74. This relative risk remained fairly constant as fish consumption increased (ranging from 0.86 to 1 meal/week to 0.54 for 4-5 meals/week) but confidence levels were very wide. These results suggest that as little as one fish meal a week could have a protective effect against death from CHD, and increasing fish consumption above this would likely not confer additional benefits. For other CHD endpoints, there were no apparent relationships with fish consumption, and the authors

suggested that eating fish might reduce the likelihood of death from a myocardial infarction but not reduce the risk of a MI event.

2.2.1.10 Gramenzi, Gentile, Fasoli, Negri, Parazzine and La Vecchia, 1990. (10)

This retrospective case control study matched 287 Northern Italian women aged 22 to 69 years who had suffered acute myocardial infarctions, with 649 controls hospitalised for conditions unrelated to CHD, cancer, smoking, alcohol, or digestive, hormonal, or reproductive disorders. The investigators relied upon participants' assessments of their level of fish consumption (low, intermediate, high consumption). Age adjusted odds ratios using 'less than 1 fish meal weekly' as the reference category showed that the risk of MI was 0.7 for those eating 1 fish meal per week, and dropped to 0.6 for more than 1 fish meal weekly; this trend was statistically significant at $p<0.05$.

2.2.1.11 Siscovick *et al*., 1995. Case-control Study in Seattle and King County, Washington. (11)

In this case control study, the association between dietary intake of long-chain n-3 fatty acids from seafood and risk of cardiac arrest was examined, based on cases of out-of-hospital primary cardiac arrests. Cases (n=334) were identified by paramedics (death certificates, and medical examiner and autopsy reports were also reviewed) and were matched to randomly selected controls (n=493) from the community. Spouses of cases and controls were interviewed to determine dietary intake of n-3 fatty acids from seafood during the previous month, and blood samples were collected from 82 cases and 108 controls to determine red blood cell membrane fatty acid composition (thought to be a biomarker of dietary n-3 fatty acid intake). Using a conditional logistic regression model, an inverse association was found between dietary intake of n-3 fatty acids and the risk of primary cardiac arrest. An intake of 2.9 g of n-3 fatty acids per month (equivalent of 2 fatty fish meals/month) compared to no seafood meals resulted in a 30% reduction in the risk of primary cardiac arrest (OR=0.70). There was a further reduction of risk (OR=0.50) with consumption of 5.5 g of n-3 fatty acids (equivalent to one fish meal/week), after adjustment for many potential confounding variables. There was also an inverse relationship between red blood cell membrane-combined EPA and DHA levels and risk of cardiac arrest: when n-3 fatty acids comprised 3.3% of total fatty acids in red blood cells, there was a 50% reduction (OR=0.50) in risk of primary cardiac arrest; a level of n-3 fatty acids of 5.0% of total fatty acids was associated with a 70% reduction (OR=0.30). However, after taking into account the effect of red blood cell membrane levels, dietary intake of n-3 fatty acids was not related to the risk of primary cardiac arrest. This may suggest that the effect of dietary fatty acids occurs through changes in cell membrane fatty acid composition.

2.2.1.12 Burr, Gilbert, Holliday, Elwood, Fehily, Rogers, Sweetnam and Deadman, 1989. "The Diet and Reinfarction Trial (DART)" (12)

The purpose of this randomised, controlled clinical trial was to determine if changes in fat, fish and dietary fiber intakes of men who had had nonfatal myocardial infarctions could affect the incidence of second MIs. A total of 2033 men were randomised to receive dietary counselling to reduce their fat intakes, eat at least 2 servings a week of fatty fish (e.g., mackerel, salmon, trout),

or eat more dietary fiber. Those in the fish group who disliked fish were given 3 fish oil capsules daily instead. A subset of 25 study participants completed 7 day weighed food records, and subjects in the fat and fish advice groups had serum cholesterol and fatty acid profiles done, as cross-checks for compliance. After two years, the groups receiving fat and fiber advice showed no significant differences in death rates. Although there is a confounding of fish consumption with fish oil consumption, the fish advice group showed a 29% lower risk of death from all causes than the group which received no fish advice, even after analyses were adjusted for 10 potentially confounding factors. This was the first randomised, controlled trial to investigate the effectiveness of increased fish consumption on the secondary prevention of MI.

2.2.1.13 Daviglus *et al*., 1997. "The Western Electric Study" (13)

The relationship between baseline fish consumption and the 30-year risk of CHD was assessed in 1822 men aged 40 to 55 years, as part of the Chicago Western Electric Study. Fish consumption was determined from a detailed diet history and was stratified into 4 categories: 0, 1-17 g/day, 18-34 g/day, and >35 g/day. Annual examinations, conducted for the first 10 years, and mailed questionnaires or telephone interviews done over the next 15 years, were used to obtain information on the status of the study participants. Dietary information was collected at the first and second annual examination. During the 31st year vital status was determined from the National Death Index, the Health Care Financing Administration, and surviving participants. Deaths due to CHD were classified as death from MI (sudden or nonsudden) or death from other coronary causes. Cox proportional hazards regression was used to estimate the RR of death for each of the four levels of fish consumption, after controlling for 13 possible confounders. Age-adjusted death rates from MI, coronary heart disease, cardiovascular disease, and all causes were the lowest in men who had the highest consumption of fish. The relative risks of death from any MI (sudden or nonsudden), sudden MI, and nonsudden MI were 0.56, 0.68, and 0.33 respectively for men who consumed >35 g of fish per day, compared to the group who consumed no fish. There was a significant trend towards a lower relative risk as the level of fish in the diet for nonsudden MI ($p=0.007$) and all CHD ($p=0.040$) but not for sudden MI. The results of this study indicated a significant inverse relationship between fish consumption and 30-year risk of death from coronary heart disease, including nonsudden MI.

2.2.1.14 Conclusions and Weight of Evidence for an Association between Coronary Heart Disease and Fish Consumption

The 13 studies chosen for this review included 1 clinical (randomised, controlled) trial and 12 epidemiological studies (2 case-control and 10 prospective cohort studies) with strong designs and large sample sizes. All the prospective studies had good rates of follow-up (i.e., they had few study dropouts), although there were large differences in the lengths of follow-up. Earlier studies relied upon information on death certificates; later studies used international guidelines for diagnostic criteria, autopsies, physician and hospital records (ECG results, cardiac enzymes, blood lipid profiles), and interviews with relatives, to improve the accuracy of CHD endpoints diagnosed. Later studies also expanded their exclusion criteria and did not recruit subjects with pre-existing or early symptoms of CHD (e.g., angina pectoris, angioplasty procedures, coronary artery bypass grafting, ischemic stroke, strokes due to injury or tumors, silent infarctions, etc.). More recent prospective studies have collected information during the follow-up period, not just

at baseline, to determine if and when health conditions, family history, or diet changes. They also controlled for substances and lifestyle factors believed to lower CHD risk, such as aspirin, anti-oxidant vitamins, alcohol, and regular exercise, in addition to other potential confounding health and socio-demographic variables. Dietary assessment methods have improved as well, with the use of instruments with known validity and reliability, and crosschecks for assessing the accuracy of recalls or compliance with dietary advice.

Findings from five (of eight) prospective population studies B Zutphen (Kromhout *et al*., 1985), Rotterdam (Kromhout, 1995), Sweden (Norell *et al*., 1985), U.S. physicians 12-year study (Albert *et al*., 1998), and Chicago Western Electric (Daviglus *et al*., 1997) are broadly concordant in showing a significant inverse relation between fish intake and risk of CHD mortality, as are also results from the two case-control studies (Gramenzi *et al*., 1990, Siscovick *et al*., 1995) and the one intervention trial (Burr *et al*., 1989). For the specific endpoints of non-sudden vs. sudden CHD death, findings in the Physicians' Health Study (Albert *et al*., 1998) and the Seattle Study (Siscovick *et al*., 1995), appear different from those in the Chicago Western Electric Study (Daviglus *et al*., 1997). Both of the former found an association between reported fish intake and rate of sudden death, whereas the Chicago Western Electric data found a lower rate of non-sudden MI death (not sudden MI death).

Three prospective studies, the Bergen Norway (Vollset *et al*., 1985), Hawaii (Curb & Reed, 1985), and U.S. Health Professionals (Ascherio *et al*., 1995) studies, did not find a relationship between fish intake and CHD-MI. There were many differences among the prospective epidemilogic investigations, one or more of which may account for this apparent inconsistency in results:

1. different methods to assess diet and to array men by fish intake;

2. different distributions of reported fish intake, such that in some cohorts (e.g., Bergen and Hawaii) there were few or no people in the group consuming little or no fish; hence, there was no fully suitable reference group;

3. different study sites and times, with populations that have quite different diets (resulting in different dietary intakes of cholesterol, saturated fats, antioxidants, fiber, etc.). For example, the cohorts of Norwegian, Hawaiian Japanese-American and U.S. health professionals were studied during the 1980s and 1990s, at a time of widespread awareness of general dietary advice about `heart healthy eating', as well as some awareness of the idea that fish may "protect" against CHD;

4. the possibility of bias due to this recent awareness, i.e., people who know they have some risk factors for CHD may have differentially become greater fish eaters in the 1980s. This could potentially cause an inversion of the fish-CHD relationship, i.e., the people who eat more fish have higher relative risks of death from CHD (e.g., the Health Professionals Follow-Up Study finding re: fish and CABG?);

5. different durations of follow-up, ranging from decades to 4-6 years (e.g., findings in Physicians' Health Study with 4- and with 12-year follow-up, compared to findings in the Chicago Western Electric Study with 30 year follow-up -- Table 2-1);

6. different CHD endpoints, with only a few studies reporting on fish and fatal MI, and only two prospective studies (Chicago Western Electric Study and Physicians' Health Study) reporting on fish and the suddenness of CHD death;

7. differences in the interpretation of findings (e.g., in the Health Professionals Follow-up Study, are data on CHD death more soundly interpreted as indicating no relation or an inverse relation of fish intake to this end point?);

8. chance, that is, random variation across studies in results.

Although the data available at this time do not allow us to say definitively that these factors account for the apparent discrepancies in findings, the 'weight of evidence' supports an association between fish consumption and lower risk of CHD in men with no previous history or symptoms of CHD. It appears that this relation is evident with as little as one to two meals of fish (lean or fatty) per week.

This inverse relation seems unlikely to be due to n-3 FA content of fish, for several reasons. First, lean fish have lower levels of n-3 FA than fatty fish, yet both appear to protect against sudden cardiac death. Second, fish oil supplementation trials have observed effects at high doses, the equivalent of enormous amounts of fish in the diet; however, there is evidence of an association between a reduced risk of sudden death from CHD and MI when as little as one meal of fish a week is consumed. It is possible that a component or combination of substances in fish, through some mechanism not yet discovered, confers the cardio-protective benefits.

With the exception of the DART study (Burr *et al*., 1989), a randomised controlled clinical trial which examined the effects of three different interventions on the secondary prevention of MI, studies have not been designed to suggest a 'cause and effect' relationship between eating fish and rates of CHD. These epidemiological studies can indicate associations between variables, but randomised controlled clinical trials are needed in order to answer the question, 'Does eating fish lead to a lower risk of CHD?'

2.2.2 Studies of Other Possible Health Effects of Fish Consumption

The following sections briefly describe investigations of benefits of fish consumption with respect to other health endpoints (Table 2-2). These endpoints have not been studied as well as coronary heart disease. Table 2-2 summarizes this research.

Table 2-2. Studies of Fish Consumption and Other Endpoints

Condition	**Key Studies**	**Evidence to Date**
Smoking-Related Chronic Obstructive Pulmonary Disease	ARIC Study (Shahar *et al*., 1994)	fish consumption associated with better lung function for Whites who currently or formerly smoked, but not Blacks
Lung Damage from Smoking	ARIC Study (Shahar *et al*., 1994) and Honolulu Heart Program (Sharp *et al*., 1994)	frequent fish consumption may protect the lungs of 35+ yr. smokers from damage; smokers of 30+ cigarettes daily not protected though
Rheumatoid Arthritis	Shapiro *et al*., 1996	2 or more servings of broiled/baked fish/week reduced risk of rheumatoid arthritis (OR=0.57); no association for other types of fish (fried, shellfish, canned tuna)
Childhood Asthma	Hodge *et al*., 1996 (fish) Hodge *et al*, 1998 (n-3 oil) Thien 1996	1996 study of 71 children with asthma found 1+ meals of oily fish/month reduced risk of asthma (OR=0.26); not supported by Nurses' Health Study (Thien, 1996); 1998 study using n-3 oil found no effect on severity of asthma
Plaque Psoriasis	Collier *et al*., 1993	small clinical trial (cross-over design) with diets including 6 oz oily or 6 oz lean fish/day; 11-15% improvement of psoriasis symptoms with oily fish
Colon Cancer	Nurses Health Study (Willett *et al*., 1990)	no association with fish alone, but ratio of $\geq$5.2 red meat:fish + chicken was 2.5 x more likely to get colon cancer than ratio of <1.2 red meat: fish + chicken
Gastrointestinal Disease	[reviewed in O'Keefe, 1996]	ulcerative colitis and adenomatous polyps successfully treated with fish oil supplements; no data re: intake of fish and incidence/severity

Condition	**Key Studies**	**Evidence to Date**
Dyslipidemia in Non-Insulin-Dependent Diabetes Mellitus	Dunston *et al*., 1997	NIDDM patients who ate 1 fish meal/day as part of a low fat diet had reduced triglyercide and increased HDL levels, but poorer glycemic control; when exercise was added, glycemic control was maintained
Antioxidant Levels	Anttolainen *et al*., 1996	comparison of 82 Finns with very high fish consumption to group eating <1 meal/month showed similar levels of antioxidants (beta-carotene & vitamin E)

2.2.2.1 Smoking-Related Chronic Obstructive Pulmonary Disease (COPD)

Shahar *et al*. (1994) looked at COPD in current and former smokers participating in the Atherosclerosis Risk in Communities (ARIC) study. They defined COPD as chronic bronchitis, physician-diagnosed emphysema, or spirometrically detected COPD. Current or former smokers in the third and fourth quartiles of fish consumption ($\geq$ 1.5 servings/week) were significantly less likely to have COPD than those who ate little or no fish. Fish consumption was also associated with improved lung function (greater forced expiratory volume in one second [FEV_1] and greater FEV_1/Forced vital capacity [FVC]) in white current and former smokers. Oddly, this relationship was not seen in black participants. Fish consumption was not related to lung function in ARIC participants who had never smoked, suggesting that fish consumption does not actually improve lung function directly, but rather protects the lungs from damage caused by smoking.

2.2.2.2 Lung Damage from Smoking

Like the results of the ARIC study summarized above, the results of the Honolulu Heart Program (HHP) study (Sharp *et al*., 1994) suggest that frequent fish consumption may protect the lungs of long-term cigarette smokers from damage. Male cigarette smokers who reported eating fish at least 2 times/week showed less of a relationship between duration of tobacco exposure and reduced FEV_1 than did smokers who ate fish less frequently. However, fish consumption only seemed to be protective among smokers who had smoked for more than 35 years. There was also some evidence that heavy smokers (> 30 cigarettes/day) were not protected by frequent fish consumption.

The authors of both the ARIC and the HHP studies speculate that fish consumption may exert its protective effect by inhibiting the production of various mediators of lung inflammation, some of which have been associated with cigarette smoking. Supplementation of the diet with fish oil has been shown to inhibit the production of a number of known and putative mediators of lung inflammation, and fish itself might produce similar effects. However, the average intake of n-3 fatty acids by study participants was much lower than the dosage contained in fish oil supplements, so some factor other than n-3 fatty acids may be at work.

2.2.2.3 Rheumatoid Arthritis

In a case-control study by Shapiro *et al*. (1996), consumption of broiled or baked fish was associated with a decreased risk of rheumatoid arthritis in women. The adjusted OR for $\geq$2 servings of broiled or baked fish/week, compared with <1 serving, was 0.57 (95%CI=0.35-0.93). However, consumption of other types of fish (fried fish, canned tuna, and shellfish) was not associated with rheumatoid arthritis, and neither was a combined measure including all types of fish consumed. In addition, there was no significant association between the estimated amounts of n-3 fatty acids in the participants' diets and rheumatoid arthritis when all cases were included in the analysis. When the analysis was restricted to cases who were rheumatoid factor positive (RF+), the association with consumption of broiled or baked fish remained significant, and there was also an association between n-3 fatty acid consumption and reduced risk of arthritis.

However, the latter association appeared to be weaker than the former; the association between n-3 fatty acid consumption and rheumatoid arthritis was only statistically significant when participants in the top 10% of n-3 consumption were compared to those in the first quartile.

2.2.2.4 Childhood Asthma

In a study of 71 children with asthma and 263 controls, Hodge *et al*. (1996) found that consumption of fresh, oily fish was associated with a reduced risk of current asthma. The adjusted OR for those who ate oily fish at least monthly versus those who never ate oily fish was 0.26, with a 95% C.I. of (0.09-0.72). There was no statistically significant association between asthma and consumption of non-oily fish or of canned or processed fish. Thien *et al*. (1996) were somewhat dubious about these results, since other studies had suggested that fish in the diet would have no effect on risk of asthma or on reducing the severity of asthma. For instance, the Nurses' Health Study had shown no relationship between adult-onset asthma and fish in the diet, and most clinical trials of fish oil supplements as a treatment for asthma had yielded disappointing results. In fact, a small clinical trial by Hodge *et al*. (1998) showed that n-3 oil supplements had no effect on the severity of symptoms in asthmatic children. However, it is possible that the association observed in the 1996 study was genuine, and that some compound in fish other than n-3 fatty acids was responsible for the protective effect.

2.2.2.5 Plaque Psoriasis

Collier *et al*. (1993) carried out a small clinical trial to examine whether a diet containing 6 oz. of oily fish/day could improve psoriasis symptoms; the control diet contained 6 oz. of white fish/day. Patients on the oily fish diet showed a small (between 11% and 15%) but statistically significant improvement after 6 weeks on the diet, and symptoms worsened again when patients switched from the oily fish diet to the white fish diet. The oily fish diet contained high levels of both vitamin D and n-3 fatty acids, and the authors speculated that one or both of these factors might have been responsible for the beneficial effect of the diet.

2.2.2.6 Colon Cancer

There was no significant relationship between fish consumption and colon cancer among the Nurses' Health Study cohort (Willett *et al*., 1990). However, the total amount of chicken and fish in the diet was associated with a reduced risk of colon cancer, and the ratio of red meat to chicken and fish in the diet was associated with an increased risk of colon cancer. Women who ate $\geq$ 5.2 times more red meat than chicken and fish (the highest quintile) were 2.5 times more likely to have colon cancer than women in the lowest quintile (< 1.2 times more red meat than chicken and fish). In this case, it seems likely that fish and chicken exerted their protective effect by substituting for red meat, thus decreasing the amount of animal fat and other potentially hazardous components of red meat in the diet.

2.2.2.7 Gastrointestinal Disease

O'Keefe (1996) cites a number of studies in which fish oil supplements were successfully used to treat patients with ulcerative colitis or adenomatous polyps. However, there seem to be no

published studies of the effect of fish in the diet on the incidence or severity of colitis or other gastrointestinal disorders.

2.2.2.8 Dyslipidemia in Non-Insulin-Dependent Diabetes Mellitus

Dunston *et al*. (1997) conducted a small clinical trial to test whether fish consumption (1 meal/day) could improve serum lipid levels in dyslipidemic NIDDM patients without increasing levels of plasma glucose and glycated hemoglobin. The addition of one fish meal per day to a low-fat diet ($\leq$ 30% of energy intake) did cause triglyceride levels to fall and HDL_2 levels to rise, but it also caused glycated hemoglobin and serum glucose to rise. However, in patients who ate one fish meal per day and participated in an exercise program (riding a stationary bicycle for 30' at 55-65% of V_{O2max}), plasma lipid levels improved with no deterioration in glycemic control.

2.3 Antioxidant Levels

Several researchers have speculated that a high-fish diet might reduce antioxidant levels in the diet or in the blood, since n-3 fatty acids have a tendency to oxidize *in vitro*, and since fish oil contains less of the antioxidant vitamin E than vegetable oils. Anttolainen *et al*. (1996) studied 82 Finns to determine whether men and women with very high levels of fish consumption do in fact have lower levels of antioxidants in their diet and in their plasma than people who eat little or no fish. When compared to participants who ate fish less than once per month, participants who ate fish every day or almost every day had equivalent or higher levels of vitamin E, vitamin C, ß-carotene, and selenium in their diets. Similarly, levels of plasma tocopherol (vitamin E) and ß-carotene were very similar in the high-fish and low-fish groups. Although this study could not measure the vitamin E stored in tissue, the results do suggest that a diet high in fish does not dangerously reduce antioxidant levels.

2.4 Health Benefits During Pregnancy, Lactation and Infancy

As mentioned earlier, fish is a good dietary source of the omega-3 fatty acids docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). DHA is incorporated into the cell membranes of the retina, brain and other parts of the central nervous system. Several animal studies have demonstrated that if DHA levels are low when these tissues are developing, vision and learning problems may result (see Neuringer, Reisbick and Janowsky, 1994 for a review). This is most important during the third trimester of pregnancy when the brain of the unborn child is rapidly developing, but is also important during the first year after birth when the brain continues to grow. Thus, there has been an interest in the possible health benefits of consuming fish during pregnancy. The unborn child may benefit from the omega-3 fatty acids from fish the mother consumes during pregnancy, and may be born with greater body stores of these fatty acids to draw upon during the first year of life.

Human milk contains many long-chain polyunsaturated fatty acids, including DHA and arachidonic acid (AA). DHA accounts for 0.1% to 1.5% of total fatty acids in human milk depending upon the amount of pre-formed n-3 fatty acids, the main source of which is fish, in the mother's diet. Currently, commercial infant formulas in the U.S. contain the n-6 fatty acid linoleic acid (precursor to arachidonic acid), and the n-3 fatty acid linolenic acid (precursor to

DHA & EPA), but do not contain AA, DHA or EPA (Auestad *et al.*, 1997). Thus, mothers who consume fish while provide pre-formed n-3 fatty acids to their infants through breast milk, during the first year of life when the brain is still developing.

In the Faroe Islands study, women who ate high amounts of marine fish and marine animals during their pregnancies were observed to have longer gestations and correspondingly heavier babies (Olsen, Hansen and Sorensen, 1986). A subsequent study of Danish women hypothesized that it was the n-3 fatty acids in marine fish and animals that conferred these benefits; indeed, the results showed that women who received fish oil supplements in their third trimesters had pregnancies that were an average of four days longer than women who received olive oil supplements or no supplements (Olsen, *et al*., 1992). Comparisons among the three groups of mothers showed that those given fish oil supplements had significantly higher levels of n-3 fatty acids, particularly docosahexaenoic acid (DHA), in their umbilical cord blood than the two other groups (Van Houwelingen, Sorensen, Hornstra *et al*., 1995). Thus, the extra n-3 fatty acids consumed by the supplemented pregnant mothers led to higher n-3 fatty acid levels in their babies at birth. The authors concluded that "it is, indeed, possible to interfere with the DHA status at birth: children born to mothers supplemented with fish oil in the last trimester of pregnancy start with a better DHA status at birth, which may be beneficial to neonatal neurodevelopment" (Van Houwelingen *et al*., 1995, p.723).

A study of 300 Canadian Inuit women provides some preliminary evidence that consuming marine fish and mammals during pregnancy may reduce the likelihood of pregnancy-induced hypertension for women at risk (Popeski *et al*., 1991). Women from communities harvesting large amounts of marine foods had significantly lower diastolic blood pressure levels in the last six hours of their pregnancies, compared with women from communities where less marine fish and sea animals, and more caribou, were eaten. Among the 53 women who developed hypertension, 12 were from communities with high fish and sea mammal consumption and 41 from communities eating lower amounts. Although these differences in blood pressure levels could reflect other dietary differences not assessed in this study (e.g., sodium intake), levels of the n-3 fatty acids eicosapentaenoic acid (EPA) and DHA in cord blood were higher in the communities with more marine foods in their diets, lending support to the hypothesis that the differences were related to diet.

2.5 Health Benefits for Children Consuming Fish

All fish is a good source of high-quality protein, essential fatty acids, and minerals such as iron and zinc (see Chapter 3 *Nutritional Benefits of Eating Fish Compared to Other Protein Sources*), and thus is an important food in the diets of growing children. Consuming other protein foods, particularly fast foods that are popular among children and teens, can result in more saturated fats in a meal. Given the increasing rates of obesity among American children, and the evidence that obese children tend to become obese adults, high dietary fat intakes among children are a public health concern. Learning to enjoy a healthful diet and to maintain an appropriate body weight during childhood may help children to reduce their risks of cardiovascular disease, Type II diabetes mellitus, and some forms of diet-related cancers, as adults.

Some children and adolescents follow strict vegetarian (vegan) diets, or variations that include dairy products and eggs (lacto-ovo-vegetarians), or dairy products, eggs and fish (lacto-ovo-pesco-vegetarians or semi-vegetarians). A recent Slovakian study examined the fatty acid profiles of children following such diets and children who were omnivores (Krajcovicova-Kudlackova *et al*., 1997). The children following semi-vegetarian, lacto-ovo-vegetarian, and vegan diets had significantly lower blood levels of saturated fatty acids compared to the omnivore children. The semi-vegetarians, who consumed fish but not poultry or meats, had significantly higher levels of EPA and DHA than lacto-ovo-vegetarians; vegans had the lowest levels of both n-3 fatty acids. There were no significant differences among the groups in the long-chain n-6 AA or in monounsaturated fatty acids. The authors warned that the "significantly reduced n-3 fatty acid content and significantly higher ratio n-6/n-3 may represent a health risk in vegans," with respect to cardiovascular diseases. However, the high EPA and DHA levels and low n-6/n-3 ratio found in semi-vegetarians, who reported eating an average of 1.9 fish meals weekly, was considered important for the prevention of cardiovascular diseases.

While children in our culture seem to love hamburgers, hot dogs, and macaroni and cheese by an early age, they may not appear to have the same preference for a lower-fat meal of baked, broiled or steamed fish. Leann Birch (1996), an authority in children's food acceptance patterns, notes that some taste preferences are "built-in" and "unlearned," infants have a preference for sweet and salty tastes, and an aversion to sour and bitter tastes. Other food likes, such as for fatty, crunchy, or creamy foods, get established through repeated experiences with the food. Therefore, "early experiences have a profound effect on food preferences" and "repeated opportunities to taste the food enhance food acceptance" (Birch, 1996; p.235). Children can learn to accept and like fish (or any other new food) if they are introduced to it at an early age and are given time to become familiar with its taste and texture. If children have ample opportunities to become familiar with fish while they are young, chances are greater they will learn to like it and continue eating it as an adult. Thus, if we are interested in promoting the cardiovascular and other nutritional/health benefits of eating fish to adults, we should encourage parents to serve fish to young children so they can develop a liking for it and a willingness to include it in their diets at an early age.

2.6 Conclusions and Research Needs

The above data provide some evidence for an association between decreased risk of CHD or MI and consumption of small amounts of fish, including mainly lean (non-fatty) fish. However, it seems unlikely that decades-long intake of small amounts of fish protect, if fish is indeed etiologically protective, via the very small amounts of omega-3 long-chain polyunsaturated fatty acids so ingested. The resolution of this issue has important implications for public health and nutritional recommendations. Thus, further studies -- observational and interventional, particularly trials -- are needed to resolve whether there is an etiologically significant protection against CHD or MI afforded by regular ingestion of modest amounts of fish. Similarly, more research is needed on the relationship of fish intake and health endpoints other than CHD or MI.

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