〈原　　著〉

An epidemiological study of the preventive effect of dietary fish on bronchial asthma

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To examine whether the intake of fish containing a high amount of eicosapentaenoic acid, such as sardines or herrings, ameliorates bronchial asthma, we investigated the relationship between consumption of fish of this type and the frequency of asthma in 5,102 elementary school children attending 25 schools located in coastal areas, where fresh fish is easily obtainable and eaten in large amounts, and in 2,640 children at 18 schools located in inland areas. There was a significant negative correlation between the frequency of fish consumption and the prevalence of asthma ($p<0.01$). The prevalence of asthma in the children who ate such fish four or more times a week was 7.3%, while it was 11.1% in those who ate such fish less than once a month. This dose-response relationship was observed consistently even when children with each of 13 confounding variables were excluded. These results suggest that the consumption of fish is an independent preventive factor against asthma episodes.

Key Words bronchial asthma, eicosapentaenoic acid, fish, SRS-A, leukotriene, arachidonic acid

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INTRODUCTION

Such chemical mediators as slow-reactive substance of anaphylaxis (SRS-A), which is released from the mast cells or basophilic leukocytes of the respiratory tract, histamine and prostaglandins are considered to play an important role in bronchial asthma episodes.

Samuelsson described SRS-A as a chemical mediator and confirmed that leukotriene resulting from the arachidonic acid cascade has pharmacologial characteristics resembling those of SRS-A[1].

Leukotriene, a potential chemical mediator of asthma episdes, is formed from arachidonic acid more abundantly in asthmatic patients than in normal subjects. Eicosapentaenoic acid is incorporated in vivo into phospholipids in the same manner as arachidonic acid in vivo and is also utilized in leukotriene formation, although it is released much earlier than arachidonic acid.

The bioactivity of leukotriene varies depending upon the condition of the organism or tissues. Leukotriene has been reported to have 1,000 to 10,000 times the effect of histamine[2].

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The leukotrienes formed from eicosapentaenoic acid have less than one tenth to one hundredth of the bioactivity of those formed from arachidonic acid.

The capacity has also been reported to form leukotriene from arachidonic acid in leukocytes of asthma patients to be higher than that of healthy subjects[3].

Conventional histamine suppressing drugs have not always been effective in treating asthma, and drugs inhibiting leukotriene may be more effective for the treatment of asthma.

Dyerberg et al. pointed out in a series of epidemiological investigations, that the polyunsaturated fatty acids found in fish, such as eicosapentaenoic acid or docosahexaenoic acid, demonstrated a potential preventive effect against cardiac infarction[4-8].

Lee et al. reported that the daily administration of either of these fatty acids to healthy subjects increased the level of eicosapentaenoic acid in leukocytes, resulting in a decrease in the formation of leukotriene[9]. This suggests that the eating of fish containing a high concentration of eicosapentaenoic acid would prevent not only cardiovascular diseases but also asthmatic episodes.

To examine whether the frequency of asthmatic episodes could be reduced by increased consumption of fish, especially that rich in fat content, we selected 25 coastal and 18 inland elementary schools and studied the relationship between history of asthma and diet, especially the consumption of high fat content fish, in children attending these schools.

SUBJECTS AND METHODS

The subjects surveyed were a total of 7,742 first-, third- and fifth-grade pupils attending elementary schools located in coastal and inland areas (Fig. 1 and Table 1). The ages of the first-, third- and fifth-grade pupils ranged from six-to-seven, eight-to-nine and ten-to-eleven years, respectively.

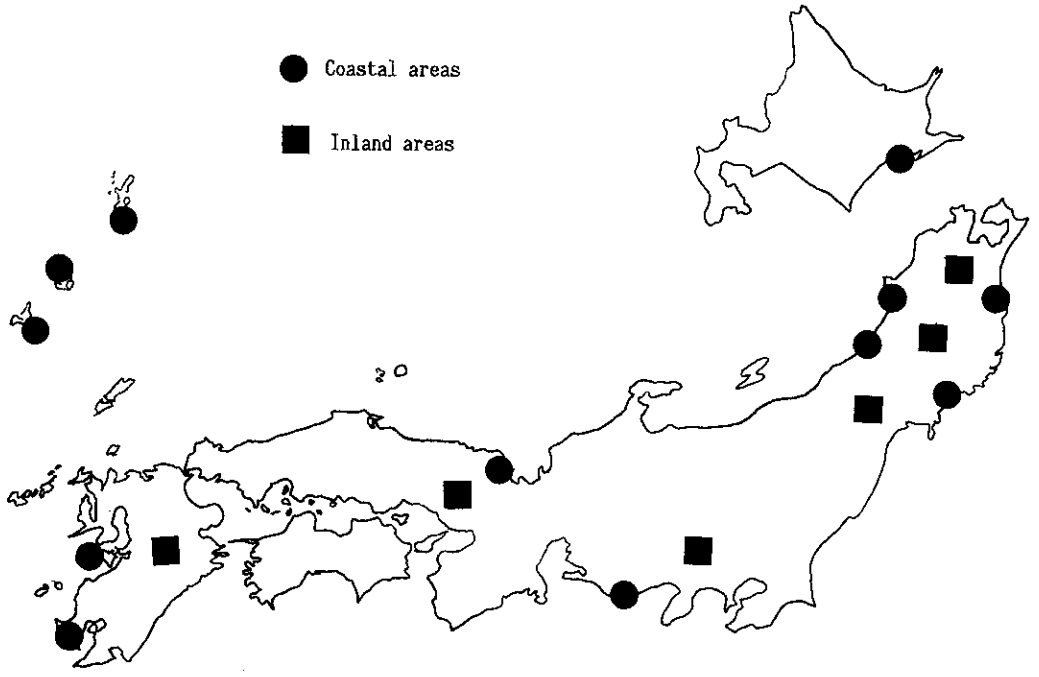

Fig. 1 Location of subjected elementary schools

Table 1 Number of Primary School Chilren Surveyed

Location of schools	First-grade		Third-grade		Fifth-grade		Total
	Boys	Girls	Boys	Girls	Boys	Girls	
Coastal area	813	809	855	783	952	890	5,102
Inland area	452	411	440	449	451	439	2,640
Total	1,265	1,220	1,295	1,232	1,403	1,327	7,742

The "Annual Statistics of Fishery Products Marketing" was used to select elementary schools in coastal areas where both fish harvest and consumption are particularly high[10]. The inland schools were selected from among those located far from the sea but near the coastal school districts.

The questionnaire described below was distributed to the parents of the children selected for this survey during the one-month period from October 1 to 31, 1985.

The questionnaire included the following items: sex, date of birth, family composition, occupation of parents, history of growth, history of allergies, symptoms of allergic diseases, presence of allergic diseases in siblings, local and domestic environment, and diet, including the type of milk used at the time of weaning, specific foods liked and disliked, frequency of consumption of various foods, and mother's diet during pregnancy.

The questionnaire included a query on whether the child was seen by a doctor for asthma. The asthma history inventory included characteristic symptoms both in the past and at the present.

The frequency of intake of various foods was classified according to the following five categories: 4-5 or more times, 2-3 times, once a week, once or twice a month, and less than once a month (Table 2). Fish was classified as reddish fish which contains a great deal of eicosapentaenoic or docosahexaenoic acid, or pale fish which has lower fat content. The consumption of other marine products, such as shellfish, seaweed, dried fish and fish-paste products, was also surveyed (Table 3).

ANALYSIS

1. Statistical Test

Chi-square test (2x2 Table) and the Cochran-Armitage test for dose-response relationship were used to analyze the relationship between the history of asthma and the consumption of each type of food. The monthly frequency of consumption of food of each type was assessed and used as a score in the Cochran-Armitage test (Table 2).

Table 2 Frequency of Cnsumption and Cochran-Armitage Test Score

Ranked frequency of consumption	Weekly (or monthly)	Score
Very often	More than 4 - 5 times/week	17
Relatively often	2 - 3 times/week	9
Often	Once a week	4
Infrequently	Once or twice a month	1
Seldom	Less than once a month	0

2. Adjustment for Confounding Factors

The relationship between fish intake and asthma was examined after the exclusion of children with possible confounding factors, which were identified during the course of this study. These included a past history of pneumonia, food allergy, or parasitic disease, domestic or environmental factors, and other allergy manifestations.

RESULTS

1. Response to the Questionnaire

A total of 7,588 returned questionnaires were collected from the parents of the 7,742 children (98.0% return). Responses were obtained regarding 3,746 boys, 3,689 girls, and 153 children whose sex was not identified on the returned questionnaire. In the coastal areas, 4,742 responses, regarding 2,388 boys, 2,333 girls and 21 children whose sex was not identified, were collected. In the inland areas, 2,433 responses, regarding 1,213 boys, 1,210 girls, and 10 children whose sex was not identified, were collected.

Table 3 Prevalence of History of Asthma by Frequency of Consumption of Various Foods

Type of food	Very often (More than 4-5 times/week)		Relatively often (2-3 times/week)		Often (once a week)		Infreqently (once or twice a month)		Seldom	
	Number of children	Asthma (%)	Number of children	Asthma (%)	Number of children	Asthma(%)	Number of children	Asthma(%)	Number of children	Asthma(%)
Reddish fish (sardine, mackerel, pike)	385	32(7.8)	1,723	142(8.2)	2,751	290(10.5)	1,612	152(9.4)	413	45(10.9) *
Pale fish (flatfish, sea bream, turbot)	326	25(7.7)	1,349	137(10.2)	2,408	233(9.7)	2,100	199(9.5)	702	64(9.1)
Shellfish	107	8(7.5)	440	53(12.0)	1,929	191(9.9)	3,412	320(9.4)	990	85(8.6)
Fish-paste	128	11(8.6)	823	87(10.6)	2,261	208(9.2)	2,589	259(10.0)	1,020	86(8.4)
Seaweed	781	85(10.9)	2,533	246(9.7)	2,308	213(9.2)	953	86(9.0)	307	28(9.1)
Dried fish	352	25(7.1)	1,185	110(9.3)	2,259	237(10.5)	1,989	191(9.6)	1,094	95(8.7)
Boiled rice	5,844	555(9.5)	939	85(9.1)	86	11(12.8)	22	4(18.2)	15	2(13.3)
Noodles, buckwheat noodles	353	36(10.2)	1,551	136(8.8)	3,087	294(9.5)	1,809	182(10.1)	100	10(10.0)
Cup-noodles	136	16(11.8)	396	34(8.6)	1,777	178(10.0)	3,264	288(8.8)	1,309	141(10.8)
Milk	4,183	399(9.5)	1,413	131(9.3)	653	53(8.1)	368	39(10.6)	277	36(13.0)
Mayonnaise	642	59(9.2)	2,401	231(9.6)	2,251	209(9.3)	1,106	113(10.2)	481	46(9.6)
Pork	693	58(8.4)	3,215	308(9.6)	2,081	213(10.2)	680	60(8.9)	219	19(8.7)
Chicken	353	22(6.2)	2,199	217(9.9)	2,871	286(10.0)	1,255	109(8.7)	207	22(10.6)
Sausage	257	19(7.4)	1,217	129(10.6)	2,401	238(9.9)	2,209	206(9.3)	793	66(8.3)
Bean curd	1,302	117(9.0)	2,887	267(9.2)	1,897	191(10.1)	627	67(10.7)	173	14(8.1)
Bean paste	4,580	434(9.5)	1,517	144(9.5)	499	56(11.2)	209	11(5.3)	87	131(14.9)
Bamboo shoot	35	2(5.7)	118	6(5.1)	559	55(9.8)	2,963	283(9.6)	3,192	309(9.7)
Yam	64	5(7.8)	242	24(9.9)	838	73(8.7)	2,793	251(9.0)	2,938	301(10.3)
Bread	2,178	224(10.3)	2,780	259(9.3)	1,453	130(8.9)	428	40(9.3)	57	6(10.5)
Spaghetti	195	17(8.7)	613	64(10.4)	2,206	200(9.1)	3,431	342(10.0)	443	35(7.9)
Egg	2,406	218(9.1)	3,269	303(9.3)	931	104(11.2)	205	24(11.7)	80	9(11.3)
Cheese	253	22(8.7)	946	81(8.6)	2,051	190(9.3)	2,316	238(10.3)	1,317	125(9.5)
Ice cream	1,323	146(11.0)	2,183	217(9.9)	1,865	161(8.6)	1,223	112(9.2)	287	21(7.3)*
Beef	279	25(9.0)	1,067	109(10.2)	1,816	184(10.1)	2,238	211(9.4)	1,481	129(8.7)
Ham	418	40(9.6)	1,966	193(9.8)	2,743	260(9.5)	1,460	135(9.2)	297	29(9.8)
Liver and other organ meats	54	4(7.4)	248	24(9.7)	1,033	96(9.3)	2,528	248(9.8)	3,015	284(9.4)
Fermented beans	645	52(8.1)	1,726	155(9.0)	1,838	170(9.2)	1,128	115(10.2)	1,540	165(10.7)*
Chocolate	426	42(9.9)	1,214	107(8.8)	2,048	215(10.5)	2,274	218(9.6)	924	76(8.2)
Taro	96	10(10.4)	520	36(6.9)	1,648	141(8.6)	2,487	250(10.1)	2,128	220(10.3)*
Eggplant	158	5(3.2)	825	66(8.0)	1,869	164(8.8)	2,029	231(11.4)	1,986	190(9.6)**

* $0.01 < p < 0.05$ ** $p < 0.01$ (Cochran-Armitage Test)

2. Relationship between History of Asthma and Amount of Fish Consumption

There was a significant negative correlation between the history of asthma and the frequency of fish consumption (Cochran-Armitage test ; $p<0.05$) (Table 3). The frequency of a history of asthma was also significantly decreased in those who frequently ate eggplant ($p<0.01$), taro ($p<0.05$), and fermented soybeans ($p<0.05$), while those who frequently ate ice cream had a significantly higher frequency of history of asthma ($p<0.05$). No significant relationship with history of asthma was observed for any other food.

3. History of Asthma and Sex Difference

The total of 706 children with a history of asthma consisted of 411 boys (11.1%) and 280 girls (7.6%). The boy-to-girl ratio was 1.35 : 1.

Of the children in coastal areas, 445 (9.5%) had a history of asthma, (267, boys, (11.2%) ; 178, girls, (7.6%) ; boy-to-girl ratio, 1.47 : 1 (Table 4).

In inland areas, 221 children (9.1%) had a history of asthma, numbering 126 boys (10.4%) and 95 girls (7.9%) with the boy-to-girl ratio being 1.32 : 1. There was little difference between the children at coastal and inland schools in the prevalence of history of asthma (Table 4).

Table 4 Prevalence of History of Asthma in Coastal and Inland Schoolchildren

Grade in school	Coastal schools		Inland schools	
	Number of Children	with History of Asthma (%)	Number of Children	with History of Asthma (%)
First-grade	1,533	132(8.6)	783	73(9.3)
Third-grade	1,542	153(9.9)	820	77(9.4)
Fifth-grade	1,667	165(9.9)	830	71(8.6)
Total	4,742	450(9.5)	2,433	211(9.1)

4. History of Asthma and Consumption of Reddish Fish

In elementary school children in coastal areas, there was a significantly lower frequency of history of asthma in those who very often ate reddish fish compared to those who seldom ate it (Cochran-Armitage test, $p<0.01$; Table 5). On the other hand, in the children in inland areas, no significant difference was found between those groups in the history of asthma. The prevalence of a history of asthma in the children in inland areas, however, was significantly higher in those who ate either pale fish or seaweed very often compared to those who ate it seldom ($p<0.01$; Table 5).

5. Confounding Factors for Frequency of History of Asthma in Children in Coastal Areas

1) History of Other Diseases

The diseases either present currently or past which were correlated with history of asthma were pneumonia, eczema during weaning, general eczema, urticaria, and food allergy ($p<0.01$; Table 6). The prevalence of history of asthma was significantly higher in children with any of these diseases than in those without ($p<0.05$), Nevertheless, the latter children relationship for Reddish Fish consumption and history of asthma ($p<0.05$; Table 7).

2) Environmental Factors

Significantly more children with asthma in the coastal areas had air conditioners in their homes than did those without ($p<0.05$; Table 8). There was a significant difference between those who reported the air in their house to be dusty and those who did not in the prevalence of asthma ($p<0.01$) as

Table 6 Relationship between History of Asthma and Other Disease, in Children in Coastal Areas

Past history of disease	Presence	Number of children	Asthma (%)
Pneumonia	Yes	230	40(17.4)
	No	4,512	410(9.1) **
Eczema or pimple-like growths during weaning	Yes	1,037	169(16.2)
	No	3,591	278(7.7) **
Eczema, hives	Yes	385	65(16.9)
	No	4,357	385(8.8) **
Food allergy	Yes	156	36(23.1)
	No	4,586	414(9.0) **

** $p<0.01$ (χ^2test)

Table 5 Prevalence of History of Asthma and Frequency of Consumption of Various Foods in Children at Coastal and Inland Schools

Location of shools and Type of food	Very often (More than 4-5 times/week)		Relatively often (2-3 times/week)		Often (once a week)		Infreqently (once or twice a month)		Seldom	
	Number of children	Asthma (%)	Number of children	Asthma (%)	Number of children	Asthma(%)	Number of children	Asthma(%)	Number of children	Asthma(%)
Coastal Inland Schools										
Reddish fish (sardine, mackerel pike)	275	20(7.3)	1,140	88(7.7)	1,727	187(10.8)	1,099	114(10.4)	289	32(11.1) **
Pale fish (flatfish, sea bream, turbot)	247	15(6.1)	993	89(9.0)	1,548	160(10.3)	1,296	134(10.3)	448	42(9.4)
Shellfish	78	5(6.4)	289	35(12.1)	1,281	129(10.1)	2,236	213(9.5)	642	59(9.2)
Fish-paste	94	8(8.6)	499	55(11.0)	1,487	139(9.3)	1,723	175(10.2)	890	58(8.4)
Seaweed	514	52(10.1)	1,710	161(9.4)	1,492	152(10.2)	620	57(9.2)	191	19(9.9)
Dried fish	259	18(6.9)	792	75(9.5)	1,428	156(10.9)	1,283	119(9.3)	763	73(9.6)
Inland Schools										
Reddish fish (sardine, mackerel pike)	110	10(9.1)	583	54(9.3)	1,024	103(10.1)	513	38(7.4)	124	13(10.5)
Pale fish (flatfish, sea bream, turbot)	79	10(12.7)	356	48(13.5)	860	73(8.5)	804	65(8.1)	254	22(8.7) **
Shellfish	29	3(10.3)	151	18(11.9)	648	62(9.6)	1,176	107(9.1)	348	26(7.5)
Fish-paste	34	3(8.8)	324	32(9.9)	774	69(8.9)	866	84(9.7)	330	28(8.5)
Seaweed	267	33(12.4)	823	85(10.3)	816	61(7.5)	333	29(8.7)	116	9(7.8) *
Dried fish	93	7(7.5)	393	35(8.9)	831	81(9.7)	706	72(10.2)	331	22(6.6)

* $0.01<p<0.05$, ** $p<0.01$ (Cochran-Armitage Test)

Table 7 Prevalence of History of Asthma and Frequency of Reddish fish Consumption in Coastal School Children without Past History of the Diseases shown in Table 6

Excluded	Very often (More than 4-5 times/week)		Relatively often (2 - 3 times/week)		Often (once a week)		Infreqently (once or twice a month)		Seldom	
	Number of children	Asthma(%)	Number of children	Asthma(%)	Number of children	Asthma(%)	Number of children	Asthma(%)	Number of children	Asthma(%)
Pneumonia	265	20(7.5)	1,084	78(7.2)	1,634	168(10.3)	1,050	106(10.1)	276	29(10.5) *
Eczema or pimple-like growths during weaning period	215	12(5.6)	889	50(5.6)	1,276	105(8.2)	819	80(9.8)	229	24(10.5) **
Eczema, hives	257	15(5.8)	1,052	80(7.6)	1,578	163(10.3)	1,010	94(9.3)	260	26(10.0) *
Alimentary allergy	263	18(6.8)	1,112	83(7.5)	1,664	171(10.3)	1,060	105(9.9)	282	31(11.0) *

* 0.01<p<0.05, ** p<0.01 (Cochran-Armitage Test)

Table 8 prevalence of History of Asthma in Children in Coastal Areas and Their Domestic Environment

Factors	Presence	Number of Children	Asthma(%)
Carpet	Yes	2,956	285(9.6)
	No	1,786	165(9.2)
Down quilt	Yes	634	48(7.6)
	No	4,108	402(9.8)
Air conditioner	Yes	1,197	132(11.0)
	No	3,545	318(9.0) **
Fanning heater	Yes	1,495	147(9.8)
	No	3,247	303(9.3)
Heater (Standard type)	Yes	2,964	273(9.2)
	No	1,778	177(10.0)
Dust	Yes	413	57(13.8)
	No	4,329	393(9.1) **
Bed (or futon)	Yes	1,965	195(9.9)
	No	2,777	255(9.2)
Pet	Yes	1,763	154(8.7)
	No	2,979	296(9.9)
Steamer	Yes	471	41(8.7)
	No	4,271	409(9.6)
Pillow (Buckwheat-hull type)	Yes	2,553	204(8.0)
	No	2,189	246(11.2) **
Flowers in room	Yes	908	87(8.9)
	No	3,762	363(9.6)
Smoker in family	Yes	2,793	288(10.3)
	No	1,949	162(8.3) **

* 0.01<p<0.05, ** p<0.01 (χ^2test)

Table 9 Prevalence of History of Asthma and Presence of Specific Environment of Children in Coastal Areas

Factors	Presence	Number of Children	Asthma (%)	
Strawberry field	Yes	238	22	(9.2)
	No	4,504	428	(9.5)
Hen-house	Yes	577	63	(10.9)
	No	4,165	387	(9.3)
Pasture	Yes	200	28	(14.0)
	No	4,542	422	(9.3) *
Livestock house	Yes	508	58	(11.0)
	No	4,234	394	(9.3)
Mushroom plantation	Yes	131	9	(6.9)
	No	4,611	441	(9.6)
Rice field	Yes	1,513	142	(9.4)
	No	3,229	308	(9.5)
Cryptomeria wood	Yes	548	47	(8.6)
	No	4,194	403	(9.6)
Dry riverbed	Yes	433	38	(8.8)
	No	4,309	412	(9.6)
Chemical factory	Yes	42	6	(14.3)
	No	4,700	444	(9.4)
Humid environment	Yes	660	77	(11.7)
	No	4,082	373	(9.1) *
Air pollution	Yes	92	9	(9.8)
	No	4,650	441	(9.5)
Considerable temperature difference day/night	Yes	701	93	(13.3)
	No	4,041	357	(8.8) *

* 0.01<p<0.05, ** p<0.01 (χ^2test)

was also found for those who reported a considerable temperature difference between day and night ($p<0.01$; Table 9). Asthma was more frequently observed in children with at least one who smoked ($p<0.01$). The prevalence of asthma in those who lived near pasture land was significantly higher ($p<0.05$) than that in those who did not.

The prevalence of asthma after exclusion of each associated factor and its relationship to reddish fish consumption are shown in Table 10. The history of asthma decreased as the frequency of fish consumption increased even after exclusion of these confounding factors.

Table 10 Prevalence of History of Asthma in Children at Coastal Areas after Exclusion of Each Confounding Factor with Reddish Fish Consumption

Excluded Confounding Factor	Very often (More than 4-5 times/week)		Relatively often (2-3 times/week)		Often (once a week)		Infreqently (once or twice a month)		Seldom	
	Number of children	Asthma (%)	Number of children	Asthma (%)	Number of children	Asthma(%)	Number of children	Asthma(%)	Number of children	Asthma(%)
Air-conditioned house	226	14(6.2)	891	66(7.4)	1,288	135(10.6)	784	75(9.6)	201	22(10.9) *
Dustiness	258	19(7.4)	1,050	80(7.6)	1,576	165(10.5)	995	96(9.6)	253	28(11.1) *
Pasture	260	20(7.7)	1,102	84(7.6)	1,651	174(10.5)	1,052	105(10.0)	278	31(11.2) *
Considerable temperature difference of day/night	225	17(7.6)	963	69(7.2)	1,448	145(10.0)	950	94(9.9)	255	25(9.8) *
Humid house	232	17(7.3)	976	71(7.3)	1,479	157(10.6)	942	95(10.1)	250	24(9.6) *
Smoker in family	111	4(3.6)	443	31(7.0)	663	66(10.0)	430	40(9.3)	127	14(11.0) *
Pillow (buckwheat-hull type)	134	15(11.2)	453	34(7.5)	761	97(12.7)	552	76(13.8)	161	17(10.6) *
Ingestion of fermented beans (during pregnancy)	246	15(5.8)	1,038	77(7.4)	1,534	163(10.6)	993	98(9.9)	284	28(9.8) *
Ingestion of mushrooms (during pregnancy)	258	20(7.8)	1,069	80(7.5)	1,627	172(10.6)	1,014	104(10.3)	289	26(9.7) *

* 0.01<p<0.05 (Cochran-Armitage Test)

Table 11 Prevalence of History of Asthma and Frequency of Eating Specific Foods during Pregnancy

Diet	Consumption Prevalence	Number of children	Asthma (%)
Fermented beans	>= Often	460	63 (13.7)
	=< Infrequently	4,282	387 (9.0) **
Mushrooms	>= Often	303	39 (12.9)
	=< Infrequently	4,439	411 (9.3) *

* 0.01<p<0.05 ** p>0.01 (χ^2test)

3) Maternal Diet During Pregnancy

The types of food which had been more frequently eaten intentionally during pregnancy by mothers of children with asthmatic history included fermented beans ($p<0.01$) and mushrooms ($p<0.05$; Table 11). The Cochran-Armitage test after excluding these dietary factors showed that reddish fish was still significantly associated with a lower frequency of asthma (Table 10). There was no relationship between any food eaten during the weaning period and the history of asthma.

6. Other Allergic Diseases

The children in the coastal areas with asthma only showed a significant relationship between fish consumption and prevalence of asthma, while those with asthma complicated with other allergic manifestations such as rhinitis or atopic dermatitis did not. (Cochran-Armitage test, $p<0.05$; Table 12).

DISCUSSION

The leukotrienes formed from eicosapentaenoic acid, than those formed from arachidonic acid, have been reported to have much weaker bioactivity.

Table 12 History of Asthma with or without Other Allergic Complications and Frequency of Consumption of Reddish fish in Children at Coastal Areas

Allergic complication	Very often (More than 4-5 times/week)	Relatively often (2-3 times/week)	Often (once a week)	Infreqently (once or twice a month)	Seldom
	Number of children (%)	Number of children (%)	Number of children (%)	Number of children (%)	Number of children (%)
Non-asthmatic	255 (92.7)	1,052 (92.3)	1,540 (89.2)	985 (89.6)	257 (88.9)
Asthma only	10 (3.6)	42 (3.7)	84 (4.9)	54 (4.9)	21 (7.3) *
Asthma with rrinitis	4 (1.5)	12 (1.1)	49 (2.8)	21 (1.9)	5 (1.7)
Asthma with atopic dermatitis	4 (1.5)	16 (1.4)	29 (1.7)	16 (1.5)	1 (0.3)
Asthma with rhinitis and atopic dermatitis	2 (0.7)	18 (1.6)	25 (1.4)	23 (2.1)	5 (1.7)
Total	275 (100.0)	1,140 (100.0)	1,727 (100.0)	1,099 (100.0)	289 (100.0)

* 0.01<p<0.05, ** p<0.01 (Cochran-Armitage Test)

This finding may be related to various mechanisms in the pathogenesis of asthma, including enhancement of vascular permeability, chemotaxis, chemokinesis or aggregation of leucocytes[11-13]. Kromann et al., in their follow-up study of Eskimos in Greenland, reported that the frequency of bronchial asthma is only 1/25th that in Danish people[14]. Although the mechanisms involved in the physiological actions of the eicosapentaenoic acid in fish require further investigation, our results are consistent with these previous observations. Miyake et al. reported that the prevalence of asthma in suburban children assessed using a questionnaire was 11.2% (135% in boys and 9.0% in girls), which is similar to the 9.3% (boys 11.0% and girls 7.6%) found in the present study[15].

A relationship between asthma history and frequency of reddish fish consumption was found in children in the coastal areas, but not in those in the inland areas. This difference is thought to be due to the amount of fish eaten and its freshness.

National Nutrition Survey reports indicate that the average daily intake of marine products per capita in Japanese was 94g in 1975 and 91.5g in 1984[16]. These figures indicate a slight decrease. According to Hirai et al., in Chiba prefecture, the average daily per capita fish consumption in agricultural villages was about 90g, while that in fishing 250g per person respectively[17]. Kagawa et al. reported that the average daily consumption of fish, other than dried fish of people over 65 years of age in isolated small islands in Okinawa Prefecture was to 147g, and that their serum concentrations of eicosapentaenoic and docosahexaenoic acids were high[18].

They pointed out that the values they obtained in Okinawa were intermediate between those of Eskimos, whose mainstay is fish, and those of Caucasians, who eat fish less frequently. This finding suggests that the amount of fish eaten in coastal areas may differ from that in inland areas, even though the frequency of consumption in the two areas is similar. It is possible that even when the frequency of eating reddish fish in inland areas is high, the quantity is in sufficient to reduce the prevalence of asthma episodes.

Eicosapentaenoic and docosahexaenoic acids are easily oxidized because of the presence of double bonds in their molecular structures. Accordingly, the freshness of fish be an important factor in the difference between the coastal and inland areas in the relationship of fish intake to asthma history; while fresh, non-oxidized fish is readily available in coastal areas, This is not necessarily so in inland areas.

The prevalence of history of asthma was high in the children in inland area who frequently ate pale fish and sea-weed. The parents of asthmatic children may have avoided serving reddish fish, which can induce increased level of histamine, a possible cause of urticaria, when stale.

The rate of oxidation of the eicosapenaenoic and docosahexaenoic acids in pale fish is lower than that in reddish fish. This factor have been involved in the preference for pale fish shown the parents whose children suffered from allergic diseases. Thus, even when a considerable amount of fish is eaten in inland areas, it may not be effective in preventing asthma.

There was also a significant dose-response relationship between the frequency of history of asthma and consumption of eggplant and taro. This finding would be due to parental restriction of eating such vegetables in the hope of preventing asthma episodes. Vegetables such as eggplant, and taro which contain choline are defined as pseudoallergens, and it is recommended that the they be avoided in a widely distributed guide book on allergic diseases for lay readers[18].

When the asthmatic children were classified as having asthma only or asthma complicated with rhinitis or atopic dermatitis, only the former group

showed significant effect due to the frequent consumption of reddish fish. Dietary fish can suppress asthmatic attacks effectively when the asthma is not severe and is without complications, but it may not be effective for severer asthma associated with other allergic complications.

In the present study, the current diet rather than long-term dietary habits was examined. On of the entire dietary history could not the limitations of our study was that be thoroughly examined. The dietary habits of school children, however, were found to be rather stable, and the recent diet probably also reflects long-term dietary habits. We consider that an intervention study in which asthmatic children are treated with dietary fish would be useful in determining whether the present conclusions are correct.

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