

Maternal meat and fat consumption during pregnancy and suspected atopic eczema in Japanese infants aged 3–4 months: The Osaka Maternal and Child Health Study

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Interest has increased in the possibility that maternal dietary intake during pregnancy might influence the development of allergic disorders in children. The present prospective study examined the association of maternal intake of selected foods high in fatty acids and specific types of fatty acids during pregnancy with the risk of suspected atopic eczema among Japanese infants aged 3–4 months. Subjects were 771 mother–child pairs. Information on maternal dietary intake during pregnancy was assessed with a validated self-administered diet history questionnaire. The term ‘suspected atopic eczema’ was used to define an outcome based on results of our questionnaire completed by mothers 3–4 months postpartum. The risk of suspected atopic eczema was 8.4% ($n = 65$). Higher maternal intake of meat during pregnancy was significantly associated with an increased risk of suspected atopic eczema in the offspring: the multivariate odds ratio (OR) for the highest vs. lowest quartile was 2.59 [95% confidence interval (CI): 1.15–6.17, p for trend = 0.01]. The positive association was strengthened when the definition of the outcome was confined to a definite physician’s diagnosis of atopic eczema ($n = 35$): the multivariate OR between extreme quartiles was 3.53 (95% CI: 1.19–12.23, p for trend = 0.02). No material exposure–response relationships were observed between maternal intake of eggs, dairy products, fish, total fat, saturated fatty acids, monounsaturated fatty acids, n-3 polyunsaturated fatty acids, α -linolenic acid, eicosapentaenoic acid, docosahexaenoic acid, n-6 polyunsaturated fatty acids, linoleic acid, arachidonic acid and cholesterol and the ratio of n-3 to n-6 polyunsaturated fatty acid consumption and the risk of suspected atopic eczema. Higher maternal meat intake may increase the risk of infantile atopic eczema, whereas we found no evidence that maternal intake of fish and n-3 polyunsaturated fatty acids are preventive against infantile atopic eczema.

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Although atopic eczema is a multifactorial disease, there is little convincing evidence regarding risk factors for the disease (1). One possible risk factor is diet. The increase in the prevalence of atopic eczema over the past decades might be

partially ascribed to westernization of eating habits. A study of Japanese male adults found an increase in intake of fat from 5% to 20%, of fish from 56 to 71 g/day and of meat from 13 to 92 g/day from 1958 to 1999 (2).

A growing body of literature has addressed the issue of the role of dietary fatty acids in allergic disorders, especially in asthma and allergic rhinitis (3–7). Also, a few studies investigated the associations between intake of fatty acids and/or foods high in fat and atopic eczema (8–10). Among Norwegian female adult patients with moderate-to-severe atopic eczema, saturated fatty acid intake was higher whereas eicosapentaenoic and docosahexaenoic acid consumption was lower compared with the reference group (8). A case-control study in Finland showed that children with atopic eczema consumed more margarine and less butter than non-atopic children and that serum eicosapentaenoic and docosahexaenoic acid levels were significantly lower in those with atopic eczema (9). In a cross-sectional study of German adults, intake of butter and margarine was not related to the prevalence of atopic eczema whereas inverse dose-response relationships of α -linolenic acid intake and the ratio of n-3 to n-6 fatty acids with atopic eczema were statistically significant in females (10).

Recently, interest has increased in the possibility that maternal dietary intake during pregnancy may influence the development of allergic disorders in children. Especially, variations in fat intake during pregnancy might influence the developing immune response (11). A cohort study of the UK infants reported that maternal intake of fish during pregnancy was related to a decreased risk of eczema in these children whereas no material associations were observed between maternal consumption of fat from dairy products or butter vs. margarine/low fat spread use and the risk of eczema (12). In a prospective study among German infants, maternal intake of margarine and vegetable oils during pregnancy was positively associated and maternal fish intake was inversely associated with the risk of eczema in the offspring (13). A significant inverse relationship between maternal fish intake during pregnancy and the risk of eczema at 1 yr was found in a Spanish cohort study (14).

In view of the paucity of epidemiological information regarding the relationship between maternal intake of high-fat foods and fatty acids and the risk of atopic eczema in the offspring, the present prospective study examined the association of maternal intake of selected foods high in fatty acids, specific types of fatty acids and cholesterol during pregnancy with the risk of suspected atopic eczema among their infants aged 3–4 months using data from the Osaka Maternal and Child Health Study (OMCHS).

Methods

Study population

The OMCHS is a prospective cohort study that investigates preventive and risk factors for maternal and child health problems such as allergic disorders. Pregnant women were recruited for the baseline survey of the OMCHS. Eligible pregnant women were those who lived in Neyagawa City, which is one of the 43 municipalities in Osaka Prefecture, a metropolis in Japan with a total population of approximately 8.8 million. In Japan, when females become pregnant, they notify the municipality of the domicile of the expectant mother and the municipality provides them with a maternal and child health handbook. During the period from November 2001 to March 2003, the Neyagawa City Government provided all pregnant females with a set of leaflets explaining the OMCHS, an application form to become part of the study, and a self-addressed and stamped return envelope together with the maternal and child health handbook. Women who wanted to take part in the OMCHS filled out the application form and returned it to the data management centre. Research technicians contacted all eligible women who had not returned the application form and asked if they would participate in the OMCHS. Of the 3639 eligible subjects in Neyagawa City, 627 pregnant females (17.2%) participated in the OMCHS.

In order to increase the sample size, pregnant women living in municipalities other than Neyagawa City were also recruited. However, the exact number of eligible subjects among the sources from which these women were recruited was not available. Eight pregnant females who did not live in Neyagawa City but who had become aware of the OMCHS at an obstetric clinic before August 2002 decided by themselves to participate in the OMCHS. Also, there were 77 participants who received explanations of the OMCHS from public health nurses in six other municipalities from August 2002 to March 2003. From October 2002 to March 2003, 290 participants were recruited from a university hospital and three obstetric hospitals in three other municipalities; these women were recommended for participation in the OMCHS by an obstetrician.

Finally, a total of 1002 women at any stage of pregnancy gave their fully informed consent in writing and completed the baseline survey. Of the 1002 females, 867 mother-child pairs participated in the second survey. The second survey was done from 2 to 9 months postpartum, with 432, 339 and 63 parent-child pairs participating

at 3, 4 and 5 months after delivery respectively. The remaining 31 pairs completed the survey at 2, 6, 7, 8 or 9 months postpartum. After excluding 96 mother-child pairs who participated in the second survey at 2, 5, 6, 7, 8 and 9 months postpartum, the final sample for analysis comprised 771 mother-child pairs. The ethics committee of the Osaka City University School of Medicine approved the OMCHS.

Measurements

At baseline, each participant filled out a set of two self-administered questionnaires and collected a dust sample from a 1 m² area of the bedclothes [futon (Japanese-style bedding) or mattress surface] for 1 min using a non-woven fabric bag, which was sent to participants together with instructions for its use and was then inserted into the participant's home electric vacuum cleaner having a motor of 1000 W or less. A third self-administered questionnaire was additionally answered in the second survey. Participants mailed these materials to the data management centre at the time of each survey. Research technicians completed missing or illogical data by telephone interview.

In the baseline survey, dietary habits during the preceding month were assessed with a self-administered, comprehensive, diet history questionnaire (DHQ) (15, 16). Estimates of daily intake for a total 150 food items, energy and selected nutrients were calculated using an *ad hoc* computer algorithm for the DHQ, which was based on the Standard Tables of Food Composition in Japan (17, 18). Information on dietary supplements was not used in the calculation of dietary intake. Detailed descriptions of the methods used for calculating dietary intake and the validity of the DHQ were published elsewhere (15, 16). Regarding the current study, the correlation coefficients for nutrient intake between those estimated from the DHQ and those observed by a 3-day dietary record were 0.75, 0.50, 0.37 and 0.49 for saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids and cholesterol, respectively, in women (15). A highly positive correlation was also observed between marine-origin n-3 polyunsaturated fatty acid intake estimated by the DHQ and the corresponding concentration in the serum phospholipid fraction in women ($r = 0.69$) (16). Energy-adjusted intake by the residual method was used for the analyses (19).

A second questionnaire at baseline asked about maternal age, gestation, family income, maternal and paternal education, maternal and

paternal history of asthma, atopic eczema and allergic rhinitis, vacuuming practices, presence of mould in the kitchen and changes in diet in the previous 1 month. A paternal or maternal history of asthma, atopic eczema and allergic rhinitis was defined as positive if the respective parent had been treated with medications for any of these allergic disorders at some time prior to the start of the survey. Antigen levels from extracts of fine dust fractions were determined by a commercially available simple semi-quantitative test (Mitey checker[®]; Shinto Fine Co., Ltd, Osaka, Japan) (20, 21). Mitey checker[®] is a double-antibody sandwich enzyme-linked immunosorbent assay using a soluble antigen prepared from whole *Dermatophagoides farinae* mite bodies as a reference standard. Antigen levels were semi-quantitatively classified with scores of $- (< 2 \mu\text{g}/\text{m}^2)$, $\pm (5 \mu\text{g}/\text{m}^2)$, $+(10-15 \mu\text{g}/\text{m}^2)$ and $++ (> 35 \mu\text{g}/\text{m}^2)$.

A self-administered questionnaire in the second survey inquired about the baby's sex, birth weight, date of birth of the infant born after the baseline survey, number of baby's older siblings, breastfeeding duration, frequency of bathing or showering the infant and atopic eczema status. Suspected atopic eczema was considered to be present if the mother selected any one of the following answers to the written question 'Has your child been diagnosed by a physician as having atopic eczema and treated with topical steroids?': (i) my child has been diagnosed with atopic eczema and treated with topical steroids ($n = 23$); (ii) my child has been diagnosed with atopic eczema but has not been treated with topical steroids ($n = 11$); (iii) my child has been diagnosed with atopic eczema and treated with a unknown ointment ($n = 1$); (iv) my child has been diagnosed as possibly having atopic eczema and has been treated with topical steroids ($n = 29$) or (v) my child has been diagnosed as possibly having atopic eczema but has not been treated with topical steroids ($n = 1$).

Statistical analysis

Intake of selected foods rich in fat and specific types of fatty acids under study was categorized at quartile points based on the distribution in 771 subjects. Maternal age (continuous), gestation (continuous), family income ($< 4,000,000$, $4,000,000-5,999,999$ and $6,000,000+$ yen/yr), maternal and paternal education (< 13 , $13-14$ and $15+$ yr), maternal and paternal history of asthma, atopic eczema and allergic rhinitis, changes in maternal diet in the previous month (none or seldom, slight and substantial), season

when data at baseline were collected (spring, summer, autumn and winter), baby's older siblings (0 and 1 +), baby's sex, baby's birth weight (continuous) and breastfeeding (never or stopped sometime before the second survey and still breastfeeding at the second survey) were selected *a priori* as potential confounding factors. The following variables associated with the home environment were also adjusted for in the multivariate model because they were significantly related to the risk of suspected atopic eczema in our previous analyses (22): mite allergen level in house dust at baseline (–, ±, + and ++), vacuuming living room at baseline (< 3 times and three times or more per week), mould in the kitchen at baseline and bathing or showering the infant (less than and at least once a day).

Logistic regression analysis was used to calculate crude odds ratios (ORs) and 95% confidence intervals (CIs) of suspected atopic eczema in relation to consumption of the selected dietary factors under study. Multiple logistic regression analysis was used to adjust for the potential confounding factors under investigation. Trend of association was assessed by a logistic regression model assigning consecutive integers (1–4) to the quartiles of the exposure variables. All computations were performed using SAS software, version 9.1 (SAS Institute, Inc., Cary, NC, USA).

Results

Of the 771 infants, 65 (8.4%) had suspected atopic eczema during the period from birth until the second survey. The mean age of the 771 mothers was 29.9 yr at baseline (Table 1). Slight or substantial changes in diet in the previous 1 month were reported by 559 mothers caused by nausea gravidarum (n = 463), maternal and foetal health (n = 88) and other reasons (n = 8). Mean daily total energy and energy-adjusted consumption of meat and total fat were 7638 kJ, 59.7 g and 61.7 g, respectively (Table 2).

Table 3 provides ORs and the 95% CIs for the risk of suspected atopic eczema associated with maternal intake of selected foods high in fat during pregnancy. Compared with maternal meat intake in the first quartile, consumption of that in the fourth quartile was significantly associated with an increased risk of suspected atopic eczema in the offspring, showing a clear positive exposure–response relationship. The positive association was slightly strengthened after adjustment for maternal age, gestation at baseline, family income, maternal and paternal

Table 1. Distribution of selected characteristics of 771 parent–child pairs, OMCHS, Japan

Variable	n (%) or mean (s.d.)
Baseline characteristics	
Maternal age (years)	29.9 (4.0)
Gestation (weeks)	17.8 (6.8)
Family income (% Japanese yen/year)*	
<4,000,000	224 (29.1)
4,000,000–5,999,999	306 (39.7)
6,000,000+	241 (31.3)
Maternal education (% years)	
<13	221 (28.7)
13–14	327 (42.4)
15+	223 (28.9)
Paternal education (% years)	
<13	300 (38.9)
13–14	122 (15.8)
15+	349 (45.3)
Maternal history of asthma (%)	81 (10.5)
Maternal history of atopic eczema (%)	122 (15.8)
Maternal history of allergic rhinitis (%)	267 (34.6)
Paternal history of asthma (%)	67 (8.7)
Paternal history of atopic eczema (%)	78 (10.1)
Paternal history of allergic rhinitis (%)	154 (20.0)
Mite allergen level from maternal bedclothes (%)†	
–	342 (44.4)
±	233 (30.2)
+	148 (19.2)
++	48 (6.2)
Vacuuming living room (%)	
Less than 3 times/week	333 (43.2)
3 times or more/week	438 (56.8)
Mould in kitchen (%)	165 (21.4)
Changes in diet in the previous 1 month (%)	
None or seldom	212 (27.5)
Slight	343 (44.5)
Substantial	216 (28.0)
Season when data were collected (%)	
Spring	250 (32.4)
Summer	125 (16.2)
Autumn	170 (22.1)
Winter	226 (29.3)
Characteristics at the postnatal assessment	
Baby's older siblings (% 1 or more)	378 (49.0)
Baby's sex (% male)	406 (52.7)
Baby's birth weight (g)	3076.6 (407.4)
Breastfeeding (%)	
Never or stopped sometime before the second survey	133 (17.3)
Still breastfeeding at the second survey	638 (82.8)
Bathing or showering infant (%)	
Less than once a day	39 (5.1)
At least once a day	732 (94.9)

*€1 = 160 yen.

†Antigen levels were semi-quantitatively classified with scores of –(<2 µg/m²), ±(5 µg/m²), +(10–15 µg/m²) and ++(>35 µg/m²).

education, maternal and paternal history of asthma, atopic eczema and allergic rhinitis, mite allergen level from maternal bedclothes, vacuuming living room, mould in kitchen, changes in maternal diet in the previous 1 month, season when data at baseline were collected, baby's older siblings, baby's sex, baby's birth weight,

Table 2. Distribution of daily nutrients and food intake in 771 pregnant women, OMCHS, Japan*

Variable	Mean (s.d.)
Daily intake	
Meat (g)	59.7 (28.7)
Eggs (g)	33.8 (24.6)
Dairy products (g)	173.7 (118.6)
Fish (g)	47.8 (27.2)
Daily nutrient intake	
Total energy (kJ)	7638.4 (1931.5)
Total fat (g)	61.7 (10.8)
Saturated fatty acids (g)	17.5 (3.9)
Monounsaturated fatty acids (g)	21.3 (5.0)
n-3 Polyunsaturated fatty acids (g)	2.4 (0.8)
α -Linolenic acid (g)	1.8 (0.6)
Eicosapentaenoic acid (g)	0.17 (0.12)
Docosahexaenoic acid (g)	0.30 (0.18)
n-6 Polyunsaturated fatty acids (g)	11.5 (2.7)
Linoleic acid (g)	11.2 (2.7)
Arachidonic acid (g)	0.14 (0.04)
Cholesterol (mg)	307.8 (111.5)

*Nutrient and food intake were adjusted for total energy intake using the residual method.

breastfeeding and bathing or showering infant: the multivariate OR for comparison of the fourth with the first quartile was 2.59 (95% CI: 1.15–6.17, p for trend = 0.01). There were no evident

associations of maternal intake of eggs, dairy products and fish with the risk of suspected atopic eczema after multivariate adjustment.

Results for maternal intake of specific types of fatty acids and cholesterol are listed in Table 4. No significant exposure–response relationships were observed between maternal intake of total fat, saturated fatty acids, monounsaturated fatty acids, n-3 polyunsaturated fatty acids, α -linolenic acid, eicosapentaenoic acid, docosahexaenoic acid, n-6 polyunsaturated fatty acids, linoleic acid, arachidonic acid and cholesterol and the ratio of n-3 to n-6 polyunsaturated fatty acid consumption and the risk of suspected atopic eczema in the multivariate model. However, significant positive associations with maternal total fat, monounsaturated fatty acid and n-6 polyunsaturated fatty acid intake in the second quartile and α -linolenic acid intake in the third quartile were found.

The significant positive association with maternal meat intake during pregnancy was strengthened when the definition of the outcome was confined to a definite physician's diagnosis of atopic eczema ($n = 35$): the multivariate OR for the highest vs. lowest quartiles was 3.53 (95% CI: 1.19–12.23, p for trend = 0.02).

Table 3. Odds ratios (ORs) and 95% confidence intervals (CIs) for suspected atopic eczema by quartiles of maternal intake of selected foods high in fat during pregnancy in 771 infants aged 3–4 months, OMCHS, Japan

Variable	Quartile				p for trend
	1 ($n = 192$)	2 ($n = 193$)	3 ($n = 193$)	4 ($n = 193$)	
Meat					
Intake (g/day)*	33.4	49.1	63.6	89.8	
No. cases	10	14	19	22	
Crude OR (95% CI)	1.00	1.42 (0.62–3.38)	1.99 (0.92–4.56)	2.34 (1.10–5.30)	0.02
Multivariate OR (95% CI)†	1.00	1.46 (0.61–3.62)	2.41 (1.06–5.75)	2.59 (1.15–6.17)	0.01
Eggs					
Intake (g/day)*	9.7	22.9	40.7	61.3	
No. cases	17	15	19	14	
Crude OR (95% CI)	1.00	0.87 (0.42–1.79)	1.12 (0.57–2.25)	0.81 (0.38–1.68)	0.76
Multivariate OR (95% CI)†	1.00	0.87 (0.40–1.89)	1.37 (0.66–2.86)	0.73 (0.33–1.61)	0.74
Dairy products					
Intake (g/day)*	52.7	126.0	191.0	288.3	
No. cases	13	16	18	18	
Crude OR (95% CI)	1.00	1.24 (0.58–2.71)	1.42 (0.68–3.04)	1.42 (0.68–3.04)	0.33
Multivariate OR (95% CI)†	1.00	1.39 (0.62–3.20)	1.63 (0.73–3.72)	1.84 (0.82–4.27)	0.13
Fish					
Intake (g/day)*	23.0	37.8	51.4	73.1	
No. cases	14	15	21	15	
Crude OR (95% CI)	1.00	1.07 (0.50–2.31)	1.55 (0.77–3.21)	1.07 (0.50–2.31)	0.61
Multivariate OR (95% CI)†	1.00	0.93 (0.41–2.13)	1.60 (0.75–3.51)	1.15 (0.51–2.62)	0.44

*Values for intake are medians for adjusted energy intake using the residual method for each quartile.

†Multivariate models included the following: maternal age, gestation at baseline, family income, maternal and paternal education, maternal and paternal history of asthma, atopic eczema and allergic rhinitis, mite allergen level from maternal bedclothes, vacuuming living room, mould in kitchen, changes in maternal diet in the previous 1 month, season when data at baseline were collected, baby's older siblings, baby's sex, baby's birth weight, breastfeeding and bathing or showering infant.

Table 4. Odds ratios (ORs) and 95% confidence intervals (CIs) for suspected atopic eczema by quartiles of maternal intake of specific fats during pregnancy in 771 infants aged 3–4 months, OMCHS, Japan

Variable	Quartile				p for trend
	1 (n = 192)	2 (n = 193)	3 (n = 193)	4 (n = 193)	
Total fat					
Intake (g/day)*	50.2	58.6	64.6	72.6	
No. cases	11	25	15	14	
Crude OR (95% CI)	1.00	2.45 (1.20–5.33)	1.39 (0.62–3.18)	1.29 (0.57–2.97)	0.94
Multivariate OR (95% CI)†	1.00	2.73 (1.27–6.24)	1.51 (0.64–3.63)	1.38 (0.58–3.33)	0.93
Saturated fatty acids					
Intake (g/day)*	13.4	16.0	18.4	21.7	
No. cases	16	16	19	14	
Crude OR (95% CI)	1.00	0.99 (0.48–2.06)	1.20 (0.60–2.44)	0.86 (0.40–1.82)	0.85
Multivariate OR (95% CI)†	1.00	0.84 (0.38–1.84)	1.34 (0.63–2.87)	0.95 (0.42–2.09)	0.82
Monounsaturated fatty acids					
Intake (g/day)*	16.6	19.9	22.3	25.7	
No. cases	10	25	17	13	
Crude OR (95% CI)	1.00	2.71 (1.30–6.07)	1.76 (0.80–4.08)	1.31 (0.56–3.15)	0.97
Multivariate OR (95% CI)†	1.00	3.50 (1.58–8.33)	1.87 (0.80–4.59)	1.48 (0.61–3.73)	0.88
n-3 Polyunsaturated fatty acids					
Intake (g/day)*	1.7	2.1	2.5	3.0	
No. cases	13	22	14	16	
Crude OR (95% CI)	1.00	1.77 (0.88–3.72)	1.08 (0.49–2.38)	1.25 (0.58–2.71)	0.97
Multivariate OR (95% CI)†	1.00	2.06 (0.97–4.55)	1.33 (0.57–3.11)	1.45 (0.64–3.31)	0.65
α-Linolenic acid					
Intake (g/day)*	1.3	1.6	1.9	2.3	
No. cases	13	19	23	10	
Crude OR (95% CI)	1.00	1.50 (0.73–3.21)	1.86 (0.93–3.90)	0.75 (0.31–1.75)	0.76
Multivariate OR (95% CI)†	1.00	1.59 (0.73–3.57)	2.26 (1.06–5.03)	0.76 (0.30–1.87)	0.91
Eicosapentaenoic acid					
Intake (g/day)*	0.07	0.13	0.18	0.27	
No. cases	13	20	13	19	
Crude OR (95% CI)	1.00	1.59 (0.78–3.37)	0.99 (0.45–2.22)	1.50 (0.73–3.21)	0.53
Multivariate OR (95% CI)†	1.00	1.57 (0.72–3.53)	0.98 (0.41–2.31)	1.84 (0.84–4.15)	0.29
Docosahexaenoic acid					
Intake (g/day)*	0.15	0.24	0.31	0.46	
No. cases	16	14	16	19	
Crude OR (95% CI)	1.00	0.86 (0.40–1.82)	0.99 (0.48–2.06)	1.20 (0.60–2.44)	0.53
Multivariate OR (95% CI)†	1.00	0.96 (0.43–2.11)	0.93 (0.42–2.05)	1.43 (0.68–3.07)	0.38
n-6 Polyunsaturated fatty acids					
Intake (g/day)*	9.0	10.6	12.1	14.1	
No. cases	11	22	20	12	
Crude OR (95% CI)	1.00	2.12 (1.02–4.66)	1.90 (0.90–4.22)	1.09 (0.47–2.58)	0.97
Multivariate OR (95% CI)†	1.00	2.42 (1.11–5.55)	2.06 (0.92–4.81)	1.14 (0.47–2.81)	0.92
Linoleic acid					
Intake (g/day)*	8.8	10.4	11.8	13.8	
No. cases	12	21	20	12	
Crude OR (95% CI)	1.00	1.83 (0.89–3.95)	1.73 (0.83–3.76)	0.99 (0.43–2.30)	0.94
Multivariate OR (95% CI)†	1.00	2.06 (0.96–4.64)	1.87 (0.85–4.27)	1.04 (0.43–2.49)	0.98
Arachidonic acid					
Intake (g/day)*	0.09	0.12	0.15	0.19	
No. cases	17	11	22	15	
Crude OR (95% CI)	1.00	0.62 (0.28–1.35)	1.32 (0.68–2.61)	0.87 (0.42–1.79)	0.78
Multivariate OR (95% CI)†	1.00	0.62 (0.26–1.42)	1.58 (0.78–3.29)	0.81 (0.36–1.79)	0.80
n-3/n-6 Polyunsaturated fatty acid ratio					
Intake*	0.17	0.19	0.21	0.24	
No. cases	15	16	19	15	
Crude OR (95% CI)	1.00	1.07 (0.51–2.24)	1.29 (0.64–2.65)	0.99 (0.47–2.11)	0.87
Multivariate OR (95% CI)†	1.00	0.95 (0.43–2.11)	1.27 (0.59–2.78)	1.17 (0.52–2.62)	0.55
Cholesterol					
Intake (mg/day)*	199.0	261.7	332.7	431.2	
No. cases	16	15	18	16	

Table 4. Continued

Variable	Quartile				p for trend
	1 (n = 192)	2 (n = 193)	3 (n = 193)	4 (n = 193)	
Crude OR (95% CI)	1.00	0.93 (0.44–1.94)	1.13 (0.56–2.31)	0.99 (0.48–2.06)	0.87
Multivariate OR (95% CI)†	1.00	0.96 (0.44–2.11)	1.22 (0.57–2.62)	0.96 (0.44–2.12)	0.92

*Values for intake are medians for adjusted energy intake using the residual method for each quartile, except for the ratio of n-3 to n-6 polyunsaturated fatty acids, which was based on crude intake in g/day.

†Multivariate models included the following: maternal age, gestation at baseline, family income, maternal and paternal education, maternal and paternal history of asthma, atopic eczema, and allergic rhinitis, mite allergen level from maternal bedclothes, vacuuming living room, mould in kitchen, changes in maternal diet in the previous 1 month, season when data at baseline were collected, baby's older siblings, baby's sex, baby's birth weight, breastfeeding and bathing or showering infant.

Discussion

The current prospective study demonstrated that higher maternal intake of meat during pregnancy was independently associated with an increased risk of suspected atopic eczema in infants aged 3–4 months. No material exposure–response relationships were observed between maternal intake of eggs, dairy products, fish and any of the types of fatty acids considered and the risk of suspected atopic eczema. However, an inverted *U*-shaped relationship was seen for maternal intake of total fat, monounsaturated fatty acids, α -linolenic acid and n-6 polyunsaturated fatty acids although these significant positive relationships may be caused by a type I error. Our findings are in agreement with a previous study that showed no relationships between maternal intake of milk, yogurt and eggs during pregnancy and the risk of eczema in the offspring at the age of 2 (13), but are at variance with studies showing an inverse association between maternal intake of fish and the risk of childhood eczema (12–14).

To our knowledge, no prospective study has addressed the relationship between maternal intake of meat during pregnancy and the risk of atopic eczema in the children. Moreover, no epidemiological study has investigated the association between dietary intake of meat and atopic eczema in adults or children. A few studies have examined the relationship between meat intake and asthma and/or wheeze. A cross-sectional study in schoolchildren in New Zealand showed that consumption of meat was not associated with the prevalence of wheeze or asthma (23). In a nested case–control study from the European Prospective Investigation into Cancer and Nutrition, meat intake was not related to the risk of onset of asthma in adulthood (24). The current results are in disagreement with these observations. We have no immediate explanation as to the underlying mechanisms for the positive

relationship between maternal meat intake and childhood suspected atopic eczema. Certain components of meat may affect foetal immune responses. Meat is a primary source of saturated fatty acids. However, the present study found no association between maternal intake of saturated fatty acids and the risk of suspected atopic eczema. The formation of heterocyclic amines during cooking and nitroso compounds in processed meat are indicated as plausible mechanisms whereby meat intake may contribute to cancer risk (25). Our results in relation to maternal meat intake and childhood suspected atopic eczema might be attributable to these possible carcinogens although epidemiological evidence regarding heterocyclic amines and nitroso compounds and allergy was not available at the time of our analysis. Alternatively, uncontrolled dietary or non-dietary factors may have confounded the relationship between maternal meat intake and suspected atopic eczema in the offspring. In Japan, a high intake of meat is likely to be linked to a westernized lifestyle that may increase the risk of childhood atopic eczema.

In Japan, fish intake is high. Among 20 Canadian pregnant women, mean intake of eicosapentaenoic and docosahexaenoic acids was estimated to be 35 and 82 mg/day respectively (26). In a US prospective study, the daily mean value of the ratio of n-3 to n-6 polyunsaturated fatty acid intake among 1540 pregnant women with normal blood pressure was 0.09 (27). The values were about half of the median values for the first quartile of eicosapentaenoic and docosahexaenoic acid intake and the ratio of n-3 to n-6 polyunsaturated fatty acid intake in our population. A beneficial association of maternal intake of fish and marine-origin n-3 polyunsaturated fatty acids and the ratio of n-3 to n-6 polyunsaturated fatty acid maternal intake with the risk of atopic eczema might be validated when fish consumption is very low. In addition, lack of relationships with maternal intake of fish

and the related fatty acid in this study may be ascribed to the hypothesis that methylmercury and dioxins that are accumulated in fish and shellfish through the marine food web might have counteracted the advantage of intake of fish in reducing the incidence of childhood suspected atopic eczema.

A methodological strength of the present study is the prospective design, which reduced the possibility of recall bias. Study subjects were homogeneous in terms of having the same residential background. We controlled for a wide range of potential confounding factors.

Weaknesses of the current study should also be discussed. The dietary intake under study was estimated using a self-administered semi-quantitative dietary assessment questionnaire. Our DHQ could only approximate consumption although this questionnaire had been validated (15, 16). Because such exposure misclassification was non-differential, the consequence would bias the magnitude of the observed association toward the null. Our DHQ was designed to assess recent dietary intake, i.e. for 1 month prior to completing the questionnaire. This disadvantage is likely to be alleviated after adjustment for the season when data were collected, however. Changes in diet in the past 1 month were controlled for because pregnant females are likely to change their diet for reasons such as nausea gravidarum. In this study, there was no significant interaction between changes in maternal diet in the previous 1 month and maternal meat intake during pregnancy in relation to the risk of suspected atopic eczema (data not shown). Potential misclassification associated with variability across subjects with regard to the stability of the maternal diet during pregnancy is likely to be negligible. However, residual confounding effects could not be ruled out because changes in maternal diet in the past 1 month may be a crude discriminator of the actual change in maternal diet.

The second survey was sent at 2–9 months postpartum; 88.9% of those who completed it were at 3–4 months postpartum. Because an accurate assessment of the presence of atopic eczema at the time of the second survey would be difficult, we used the term ‘suspected atopic eczema’ to define outcome in this questionnaire. The resulting bias would give rise to an underestimation of our results because of non-differential outcome misclassification.

At baseline, the participation rate in Neyagawa City was low (17.2%) and that in other areas could not be calculated. The mothers in the current study were not a representative sample of

Japanese women in the general population and the present findings may not be generalized. Educational levels in the present study population were higher than in the general population. According to the 2000 population census of Japan, the proportions of females aged 30–34 yr in Osaka Prefecture with years of education of <13, 13–14, 15+ and unknown were 49.2%, 32.3%, 13.6% and 4.9% respectively (28). The corresponding figures for the current study were 28.7%, 42.4%, 28.9% and 0.0% respectively. The lifetime prevalence of atopic eczema might be higher among our parents than among the general population. Muto et al. (29) reported that the lifetime prevalence of atopic eczema was 4.2% and 4.4%, respectively, for Japanese men and women aged 30–39 yr according to the UK Working Party’s diagnostic criteria. On the other hand, the prevalence of atopic eczema might be lower among our infants than among the general population. Another study from Japan showed that eczema based on the morphological appearance and distribution of skin lesions was observed in 30% of the 4-month-old infants who came to public health examinations (30).

In conclusion, the current prospective study in Japan found that higher maternal intake of meat is associated with an increased risk of suspected atopic eczema in children aged 3–4 months. However, our study provides no evidence that maternal intake of fish and marine-origin n-3 polyunsaturated fatty acids and the ratio of n-3 to n-6 polyunsaturated fatty acid maternal intake are preventive against the risk of suspected atopic eczema. Continued follow-up of our cohort as well as additional studies in various populations are required to confirm these findings.

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