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Bronchial reactivity and dietary antioxidants

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Abstract

***Background* – It has been postulated that dietary antioxidants may influence the expression of allergic diseases and asthma. To test this hypothesis a case-control study was performed, nested in a cross sectional study of a random sample of adults, to investigate the relationship between allergic disease and dietary antioxidants.**

***Methods* – The study was performed in rural general practices in Grampian, Scotland. A validated dietary questionnaire was used to measure food intake of cases, defined, firstly, as people with seasonal allergic-type symptoms and, secondly, those with bronchial hyperreactivity confirmed by methacholine challenge, and of controls without allergic symptoms or bronchial reactivity.**

***Results* – Cases with seasonal symptoms did not differ from controls except with respect to the presence of atopy and an increased risk of symptoms associated with the lowest intake of zinc. The lowest intakes of vitamin C and manganese were associated with more than fivefold increased risks of bronchial reactivity. Decreasing intakes of magnesium were also significantly associated with an increased risk of hyperreactivity.**

***Conclusions* – This study provides evidence that diet may have a modulatory effect on bronchial reactivity, and is consistent with the hypothesis that the observed reduction in antioxidant intake in the British diet over the last 25 years has been a factor in the increase in the prevalence of asthma over this period.**

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Keywords: asthma, hay fever, bronchial reactivity, diet, antioxidants.

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The well known increase in the prevalence of asthma and other allergic diseases in westernised countries remains unexplained.[1–6] We have argued that such a large increase in asthma, eczema, and hay fever is unlikely to be explained by changes in the air we breathe, either in terms of its allergen content or in the amount of pollutants such as cigarette smoke or those derived from traffic and industrial sources. Rather, we have proposed that the populations of economically advanced countries have eaten a diet which has included progressively less fresh fruit and vegetables and that this diet has increased the susceptibility of the population as a whole to potentially harmful inhaled substances by reducing the antioxidant defences of the lung against the effects of inhaled irritants and allergens.[7] It is likely that, if this hypothesis were true, the diets that would influence the prevalence of allergic disease in children most critically would be those of the mother in pregnancy and during lactation and of the child in the first year or two of life. However, since asthma may start at any age an effect may be demonstrable at any time, and we have taken the opportunity to investigate diet in adults, with and without increased bronchial reactivity, derived from a random sample of a rural population.

Methods

SELECTION OF INDIVIDUALS

The original cross sectional study population consisted of 2000 individuals, an approximately one in 10 random sample of all adults registered with the general practitioners of three villages in rural Grampian, Scotland.[8] All had completed questionnaires on the presence or absence of a range of seasonal symptoms including those classically associated with allergy. Cases were first defined as those who had responded positively to questions about recurrent eye, nasal, or respiratory symptoms any time between April and August[8] and controls were those with no such seasonal symptoms. The cases selected from the original population for the present study were all those from one of these villages who had recorded seasonal symptoms on the questionnaire, together with age and sex matched controls without symptoms from the same village. They were contacted by telephone and those who agreed to participate were sent a detailed dietary questionnaire through the post with instructions on how to complete it. Of 78 cases and 68 controls approached, 52 and 38, respectively, took part. The main reasons for not participating did not differ between cases and controls, 10 and 13, respectively, having moved, six and four being ill or having died, and 10 and 13 being unwilling or unable to attend.

Subjects taking bronchodilators or antihistamines were asked to stop them six or 48 hours, respectively, before attending for further tests. They were then seen and the completed questionnaire was checked. A second questionnaire to confirm the presence or absence of symptoms was administered and a clinical history taken. Skin prick tests and a methacholine challenge test were then carried out. A second group of cases was defined as those who showed a fall of 20% or greater in forced expiratory volume in one second (FEV_1) in response to 12.25 μmol or less of methacholine, controls being those who showed no such change at this level.

All tests were carried out during the winter and care was taken to ensure that no subject had suffered a viral infection in the six weeks prior to the test.

Table 1 Characteristics of those with (cases) and without (controls) a history of seasonal symptoms

	Cases (n=51)	*Controls (n=38)*	*p value*
M:F	16:35	14:24	0.589
Mean (SD) age	36.6 (11.09)	38.3 (10.42)	0.451
Smoking habits:			
Current smokers	12	10	
Ex-smokers	7	9	0.389
Never smokers	32	19	
Atopy	39	2	<0.001
Mean (SD) FEV_1 (% predicted)	115.1 (16.08)	111.7 (14.01)	0.296
Mean (SD) FVC (% predicted)	113.6 (13.97)	108.9 (14.74)	0.131
Mean (SD) PD_{20} (μmol)	7.8 (2.59)	11.7 (1.95)	0.038
Previously diagnosed:			
Asthma	7	1	0.070
Hay fever	40	0	<0.001
Eczema	9	2	0.079
Allergy	13	3	0.032

FEV_1=forced expiratory volume in one second; FVC=forced vital capacity; PD_{20}=dose of methacholine provoking a 20% fall in FEV_1.

Table 2 Daily antioxidant and total energy intake for those with symptoms (cases) and those without (controls)

	Cases		*Controls*	
	Geometric mean	*Confidence interval*	*Geometric mean*	*Confidence interval*
Retinol (μg)	756	637 to 898	784	619 to 992
β-carotene (μg)	1951	1630 to 2335	2107	1842 to 2409
Vitamin C (mg)	97.3	82.2 to 115.2	104.0	87.0 to 124.3
Vitamin E (mg)	6.99	6.07 to 8.06	7.92	6.85 to 9.15
Magnesium (mg)	294	267 to 322	331	302 to 362
Zinc (mg)	9.32	8.56 to 10.14	10.92	9.80 to 12.18
Manganese (mg)	2.93	2.59 to 3.32	3.33	2.85 to 3.90
Selenium (μg)	62	55 to 70	73	63 to 85
Energy intake (kcal)	1947	1767 to 2145	2169	1952 to 2410

The study protocol was approved by the local ethical committee and all subjects gave fully informed consent to their participation.

DIETARY QUESTIONNAIRE

The questionnaire, which has been validated previously against weighed intake and in epidemiological studies of heart disease,[9 10] established present and past dietary intake. Mean daily intake is estimated from daily frequency of food consumption over a seven day period. Information on any vitamin, mineral, and food supplements taken was recorded – that is, type, brand, strength, and frequency of consumption. This was not dealt with by the computer program and such information had to be input separately and the intakes altered accordingly.

ALLERGY TESTS

Skin prick tests were performed to 10 common allergens: house dust mite (*Dermatophagoides pteronyssinus*), grass pollen mix, tree pollen mix, birch pollen, nettle pollen, *Cladosporium herbarum*, *Alternaria alternata*, cat fur, dog hair and a saline control (Bencard, Brentford, Middlesex, UK). The skin test responses were read after 15 minutes and measured as the mean of two right angled diameters, one of which was the largest. Tests were regarded as positive if the mean diameter of the weal was 3 mm or more, corrected for the mean diameter of the negative control weal if necessary. Individuals were regarded as being atopic if they had one or more positive skin prick tests.

METHACHOLINE CHALLENGE TEST

Where relevant, subjects were asked to refrain from smoking for at least two hours beforehand. Those who had had any symptoms of a viral illness during the preceding six weeks were excluded. The FEV_1 was measured as the best of three blows using a Vitalograph spirometer. Methacholine challenge testing was not carried out on any subject who had an FEV_1 of <70% of that predicted or less than 1.5 l. Methacholine challenge was performed according to the method of Yan *et al.*[11] Saline, followed by successive doubling doses of methacholine from 0.016 μmol to 16.4 μmol, was administered. The test was stopped when FEV_1 had fallen by 20% or more from the saline control or the highest concentration had been administered. The methacholine dose provoking a 20% fall in FEV_1 (PD_{20}) was calculated by interpolation. If a fall of 20% or more was not attained, PD_{20} was recorded as >16.4 μmol.

STATISTICAL ANALYSIS

Statistical analysis was carried out using the SPSS for Windows v. 6.0 program. Those who reported seasonal symptoms were compared with those who had no symptoms and reactors, defined as those who had a PD_{20} of 12.25 μmol or less, were compared with non-reactors. For the analysis of the dietary information the method of Willet[12] was employed. Residuals were calculated for the log transformed nutrients regressed on energy intake and tertiles for each nutrient determined. Logistic regression analyses were carried out to estimate the effects of low nutrient intakes on having symptoms or being a reactor. Adjusted analyses were carried out to control for the potential confounding effects of sex, age, and smoking habits (smokers versus non-smokers). The two sample *t* test was used to compare age, FEV_1, the log transformed PD_{20}, and energy intake. The χ^2 test was used to compare categorical data (smoking habits, atopy, and sex).

Results

Ninety individuals (60 women) agreed to participate in the study after explanation of the details over the telephone. Methacholine challenge was successfully carried out on 88 of them. It was not possible to obtain reliable information on the usage of food supplements from two individuals and they were omitted from subsequent dietary analysis. Subjects were initially allocated to one of two groups, with and without seasonal symptoms. Both groups were similar with respect to age, sex, smoking habits, and FEV_1. As expected, a significantly higher proportion of cases, though not all, were atopic (relative risk 58, 95% confidence interval (CI) 12.2 to 279.5) and PD_{20} was higher in controls (table 1), though the difference was not significant.

Antioxidant and energy intakes of cases and controls are shown in table 2. Total energy intake was slightly higher in controls, though not significantly so (p=0.132). Controls had slightly higher intakes of all antioxidants which

Table 3 Odds ratios for symptoms versus no symptoms in relation to antioxidant intake

	Unadjusted odds			*Adjusted odds**		
	Odds ratio	*95% CI*	*p value*	*Odds ratio*	*95% CI*	*p value*
Retinol						
Low	0.62	0.22 to 1.73	0.359	0.64	0.23 to 1.80	0.397
Middle	1.41	0.49 to 4.07	0.524	1.53	0.52 to 4.53	0.444
β-carotene						
Low	1.11	0.61 to 2.02	0.728	0.92	0.31 to 2.71	0.881
Middle	0.74	0.41 to 1.34	0.321	0.67	0.23 to 1.94	0.458
Vitamin C						
Low	0.92	0.32 to 2.61	0.871	0.95	0.32 to 2.77	0.918
Middle	0.61	0.22 to 1.72	0.352	0.59	0.21 to 1.71	0.333
Vitamin E						
Low	1.41	0.49 to 4.07	0.524	1.50	0.51 to 4.41	0.467
Middle	0.62	0.22 to 1.73	0.359	0.61	0.21 to 1.73	0.351
Magnesium						
Low	1.61	0.58 to 4.50	0.364	1.68	0.57 to 4.94	0.346
Middle	2.87	0.98 to 8.37	0.053	2.95	0.98 to 8.86	0.054
Zinc						
Low	3.52	1.15 to 10.75	0.027	4.70	1.33 to 16.53	0.016
Middle	0.94	0.33 to 2.61	0.902	1.03	0.36 to 2.94	0.958
Manganese						
Low	1.22	0.44 to 3.40	0.703	1.18	0.42 to 3.35	0.758
Middle	1.61	0.57 to 4.56	0.368	1.54	0.53 to 4.49	0.432
Selenium						
Low	1.62	0.57 to 4.66	0.367	1.64	0.56 to 4.84	0.367
Middle	0.81	0.29 to 2.26	0.691	0.81	0.29 to 2.28	0.687

* Adjusted for sex, age and smoking.

Table 4 Characteristics of methacholine reactors and non-reactors

	Reactors (n=29)	*Non-reactors (n=58)*	*p value*
M:F	6:23	24:34	0.056
Mean (SD) age (years)	36.7 (9.70)	37.5 (11.44)	0.766
Smoking habits:			
Current smokers	9	13	
Ex-smokers	5	11	0.683
Never smokers	15	34	
Atopy	16	24	0.223
Mean (SD) FEV_1 (% predicted)	110.2 (14.90)	116.1 (14.44)	0.077
Mean (SD) FVC (% predicted)	111.1 (14.28)	111.6 (14.67)	0.934
Previously diagnosed:			
Asthma	6	2	0.009
Hay fever	16	23	0.170
Eczema	5	5	0.235
Allergy	8	8	0.117

FEV_1 = forced expiratory volume in one second; FVC = forced vital capacity.

Table 5 Daily antioxidant and total energy intake for reactors and non-reactors

	Reactors		*Non-reactors*	
	Geometric mean	*Confidence interval*	*Geometric mean*	*Confidence interval*
Retinol (μg)	772	615 to 969	759	636 to 906
β-carotene (μg)	1673	1291 to 2169	1099	1963 to 2486
Vitamin C (mg)	77.3	62.8 to 95.2	115.0	100.0 to 132.4
Vitamin E (mg)	6.65	5.56 to 7.96	7.75	6.85 to 8.78
Magnesium (mg)	286	252 to 323	322	298 to 348
Zinc (mg)	9.68	8.77 to 10.69	10.10	9.23 to 11.05
Manganese (mg)	2.75	2.26 to 3.34	3.30	2.95 to 3.68
Selenium (μg)	64	53 to 77	68	61 to 76
Energy intake (kcal)	1979	1729 to 2265	2067	1879 to 2252

Table 6 Odds ratios for reactors versus non-reactors in relation to antioxidant intake

	Unadjusted odds			*Adjusted odds**		
	Odds ratio	*95% CI*	*p value*	*Odds ratio*	*95% CI*	*p value*
Retinol						
Low	1.12	0.36 to 3.51	0.839	1.13	0.35 to 3.64	0.840
Middle	1.67	0.56 to 5.00	0.362	2.00	0.63 to 6.33	0.240
β-carotene						
Low	2.59	0.81 to 8.31	0.110	3.43	0.97 to 12.11	0.056
Middle	2.12	0.66 to 6.83	0.207	2.37	0.70 to 8.03	0.166
Vitamin C						
Low	5.66	1.68 to 19.04	0.005	7.13	1.91 to 26.71	0.004
Middle	1.67	0.47 to 5.90	0.424	1.62	0.44 to 5.98	0.467
Vitamin E						
Low	1.53	0.50 to 4.64	0.455	1.89	0.59 to 6.11	0.284
Middle	1.25	0.41 to 3.82	0.696	1.40	0.44 to 4.41	0.569
Magnesium						
Low	5.07	1.40 to 18.33	0.013	5.63	1.42 to 22.33	0.014
Middle	4.41	1.22 to 15.99	0.024	4.03	1.07 to 15.20	0.039
Zinc						
Low	1.32	0.43 to 4.04	0.632	1.90	0.53 to 6.82	0.323
Middle	1.45	0.48 to 4.38	0.512	1.76	0.55 to 5.62	0.337
Manganese						
Low	5.91	1.76 to 19.81	0.004	8.14	2.11 to 31.39	0.002
Middle	1.82	0.52 to 6.46	0.348	1.59	0.43 to 5.89	0.485
Selenium						
Low	1.29	0.44 to 3.80	0.648	1.61	0.51 to 5.08	0.412
Middle	1.05	0.34 to 3.22	0.928	1.18	0.37 to 3.75	0.780

* Adjusted for sex, age and smoking.

may be a reflection of their higher energy intakes. The unadjusted and adjusted odds ratios and associated 95% confidence intervals are presented in table 3. For each antioxidant the odds ratios are given relative to the highest tertile. Adjusting for age, sex, and smoking habits made little difference to the odds ratios. The only significant result was for zinc, with those individuals in the lowest tertile of intake being observed to have an adjusted odds ratio 4.7 times those in the highest tertile.

Characteristics of methacholine reactors and non-reactors are given in table 4. The two groups did not differ significantly with respect to age, smoking habits, FEV_1, and atopy. The proportion of female reactors was somewhat higher, with the relative risk of a woman being a reactor of 2.71 (95% CI 0.96 to 7.6).

Antioxidant and energy intakes of reactors and non-reactors are shown in table 5. With the exception of retinol and β-carotene, non-reactors had higher intakes of antioxidants. Again non-reactors had a higher energy intake, though this was not significant ($p = 0.570$). The difference in vitamin C intakes is particularly striking and it is unlikely that this is solely due to differences in energy intake. The unadjusted and adjusted odds ratios and associated 95% CI are presented in table 6. Odds ratios are again given relative to the highest tertile. In general, lower levels of antioxidant intake have associated odds ratios which are greater than one. After adjustment for age, sex and smoking habits, the lowest intakes of vitamin C, magnesium, and manganese were significant. These differences in antioxidants were reflected in intakes of macronutrients (table 7). Reactors consumed more fats and less carbohydrates, fibre, and alcohol than non-reactors. The unadjusted and adjusted odds ratios along with 95% CI are presented in table 8. Odds ratios are again given relative to the highest tertile. Adjusting for sex, age, and smoking habit did not alter the results to any significant extent. In general, lower intakes of any kind of fats were associated with a decreased risk of being a reactor. This decreased risk was significant for low intakes of fat, saturated fatty acids, and monounsaturated fatty acids. Lower tertiles of carbohydrates, fibre, and alcohol were associated with an increased risk of being a reactor. Both lower tertiles of carbohydrate intake were associated with a significantly increased risk of being a reactor. Those with the lowest intakes of fibre also had significantly increased risks of being a reactor.

It is recognised that, when a large number of independent tests are carried out, some of the tests may be expected to be statistically significant by chance. However, the very small p values for vitamin C ($p = 0.004$) and manganese ($p = 0.002$) suggest that, in these cases, the differences are unlikely to be due to chance.

Discussion

The objectives of this study were to test the hypothesis that differences in antioxidant intake are a factor in determining whether or not people develop seasonal symptoms and to in-

Table 7 Daily macronutrient intake for reactors and non-reactors

	Reactors (n=29)		*Non-reactors (n=58)*	
	Geometric mean	*Confidence interval*	*Geometric mean*	*Confidence interval*
Protein (g)	80.4	72.9 to 88.8	82.0	75.2 to 89.4
Fat (g)	83.8	72.1 to 97.3	76.0	67.9 to 85.2
Saturated fatty acids (g)	34.5	29.9 to 39.9	30.3	26.9 to 34.2
Monounsaturated fatty acids (g)	31.3	27.0 to 36.2	29.2	26.4 to 32.3
Polyunsaturated fatty acids (g)[1]	12.5	10.0 to 15.6	12.5	11.1 to 14.0
Cholesterol (mg)	339.3	297.4 to 387.0	309.7	279.3 to 343.5
Carbohydrates (g)	220.2	188.5 to 257.3	254.4	232.9 to 278.1
Starch (g)	117.5	99.8 to 138.3	123.8	111.3 to 137.8
Fibre (g)	12.4	10.4 to 14.9	15.9	14.6 to 17.4
Alcohol (g)[2]	4.5	2.5 to 7.7	7.3	5.4 to 9.8

[1] No. of reactors = 28, no. of non-reactors = 50.
[2] Weekly intake.

Table 8 Odds ratios for reactors versus non-reactors in relation to macronutrient intake

	Unadjusted odds			*Adjusted odds**		
	Odds ratio	*95% CI*	*p value*	*Odds ratio*	*95% CI*	*p value*
Protein (g)						
Low	1.29	0.43 to 3.84	0.647	1.81	0.54 to 6.02	0.336
Middle	0.90	0.30 to 2.75	0.860	1.01	0.31 to 3.27	0.982
Fat (g)						
Low	0.23	0.07 to 0.78	0.018	0.25	0.07 to 0.87	0.029
Middle	0.71	0.25 to 2.03	0.517	0.71	0.24 to 2.11	0.543
Saturated fatty acids (g)						
Low	0.10	0.03 to 0.42	0.002	0.11	0.03 to 0.44	0.002
Middle	0.60	0.21 to 1.73	0.347	0.56	0.19 to 1.65	0.292
Monounsaturated fatty acids (g)						
Low	0.25	0.08 to 0.80	0.019	0.28	0.09 to 0.92	0.036
Middle	0.45	0.15 to 1.33	0.148	0.48	0.16 to 1.47	0.197
Polyunsaturated fatty acids (g)[1]						
Low	0.46	0.15 to 1.43	0.177	0.52	0.15 to 1.77	0.296
Middle	0.48	0.15 to 1.51	0.211	0.45	0.13 to 1.58	0.212
Carbohydrates (g)						
Low	6.25	1.72 to 22.67	0.005	10.52	2.41 to 45.89	0.002
Middle	3.62	1.00 to 13.14	0.051	5.77	1.41 to 23.56	0.015
Cholesterol (mg)						
Low	0.44	0.15 to 1.32	0.144	0.50	0.16 to 1.59	0.238
Middle	0.42	0.14 to 1.26	0.121	0.42	0.13 to 1.29	0.129
Starch (g)						
Low	0.89	0.29 to 2.77	0.839	0.93	0.28 to 3.07	0.906
Middle	1.48	0.51 to 4.33	0.473	1.47	0.49 to 4.43	0.490
Fibre (g)						
Low	5.14	1.54 to 17.21	0.008	6.08	1.65 to 22.40	0.007
Middle	2.16	0.62 to 7.49	0.225	2.24	0.61 to 8.29	0.226
Alcohol (g)[2]						
Low	2.36	0.76 to 7.32	0.138	2.54	0.72 to 9.01	0.149
Middle	1.57	0.50 to 4.91	0.437	2.00	0.59 to 6.77	0.266

* Adjusted for sex, age, and smoking.
[1] No. of reactors = 28, no. of non-reactors = 50.
[2] Weekly intake.

vestigate the relationship, if any, between diet and bronchial reactivity. The results of our first analysis showed no significant differences in antioxidant intake between those with seasonal symptoms and those without. However, when cases were defined as those reacting to less than 12.25 μmol of methacholine, highly significant differences were observed. These differences were in the amount of antioxidant vitamins and cofactors consumed, and thus suggest that a diet relatively low in antioxidants may have some effect in potentiating the development of bronchial hyperreactivity and, by inference, asthma – even though it is apparently not influential in determining whether or not individuals manifest the symptoms of hay fever. The results from the macronutrient analysis indicate, moreover, that a good diet has an important protective part to play in the prevention of bronchial reactivity. Little change in the odds ratios was observed when the potential confounding effects of sex, age, and smoking habit were adjusted for.

We have considered the possibility that the differences observed between reactors and non-reactors may have been due to a selection bias. All subjects were originally selected from a random population sample and there were no obvious differences between cases and controls in their reasons for inability to participate. It is possible that the controls were a particularly fit and health conscious group who might have had a better diet than the cases on that account. If that were the case, it is hard to explain why differences were not found between the original cases with symptoms and controls, rather than between the reactors and non-reactors. A general comparison of the diets of our subjects with those from another sample of a local population (which will necessarily include individuals with increased reactivity) suggests that both cases and controls in our study tended to eat less fat, fibre, retinol, and vitamin E and more vitamin C than people living in a nearby town.

On the other hand, there is already some evidence that our results reflect a real relationship between diet and asthma as our results are consistent with those of some earlier studies which concluded that individuals with bronchial hyperreactivity have reduced antioxidant intake or vice versa. Two studies have shown relatively low blood levels of selenium in subjects with asthma.[13 14] Selenium is essential to the activity of the glutathione peroxidase enzymes which are believed to be an important component of pulmonary antioxidant systems. Another study has shown that a low intake of magnesium, which is involved in the relaxation of smooth muscle, is associated with reduced lung function, bronchial hyperreactivity, and self-reported wheezing.[15] Moreover, low intakes of fresh fruit and fruit juice have been shown to be associated with reduced lung function[16] while a low vitamin C intake has been associated with reduction in FEV_1.[17 18] One study has shown that airways obstruction is associated with lower levels of serum retinol[19] while another has suggested that various factors, including reduced serum levels of vitamin C, were related to wheezing and bronchitis.[20] The literature relating to vitamin C and asthma has recently been reviewed.[21] Some studies have shown a beneficial effect and others none. Administration of vitamin C has been shown to attenuate bronchoconstriction induced by inhaling nitrogen dioxide[22] and ozone[23] in normal subjects, and also to reduce bronchial reactivity to histamine and methacholine.[24 25]

The accumulating evidence suggests that diet does have an influence in modulating the response of the lung to inhaled allergens and irritants. Clearly, genetic factors are influential in determining atopy, but genetic change is not the explanation for the remarkable rise in the prevalence of the three atopic diseases over the last 25 years. Substantial changes in the average household consumption of food have been documented in Britain over this period and these have included a marked fall in consumption of antioxidants and mineral cofactors in fresh fruit and vegetables, fresh fish, and

meat.[7 26] We have proposed that this change, operating over the whole population, has produced a general reduction in the ability of the lung to counter inflammatory reactions due to inhalation of irritants or allergens.

In the case of the newborn child, a low antioxidant level may make it more susceptible to the initial exposure to mite antigen that it encounters when arriving home, and later to exposure to grass pollen. Later in life a diet low in antioxidants may increase the risk of an atopic individual developing symptoms in response to exposure to higher doses of allergen. Our study, taken with the others quoted, suggests that diet may have such an influence throughout adult life. If it does, its importance is likely to be greater from an epidemiological point of view – shifting the population curve of susceptibility – than from a clinical point of view.

A dietary hypothesis would not explain all the epidemiological features of asthma and atopic disease. In particular, it does not explain why the first born child is more at risk than subsequent children, nor why members of large sibships are relatively protected, and it is possible that childhood infections may also play a part in modulating the expression of atopy.[27 28] It is, however, an attractive hypothesis in that, if true, it points the way to a means of reversing the progressive upward trend in atopic disease. Studies of the influence of dietary factors in pregnancy and early childhood on the expression of atopic disease are desirable.

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