Health effects of passive smoking · 5

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Parental smoking and allergic sensitisation in children

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Abstract

Background – A systematic review was conducted of the effects of parental smoking on immunoglobulin (IgE) levels, skin prick positivity, and allergic rhinitis or eczema in children. Asthma was excluded in order to distinguish more clearly the effect of passive smoke exposure on allergic sensitisation.

Methods – Thirty six relevant publications were identified after consideration of 692 articles selected by electronic search of the Embase and Medline databases using keywords relevant to passive smoking in children. The search was completed in April 1997 and identified nine studies of IgE in neonates, eight of IgE in older children, 12 which included skin prick tests, and 10 describing symptoms of allergic disease other than asthma or wheezing. A quantitative meta-analysis was possible only for the studies reporting skin prick tests.

Results – Several large studies failed to confirm early reports of a substantial or statistically significant association of maternal smoking with concentrations of total serum IgE in neonates or in older children. No consistent association emerged between parental smoking and allergic rhinitis or eczema. Few of these studies adjusted for potential confounding variables. The quantity and quality of evidence was greatest for skin prick tests, and studies of parental smoking during pregnancy or infancy were broadly consistent in showing no adverse effect on prick positivity (pooled odds ratio 0.87, 95% confidence interval 0.62 to 1.24). There was much greater and statistically significant ($p=0.002$) heterogeneity of odds ratios relating current parental smoking to skin prick positivity.

Conclusions – Parental smoking, either before or immediately after birth, is unlikely to increase the risk of allergic sensitisation in children.

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Keywords: parental smoking, allergic sensitisation, children.

Active smoking is associated with an increase in total serum immunoglobulin E (IgE) con-

centrations¹ and an elevated risk of allergic sensitisation to some, but not all, occupational allergens.²⁻⁴ The suggestion that passive exposure to tobacco smoke might influence allergic sensitisation in children was first made in 1981⁵ and subsequently a number of studies have investigated the relationship of parental smoking to IgE concentrations in cord blood, total and allergen specific IgE levels later in childhood, positive skin prick reactions to common aeroallergens, and allergic symptoms. This paper systematically reviews the evidence relating to IgE levels, skin prick tests, and allergic rhinitis. The larger number of studies relating parental smoking to the development of asthma will be reviewed separately.

Methods

Published papers, letters and review articles were selected by an electronic search of the Embase and Medline databases using the search strategy described in detail elsewhere.⁶ Briefly, all passive smoking references were selected by the MESH heading *tobacco smoke pollution* and/or textword combinations (*{passive, second-hand, second hand, involuntary, parent*, maternal, mother*, paternal, father* or household}* and *{smok*, tobacco* or cigarette*}*). Papers were then restricted to children by relevant textwords or by the age group as specified in the title or abstract. This search, completed in April 1997, yielded 3625 references of which 1593 contained keywords relevant to respiratory or allergic disease. These 1593 abstracts were reviewed and papers relevant to allergy were selected by the textwords *globulin E, IgE, atopic, atopy, allergy or skin prick*. Papers relating solely to asthma or wheezing illness were excluded by review of the on-line abstracts. Thirty four publications included quantitative information relevant to this review and a further two were identified by citations in the studies reviewed. The 36 papers described the results of 23 cross-sectional surveys, two case-control studies, eight longitudinal studies, and three controlled trials of intervention in high-risk families (table 1).

Studies were grouped according to the outcome measure as follows: IgE in neonates (nine studies), IgE in older children (eight studies), skin prick tests (12 studies), and symptoms of

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Table 1 Studies relating parental smoking to manifestations of allergic sensitisation in children

Reference	Year	Country	Age	Design	Outcome measure	Sample size	Sample selection
Neonatal IgE concentrations							
8	80	France	0	Survey	Cord IgE (GM)	136	Unselected births
5	81	Sweden	0	Survey	Cord IgE (GM)	46	Not stated (letter only)
7	86	Sweden	0	Survey	Cord IgE >1.2 kU/l	186	Unselected European births
14	89	USA	0	Survey	Cord IgE (GM)	325	Not stated (abstract only)
11	91	France	0	Survey	Cord IgE (GM)	99	Singletons born in working hours
13	93	Italy	0	Survey	Cord IgE (GM)	215	Newborns >2.5 kg birthweight
12	95	Turkey	0	Survey	Cord IgE (GM)	1251	Consecutive births in 1 hospital
10	95	Germany	0	Survey	Cord IgE >0.7 kU/l	4793	Singletons born in 6 hospitals
9	96	Poland	0	Survey	Cord IgE (GM)	110	Consecutive births in 1 hospital
Postnatal IgE concentrations							
5	81	Sweden	0-3	Cohort	Total IgE (GM)	46	Not stated (letter only)
15	87	Israel	1-4	Cohort	Total IgE (increase)	80	Wheezy bronchitis plus atopy
16	87	UK	0-5	Cohort	Total IgE (GM)	73	Children with 1 atopic parent
17	88	USA (MI)	2-17	Survey	Total and specific IgE	100	General paediatric outpatients
21	90	Italy	9	Survey	Total IgE, eosinophilia	159	Random sample of schoolchildren
18	94	Turkey	1-17	Survey	Total IgE (GM)	558	Allergy clinic outpatients
19	94	Germany	6-12	Survey	Total IgE (GM)	703	Random sample of schoolchildren
20	96	Egypt	~10	Survey	Total IgE, eosinophils, IL-4	120	Children of smokers and non-smokers
Skin prick tests - population surveys							
24	85	USA (MA)	12-16	Cohort	Any of 4 SPT >0 mm	163	Follow up of random sample at 5-9
22	88	Italy	9	Survey	"Skin test index"	159	Random sample of schoolchildren
23	92	Italy	13	Cohort	Any of 10 SPT +ve	142	4-year follow up of refs 21 and 22
31	92	Germany	6-8	Survey	Any of 7 SPT ≥ 3 mm	1470	All children starting school
30	94	Germany	9-11	Survey	Any of 6 SPT ≥ 3 mm	8653	All 4th grade schoolchildren
25	95	USA (NC)	7-12	Survey	Any of 14 SPT ≥ 4 mm	219	Random sample of paediatric patients
28	95	Baltics	10-12	Survey	Any of 8 SPT >0 mm	2594	Schoolchildren in 3 countries
29	95	Norway	7-13	Survey	Any of 8 SPT ≥ 3 mm	529	Random sample of schoolchildren
Skin prick tests - patients							
33	90	Italy	1-12	C-C	Any of 6 SPT ≥ 3 mm	302	Asthmatic patients
32	92	Sweden	3-17	C-C	Any of 8 SPT +ve	169	Patients with atopic disease
Skin prick test and atopic disease							
27	93	UK	0-2	Cohort	SPT +ve, atopic disease	1174	All births in Isle of Wight
43	95	USA (CA)	0-7	Trial	SPT +ve, atopic disease	165	Children of ≥ 1 atopic parent(s)
Atopic disease							
39	83	UK	0-5	Cohort	Hay fever ever	13315	National birth cohort
41	89	UK	0-1	Trial	Eczema, nasal discharge	483	Children of ≥ 1 atopic parent(s)
40	92	UK	0-1	Trial	Eczema, food allergy	120	2 atopic parents or siblings
34	92	Germany	6-8	Survey	Clinical atopic disease	903	Children starting school
35	94	Sweden	14	Survey	Rhinoconjunctivitis	985	Schoolchildren
38	94	USA (AZ)	0-6	Cohort	Allergic rhinitis (PD)	747	HMO-based birth cohort
37	96	UK	12	Survey	Hay fever, eczema	1503	Schoolchildren
36	97	Turkey	7-12	Survey	Rhinoconjunctivitis	5412	Schoolchildren

GM=geometric mean; C-C=case-control; SPT=skin prick test; PD=physician diagnosed.

Table 2 Association of parental smoking with positive skin prick reactions

Reference	Year	Country	Age	Outcome measure	Exposure measure	Odds ratio (95% CI)
Perinatal ETS exposure:						
31	92	Germany	6-8	Any of 7 SPT ≥ 3 mm	Mother smoked in pregnancy	0.6 (0.3 to 1.1)
27	93	UK	2	Any of 5 SPT +ve	Mother smoking >1 cig/day	0.9 (0.5 to 1.7)
25	95	USA (NC)	7-12	Any of 14 SPT ≥ 4 mm	Mother smoked in pregnancy	0.8 (0.4 to 2.0)
28	95	Sweden	10-12	Any of 8 SPT >0 mm	ETS in home in infancy	1.3 (0.9 to 1.8)
28	95	Estonia	10-12	Any of 8 SPT >0 mm	ETS in home in infancy	1.2 (0.9 to 1.8)
28	95	Poland	10-12	Any of 8 SPT >0 mm	ETS in home in infancy	0.6 (0.3 to 1.1)
29	95	Norway	7-13	Any of 8 SPT ≥ 3 mm	Mother smoked in pregnancy*	0.6 (0.4 to 1.0)
29	95	Norway	7-13	Any of 8 SPT ≥ 3 mm	Mother smoked age 0-1†	0.6 (0.4 to 1.0)
χ^2 test for heterogeneity (6 d.f.)						12.8 (p=0.046)
Pooled estimate (fixed effect)						0.94 (0.79 to 1.13)
Pooled estimate (random effects)						0.87 (0.62 to 1.24)
Current ETS exposure:						
24	85	USA (MA)	12-16	Any of 4 SPT >0 mm	Mother currently smoking	2.2 (1.1 to 4.4)
23	92	Italy	13	Any of 10 SPT +ve	Either parent smoking	1.7 (0.8 to 3.8)
30	94	Germany	9-11	Any of 6 SPT ≥ 3 mm	Mother currently smoking	0.8 (0.7 to 0.9)
25	95	USA (NC)	7-12	Any of 14 SPT ≥ 4 mm	Parental smoking at age 5	1.1 (0.6 to 1.9)
43	95	USA (CA)	7	Any of 9 SPT +ve	Regular smoking at home	2.9 (1.1 to 7.7)
29	95	Norway	7-13	Any of 8 SPT ≥ 3 mm	Mother currently smoking*	0.8 (0.5 to 1.2)
29	95	Norway	7-13	Any of 8 SPT ≥ 3 mm	Father currently smoking†	0.7 (0.5 to 1.1)
χ^2 test for heterogeneity (5 d.f.)						18.1 (p=0.002)
Pooled estimate (random effects)‡						1.21 (0.72 to 2.04)

SPT=skin prick test; ETS=environmental tobacco smoke.

* Results for maternal smoking in pregnancy and current maternal smoking used in the meta-analyses.

† Results for maternal smoking at age 0-1 and current paternal smoking excluded from meta-analyses.

‡ In the presence of such marked heterogeneity the fixed effect assumption is invalid and the random effects estimate should be interpreted with caution.

allergy (10 studies). Three publications contributed information on more than one outcome measure. Due to the relatively small number of articles under each heading the emphasis is on a narrative review, but a quantitative meta-analysis is presented for skin prick tests (table 2). The statistical methods used for this meta-analysis have been previously described.⁶ "Random effects" models were used because there was evidence of statistically significant heterogeneity of the passive smoking effect between studies.⁶

Results

NEONATAL IGE CONCENTRATIONS

Magnusson⁷ reported results for cord blood IgE and IgD measurements from 186 newborn European infants followed to 18 months of age, 65% of a randomly selected population sample. No information is presented on infants lost to follow up and the smoking history obtained at 18 months did not specifically relate to prenatal smoking. The proportion of offspring with IgE levels ≥ 1.2 IU/ml (≥ 1.2 kU/l) was 29% of 41 smoking mothers and 17% of 145 non-smoking

mothers (odds ratio 2.1, 95% confidence interval (CI) 0.9 to 4.7). Among 106 offspring of non-allergic parents, the equivalent odds ratio was 4.6 (95% CI 1.5 to 14.4), but it is not possible to assess whether there is a statistically significant interaction between maternal smoking and family history of allergy. Paternal smoking was not associated with increased IgE concentrations (odds ratio 1.1, 95% CI 0.5 to 2.3).

Among 1251 Turkish infants⁸ the geometric mean IgE was similar whether the mother smoked more than 10 cigarettes daily during pregnancy (0.63 kU/l, $n=119$) or was a non-smoker (0.54 kU/l, $n=1073$). This difference was not statistically significant, but confidence intervals cannot be calculated and no data are presented for 59 light or occasional smokers. In contrast to the study by Magnusson,⁷ the effect of maternal smoking appeared to be greater among children with a family history of allergy, although the statistical interaction was not formally assessed.

A smaller study of 110 Polish infants⁹ found no significant differences in geometric mean cord IgE level with parental smoking, although the effect of father's smoking (0.40 kU/l versus 0.33 kU/l) appeared more influential than smoking by the pregnant mother (0.36 kU/l versus 0.37 kU/l). Among 47 offspring of atopic parents, maternal smoking was associated with a lower geometric mean IgE concentration (0.36 kU/l versus 0.46 kU/l). This difference is not statistically significant ($p=0.06$).

As part of a more general descriptive study Bergmann *et al*¹⁰ related cord blood IgE levels to parental smoking habits during pregnancy for 4793 German infants, representing 63% of all babies born in six hospitals during 1990. The prevalence of elevated IgE concentrations (≥ 0.7 kU/l) was 11.6% among 3495 offspring of non-smoking mothers and 10.6% among 1298 babies whose mothers smoked during pregnancy (odds ratio 0.9, 95% CI 0.7 to 1.1). The equivalent odds ratio for paternal smoking was 1.0 (95% CI 0.8 to 1.2). This large study did not report upon possible effect modification by paternal family history.

Only one study has related objective measures of maternal smoking to cord blood IgE concentrations.¹¹ The geometric mean IgE level was 0.12 kU/l among the offspring of 79 non-smoking mothers and 0.11 kU/l among 20 babies whose mother smoked, a non-significant difference. Similar conclusions were drawn whether maternal smoking during pregnancy was assessed by questionnaire or by cord blood cotinine and perinatal maternal urinary cotinine concentrations, suggesting that reliance on smoking history is unlikely to have introduced bias into other larger studies.

Two earlier studies^{5,12} of small samples (46 and 136 infants, respectively) also report no significant association of parental smoking with neonatal IgE concentrations, but another of 215 infants found a positive correlation between the number of cigarettes smoked in pregnancy and cord blood IgE levels.¹³ A somewhat larger study of 325 infants found no significant association using a more sensitive assay, but it

appears to have been published only in abstract form.¹⁴ These studies offer insufficient quantitative information to be considered in detail in this review.

POSTNATAL IgE CONCENTRATIONS

Total serum IgE concentrations rise rapidly during the first few years of life and the early report by Kjellman⁵ suggested that this increase might be more rapid in infants at high risk of atopy if their parents smoked. However, a prospective study of 80 Israeli babies with wheezy bronchitis found no effect of parental smoking on the rate of increase in serum IgE concentrations from one to four years of age.¹⁵ Total IgE levels increased by more than 100 kU/l in 56% of 52 offspring of smoking parents compared with 54% of 28 non-smoking parents. No significant effect of parental smoking on total IgE levels at any age was found among 73 British children born to atopic parents and followed over five years.¹⁶

Among 100 children aged 1–17 years (mean nine years) recruited from general paediatric practice in the USA¹⁷ the geometric mean total IgE level was non-significantly lower if the mother smoked (43 versus 56 kU/l) and the concentrations of specific IgE to common aero-allergens were similar with respect to maternal smoking. However, children of smoking mothers did have significantly higher levels of serum IgD (geometric means 15 kU/l versus 10 kU/l).¹⁷ In contrast, a Turkish study of 558 patients aged 1–17 years with respiratory allergies¹⁸ found significantly higher geometric mean total IgE concentrations in the children of smokers than non-smokers (241 versus 192 kU/l). No confidence intervals were given.

These observations on patient groups are of limited value because the referral criteria are poorly specified. Greater confidence can be placed in surveys of representative population samples. Three such studies have been published.

Wjst *et al*¹⁹ presented a detailed analysis of indoor factors in relation to total serum IgE levels in 703 children, 64% of a population sample from three East German towns. Parental smoking habits were assessed by questionnaire and, in a subsample of 224 children, by urinary cotinine assay. After adjustment for family history of atopy and 30 demographic or indoor environmental factors the relative increase in total IgE associated with current parental smoking was estimated as +15% (95% CI –9% to 46%). An effect of similar magnitude was derived for past smoking, but no independent effect emerged for maternal smoking during pregnancy (95% CI –41% to +66%). Although children in the top 10% of the cotinine distribution had higher total IgE levels, no clear dose-response relationship emerged with measured tobacco smoke exposure, and was not formally evaluated by a test for trend.

El-Nawawy *et al*²⁰ compared 70 randomly selected schoolchildren of smoking parents with 50 age matched children of non-smoking parents in a rural area of Egypt. The offspring

of smokers had significantly higher arithmetic mean IgE levels (585 versus 189 kU/l), eosinophil counts (482 versus 239 cells/m³) and interleukin 4 concentrations (1.6 versus 0.8 ng/l). It is uncertain whether these reflect allergic sensitisation or immune responses to parasites.

Ronchetti *et al*²¹ measured total serum IgE concentrations in 159 nine year old children, 89% of a randomly selected sample in three Italian towns. An association of geometric mean IgE with one or more parents smoking emerged for boys (99 versus 39 kU/l) but not for girls (56 versus 59 kU/l). Statistical significance was achieved by subgroup analysis, but the interaction of sex and parental smoking was not formally assessed. The prevalence of eosinophilia ($\geq 4\%$ leucocytes) was also increased in the offspring of smoking parents, independent of the common association with IgE level. This otherwise informative study does not provide an estimate of the effect of parental smoking on serum IgE levels in both sexes combined, although it is reported to be non-significant ($p=0.2$).

SKIN PRICK REACTIONS

In the same Italian study a positive correlation was found in boys, but not in girls, between the total number of cigarettes smoked daily by parents and the number of positive reactions on skin prick tests to eight aeroallergens and two food allergens.²² Four years later 142 (86%) of the original 159 children were retested and the prevalence of positive skin prick tests related to current parental smoking.²³ Combining boys and girls, the odds ratio for one or more positive skin prick tests was 1.7 (95% CI 0.8 to 3.8), and the interaction between sex and smoking was not statistically significant. However, further subgroup analyses were reported which suggested that persistent parental smoking may enhance the development of allergic sensitisation in boys.

The relationship of current maternal smoking to atopy, defined as ≥ 5 mm erythema or a detectable weal (≥ 0 mm) to any of four aeroallergens, was analysed among a population based cohort of 196 children aged 12–16 in Boston, Massachusetts.²⁴ A positive association of similar strength to the Italian study was found (odds ratio 2.2, 95% CI 1.1 to 4.4). This was significant at the 2% level and the 95% confidence interval is derived from the published χ^2 value.

A random sample of 219 children aged 7–12 registered with a general paediatric practice in Chapel Hill, North Carolina were skin prick tested with 14 allergens using a ≥ 4 mm cut off.²⁵ Smoking by either parent at the age of five was only weakly associated with skin prick positivity (prevalence 42% in 84 smoking families versus 39% in 135 non-smoking families, odds ratio 1.1, 95% CI 0.6 to 1.9). This study also analysed skin prick reactions by a history of maternal smoking during pregnancy and found an inverse relationship (36% versus 40%, odds ratio 0.8, 95% CI 0.4 to 2.0).

A longitudinal study of consecutive births in the Isle of Wight during 1989–90 has reported

on the association of environmental factors and allergic sensitisation at the ages of one²⁶ and two years.²⁷ Only the latter study is considered here. Among the offspring of 257 smoking mothers 4.7% had positive skin prick tests to one or more of five allergens at the age of two compared with 5.3% of 915 children of non-smoking mothers, an odds ratio of 0.9 (95% CI 0.5 to 1.7). It is not clear from the publication whether this relates to current maternal smoking or smoking in pregnancy.

Skin test reactions in older children were related to passive smoke exposure in infancy in a multicentre survey of 2232 children aged 10–12 years in Sweden, Poland and Estonia.²⁸ The prevalence of sensitisation to eight aeroallergens was greater among children exposed to parental smoking in Sweden (33% versus 28%, $n=640$) and Estonia (12% versus 10%, $n=1234$), but in Poland the findings were opposite (12% versus 18%, $n=358$). None of these differences was significant at the 5% level, and thus all would be consistent with no effect of parental smoking on allergic sensitisation. Odds ratios can be calculated directly from the published figures but their confidence intervals can only be estimated on the assumption that the prevalence of exposure in each centre was approximately 50% (as cited in the paper). When specific aeroallergens were considered in all centres combined, passive smoke exposure was associated with a significant increase in risk of sensitisation to animal dander (1.4, 95% CI 1.0 to 1.9) but not grass pollen (1.2, 95% CI 0.9 to 1.6).

The possibility that early exposure may be particularly important was addressed in detail in a cross sectional survey of 529 Norwegian children, 82% of a representative sample of 7–13 year olds in two valleys.²⁹ Eight aeroallergens were used for skin prick testing with a 3 mm cut off for positivity. The prevalence of one or more positive tests was lower among children whose parents currently smoked, the odds ratios being 0.8 (95% CI 0.5 to 1.2) and 0.7 (95% CI 0.5 to 1.1) for maternal and paternal smoking, respectively. More extreme results were obtained for maternal smoking in the first year of life (0.6, 95% CI 0.4 to 1.0) and prenatally (0.6, 95% CI 0.4 to 1.0). These findings contrast with those above^{22 23 25} and suggest that selective avoidance of smoking by parents of children who develop atopic disease is unlikely to bias the results of population based studies.

A larger cross sectional study of 8653 children aged 9–11 years in three German cities³⁰ also found a reduced prevalence of skin prick positivity in children of smoking mothers. Six common aeroallergens were assessed by skin testing, using a 3 mm cut off. The relevant prevalence data are not tabulated but after adjustment for study area, family history of asthma or atopy, number of siblings, sex, maternal education, and pet ownership the odds ratio relating skin test positivity to current maternal smoking was 0.8 (95% CI 0.7 to 0.9, $p=0.02$). No information is reported on paternal smoking.

A second German study in three south-western towns performed skin prick tests to seven aeroallergens on 1470 (81%) of 1812 children aged 6–8 years.³¹ Children with a positive reaction (≥ 3 mm) to any allergen – and specifically to grass pollen, dust mites, and cat dander – were less likely than non-atopic children to have been exposed to maternal smoking in pregnancy, in the first year of life, or in the previous year. After adjustment for parental atopy, gestational age, and sex the odds ratio for maternal smoking in pregnancy was 0.6 (95% CI 0.3 to 1.1) for any skin test positivity, and ranged from 0.4 to 0.8 for sensitisation to specific allergens. The unadjusted effect of maternal smoking during pregnancy was similar in children of non-atopic parents (0.5, 95% CI 0.3 to 1.1) and those with a parental history of asthma, hay fever or eczema (0.4, 95% CI 0.2 to 1.1).

Two studies have analysed the relationship between skin prick positivity and parental smoking among patients with atopic disease. These are more difficult to interpret because parental smoking may have influenced the reason for referral and may have changed as a response to the child's illness. In a Swedish study of children aged 3–17 years referred for asthma, allergic rhinitis or eczema,³² exposure to environmental tobacco smoke was assessed retrospectively for the first two years of life and thereafter. Early exposure was reported for 57% of patients (65/115) with skin prick reactions to any of eight aeroallergens and for 41% of patients (22/54) with negative skin prick tests, an odds ratio of 1.9 (95% CI 1.0 to 3.6). Exposure after two years of age was more similar in the two groups (45% versus 41%). Among 302 asthmatic subjects aged 1–12 years diagnosed by family physicians in Italy³³ current exposure to parental smoking was less common among those with positive (≥ 3 mm) skin prick tests to any of six allergens: 77% (176/230) versus 82% (59/72), an odds ratio of 0.7 (95% CI 0.4 to 1.4).

CLINICAL ATOPIC DISEASE (EXCLUDING ASTHMA)

The relationship of maternal smoking to clinical atopic disease has been reported from the south-west German study.³⁴ Eczema was defined without reference to the skin prick tests and was inversely related to maternal smoking during pregnancy and during the previous year. Hay fever, defined on the basis of symptoms of rhinitis or conjunctivitis plus a positive skin prick test to pollen, was also less common if the mother smoked. The unadjusted odds ratio for any atopic disease in relation to maternal smoking during pregnancy was 0.7 (95% CI 0.5 to 1.1) and in relation to current maternal smoking was 0.8 (95% CI 0.6 to 1.1).

Norrman *et al*³⁵ also defined allergic rhinoconjunctivitis by a combination of reported symptoms and positive skin prick reaction to a relevant aeroallergen among 985 (85%) of a population sample of 14 year old children in northern Sweden. After adjustment for area, month of birth, sex, atopic family history, type of residence, and mould in the home there was

an increased risk of allergic rhinoconjunctivitis if the mother smoked (odds ratio 1.3, 95% CI 0.7 to 2.3) but a decreased risk if the father smoked (0.9, 95% CI 0.5 to 1.7). The relative risks were similar for a lifetime history of allergic rhinoconjunctivitis.

Two population based surveys of school-children have related histories of seasonal or perennial rhinoconjunctivitis³⁶ or hay fever³⁷ to parental smoking without corroborative evidence from skin prick tests. Among 5412 children aged 7–12 years in Turkey³⁶ rhinoconjunctivitis was more common if parents smoked after adjustment for village, sex, animal contact, breast feeding, and atopic family history (adjusted odds ratio 1.2, 95% CI 1.0 to 1.5). In contrast, among 1503 children aged 12 years in the Scottish Highlands,³⁷ reported hay fever was significantly less common if the parents smoked (unadjusted odds ratio 0.7, 95% CI 0.5 to 0.9).

In a prospective study of physician-diagnosed allergic rhinitis in a birth cohort of 747 infants in Tucson, Arizona followed to the age of six years³⁸ maternal smoking was equally common in children with and without a diagnosis of allergic rhinitis (8% in each group). Early diagnosis was more common in children of smoking parents, possibly because they were more likely to seek medical help for lower respiratory illnesses in infancy and thereby to receive investigations for allergy. In contrast, in a national British cohort born in 1970 and followed to five years of age³⁹ a lifetime history of hay fever (reported by parents) was slightly more common in children of non-smoking mothers (4.6%) than in those whose mothers smoked ≥ 15 cigarettes per day (4.0%). Insufficient detail is given to calculate confidence intervals and the results are not adjusted for possible confounding variables such as birth rank, socio-economic status, and breast feeding.

In 1172 children born in the Isle of Wight²⁷ there was a slightly reduced lifetime prevalence of eczema by the age of two in the offspring of smoking mothers (odds ratio 0.7, 95% CI 0.4 to 1.1) and little difference in the prevalence of rhinitis (0.9) or food intolerance (1.0). These odds ratios were not adjusted for possible confounding factors. Reported eczema was not associated with parental smoking among Scottish 12 year old children (unadjusted odds ratio 0.9, 95% CI 0.7 to 1.2).³⁷

STUDIES OF HIGH RISK CHILDREN

Three intervention studies recruiting infants of atopic parents have reported briefly upon the influence of parental smoking on allergic manifestations in these susceptible groups. Smoking by either parent was associated with an increased risk of physician assessed eczema (odds ratio 2.4, 95% CI 0.7 to 7.9) and food intolerance (1.5, 95% CI 0.2 to 9.7) among 120 high risk infants from the Isle of Wight who participated in a trial of perinatal allergen avoidance.⁴⁰ However, no association of maternal or paternal smoking with eczema or nasal discharge in infancy was found in a feeding trial of 468 children in South Wales, of whom

half were exposed to smoking in the home.^{41,42} Among 165 high risk children in California followed to the age of seven years as part of a dietary intervention study⁴³ there were 22 who were regularly exposed to smoking in the home. This group had a significantly higher prevalence of aeroallergen sensitisation (odds ratio 2.9, 95% CI 1.1 to 7.7) and an increased risk of atopic disorders excluding asthma (odds ratio 1.7, 95% CI 0.7 to 4.4).

Discussion

Previous reviews have concluded that parental smoking adversely affects risk of allergic disease.⁴⁴ This conclusion may be misleading because it does not adequately distinguish between the well established association of parental smoking with lower respiratory illnesses in early childhood,⁶ which may include forms of asthma,^{24,33} and the effect of prenatal or postnatal tobacco smoke exposure on allergic sensitisation which in turn may lead to asthma. This review has deliberately excluded asthma and other wheezing disorders in order to concentrate on IgE mediated allergic manifestations.

Much of the evidence reviewed is imperfect because of the play of chance in small studies, lack of control for potential confounders in most of the published analyses, and the potential for bias towards an inverse association if parents of atopic children selectively avoid smoking at critical periods of prenatal or postnatal development. Each of these limitations has been addressed in one or more publications, but no single study offers the ideal design or analysis.

Since the first and widely cited report by Magnusson⁷ several larger studies have failed to confirm a substantial or significant effect of maternal smoking on cord blood IgE concentrations. With one exception from rural Egypt²⁰ (where IgE may be elevated by parasitism), the only statistically significant associations between postnatal IgE levels in children and parental smoking are those arising from repeated significance testing⁵ or subgroup analysis,²¹ each of which increases the probability of false positive results. The balance of evidence suggests little or no effect of parental smoking on IgE concentrations in children in developed countries.

The quantity and quality of evidence is greatest for studies measuring skin prick reactivity which are summarised in table 2 and fig 1. Overall, no consistent pattern emerges: there appears to be an increased risk of sensitisation among children of smoking parents in Sweden, Estonia, Italy and USA, but a reduced risk among children of smoking parents in Poland, Norway and Germany. The German studies recruited larger samples and adjusted for multiple confounding variables, and both found a slightly decreased risk of allergic sensitisation in smoking homes.

The results are more consistent if studies of perinatal exposure are considered separately (table 2). There is evidence of heterogeneity of effects between these studies, but it is of only

Figure 1 Odds ratios and 95% confidence intervals for the effect of parental smoking on skin prick positivity. ○ = studies of perinatal exposure (see table 2); ● = studies of current exposure (see table 2). Pooled values were derived by random effects modelling. See table 2 for definitions and data points. Note that the x axis is logarithmic.

borderline statistical significance and both “fixed effect” and “random effects” methods of pooling yield similar results – namely, a non-significant reduction in risk among the offspring of smokers. It is reasonable to conclude that parental smoking during pregnancy or early childhood is unlikely to increase substantially the risk of allergic sensitisation.

The evidence is much less consistent with regard to current exposure (table 2). There is marked and statistically significant heterogeneity across studies, which is not readily explained by location, design, age group, or method of exposure assessment. There is uncertainty about both the direction and magnitude of this association and a quantitative summary is problematic. Further studies are required to shed further light on the relationship of parental smoking after the perinatal period to allergic sensitisation, taking into account confounding variables and possible smoking cessation in response to the child's illnesses.

The results relating to allergic rhinitis and eczema are derived from competent studies but are generally reported in too little detail to permit a comprehensive reanalysis. There is no consistent evidence of an increased risk among the offspring of smokers, except in two small intervention studies of high risk infants.^{40,43} However, in the single study which has formally evaluated the interaction between parental atopic history and prenatal smoke exposure³¹ the effects of maternal smoking were similar in children with and without a parental history of

allergic disease. This argues against, but does not entirely exclude, a stronger effect of passive smoking among children genetically at high risk of allergy.

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