

PARENTAL SMOKING AND CHRONIC EAR INFECTIONS

SUMMARY OF THE EVIDENCE

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Introduction

The possible adverse effects of passive smoking on children's health have been known for some time, but it is only recently that attention has been focused on middle ear problems in particular. Indeed, the earliest study to consider this group of diseases was not published until 1979 [2], since when at least 25 other studies have presented data on this subject. Three reviews of the evidence on the relationship between childhood middle ear disease and smoking by household members have also been published [7,26,32]. All three failed to find convincing evidence that a causal relationship exists.

The objective of this report is to provide a summary of the epidemiological evidence relating to the possible association between environmental tobacco smoke exposure and childhood middle ear diseases of all types.

The Studies

Twenty-six studies were found which were relevant to the subject under investigation. Six of the studies were of prospective design, 4 were cross-sectional, 1 was experimental, 1 contained a prospective and a case-control section, and 14 were of the case-control type, although 3 of these took the cases and controls from a cross-sectional study, and 1 was also experimental. Brief details of the studies are given in Table 1. The studies by Etzel and Maw were not considered for further analysis, as information on an adequate control series was not available. Also, as the

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aim of the study by Maw was to measure the outcome of surgery for glue ear, rather than to investigate the causes of the disease, it was not really comparable to the other studies. Additionally, the results from the case-control section of the study by Zielhuis were not included, as it was felt that this was not a separate study as such.

The age range of the cases in the studies went from birth to 14 years. Only one of the studies measured smoke exposure objectively, by salivary cotinine assay, with the others relying upon data gathered from questionnaires. With the exception of two studies in which the source of information was not stated, data was collected from the parents or guardians. Tympanometry was the most commonly used method of diagnosing middle ear disease, although most of the studies used a combination of several techniques, including myringotomy, otoscopy, audiometry, impedance tests, grommet insertion, and reporting by physician or parents. Most of the case-control studies carried out matching for age, as well as for one or more other factors. Levels of non-response were frequently not reported, but where they were, a much higher level of non-response among controls than cases was found by one study (Visscher: controls 55%, cases 9%), while another found no real difference in response rate in one set of controls, but a higher non-response rate in the other set (Black: cases 1%; hospital controls 2%; home controls 10%).

Smoking by Household Members

Table 2 summarizes the results for smoking by any household member, presenting unadjusted relative risk estimates where possible, and showing the ninety-five percent confidence intervals so that the significance of the findings can be seen. The specific disease to which the risk estimate relates is also given, as several of the studies investigated more than one disease.

Meta-analysis of the unadjusted relative risks was then performed, with risk estimates being calculated from the numbers of exposed and unexposed cases and controls where possible, if this had not already been done. Nine of the studies, all of which reported finding no association (see Table 2), gave insufficient information to permit inclusion, meaning that the meta-analysis was based almost entirely on raised relative risks, which obviously biased the results. Additionally, the study by Fleming did not give confidence limits and so could not be included, and

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for the same reason the adjusted relative risk given by Black was used in place of the unadjusted one. For the study by Lyons, only the relative risk given for hearing loss was included, as it was felt that this was a better index of current ear disease than abnormalities of the tympana, which could have been present from an earlier episode of ear disease. Using a fixed effects model, a relative risk estimate of 1.35 (95% CI 1.21-1.50) was found from meta-analysis.

The risk of middle ear disease in relation to the level of exposure was examined in one of two ways, based on either the number of cigarettes smoked per day, or by recording the number of smokers in the household. The results are summarized in Table 3 and Table 4 respectively. One study found a significant trend in increasing risk with an increasing number of cigarettes smoked, and one study found a significant trend with the number of smokers present in the household. The other studies failed to find any clear pattern of increasing risk with increasing exposure to tobacco smoke.

The studies were also analysed according to the specific disease considered, and these findings are summarized in Table 5. Of all the diagnostic subgroups looked at, only one failed to show a significantly positive result where meta-analysis was carried out, although the relative risk estimate was still above 1.00.

Maternal Smoking During Pregnancy

Two studies considered this index of exposure, and their findings are summarized in Table 6. One study failed to find an association, while the other found positive associations for both acute and secretory otitis media. None of the results were detailed enough to allow meta-analysis to be performed.

Maternal Smoking After Pregnancy

Three studies presented results for maternal smoking after pregnancy, as shown in Table 7. Two studies found raised relative risks, although only one of these was significantly so, while the other study failed to find an association for either of the two diagnostic subgroups considered. Meta-analysis of the available results gave a risk estimate of 1.58 (95% CI 1.13-2.23).

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Paternal Smoking

Table 8 summarizes the results from the two studies which considered paternal smoking, neither of which found a significantly positive association.

Separation of Potential Effects of Maternal Smoking During and After Pregnancy

Most of the studies did not consider the possible effects of maternal smoking during pregnancy, concentrating solely on the child's exposure to smoke after birth. Bearing in mind that women who smoke during pregnancy tend to continue to do so after the birth of their child, separating out the effects of transplacentally-received smoke and exposure to tobacco smoking after birth will be very difficult, but if, as has been suggested, smoking during pregnancy is more important than smoking after pregnancy [32], it could confound the results of the studies which failed to measure this factor, and produce spurious associations. Of the two studies which did look at maternal smoking during pregnancy, one presented separate results for maternal smoking after pregnancy, while the other presented results only for smoking by all household members.

Misclassification of Exposure

Several of the studies measured only parental smoking, and did not record smoking by other members of the household. It is possible that neither of the child's parents were smokers but that another occupant of the house may have been, and in such cases a child classified as coming from a non-smoking household may be wrongly classed as such. If this type of misclassification is random it will have the effect of weakening any association between exposure to tobacco smoke and the risk of childhood middle ear disease.

None of the studies which included older children appeared to have considered the fact that some of these children may themselves be active smokers. Indeed, Strachan found cotinine levels in six children which were too high to be explained by passive smoking alone. If active smoking were more likely to produce symptoms than passive smoking then the

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inclusion of such children in the analysis may lead to a stronger association between environmental tobacco smoke exposure and middle ear disease.

Additionally, misclassification of exposure may occur in prospective studies if smoking habits are not recorded throughout the period of follow-up, as any subsequent changes in smoking behaviour will not be taken into account and bias may be introduced. One study measured parental smoking habits at the beginning of the study period only, another recorded smoking data at the end of the study period only, and one collected information at the beginning of the study for some respondents and at the end for others. Only the study by Zielhuis recorded parental smoking habits throughout the study period, although the analysis was based solely on measurements taken at the fifth screening round.

Effect of Adjustment for Confounding Variables on Estimates of Relative Risk

The available adjusted relative risks, along with the unadjusted relative risks, the factors adjusted for, and the disease being investigated, are given in Table 9. The overall effect of adjustment is not clear, with one of the studies finding a lower relative risk after adjustment, and three reporting that the observed association became stronger. In fact, in two of the studies the results became significant after adjustment had been carried out. The effect of adjustment in the study by Fleming was difficult to judge, due to the failure to present an unadjusted relative risk for comparison. Generally, there was a failure of studies which found positive unadjusted relative risks to have carried out any adjustment for potential confounders, and those which did adjust their results often had not considered many of the other known risk factors for middle ear disease. These include existing medical conditions, such as a recent episode of rhinorrhoea or similar viral infection [1,5,7-9,11,12,15,17,20,22,24,28,30,33], presence of nasal congestion [4,6-8,33], the presence of an allergic condition [1,4,5,9,10,12,16,17,19,24,30,33,35], and a family history of ear disease [4,9,10,15,16,18,22,29]; environmental factors such as season and climate [3-5,8,10,16,23,25-27,29,31]; and social factors, particularly contact with other children [4], either through the presence of older siblings

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[9,11-13,26,27] or through attendance at a public day-care centre or school [2,5,8-12,17,19-21,26-28,33]. The possibility exists, therefore, that these factors could be confounding any associations between smoking by household members and the risk of childhood middle ear disease.

Other Study Weaknesses

Various other problems were noted in some of the studies, including an apparent failure to conduct any of the studies blind which may have caused recall bias and/or affected the depth of questioning, failure to adequately match the cases and controls, and a general lack of information about the design and execution of the studies. Possible misclassification of diagnosis may also have occurred, due partly to the varying quality of diagnostic techniques used, and differences in the "health culture" of families which may determine whether or not a child is taken to a doctor. The effects of such a selection bias are not clear, and will depend on whether parents who smoke are more or less likely to report symptoms in their children.

Difficulties in Interpretation of Meta-analysis

Variation in the quality of the studies, due to the differing methodologies used, makes it unclear what weight should be given to each study in meta-analysis. Also, although studies which did not find significantly positive associations were published, the noticeable tendency for such studies to fail to present their results in enough detail to allow inclusion in the meta-analysis data set means that the meta-analysis was based almost solely on raised relative risk values. It is therefore not surprising that the overall results showed an apparently significant positive association. However, it must be borne in mind that no significantly negative associations were found by any of the studies, but five significantly positive associations were reported. Also, even if it is assumed that all of the studies which failed to present their results had in fact found a negative relationship, this would still leave over half of the studies reporting a positive association, which is more than would be expected by chance alone.

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Conclusions

It is possible that exposure to environmental tobacco smoke may convey a small risk of developing middle ear disease in childhood. However, the risk attributable to this factor, calculated as lying between 8% and 75% [11,24,33,34], still leaves a large number of cases unexplained, pointing to the existence of one, or more, other major risk factors. This fact, along with the study weaknesses discussed above, such as the failure to separate out the effects of maternal smoking during and after pregnancy, potential misclassification, the failure of many studies to adjust for confounding variables, and the problems in interpreting the results of meta-analysis, leads to the overall conclusion that the epidemiological data do not really provide convincing evidence that the observed associations between the risk of childhood middle ear disease and smoking by other members of the child's household result from a causal relationship.

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Table 1 Details of the studies

Study	Ref.	Location	Study design	No. of cases	Control type	Matching factors
Vinther	2	Denmark	C-S	203 ¹		
Kraemer	4	USA	C-C	76	Patients	A, S, TS
Pukander I	5	Finland	C-CS	134	Healthy ²	A
Van Cauwenberge	7,8	Belgium	PR	138		
Visscher	9	USA	C-CS	300	Patients	C
Black	10	England	C-C	150	Patients/ School	A, S
Iversen	11	Denmark	PR	78 ¹		
Pukander II	12	Finland	C-C	264	Patients	A, U
Birch	13	Denmark	PR	185		
Kallail	14	USA	C-C	119	School	A, S,
Hinton I	15	England	C-C/E	34	Patients	A, S, C, SC
Marchisio	16	Italy	C-CS	81	Patients	C
Reed	17	USA	C-C	45	Patients	C, TS
Rockley	18	USA	C-C	78	Patients	A, C
Tainio	19	Finland	PR	101		
Zielhuis	20,26	Netherlands	PR/C-C	<1439		
Fleming	21	USA	C-S	139		
Hinton II	22	England	C-C	115	Patients	A, S, C, U
Strachan	24,28	Scotland	C-S	82		
Ross	27	England	PR	156		
Barr	29	England	C-C	115	Patients	A, S, R, SC
Green	30	W. Germany	C-C	217	Patients	A, S,
Etzel	33	USA	PR	132		
Lyons	34	Ireland	C-S	34		
Maw	35,37	England	E	201		
Rowe-Jones	36	England	C-C	163	Patients	SC, U

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Footnote for Table 1

1 Estimated from given data

2 Source not stated

A - Age; C - Clinic/hospital; C-C - Case-control; C-CP - Case-control from within a cross-sectional study; C-S - Cross-sectional; E - Experimental; PR - Prospective; R - Race; S - Sex; SC - Social class; TS - Time of surgery/diagnosis; U - Urban area
Studies listed in order of publication - see references

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Table 2 Risk of childhood middle ear disease of all types for smoking by household members

Study	Dis- ease	Relative risk (95% limits)	Notes
Vinther	SOM	No association ¹	No details given
Kraemer	PMEE	1.45(0.76-2.76)	Estimated from data given
Pukander I	AOM	No association ¹	No details given
Van Cauwenberge	SOM AOM	No association ¹ No association ¹	No details given No details given
Visscher	OM	No association ¹	No details given
Black	SOM	1.37(p > 0.05) ¹	Estimated from data for two control groups
Iversen	MEE	1.55(0.999-2.40)	Estimated from data given
Pukander II	AOM	1.89(1.30-2.74)	Estimated from data given
Birch	SOM	No association ¹	No details given
Kallail	MEP	1.55(0.93-2.59)	Estimated from data given
Hinton I	MEE	2.24(0.86-5.84)	Estimated from data given
Marchisio	POME	No association ¹	No details given
Reed	MEE	4.51(1.26-16.1)	Estimated from data given
Rockley	PSOM	No association ¹	No details given
Tainio	ROM	3.00(1.15-7.84)	Estimated from data given
Zielhuis	OME	1.07(0.90-1.26)	
Fleming	URTI EI	1.70(p = 0.01) ¹ 1.10(p = 0.82) ¹	Adjusted for family income, race, crowding, no. of children aged <5 years, age
Hinton II	OME	1.64(0.88-3.05)	Estimated from data given
Strachan	MEE	1.41(0.89-2.23)	Estimated from data given
Ross	URTI AOM	No association ¹ No association ¹	No details given No details given
Barr	OME	0.76(0.45-1.27)	Estimated from data given
Green	MEE	1.70(1.08-2.69)	Estimated from data given
Lyons	HL AT	8.74(1.88-40.6) 4.86(1.29-18.3) ²	Estimated from data given Estimated from data given
Rowe-Jones	POME	1.21(0.64-2.28)	Estimated from data given

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Footnote for Table 2

1 Insufficient information given to permit inclusion in meta-analysis

2 Not included in meta-analysis, as not an index of current ear disease

AOM - acute otitis media; AT - abnormal tympana; EI - ear infections; HL - hearing loss; MEE - middle ear effusion; MEP - middle ear problems; OM - otitis media; OME - otitis media with effusion; PMEE - persistent middle ear effusion; POME - persistent otitis media with effusion; PSOM - persistent secretory otitis media; ROM - recurrent otitis media; SOM - secretory otitis media; URTI - upper respiratory tract infections

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Table 3 Risk of childhood middle ear disease in relation to the number of cigarettes smoked per day by household members

Study	Grouping (packs per day)	Relative risk by grouping	Trend
Kraemer	0 .1-.9 1-1.9 2-2.9 ≥ 3.0	1.0 1.9 1.1 1.0 4.1	NS
Kallail	0 <1 1-2 2-3 $\geq 3^1$	1.0 1.49 1.11 2.46	NS
Hinton I	0 1-19 20-39 40+ ²	1.0 2.75 2.62 1.57	NS
Reed	0 ≤ 1 >1	1.0 3.64 5.67	p=0.02
Green	Five point scale(0-40 cigs)	No correlation found	NS

1 Groupings as stated by author. It is not clear into which category 2 packs a day smokers were included

2 Cigarettes per day

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Table 4 Risk of childhood middle ear disease in relation to the number of smokers in the household

Study	Grouping			Relative risk by			Trend
	(number of smokers)			grouping			
Kraemer	0	1	2+	1.0	1.0	2.8	NS
Kallail	0	1	2+	1.0	1.49	1.53	NS
Strachan	0	1	2+	1.0	1.17	1.89	p<0.05

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Table 5 Summary of results for childhood middle ear diseases by type of disease for smoking by household members

Disease	No. of studies	Negative		RR=1	Positive		Meta-analysis
		S	NS		NS	S	
All diseases	24	0	1	8*	10	5	1.36 (1.22-1.51)
Acute infections	7	0	0	4*	1	2	2.01 (1.41-2.84)
Acute otitis media	4	0	0	3*	0	1	1.89 (1.30-2.74)
Recurrent otitis media	1	0	0	0	0	1	3.00 (1.15-7.84)
Otitis media	1	0	0	1*	0	0	Not performed
Ear infections	1	0	0	0	1	0	Not performed
Upper respiratory tract infections	2	0	0	1*	0	1	Not performed
Chronic infections	15	0	1	5*	7	2	1.27 (1.13-1.43)
Middle ear effusion	5	0	0	0	3	2	1.65 (1.29-2.12)
Persistent middle ear effusion	1	0	0	0	1	0	1.45 (0.76-2.76)
Secretory otitis media	4	0	0	3*	1	0	1.57 (1.17-2.09)+
Persistent secretory otitis media	1	0	0	1*	0	0	Not performed
Otitis media with effusion	3	0	1	0	2	0	1.07 (0.91-1.24)
Persistent otitis media with effusion	2	0	0	1*	1	0	1.21 (0.64-2.28)
Middle ear problems	1	0	0	0	1	0	1.55 (0.93-2.59)
Hearing loss	1	0	0	0	0	1	8.74 (1.88-40.6)
Anormal tympana	1	0	0	0	0	1	4.86 (1.29-18.3)

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Footnote for Table 5

* No association reported but no detailed results given, therefore not included in meta-analysis where available

+ Meta-analysis based on adjusted relative risks only

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Table 6 Risk of ear disease in children in relation to maternal smoking during pregnancy

Study	Disease	Relative risk (95% limits)
Van Cauwenberge	Acute otitis media	Positive association (p<0.05)
	Secretory otitis media	Positive association (p<0.05)
Black	Secretory otitis media	No association

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Table 7 Risk of ear disease in children in relation to maternal smoking after pregnancy

Study	Disease	Relative risk (95% limits)
Van Cauwenberge	Acute otitis media	No association
	Secretory otitis media	No association
Barr	Otitis media with effusion	1.23(0.67-2.26)
Green	Middle ear effusion	1.92(1.23-2.99)

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Table 8 Risk of ear disease in children in relation to paternal smoking

Study	Disease	Relative risk (95% limits)
Van Cauwenberge	Acute otitis media	No association
	Secretory otitis media	No association
Green	Middle ear effusion	1.37(0.89-2.12)

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Table 9 Effect of adjustment for confounding variables on estimates of middle ear disease risk for smoking by household members

Study	Dis- ease	Adjustment factors	Relative risks (95% limits)
Kraemer	PMEE	None	1.45(0.76-2.76)
		Nasal congestion, atopy	1.10(0.50-2.90)
Black	SOM	None	1.37(p > 0.05)
		Employment status of parents, day-care, place of birth, use of unsealed heating system	1.57(1.17-2.09)
Iversen	MEE	None	1.55(0.999-2.40)
		Age	1.60(1.001-2.57)
Reed	MEE	None	4.51(1.26-16.1)
		Breast-feeding, previous episode of OM, recent common cold, day-care	Associations more pronounced

MEE = Middle ear effusion; OM = Otitis media; PMEE = Persistent middle ear effusion; SOM = Secretory otitis media

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