Relation of passive smoking as assessed by salivary cotinine concentration and questionnaire to spirometric indices in children

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Abstract

Background Previous studies of the effects of passive exposure to smoke on spirometric indices in children have largely relied on questionnaire measures of exposure. This may have resulted in underestimation of the true effect of passive smoking. Biochemical measures offer the opportunity to estimate recent exposure directly.

Methods The relation between spirometric indices and passive exposure to tobacco smoke was examined in a large population sample of 5-7 year old children from 10 towns in England and Wales. The effects of passive exposure to smoke on lung function were assessed by means of both salivary cotinine concentration and questionnaire measurements of exposure. Analyses of the relation between spirometric values and cotinine concentrations were based on 2511 children and of the relation between spirometric values and questionnaire measures on 2000 children.

Results Cotinine concentration was negatively associated with all spirometric indices after adjustment for confounding variables, which included age, sex, body size, and social class. The strongest association was with mid expiratory flow rate (FEF₅₀), the fall between the bottom and top fifths of the cotinine distribution being 6%, equivalent to a reduction of 14.3 (95% confidence limits (CL) 8.6, 20.0) ml/s per ng/ml cotinine. Salivary cotinine concentrations were strongly related to exposure to cigarette smoke at home but 88% of children who were from non-smoking households and not looked after by a smoker had detectable cotinine concentrations, 5% being in the top two fifths of the cotinine distribution. A composite questionnaire score based on the number of regular sources of exposure was as strongly related to mid and end expiratory flow rates as the single cotinine measure. The fall in FEF₅₀ per smoker to whom the child was exposed was 51.0 (26.5, 75.5) ml/s. The relationships be-

tween the questionnaire score and forced vital capacity (FVC) or forced expiratory volume in one second (FEV₁) were not statistically significant.

Conclusions These effects of passive smoking on respiratory function are consistent with the results of previous studies and, although small in absolute magnitude, may be important if the effects of exposure are cumulative. In children aged 5-7 years the use of a single salivary cotinine concentration as a marker of passive exposure to smoke resulted in clear relationships between exposure and FVC and FEV₁, whereas the associations were much weaker and not significant when based on the questionnaire score. The associations between exposure and mid or end expiratory flow rates were of similar magnitude for cotinine concentration and the questionnaire score. The use of salivary cotinine concentration in longitudinal studies may help to determine the extent to which these effects are cumulative or reversible.

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The health hazards of passive smoking for children have been extensively reviewed.¹⁻³ Although the effect of parental smoking on acute respiratory illnesses in infancy is clear and consistent, not all studies have shown effects on respiratory symptoms and ventilatory function in older children. Many of these studies were small, however, and all relied on questionnaire measures of parents' smoking habits to characterise passive exposure to smoke. Such measures ignore exposure outside the household, the extent to which the parents are smoking in the presence of the child, and other modifying factors, such as the ventilation of the room at the time, raising the possibility that studies based on exposure as assessed by questionnaire may have underestimated the real effect of passive smoking in children. Biochemical measures

offer the opportunity to estimate recent exposure directly.

Cotinine, a metabolite of nicotine, is the biochemical marker of choice for quantifying passive exposure to smoke.⁴ It is specific to tobacco, with a half life of about 20 hours, and can be assayed at low concentrations by gas-liquid chromatography.⁵ Salivary concentrations are in approximate equilibrium with those in the blood⁶ and provide a non-invasive way of measuring passive exposure to smoke. The only previous study relating lung function to passive smoking by using a biochemical marker was a study of 770 seven year old children in Edinburgh, which found negative associations between spirometric indices and salivary cotinine, the effect being significant for end expiratory flow rates.⁷

In this paper we examine the relation between spirometric indices and passive exposure to smoke in a large sample of children from 10 towns in England and Wales. In particular, we compare salivary cotinine concentrations with questionnaire measures of exposure in relation to spirometric indices in an age group, 5.5–7.9 years, where active smoking was unlikely to confound the issue. We measured mid and end expiratory flow rates (FEF₅₀ and FEF₇₅) as well as forced vital capacity (FVC) and forced expiratory volume in one second (FEV₁) as there is some evidence that these are most affected.⁷

Methods

SAMPLE SELECTION

The study was carried out in 10 towns in England and Wales, five with exceptionally high adult cardiovascular mortality rates (Wigan, Burnley, Rochdale, Port Talbot, and Rhondda) and five with exceptionally low rates (Esher, Leatherhead, Chelmsford, Bath, and Tunbridge Wells). The selection of these towns has been described in detail elsewhere.⁸ Because of the strong geographic association between mortality from cardiovascular and respiratory disease, this resulted in five towns with high mortality from respiratory diseases and five with low mortality. Within each town a sample of 10 primary schools, stratified by religious denomination and, in the case of country primary schools, by size and location, was selected. Any school unable to take part was replaced by the school matching it most closely in denomination, size, and location. Within each school two classes of children in the age range 5.0–7.9 years were randomly selected to provide a sample of 50–60 children who were invited to participate. The validation of the sampling method has been described.⁹

SURVEY PROCEDURES

During January–July 1990 a team of four trained nurses, working in pairs, visited each town. Towns in high and low mortality areas were examined alternately. The 10 schools in each town were visited over five days, each pair of nurses visiting one school for a whole day. Each nurse made about one quarter of all measurements in each town.

Standing height was measured to the last complete millimetre with shoes removed. Weight was measured to the last complete 0.1 kg. Ethnic group (European origin or non-European origin) was assessed on the basis of the child's appearance. Room temperature was measured to the nearest 0.1°C with a digital thermometer and thermocouple (RS Components). External temperatures, as recorded hourly at local meteorological stations, were provided by the Meteorological Office.

SPIROMETRY

After instruction and two practice attempts each child performed three forced expiratory manoeuvres, according to the methods recommended by the American Thoracic Society.¹⁰ Tests were performed in the standing position; nose clips were not used. Two "Compact" pneumotachographs (Vitalograph Ltd, Buckingham) with a paediatric mouthpiece adapter were used. These measure air flow through a resistive mesh, on the Fleisch principle, and determine volumes by flow integration. On three occasions each day the pneumotachographs were calibrated by pumping 10 litres through the instrument with a one litre precision syringe. This was repeated at both fast and slow rates to check the linearity of the flow integration. There were no problems with calibration drift. All spirometric indices were corrected automatically to BTPS. The following spirometric indices were automatically recorded for the "best" test as defined by the American Thoracic Society¹⁰ (that is, the spirogram with the greatest sum of FEV₁ and FVC): FVC, FEV₁, the instantaneous flow rates when 25%, 50%, and 75% of FVC had been expired (FEF₂₅, FEF₅₀ and FEF₇₅). In addition, a measure of reproducibility, the best test variation, was recorded (that is, difference between FEV₁ + FVC for the "best" test and for the "second best" test as a percentage of that for the "best" test).

SALIVARY COTININE

Subjects were asked to collect saliva in the mouth and to blow it through a plastic straw into a plastic container. Samples were frozen within eight hours of collection for later assay by gas-liquid chromatography, which can detect cotinine concentrations as low as 0.1 ng/ml.⁵

QUESTIONNAIRE

A self completion questionnaire was sent to the parents of all participants on the day of the examination. Social class was determined for both parents on the basis of present or most recent occupation, classified according to the Registrar General's six social classes. Analyses in this paper refer to the head of household (male in 93%) as defined by the Office of Population Censuses and Surveys.¹¹ Those few households to whom a social class could not be assigned were treated as a separate group; they were mostly single parent households in which the mother had never worked regularly. The parents were asked about their own current smoking habits (number of cigarettes per day

Table 1 Frequency distribution of salivary cotinine concentrations according to number of cigarette smokers to whom the child is exposed

No of smokers to whom exposed	Salivary cotinine group (ng/ml)							Total
	ND	0.1–	0.3–	0.7–	1.8–	4.1–	> 14.7	
0	143	371	397	184	51	10	1	1157
1	17	41	122	205	208	112	0	705
2	1	3	11	76	186	232	29	538
≥3	0	0	1	8	22	49	5	85
Total	161	415	531	473	467	403	35	2485

ND—not detectable.

plus pipe and cigar smoking for fathers), whether anyone else in the household smoked cigarettes, and whether the child was looked after for two hours a week or more by anyone from outside the household who smoked cigarettes. In several analyses we used a score representing the number of these four sources of exposure to which the child was exposed.

STATISTICAL METHODS

Cross tabulations and multiple regressions were performed with the FREQ and GLM procedures in SAS.¹² In multiple regression models spirometric indices were standardised for: age, sex, standing height, body mass index (weight/height²), and observer (with one observer the children achieved consistently higher lung volumes and flow rates than with the other three). Body mass index was included as a linear term in multiple regression analyses as the standard deviation and skewness did not vary substantially over the narrow age range. Social class and town of residence were also included as simple indicators of household socioeconomic status and of local environmental influences that were related to both respiratory symptoms and lung function. External air temperature was not included as any relationships with lung function were adequately controlled for by adjusting for town.

Salivary cotinine concentration was analysed both as a grouped variable and as a continuous measurement. Five groups were defined by the quintiles of cotinine in the study sample. In adults and adolescents a cotinine concentration of 14.7 ng/ml has been suggested as a cut off for active smoking¹³ and thus children with cotinine values above 14.7 ng/ml were treated as a separate group in some analyses, as were children with concentrations below the threshold of detection (0.1 ng/ml). Undetectable concentrations were coded as 0.05 ng/ml.

Results

RESPONSE RATES AND MISSING DATA

All analyses in this paper are based on children of European origin aged 5.5–7.9 years. Children aged less than 5.5 years were excluded because of the difficulty of obtaining adequate spirometric measurements. Of the 4711 children aged 5.5–7.9 invited, 78% (n = 3664) were screened and spirometric measurements were obtained on 90% (n = 3282) of these. The analyses presented in this paper are based on the 2682 children whose “best test” variation was 10% or less (we comment below on the effect of not including the restriction on best test variation). The larger number of readings available for FEV₁ and FVC than for flow rates was due to a temporary programming error on one pneumotachograph. Salivary cotinine measurements were available for 91% (n = 3327) of the children screened. Analyses of the relation of FEV₁ to cotinine concentrations were based on the 2511 children who had both a cotinine concentration and spirometric measurements and an acceptable best test variation. The questionnaire sent to parents of children who were screened was returned by 87% (n = 3184). Complete data on exposure to smoking were available for 2751. Analyses of the relation of FEV₁ to questionnaire measures of exposure to tobacco smoke were based on the 2000 children for whom acceptable spirometric and questionnaire data were available.

DELIVERY OF SALIVARY COTININE CONCENTRATIONS

Salivary cotinine concentration was strongly related to the number of smokers to whom the child was usually exposed (table 1). Undetectable cotinine was rare among those exposed to one or more smokers (18/1328 = 1.4%), whereas among those not regularly exposed there was only one reading above 14.7 ng/ml. Thirty five children had cotinine concentra-

Table 2 Mean (SD) spirometric indices and spirometric indices by quintiles of salivary cotinine,* and multiple regression estimate of the effect of a 1 ng/ml increase in cotinine concentration

	n	Mean (SD)	Salivary cotinine quintiles (ng/ml)					Change in spirometric indices per ng/ml cotinine		
			< 0.3	0.3–	0.7–	1.8–	≥ 4.1	Estimate	SE	p
FVC (ml)	2511	1509 (294)	0	3	10	–21	–32	–4.8	1.3	0.0002
FEV ₁ (ml)	2511	1330 (238)	0	11	8	–12	–30	–4.7	1.1	0.0001
FEF ₂₅ (ml/s)	2346	2546 (607)	0	–12	–65	–45	–153	–16.5	3.5	0.0001
FEF ₅₀ (ml/s)	2346	1862 (480)	0	10	–1	–44	–114	–14.3	2.9	0.0001
FEF ₇₅ (ml/s)	2345	990 (337)	0	26	32	11	–31	–5.3	2.0	0.0087
FEV ₁ /FVC (%)	2511	88.75 (8.21)	0	0.5	0.0	0.4	–0.3	–0.04	0.05	0.39

*The mean difference from the bottom quintile adjusted for confounding variables; all values adjusted for age, sex, height, body mass index, observer, and town.

FVC—forced vital capacity; FEV₁—forced expiratory volume in one second; FEF₂₅, FEF₅₀, FEF₇₅—early, mid, and end expiratory flow.

Mean FEV₁ with 95% confidence limits, by smoking habit of parents.

tions above 14.7 ng/ml. Finally, whereas children with no data from the questionnaire had cotinine concentrations above average for the study those with no data on cotinine had average exposure as assessed by questionnaire (data not presented).

SALIVARY COTININE AND SPIROMETRIC INDICES
The relationships between spirometric indices and cotinine concentration, after adjustment for age, sex, height, body mass index, observer, and town, are shown in table 2. All spirometric indices show a tendency for children with higher cotinine concentration to have poorer ventilatory function. For all except the FEV₁:FVC ratio these differences were highly significant. The strongest association (as shown by the p value) was with FEF₅₀, where each unit increase in cotinine concentration was associated with a fall of 14.3 (95% confidence limits (CL) 8.6, 20.0) ml/s. Additional adjustment for head of household's social class (which meant restricting the analyses to children for whom questionnaire data were available) had little effect on the estimated coefficients (compare the coefficients in tables 2 and 4). The coefficients for FEF₅₀ and FEF₇₅ actually increased marginally whereas those for FVC and FEV₁ were reduced in magnitude. For descriptive purposes the adjusted mean spirometric indices are given by cotinine groups, after subtraction of

the mean in the lowest fifth. The relation of spirometric values to cotinine concentrations is relatively flat over the first three fifths of the cotinine distribution. Given the small differences in cotinine between the groups this is not surprising. Because of the skewed distribution of cotinine the change in cotinine over the next two fifths is much greater and there were substantial falls in all spirometric indices. For FEF₅₀ the mean in the highest fifth of the cotinine distribution is some 6% below that in the lowest fifth. For FEV₁ the deficit is just over 2%. In table 2 the spirometric indices appear to fall linearly with increasing cotinine concentration, and this was confirmed by including quadratic terms for cotinine in regression models—all such terms were non-significant.

QUESTIONNAIRE EXPOSURE AND SPIROMETRIC INDICES

We ascertained exposure to cigarette smoke from four sources on the basis of the questionnaire: mother, father, others living in the same household, and anyone else looking after the child for more than two hours a week. The independent relationships of each of these sources of exposure to spirometric indices was examined by means of multiple regression analyses in which all sources were included simultaneously. All four sources of exposure tended to be associated with reduced spirometric measures. For FEV₁ (ml) the effects were -8.6 (95% CL -27.5, +10.3) if the mother smoked, -9.5 (-27.8, +8.9) if the father smoked, +7.9 (-37.9, +53.7) if others in the household smoked, and -21.0 (-8.8, +50.9) if a minder smoked. For FEF₅₀ (ml/s) the effects were -56.3 (-106.1, -6.5), -41.6 (-90.1, +6.9), -76.4 (-195.1, +42.4), and -74.6 (-152.0, +2.8). Because the effects from the different sources of exposure seemed broadly similar (though few were individually significant) and because there was no clear evidence of dose-response effects with number of cigarettes smoked by mother or father (data for FEV₁ presented in figure) we summarised exposure as the number of sources (0, 1, 2, ≥3; there were so few with four sources of exposure that this group was not treated separately). The relation of this summary score to each of the spirometric indices appears in table 3. For all indices except FVC there is a clear fall in respiratory function with increasing exposure. As with cotinine, the strongest association was with FEF₅₀, the estimated effect being a reduction of 51.0 (95% CL 26.5, 75.5) ml/s for each

Table 3 Multiple regression estimates of the effect of exposure (as assessed by questionnaire) on respiratory function

		No of smokers to whom regularly exposed				Change in spirometric indices per additional smoker		
	n	0	1	2	≥3	Estimate	SE	p
FVC (ml)	2000	0	2	-5	16	- 0.0	5.6	0.99
FEV ₁ (ml)	2000	0	- 0	-15	- 33	- 8.1	4.8	0.09
FEF ₂₅ (ml/s)	1863	0	-23	-62	-246	-46.2	15.2	0.0025
FEF ₅₀ (ml/s)	1863	0	-21	-95	-192	-51.0	12.5	0.0001
FEF ₇₅ (ml/s)	1862	0	-14	-43	- 75	-22.2	8.9	0.01
FEV ₁ /FVC (%)	2000	0	- 0.3	- 0.7	- 3.2	- 0.54	0.20	0.008

*Adjusted for age, sex, height, observer, body mass index, town, and social class. Abbreviations as in table 2.

Table 4 Comparison of the predictive value of cotinine and questionnaire exposure on respiratory function on reduced data set where both measures were available*

	n	Change in lung function per ng/ml of cotinine		Change in spirometric indices per additional smoker	
		Estimate	p	Estimate	p
FVC (ml)	1875	- 3.6	0.03	- 0.2	0.97
FEV ₁ (ml)	1875	- 4.3	0.002	- 7.6	0.12
FEF ₂₅ (ml/s)	1742	-15.8	0.0004	-47.6	0.002
FEF ₅₀ (ml/s)	1742	-15.8	0.0001	-52.7	0.0001
FEF ₇₅ (ml/s)	1741	- 6.3	0.01	-23.1	0.01
FEV ₁ /FVC (%)	1875	- 0.08	0.18	- 0.50	0.02

*Each variable (cotinine and number of smokers) was separately included in a model that also included age, sex, observer, height, body mass index, town, and social class. Abbreviations as in table 2.

additional source of exposure. In contrast to cotinine, exposure as assessed by questionnaire was negatively associated with FEV₁/FVC.

EFFECT OF AGE, SEX, AND EXCLUSION OF HIGH COTININE CONCENTRATIONS

For both cotinine and questionnaire exposure the regression analyses were repeated separately for boys and girls and for younger (<6.5 years) and older children. In addition, we repeated the analyses excluding subjects with a cotinine concentration greater than 14.7 ng/ml. The coefficients tended to be more strongly negative in boys than in girls and in the younger age group. None of these differences, however, was statistically significant for any of the outcome measures. Excluding the high cotinine values had only a small effect on the regression coefficients. Finally, we examined the effect of including subjects with a best test variation of more than 10%. Again there were no important changes in the estimated coefficients except for FVC and FEV₁, which increased in magnitude (to -6.1 and -5.5 in the cotinine analyses). The lack of effect of restricting the best test variation was not surprising given the very weak association between best test variation and cotinine concentrations: the geometric mean cotinine was 1.01 ng/ml in children with a best test variation of up to 10% and 1.09 ng/ml in children with a best test variation of more than 10%. Inclusion of other potential confounding variables in the models, such as birth weight and presence or absence of gas cookers, had no effect on the regression estimates.

IS COTININE CONCENTRATION OR A QUESTIONNAIRE BASED MEASURE THE BETTER PREDICTOR?

We have shown the inverse associations between spirometric indices and both salivary cotinine and a questionnaire measure of passive exposure to smoking. To assess which was the better predictor, both cotinine and number of sources of exposure were included, one at a time, in regression models fitted on a data set including only those children for whom both exposure as assessed by questionnaire and cotinine measurements were available (table 4). All estimates in table 4 are adjusted for any confounding effects of social class. Other potential confounders, such as birth weight and use

or non-use of gas cookers, were not adjusted for as they had no effect on the estimated coefficients. Judged in terms of statistical significance, cotinine was somewhat more strongly related to FVC and FEV₁, whereas the questionnaire measure was somewhat more strongly related to the FEV₁/FVC ratio. Given the strong association, however, between cotinine and questionnaire exposure (table 1), and the small magnitude of the effects in question as a proportion of the total variation in spirometric indices, too much should not be made of these patterns. What is clear is that, in our data, a questionnaire score that combined several different sources of exposure was as good a predictor of flow rates as a single measurement of cotinine in young children.

SHORT TERM VIABILITY IN COTININE CONCENTRATIONS

It was important to consider how well a single measurement of salivary cotinine characterises the average concentration for an individual. As part of the present study 111 children who were included in the pilot study had their cotinine concentrations measured in January and again in July. The mean cotinine fell from 1.59 to 1.37 ng/ml, a fall of 0.22 (SD 1.38) ng/ml. The fall was thus not statistically significant (95% CL -0.04, 0.48 ng/ml), and the correlation of the two measurements was 0.81.

Discussion

PREVIOUS STUDIES

Several cross sectional studies have sought evidence of lung damage attributable to passive exposure to tobacco smoke in childhood on the basis of exposure as assessed by questionnaire. Most^{7 14-23} but not all²⁴⁻²⁶ have observed associations in the expected direction, though not all the associations in the studies with positive results were statistically significant.

QUESTIONNAIRE MEASURES OF EXPOSURE AND SPIROMETRIC INDICES

To assess current exposure previous studies have usually asked only about the smoking habits of mothers, or of mothers and fathers. Two have reported a dose-response relationship with the mother's cigarette consumption^{21 22} and one with the father's consumption.¹⁴ In our study there were no statistically significant associations with the smoking habit of the father and only a few spirometric indices were significantly associated with that of the mother. Using a composite score based on the number of sources of exposure, however, including one from outside the home, we found a clear relation between estimated degree of exposure to tobacco smoke and respiratory function. Nevertheless, the lack of a clear dose-response relationship with number of cigarettes smoked per day by the parents and the possibility that the mother's smoking is more important than the father's, which is supported by other studies, suggest that factors that modify exposure, such as the extent to which cigarettes are smoked in the presence of children, need to be taken into account. Our results

also emphasise that questionnaire measures need to take account of other sources of exposure. Although the number of children looked after by a smoker from outside the home was small in our study ($n=156$), the effect on lung function was as great as that of smoking by the mother. For older children and adults it may prove even harder to characterise exposure by the smoking habits of a few significant others.²⁷ From this perspective the salivary cotinine concentration should provide a better index of actual exposure.

POTENTIAL VALUE OF A BIOCHEMICAL MARKER

The potential value of a biochemical marker is illustrated by the distribution of salivary cotinine concentrations among children from non-smoking households who were not regularly looked after by someone from outside the home who smoked. This identified a purer "un-exposed" reference group that that used in previous studies, yet 88% of such children in our sample had detectable cotinine concentrations in their saliva and 5% were in the upper two fifths of the distribution. This presumably reflects smoking by visitors to the family or passive exposure outside the home because none of the concentrations in children from non-smoking households was high enough to be compatible with active smoking. In adults and adolescents a cotinine of 14.7 ng/ml has been suggested as a cut off for active smoking.¹⁴ We believe, however, that most of these values were due to passive exposure because (1) only one value out of the 35 was incompatible with passive exposure (56.3 ng/ml); (2) 69% of the values over 14.7 ng/ml were in girls; and (3) the average age of children with high values was 6.2 years, below the average for the survey.

COTININE AND SPIROMETRIC INDICES

All spirometric indices were negatively associated with cotinine concentration and most of the associations were highly significant. As with the questionnaire measure, the strongest association was with FEF_{50} , the fall between the bottom and top fifths of the cotinine distribution being 6%, equivalent to a reduction of 14.3 ml/s per ng/ml of cotinine (95% CL 8.6, 20.0). Although these associations are highly significant statistically, they are small in magnitude and we must consider whether they might be due to residual confounding, in particular for social factors. This seems unlikely as adjustment for social class altered the cotinine coefficients very little and actually increased the coefficient relating cotinine concentration to FEF_{50} . The only previous study that included a biochemical marker was based on seven year old children in Edinburgh, and used similar methods.⁷ The associations seen in the present study are all consistent with the earlier results, though we found slightly stronger associations for early and mid expiratory flow rates. The suggestion that flow rates in the terminal part of the spirogram might be most sensitive to passive exposure to smoke has not been substantiated.

Even if recent exposure is most relevant cotinine concentrations vary within subjects,

which will lead us to underestimate the true relation between cotinine concentration and spirometric indices.²⁸ The correlation of the two cotinine measurements was 0.81, which is in keeping with previous estimates.²⁹ An estimate of the true relation between cotinine and spirometric indices can be obtained by multiplying the coefficients in table 2 by $0.81^{-1} = 1.24$.³⁰ Such corrections are not ideal,³¹ especially as the variability of cotinine tends to increase with average concentrations, and—given the relative ease of obtaining saliva for cotinine assay, possibly by post—we would prefer to see more than one saliva sample obtained in future studies.

COTININE CONCENTRATION AND QUESTIONNAIRE MEASURES

Whereas there is evidence that biochemical markers of active smoking are more strongly related to disease outcomes than is reported consumption of cigarettes,^{32,33} the only previous study of indirect exposure was of cotinine concentration compared with reported maternal consumption in relation to birth weight.³⁴ Cotinine concentration was clearly the better predictor. We have found that a single measurement of cotinine was similar in value to a composite questionnaire measure of passive exposure for predicting mid and end expiratory flow rates, and for FVC and FEV_1 cotinine was somewhat better. In so far as previous studies have not used a composite measure and because a single cotinine measure will have led us to underestimate the true association by 24%, previous studies will have underestimated the true effect of passive exposure to smoke on spirometric indices in children.

LONG TERM EXPOSURE

Although biochemical markers accurately reflect recent exposure to tobacco smoke, they may not adequately reflect longer term exposure. Questionnaires allow the possibility of estimating past exposure but also have problems. For example, in smoking households preschool exposure is likely to have been greater even if the parents have not altered their smoking habits. This may explain why the evidence of respiratory effects from parental smoking is most consistent in the first few years of life,¹ though an alternative explanation is that younger children are more susceptible. Within the narrow age range of the present study the estimated effects on spirometric indices were similar in younger and older children. In the present study reported changes in smoking habits among parents since the birth of the child were few and thus we could not distinguish the effects of past from present exposure.

AGENDA FOR FUTURE WORK

The smallness of the spirometric changes observed in this and other cross sectional studies raises two important questions: firstly, is recent or long term exposure important in determining the deficit and, secondly, is the effect of long term exposure cumulative? It is

difficult for cross sectional studies to address such questions as past exposure is difficult to quantify. Two prospective studies found that reduced growth in lung function (FEV₁) was associated with passive exposure to smoke,^{35 36} but one did not.³⁸ All three used questionnaire measures of exposure, one based only on whether the child's mother smoked³⁵ and the others also on whether the father smoked.^{36 37}

Ultimately the clinical and epidemiological significance of the small spirometric changes observed in cross sectional studies can be assessed only by performing ventilatory function measurements and assessing exposure repeatedly over time in children where active smoking is excluded.³⁸ In practice, exposure is likely to vary even while parental smoking habits remain constant (cotinine concentrations fell with age even within the present study) and among adolescents exposure to friends' smoking takes on greater prominence.²⁷ Repeated measurements of salivary cotinine will be needed to differentiate current from past exposure and to examine the reversibility of the effects of passive smoking on spirometric indices.

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