Passive smoking and impaired lung function in cystic fibrosis

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Abstract
Passive smoking was measured in 57 children with cystic fibrosis and in 51 controls using a questionnaire and a measurement of urinary cotinine concentration. In the cystic fibrosis group, cotinine was significantly lower than in the controls. Also in this group, when the parents smoked the child's forced expiratory volume in one second decreased by 4% and the forced vital capacity by 3% for every 10 cigarettes smoked in the household each day.
(*Arch Dis Child* 1994; 71: 353–354)

Cotinine is a metabolite of nicotine and is a reliable biochemical measure of exposure to passive smoking.[1] Passive smoking (measured by salivary cotinine concentration) has a negative, dose dependent, effect on lung function in healthy schoolchildren.[2] A similar effect (measured by urinary cotinine concentration) has been shown in children with asthma.[3] We have used the urinary cotinine concentration to study the effects of passive smoking in children with cystic fibrosis.

Subjects and methods
We studied 57 patients with cystic fibrosis and 51 controls (enrolled from the paediatric dental clinic) aged 5–16 years. All patients with cystic fibrosis were prescribed antibiotic prophylaxis against staphylococcal bacteria. An investigator administered the questionnaire. Social class was assigned according to whether the head of household was in a manual or non-manual occupation or was unemployed. Urine samples from the two groups were assayed for cotinine concentration by gas-liquid chromatography.[4] Samples from children with cystic fibrosis were also assayed for antibiotics (using a bioassay)[5] to assess compliance with antibiotic prophylaxis.

In the cystic fibrosis group, the forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) were measured using a portable spirometer (Micro Medical). The two values were expressed as a percentage

of those predicted for height using the values of Polgar and Promadhat.[6] Similarly, weight was expressed as a percentage of that predicted for height using standard centile charts (Castlemead Publications).

The logarithmic transformation of cotinine values was performed as the cotinine distribution was positively skewed. Comparisons were made using the χ^2 test (with Yates's correction), the unpaired Student's t test, and stepwise linear regression with the Arcus Pro-II statistics package.

Results
Urinary cotinine was measured in 107 (99%) subjects; urinary antibacterial substances were measured in 54 (95%) patients with cystic fibrosis and were present in 52 (96%) of these.

For all subjects, simple linear regression showed a correlation between log cotinine and smoking index (regression coefficient 0·015; 95% confidence interval 0·009 to 0·020; p<0·0001). The mean urinary cotinine concentration was significantly greater in the control group (geometric mean 8·67) than in the patients with cystic fibrosis (geometric mean 5·12; ratio 1·69; 95% confidence interval 1·07 to 2·69; p=0·028). One control subject may have been an active smoker (urinary cotinine concentration 1124·8 ng/ml) and was excluded from the statistical analysis.

No smoking was allowed in the home in 24/57 (42%) households in the cystic fibrosis group, but only 8/51 (16%) in the control group. This was a significant difference (χ^2=7·8; p=0·005).

For patients with cystic fibrosis, a stepwise linear regression analysis was performed in which the outcome variables were FEV_1, FVC, and weight (all expressed as a percentage of that value predicted for height). The following predictor variables were used: log cotinine concentration; smoking index; parental occupation; and patient's sex and age. The table shows those predictor variables which correlated significantly with each clinical end point. The smoking index was the most significant predictor of FEV_1 and female sex of FVC. For every increase in the smoking index of 10 cigarettes each day, the FEV_1 decreased by about 4% and the FVC by 3%. Only non-manual parental occupation predicted weight.

Discussion
We have shown less exposure to passive smoking in a group of patients with cystic fibrosis compared with control subjects without respiratory illness. This may be because

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Stepwise linear regression of clinical end points with predictor variables

Clinical end point*	Predictor variable	Regression coefficient	95% Confidence interval	p Value
FEV_1	Smoking index	−0·413	−0·766 to −0·060	0·022
	Female sex	−10·9	−21·7 to −0·130	0·047
FVC	Female sex	−9·93	−19·0 to −0·887	0·032
	Smoking index	−0·299	−0·596 to −0·002	0·047
Weight	Non-manual occupation	10·8	2·70 to 18·9	0·01

*Expressed as percentage predicted for height.

families of patients with cystic fibrosis were significantly more likely to forbid smoking in the home.

We have shown a negative association between passive smoking and lung function in patients with cystic fibrosis. This is likely to be a real effect of passive smoking as it is dose dependent and the major confounding variable, social class, was included in the analysis. Compliance is unlikely to be a confounding factor as we have shown good compliance, at least with prophylactic antibiotics. Log urinary cotinine did not predict lung function, perhaps because the relation between cotinine and lung function is flat over the first three fifths of the cotinine distribution.[2] The finding that nutrition tends to be better in children whose parents were in non-manual occupations, despite regular dietary advice given to all parents in the cystic fibrosis clinic, is surprising.

In conclusion, urinary cotinine in our study reflected household smoking behaviour but did not predict lung function. There was an association between increasing household smoking and impaired FEV_1 and FVC in children with cystic fibrosis. Smoking by parents of children with cystic fibrosis should be strongly discouraged.

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3 Chilmonczyk BA, Salmun LM, Megathlin KN, *et al.* Association between exposure to environmental tobacco smoke and exacerbations of asthma in children. *N Engl J Med* 1993; **328:** 1665–9.
4 Feyerabend C, Russell MAH. A rapid gas-liquid chromatographic method for determination of cotinine and nicotine in biological fluids. *J Pharm Pharmacol* 1990; **42:** 450–2.
5 Harvey KJ. Antibacterial activity in urine. *Med J Aust* 1972; i: 1072–4.
6 Polgar G, Promadhat V. *Pulmonary function testing in children: techniques and standards.* Philadelphia: Saunders, 1971.