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Exposure to Environmental Tobacco Smoke and the Risk of Adverse Respiratory Events in Children Receiving General Anesthesia

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Background: **Exposure to environmental tobacco smoke is associated with detrimental effects on pulmonary function in children. The authors investigated the relation between airway complications in children receiving general anesthesia and the passive inhalation of tobacco smoke.**

Methods: **Six hundred two children scheduled to receive general anesthesia were enrolled in this prospective study. The anesthesiologist and the recovery room nurse, unaware of the smoke exposure history, recorded the occurrence of airway complications. A history of passive smoking was assessed by measuring the urinary concentration of the major nicotine metabolite cotinine and by questionnaire.**

Results: **Airway complications occurred in 42% of the patients with urinary concentrations of cotinine ≥40 ng/ml, in 33% of the patients with concentrations of cotinine between 10.0 and 39.9 ng/ml, and in 24% of the patients with concentrations of cotinine <10 ng/ml ($P = 0.01$ for the trend among the three groups). The gender of the child ($P = 0.001$) and the educational level of the child's mother ($P = 0.0008$) significantly modified the effect of the concentration of cotinine on the incidence of adverse respiratory events.**

Conclusions: **There is a strong association between passive inhalation of tobacco smoke and airway complications in children receiving general anesthesia. The relationship is greatest for girls and for those whose mothers have a lower level of education. Passive smoking should be regarded as a risk factor in children undergoing general anesthesia. (Key words: Anesthetic complications; passive smoking; pediatric anesthesia; tobacco smoke pollution.)**

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U. S. Environmental Protection Agency: Respiratory health effects of passive smoking: Lung cancer and other disorders [EPA/600/8-90/006F]. Washington, DC, US Environmental Protection Agency, Office of Research and Development, Office of Air and Radiation, December 1992

EXPOSURE to environmental tobacco smoke is associated with several detrimental effects on the respiratory system in children. Passive smoking results in decreased lung growth. The expected increase in the forced expiratory volume in 1 s and in the forced vital capacity during childhood is diminished.[1-3] Passive inhalation of tobacco smoke by children has been associated with an increased incidence and severity of asthma and airway hyperreactivity[4-8]# and an increased rate of lower respiratory tract illness in infants.[9,10]# Second-hand smoking has also been linked with upper airway cellular and mucociliary dysfunction including higher rates of otitis media.[11,12]#

Cotinine, the major metabolite of nicotine, is the most commonly used qualitative and quantitative bio-

logic marker of exposure to environmental tobacco smoke.[4,9,13-16] The correlation between passive smoking and urinary concentrations of cotinine has been clearly established. This allows for group delineation according to low, moderate, and high levels of passive smoking.[4,14-16] Because cotinine in urine has a half-life of 19-40 h in nonsmokers, the reported values reflect exposure during the previous 3-4 days.[14]

In the United States, nearly two million surgical procedures per year are performed on children younger than 15 yr old,** so accurate identification of a patient population at increased risk for perioperative airway complications is important. Although the adverse effects of passive smoking have been reported previously,[1-13]# the effect of exposure to passive smoke on perioperative airway complications in children after the administration of general anesthesia is unknown. Accordingly, we conducted a prospective study using urine concentrations of cotinine to test the hypothesis that exposure to environmental tobacco smoke increases the incidence of airway complications in children undergoing general anesthesia.

Materials and Methods

Patients

After approval from the institutional review board of Health Sciences, Columbia University, and with written informed consent from the parents, 602 children (age range, 1 month-12 <fr11/12> yr) coming from home on the day of surgery and scheduled to receive general anesthesia at The Babies and Children's Hospital of New York/Columbia Presbyterian Medical Center between September 1993 and January 1995 were enrolled. All study participants were free of cardiovascular or severe respiratory disease and were classified as American Society of Anesthesiologists patient status I-III. Twenty-seven of the 602 patients were excluded because they inadvertently received drugs that were not part of the anesthetic protocol (see later). Urine samples for cotinine analysis were obtained successfully from 499 of the 575 remaining children. After the study was completed, three environmental tobacco smoke exposure groups were defined: those with corrected (see later) urinary concentrations of cotinine of (1) <10 ng/ml (no exposure), (2) 10.0-39.9 ng/ml (moderate exposure), and (3) ≥40 ng/ml (heavy exposure).[4,14-16]

Documentation of Environmental Tobacco Smoke Exposure

On the day of surgery, parents completed an American Thoracic Society children's respiratory questionnaire,[17] which furnished demographic and medical information on the child and family and a history of environmental exposure. The questionnaire was modified by including (1) a detailed smoking survey from the adult portion of the respiratory questionnaire and (2) qualitative and quantitative assessments of tobacco use by all persons, at home and at other places frequented by the child.

A patient was considered to have a history of reactive airways disease if the parents gave an affirmative answer to those questions related to chronic cough and wheeze as defined by the authors of the questionnaire.[17] A recent history of upper respiratory infection was defined by an affirmative parental response to the question, "Has your child had a cold in the past 6 weeks?"[18]

During their stay in the operating suite, urine samples were obtained from each child and frozen at −20°C until transportation to the laboratory for measurement of cotinine by radioimmunoassay. This method uses specific antisera produced in rabbits according to the method of Haley *et al.*[19] The inter- and intraassay variations are 9%, with a sensitivity of 2.0 ng/ml. Urinary concentration of creatinine was measured by calorimetric assay (Ectochem 500; Eastman Kodak, Rochester, NY). To account for differences in concentrations in urine among patients, concentrations of cotinine were corrected to the mean urinary concentration of creatinine of our patients using a previously published regression coefficient[4,20] between urinary concentrations of cotinine and creatinine. The values for cotinine were then standardized to the mean urinary concentration of creatinine of our patients.

Anesthetic Protocol

Anesthetic care was provided by 12 attending anesthesiologists whose practices were limited to children and residents in anesthesiology. Each physician furnished a four-digit code number, which provided ano-

** Vital and Health Statistics: National Hospital Discharge Survey: Annual Summary, 1992, Series 13: Data from the National Health Survey, No. 119. Washington, DC, US Department of Health and Human Services, Centers for Disease Control and Prevention/National Center for Health Statistics, DHSS Publication No. (PHS) 94-1779, 1992

nymity for tracking the effect of the anesthesiologist on airway complications.

After determining the oxygen saturation of hemoglobin by pulse oximetry (SpO_2) while breathing room air, anesthesia was induced by inhalation of 70% nitrous oxide in oxygen and gradually increasing concentrations of halothane without any premedication. Patients who required neuromuscular blockade received vecuronium bromide (0.1 mg/kg). Anesthesia was maintained with 65% nitrous oxide in oxygen and a concentration of halothane that allowed proper surgical conditions with the lowest variance of heart rate and blood pressure. Patients were anesthetized using a face mask only when appropriate (*i.e.,* acceptable surgical site and duration, absence of aspiration hazard). All other patients (428 of 499) were anesthetized using an endotracheal tube. One hundred six of 499 patients received intravenous fentanyl supplementation (dose range, 1.0–6.4 μg/kg; one patient received 7.9 and another 11.3 μg/kg). To provide for postoperative pain relief, 285 of 499 patients received caudal, ilioinguinal, penile, or local infiltration blocks, which were combined with the general anesthetic agent of the protocol. Patients who inadvertently received volatile anesthetic agents other than halothane, neuromuscular blocking agents other than vecuronium, narcotic agents other than fentanyl, atropine as an antisialagogue or for prevention of bradycardia, or any drugs known to release histamine were excluded because of a failure to adhere to the study protocol. No patients were excluded because of their clinical condition or an adverse event that may have occurred.

Outcome Measures

The patient's anesthesiologist, unaware of the history of exposure to environmental tobacco smoke (because obtaining a smoking history about parents or caregivers is not part of the routine preoperative history), and unaware of the concentration of cotinine, recorded the following adverse events on a separate data sheet: laryngospasm (characterized by an inability to ventilate the patient's lungs and requiring either administration of continuous positive pressure or a neuromuscular blocking agent to restore ventilation), auscultated wheezing, bronchospasm requiring treatment, airway pressure increased to higher than the baseline peak airway pressure, stridor, breath holding, severe coughing (defined as three or more paroxysms or at least one episode lasting >5 s) on induction or emergence from anesthesia, excessive mucous production requiring suctioning of the endotracheal tube, and oxygen desaturation to $SpO_2 \leq 95\%$ with regular pulsation evident on the pulse oximeter. Whether a patient experienced one or more than one adverse event, that patient was only counted once in the adverse event category. If the patient's anesthesiologist marked the section on the data sheet indicating that the event was the result of a nonpatient-related mechanical problem (*e.g.,* endobronchial intubation, tracheal tube kinking), then it was not considered an adverse event.

In the recovery room, the patient's nurse, unaware of the patient's history of passive smoking or concentration of cotinine, recorded the occurrence of adverse events as previously defined and the inability to maintain an SpO_2 of 97% after oxygen therapy was terminated when the child was fully awake.

Statistical Analysis

Correlations of covariates to urinary concentrations of cotinine and to the incidence of adverse events were made by *t* test, Pearson's correlation coefficient, or chi-square analysis. Wilcoxon's test for independent samples was used for the covariates of patient age and weight because of the nonnormality of these data. Because of the presence of extreme values for patient weight and duration of anesthesia, these values were log transformed to appear more normal before comparison *via* analysis of variance. Categories of variables for which there were not sufficient numbers of patients were collapsed into relevant categories or removed from analysis. The relation between questionnaire reports of smoking and urinary concentrations of cotinine was evaluated using Spearman's correlation because of the nonnormality of the data for these variables. Logistic regression models were fitted to determine the relation between urinary concentrations of cotinine and having one or more adverse respiratory events and to assess whether suspected risk factors modified the effect of urinary concentrations of cotinine on that relation. This effect modification was evaluated by testing the significance of a product term created from urinary concentrations of cotinine and the variable of interest. Linear trend testing for concentrations of cotinine involved testing the significance of a single variable for cotinine, coded with low, moderate, and high levels as a linear relation in the model. Confounding, the presence of an additional factor related to both the concentration of cotinine and the occurrence of adverse respiratory events that distorts their observed association, was eval-

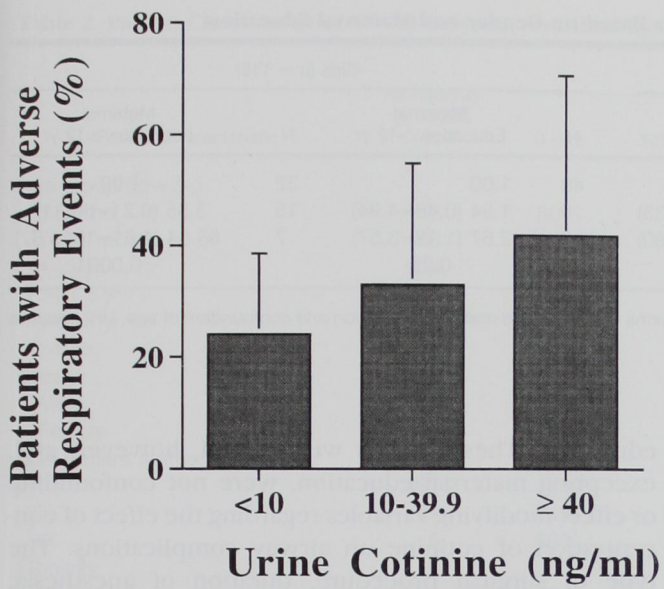

Fig. 1. Adverse respiratory events occurred in 18 of 43 (42%) children in whom the urinary concentration of cotinine was ≥40 ng/ml (odds ratio, 2.3; 95% CI, 1.2–4.5; $P = 0.02$); in 30 of 91 (33%) of those with concentrations of cotinine between 10.0 and 39.9 ng/ml (odds ratio, 1.4; 95% CI, 0.9–2.4; $P = 0.17$); and in 88 of 365 (24%) of those with a corrected concentration of cotinine <10 ng/ml. $P = 0.01$ for the trend among the three cotinine groups.

uated by fitting regression models for the effect of urinary concentrations of cotinine on adverse respiratory events, with and without the potential confounder. Any variable that altered the coefficients for cotinine >10% was considered a confounder. When evaluating whether use of an endotracheal tube *versus* face mask modified the effect of urinary concentrations of cotinine, the event of mucous requiring suctioning of the endotracheal tube was removed from the analysis. Reported odds ratios are adjusted for age, presence of an endotracheal tube, upper respiratory infection, and reactive airways disease. All tests of statistical significance were two-sided and conducted with SAS software (version 6.10 for Windows; SAS Institute, Cary, NC). A probability value of 0.05 was used to define nominal statistical significance. No adjustments were made for multiple testing.

Results

The proportion of patients experiencing adverse respiratory events increased with increasing urinary concentrations of cotinine (fig. 1). The number of adverse events in those children who experienced them ranged from one to five. Seventeen percent of the 499 patients had one event, 6.4% had two events, and 3.7% had three to five events. In addition to the relation between concentrations of cotinine and airway complications, a relation was found between reported smoking and airway complications. Five hundred seventy-two parental surveys contained answers to questions concerning the quantity of smoke exposure. Those who reported exposure to at least one individual smoking ≥30 cigarettes per day had a 44.0% incidence of adverse events compared with a 25.5% incidence of airway complications in children reportedly not exposed to cigarette smoke. Questionnaire reports of smoke exposure correlated well ($r = 0.46$, $P = 0.0001$) with concentrations of cotinine (fig. 2). All concentrations of cotinine were lower than the range typical for active smokers.

Two risk factors were found to significantly modify the effect of concentration of cotinine on the incidence of adverse respiratory events (table 1). These were the gender of the child ($P = 0.001$) and the educational level of the child's mother ($P = 0.0008$). For girls, a concentration of cotinine ≥40 ng/ml was a risk factor for adverse respiratory events. For children whose

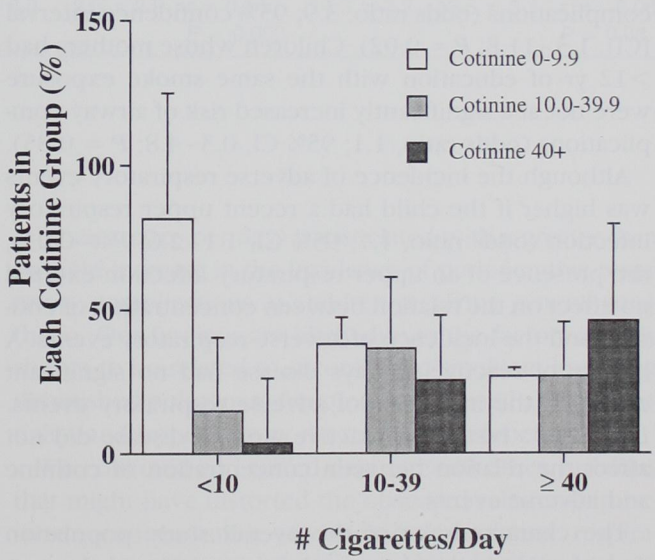

Fig. 2. For children whose reported total exposure to smoke was <10 cigarettes per day, 81.5% had urinary concentrations of cotinine <10 ng/ml. Similarly, more patients were found to have urine cotinine concentrations ≥40 ng/ml when parents reported that ≥40 cigarettes day were smoked near the child than if <10 per day were smoked (46.1% *vs.* 3.7%, respectively; $r = 0.46$; $P = 0.0001$).

Table 1. Odds Ratios* for One or More Adverse Respiratory Events Based on Gender and Maternal Education

Urinary Cotinine (mg/ml)	Boys (n = 384)				Girls (n = 115)			
	N	Maternal Education >12 yr	N	Maternal Education ≤12 yr	N	Maternal Education >12 yr	N	Maternal Education ≤12 yr
0.9.9	188	1.00	96	1.00	49	1.00	32	1.00
10–39.9	37	0.84 (0.39–1.81)	30	1.92 (0.85–4.33)	9	1.54 (0.48–4.94)	15	3.55 (0.21–60.21)
≥40	14	0.14 (0.02–1.22)	19	3.56 (1.29–9.80)	3	2.67 (1.12–3.57)	7	68.54 (4.61–1015.67)
P trend		0.08		0.007		0.23		<0.0001

* Odds ratios were taken from combined logistic regression model of interaction terms of gender and maternal education and confounders of age, URI, reactive airways disease, and ETT use.

mothers had ≤12 yr of education, a concentration of cotinine ≥10 ng/ml was a strong risk factor for airway complications. Girls whose mothers had <12 yr of education showed the greatest risk. Boys whose mothers had >12 yr of education did not have an increased risk of adverse respiratory events. Regarding reported smoke exposure to at least one individual smoking ≥30 cigarettes per day, maternal educational level, but not gender, modified the effect of smoking on the incidence of respiratory complications ($P = 0.04$). Children exposed to one individual smoking ≥30 cigarettes per day and whose mothers had ≤12 yr of education were more likely than nonexposed children to experience airway complications (odds ratio, 3.9; 95% confidence interval [CI], 1.3–11.8; $P = 0.02$). Children whose mothers had >12 yr of education with the same smoke exposure were not at a significantly increased risk of airway complications (odds ratio, 1.1; 95% CI, 0.3–4.8; $P = 0.85$).

Although the incidence of adverse respiratory events was higher if the child had a recent upper respiratory infection (odds ratio, 1.7; 95% CI, 1.1–2.6; $P = 0.03$), the presence of an upper respiratory infection exerted no effect on the relation between concentration of cotinine and the incidence of adverse respiratory events. A history of reactive airways disease had no significant effect on the incidence of adverse respiratory events. Likewise, a history of reactive airways disease did not affect the relation between concentration of cotinine and adverse events.

The characteristics of the overall study population and of each of the three cotinine groups and the two adverse respiratory event groups (none *vs.* any) are shown in tables 2 and 3. The patients in the group with the highest concentrations of cotinine were younger, had the greatest percentage of African Americans, weighed less, and their parents had a lower level of education. These factors were tested, however, and, excepting maternal education, were not confounding or effect-modifying variables regarding the effect of concentration of cotinine on airway complications. The type of surgical procedure, duration of anesthesia, mode of administration of anesthesia (endotracheal tube or face mask), American Society of Anesthesiologists patient status, and initial room air SpO_2 also were not confounding factors.

Additional factors (not shown in the tables) that also were considered and did not confound the relation between concentration of cotinine and adverse respiratory events include the attending anesthesiologist; the administration of regional/local blocks; the halothane and fentanyl doses; the home population density; the type of home cooking fuel; the household presence of dogs, cats, and birds as pets; and a history of prematurity, low birth weight, or a hospital stay beyond maternal discharge. Only three of the patients younger than 1 yr old were former premature/low-birth-weight babies. Although the type of primary home heating system was a factor by itself in the risk of adverse respiratory events, it did not affect the relation we found between concentration of cotinine and adverse respiratory events.

The proportion of patients in each cotinine group that experienced specific adverse events and the adjusted odds ratios for these events are given in table 4. The specific adverse events that were statistically significantly associated with high concentrations of cotinine were oxygen desaturation of hemoglobin in the operating room, breath holding, and severe coughing on induction of/emergence from anesthesia. Although not statistically significant, laryngospasm and severe coughing in the recovery room also were increased in the highest cotinine group. Of the 25 patients experiencing laryngospasm, 21 required only application of

Table 2. Patient Characteristics of 499 Subjects, Stratified by Urinary Cotinine and Occurrence of Respiratory Events

Patient Characteristic	All Patients (n = 499) (no.)	Cotinine (ng/ml)				Adverse Events		
		0–9.9	10–39.9	≥40	*P* Value for Trend	None	≥1	*P* Value
Age group (row %)								
1–6 mo	45	80%	11%	8%		80%	20%	
7–11 mo	46	67%	15%	17%		70%	30%	
1–3 yr	106	71%	19%	10%		67%	33%	
>3–5 yr	107	66%	24%	9%		70%	30%	
>5–8 yr	115	71%	22%	7%		75%	25%	
>8 yr	80	88%	11%	1%		79%	21%	
Gender								
Male	384	74%	17%	9%	0.69	77%	23%	0.34
Female	115	70%	21%	9%		72%	28%	
ASA patient status								
I	397	74%	18%	8%	0.52	71%	29%	0.15
II	97	71%	20%	9%		78%	22%	
III	5	60%	20%	20%		80%	20%	
Ethnicity								
White	313	79%	15%	6%	0.0001	74%	26%	0.70
Black	33	52%	24%	24%		70%	30%	
Hispanic	124	62%	26%	12%		71%	29%	
Other	29	83%	14%	3%		69%	21%	
Median age (yr)	4	4	4	2	0.005	4	3	0.27
Median weight (kg)	16.5	17	16	14	0.006*	17	16	0.08*
Father's education (mean no. of years ± standard deviation)	15.0 ± 3.6	15.4 ± 3.7	14.4 ± 2.7	12.8 ± 3.3	$r = 0.16$ $P = 0.002$	15.1 ± 3.6	14.9 ± 3.5	$r = -0.03$ $P = 0.52$
Mother's education (mean no. of years ± standard deviation)	14.1 ± 3.3	14.4 ± 3.3	13.6 ± 3.0	12.5 ± 2.9	$r = 0.14$ $P = 0.002$	14.3 ± 3.2	13.6 ± 3.3	$r = -0.08$ $P = 0.08$

Percentages may not total 100% due to rounding to whole percentages.

* Log transformed for analysis.

continuous positive pressure to restore ventilation, and 4 required neuromuscular blockade. Eleven of those 25 patients had accompanying oxygen desaturation of hemoglobin as previously defined. Because of the low frequency of occurrence, increased peak airway pressure higher than the patient's baseline (n = 0), bronchospasm requiring treatment (n = 1), auscultated wheezing (n = 3), stridor (n = 6), and recovery room desaturation after discontinuation of oxygen therapy (n = 8) are not displayed in the table.

Discussion

We have shown that exposure to environmental tobacco smoke as determined by urinary concentrations of cotinine ≥40 ng/ml (and by a history of exposure to ≥30 cigarettes per day) is associated with a greater than twofold increase in the incidence of perioperative respiratory complications in children receiving general anesthesia. Our findings are likely due to the factors already shown to be related to second-hand smoking, including diminished pulmonary function, heightened airway reactivity, and upper airway mucociliary dysfunction.

We collected and tested data on >20 other variables that might have distorted the observed relationship between concentration of cotinine and adverse respiratory events. Only two factors were found to have modified our results — female gender and socioeconomic status (as determined by maternal educational level). Girls had the greatest effect from a high concentration of cotinine. This gender difference has been well described in previous studies of passive smoking. Prior

Table 3. Surgical/Anesthetic Characteristics of 499 Subjects, Stratified by Urinary Cotinine and Occurrence of Adverse Events

		Cotinine (ng/ml)				Adverse Events		
Surgical Site	All Patients (n = 499) (no.)	0–9.9	10–39.9	≥40	*P* Value for Trend	None	≥1	*P* Value
Genitalia (hypospadius repair, circumcision, etc.)	139	74%	16%	10%	0.40	72%	28%	0.91
Kidney and bladder (ureteral reimplant, pyeloplasty, etc.)	46	83%	11%	6%		72%	28%	
Peritoneum (hernia, etc.)	122	71%	19%	9%		73%	27%	
Ear (myringotomy with tubes, otoplasty, etc.)	28	64%	29%	7%		64%	36%	
Nose and throat (tonsilectomy and adenoidectomy, etc.)	51	76%	20%	4%		80%	20%	
Head and mouth (dental restorations, etc.)	36	67%	14%	19%		72%	28%	
Integument and superficial lymph nodes	38	68%	26%	5%		79%	21%	
Musculoskeletal	38	76%	18%	5%		66%	34%	
Digestive	1	0%	100%	0%		100%	0%	
Mode of anesthesia administration								
Endotracheal tube	428	74%	18%	8%	0.82	72%	28%	0.50
Mask only	71	70%	17%	13%		76%	24%	
Mean anesthesia time (minutes ± standard deviation)	102.5 ± 64.7	103.6 ± 68.9	94.3 ± 46.6	110.8 ± 60.2	0.38*	102.2 ± 76.6	102.6 ± 60.0	0.81*
Mean Sp_{O_2} in room air (% ± standard deviation)	98.7 ± 1.3	98.7 ± 1.3	98.7 ± 1.4	98.9 ± 1.5	0.66	98.8 ± 1.3	98.7 ± 1.3	0.75

Percentages may not total 100% due to rounding to whole percentages.

* Log transformed for analysis.

publications have concluded that females were more susceptible to the effects of passive smoking.[21,22] Such gender-based differences may be related to the greater ratio of airways to lung size[22,23] in the preadolescent female, which can therefore accommodate more airborne irritant.[21] There also may be greater cholinergic irritability in females.[24] Our study included many more boys than girls because of the high number of patients undergoing urologic procedures.

The current study also found that the educational level of the mother, an indicator of socioeconomic status, was an important factor in determining the effect of passive smoking on the risk of airway complications. For children whose mothers had a lower level of education, passive smoking was a strong risk factor for adverse respiratory events. Previous studies have shown that infants of low socioeconomic status have a greater incidence of acute lower respiratory illness and that children in that group have a greater prevalence of chronic respiratory symptoms. This has been explained by factors related to the home environment, including crowding, stress, and a lower incidence of breast feeding.[25]

In evaluating the effect of passive smoking on specific adverse respiratory events, oxygen desaturation of hemoglobin, severe coughing on induction of/emergence from anesthesia, and breath holding were significantly associated with high or increasing concentrations of cotinine. Severe coughing in the recovery room and laryngospasm were also increased in passive smokers. The small numbers of patients with each individual event may create an issue of insufficient power to deter-

Table 4. Percentages of Patients, Odds Ratios (OR), and 95% Confidence Intervals (CI) of Adverse Respiratory Events for 499 Subjects According to Urinary Continine

Urinary Cotinine (ng/ml)	N	Having Selected Events									
		Severe Coughing, Induction/Emergence		Sp_{O_2} < 95% in Operating Room		Breath Holding		Severe Coughing, Recovery Room		Laryngospasm	
		%	OR (95% CI)	%	OR (95% CI)	%	OR (95% CI)	%	OR (95% CI)	%	OR (95% CI)
0.0–9.9	365	8.8	1.0*	7.7	1.0*	2.5	1.0*	4.1	1.0*	4.7	1.0*
10.0–39.9	91	15.4	1.8 (0.89–3.51	8.8	11 (0.5–2.6)	3.3	1.7 (0.4–6.7)	7.7	1.8 (0.70–4.6)	3.3	0.7 (0.2–2.4)
≥40.0	43	18.6	2.3 (0.95–5.52)	18.6	2.6 (1.1–6.2)†	7.0	5.1 (1.15–22.4)	9.3	2.3 (0.70–7.7)	11.6	2.3 (0.75–7.3)
Linear trend test (*P*)			0.03		0.07		0.04		0.10		0.31

* Reference group.

† $P = 0.04$ between cotinine groups 0–9.9 and ≥40 ng/ml.

mine statistical significance. It is noteworthy that the odds ratios for every individual event, significant or not, are ≥2.3. The consistency of risk, seen for overall airway complications and across the range of these specific events, is a compelling argument for the broad detrimental effect of exposure to environmental tobacco smoke.

Although the potential exists for detecting the odor of tobacco smoke emanating from the parents, it is unusual for anesthesiologists to seek information about the tobacco use habits of the child's parents, grandparents, other relatives, or day care staff. In addition, the anesthesiologists knew they were participating in a blinded study and therefore requested no information on the patients.

Our study results concur with two prior studies regarding perioperative adverse events related to exposure to environmental tobacco smoke. A retrospective chart review of children undergoing general anesthesia found a relative risk of laryngospasm ten times higher in children exposed to household tobacco smoke.[26] Another study found that oxygen desaturation in the recovery room was significantly more common in children exposed to parental smoking.[27] With the current comprehensive study results included, there is now substantial evidence that passive smoking is a risk factor for untoward respiratory events after general anesthesia.

The results of our study confirm the well-accepted dose-response relation between reported smoking and urinary concentrations of cotinine. Discrepancies may be explained by differences in individual smoking habits or unreliable personal histories. Although the correlation between questionnaire responses and concentrations of cotinine is high, it is not absolute. The use of cotinine measurements therefore decreases the likelihood of bias on the part of the anesthesiologist. No concentrations of cotinine were in the range typical for active smokers; therefore, older children engaging in active smoking was not a factor. Clearly, recent reports support the view that studies of passive smoking must be conducted with appropriate biologic markers to ensure accuracy.[13,28,29] Therefore, the current study focuses on cotinine as the main indicator of exposure to environmental tobacco smoke. As is the practice in research on passive smoking, the raw urinary concentration of cotinine was corrected for the concentration of the urine to best reflect the serum concentration of cotinine. The correction we used[20] has been used previously in children.[4] In effect, this method yields

the cotinine value that patients would have had all the patients had the same urinary concentration of creatinine.

Several investigators have demonstrated increased airway complications in the presence of perioperative upper respiratory infections.[30,31] The current study confirmed these findings. Passive smokers with an upper respiratory infection, however, were at no greater risk than unexposed patients with an upper respiratory infection. The presence of an upper respiratory infection may be sufficiently potent to negate the effects of passive smoking. It is noteworthy that patients with a history of reactive airways disease were not at a significantly increased risk of adverse respiratory events. This may have been due to optimal preoperative preparation of the patients, including not anesthetizing children with active bronchospasm and appropriate intraoperative management. No synergism was found between a history of reactive airways disease and passive smoking on their effect on airway complications.

Children who are exposed to environmental tobacco smoke and who undergo general anesthesia have a greatly increased incidence of respiratory complications in the perioperative period. Additional studies are indicated to delineate the synergism between passive smoking and gender or lower levels of maternal education (as a measure of socioeconomic status) on the risk of airway complications.

This study adds to the considerable body of evidence[1-13]# pointing to the public health risk posed by exposure to environmental tobacco smoke. Anesthesiologists, surgeons, pediatricians, and other health care professionals caring for children in the perioperative period should add this item to the preoperative medical history and regard its presence as a risk factor for respiratory complications. As the perioperative physician, the anesthesiologist has an important role in educating the parents of children scheduled for surgery using general anesthesia and the general public about the increased risk associated with exposure to environmental tobacco smoke.

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