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Letters to the Editor

ASTHMA AND CANCER

The interesting recent article by Vena et al. (1) indicating an apparent decreased risk for cancer among sufferers of allergy-related diseases, but a suggestively increased risk for lung cancer among men reporting a history of asthma, prompted us to more carefully examine prospective data we have suggesting a positive relation between asthma and cancer in men. We offer additional evidence for this risk relation.

Our sample consists of 6,848 men and women living in Alameda County, California, in 1965, with no known previous cancer diagnosis and selected to be representative of the county population in 1965. Details of the sampling strategy and sample characteristics for the Alameda County Study are summarized in a recent publication by Berkman and Breslow (2). In the 1965 survey, respondents were asked whether or not they had, within the previous 12 months, any of a series of chronic conditions, including asthma. Follow-up cancer incidence and mortality ascertainment has been completed for the sample through 1983 via record linkage to statewide vital statistics and San Francisco Bay Area cancer incidence surveillance (California Tumor Registry) data.

The reported prevalence of asthma in our study cohort is consistent with that reported by Vena et al.: 3.3 per cent of the males and 3.1 per cent of the females. Smoking history for asthma sufferers does not differ from that among respondents without asthma. The distribution of asthma in the study sample and by cancer outcomes can be seen in table 1.

Table 2 summarizes the results of multivariate analyses (using Cox regression) of the association between 18-year cancer incidence and mortality and report of asthma, adjusting for age and smoking history (pack-years of exposure). The estimate of risk is the relative hazard, which can be thought of as the instantaneous relative risk. There were no lung cancer deaths among women with asthma, so that the relative hazards for that outcome could not be estimated. These data suggest that the apparent positive relation between asthma and all sites of cancer among men in our sample is essentially explained by the strong risk relation between asthma and lung cancer. These results do not change appreciably (relative risk = 5.2, $p = 0.007$ for lung cancer mortality, and relative risk = 6.3, $p = 0.0006$ for lung cancer incidence) for male respondents when excluding cancer outcomes during the first five years following the baseline survey. There is also no evidence for a difference in the association between asthma and lung cancer in smokers and nonsmokers.

It is possible, as has been suggested (3), that there may be some classification error between reported asthma and bronchitis. However, analyses which either excluded those who reported chronic bronchitis or which adjusted for the presence of chronic bronchitis yielded results similar to those presented above.

We believe that the strong prospective risk relation between asthma and lung cancer among men in our study, independent of smoking, is worthy of note. This is also consistent with the prospective evidence of Robinette and Fraumeni (3). It is not clear why there should be absolutely no such relation for women. That this same contrast is evident in the well-designed study presented by Vena and associates suggests that the finding may not be purely artifactual. We do know

TABLE 1

Distribution of respondents by asthma status, by sex, and by cancer outcome, Alameda County Study, 1965–1983

Baseline asthma status	Males					Females				
	At risk*	Incidence		Mortality		At risk*	Incidence		Mortality	
		All sites	Lung	All sites	Lung		All sites	Lung	All sites	Lung
With asthma	102	11	5	8	4	115	8	1	2	0
Without asthma	3,015	204	33	125	31	3,593	249	27	142	21

* Table excludes 23 respondents for whom baseline asthma status was unavailable.

TABLE 2

Adjusted† approximate relative risks for cancer by history of asthma within 12 months prior to initial contact among 6,825 adults, Alameda County Study, 1965–1983

	Males		Females	
	Incidence	Mortality	Incidence	Mortality
All sites	2.1*	2.4*	1.1	0.5
All sites, excluding lung‡	1.3	1.5	1.1	0.6
Lung‡ cancer	6.3***	5.4**	1.2	§

* $p < 0.05$. ** $p < 0.005$. *** $p < 0.001$.
† The measure of association is the relative hazard (instantaneous relative risk), adjusting for age and smoking (pack-years).
‡ Lung, bronchus, and trachea (*International Classification of Diseases for Oncology*, code 162).
§ No lung cancer deaths occurred among women with asthma.

that lung cancer in women reflects a different pattern of histopathology and possibly a different disease process. These data may suggest, in the case of asthma and cancer, a localized risk relation rather than systemic (or immunologic) risk mechanism discussed by Vena et al. for the overall relation between allergies and cancer.

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THE AUTHORS REPLY

Reynolds and Kaplan (1) have presented additional findings regarding the association between asthma and lung cancer. Their comments and findings prompted us to take a closer look at the association between asthma and lung cancer in our data (2). Table 1 presents the report of asthma (ever versus never) among lung cancer patients and controls and the age-adjusted odds ratio by categories of cigarette smoking. Our findings concur with those of Reynolds and Kaplan in that smoking does not appear to be an effect modifier in the asthma-lung cancer association. However, our findings suggest that this association is much weaker than that reported by Reynolds and Kaplan.

A major problem in both studies is the uncertain meaning of the history of "asthma." Although we asked if the disease was diagnosed by a physician, we could not differentiate true allergic asthma from other reactive airway problems. One must wonder, in particular, whether asthma reported by smokers reflects the same pathophysiologic state as asthma reported by nonsmokers. However, additional analyses revealed an age- and smoking-adjusted odds ratio of 1.4 for those with asthma diagnosed 10 years or less prior to admission to the hospital (not statistically significant), whereas the odds ratio was 1.8 if the onset of asthma was greater than 10 years prior to admission ($p < 0.05$). This suggests that the report of asthma and the association seen are not likely due to the late complications of cigarette smoking such as chronic bronchitis.

The findings of Reynolds and Kaplan, and those reported here, suggest that more research in this area may further our understanding of the way in which the immune system and/or airway reactivity relates to lung cancer risk. Long-term prospective studies of clinically defined cohorts of individuals with allergic diseases, including asthma, may be particularly helpful in studying the relation between lung cancer and allergic disorders, their associated treatments, and complications. Such studies must, of course, include detailed and reliable measures of tobacco use, which is clearly the most important factor in lung cancer, regardless of other modifiers of risk.

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TABLE 1

Reported asthma among lung cancer patients and controls by pack-years of cigarette smoking, white males, Roswell Park Memorial Institute, 1957–1965

	Nonsmokers			1–39 pack-years			40+ pack-years		
	Total no.	No. with asthma	%	Total no.	No. with asthma	%	Total no.	No. with asthma	%
Lung cancer	91	8	8.8	262	15	5.7	699	56	8.0
Controls	583	28	4.8	554	20	3.6	437	23	5.3
Age-adjusted odds ratio*		1.58			1.65			1.64	

* Age- and smoking-adjusted odds ratio = 1.63 ($p < 0.05$). If asthma diagnosed within five years of admission is omitted, odds ratio = 1.51 ($p < 0.10$).