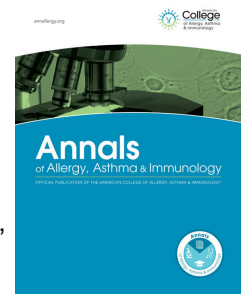


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Family History of Cancer Predicts Allergic Rhinitis and Asthma Development

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Family History of Cancer Predicts Allergic Rhinitis and Asthma Development

Letter

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Abbreviations:

CDC – Centers for Disease Control and Prevention

NHIS – National Health Interview Survey

FHC – Family History of Cancer

AR – Allergic Rhinitis

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The respiratory tract is a common entry point into the human body for both allergens and natural/manmade carcinogens, the latter of which could result in lung, gastrointestinal, and other malignancies.(1) We previously determined, in analyzing data from the National Health Interview Survey (NHIS) that there was a significant negative relationship between diagnoses of cancer with allergic rhinitis or asthma. The obstruction associated with both allergic rhinitis and asthma may act to block the entry of both allergens and carcinogens.(2) Although other studies have examined the relationship between personal cancer diagnoses in asthmatic or allergic individuals, or via biomarkers such as IgE, (3, 4), the heritability of such an effect, which may provide a survival benefit, has not been evaluated through family studies. No studies to date have investigated family history of cancer as a predictive factor for asthma and allergic rhinitis. We now report three studies that extrapolate the allergy-cancer relationship to assess inter-generational risk. These studies were conducted between 2010-2020 and examined the trans-generational relationship of a family history of cancer (FHC) with asthma and allergic rhinitis (see Table 1).

We first conducted a case-control study in collaboration with Lutheran Medical Center (2010-2011) of 488 immigrant adults with allergic rhinitis-asthma (East Asian n= 249, Hispanic n=109) randomly recruited to complete a written self-administered questionnaire regarding family history and new onset allergic rhinitis and asthma diagnosis since immigration. After excluding those (n=101) that had either a pre-existing asthma/allergic rhinitis diagnosis or were USA-born, subjects with incident allergic rhinitis/asthma (n=196) and healthy controls (n=191) were studied. Demographic information and FHC status, including relation to subject and type of cancer, was obtained. The second case-control (2016-2018) study was of inner city Afro-

Caribbean children (allergic rhinitis/asthma n=165, control n=256) aged 0-19 years receiving outpatient allergy/general pediatric care at the University Hospital of Brooklyn. Data was collected by phone, in-person or medical record review. The final study utilized data on 114,300 subjects from a U.S. sample of respondents, the NHIS (2012-2016) study to track information on asthmatic children with family members reporting physician-diagnosed cancer.(5) Every included child was linked to a corresponding representative household adult, both of whom had completed medical condition questionnaires.(6) Adult respondents with personal histories of cancer were considered a positive FHC for the linked child. All three studies conducted chi-square analyses for categorical, Student's t-tests for continuous data and multivariate logistic regression, using SPSS v26 and SAS v9.4.

In the first study of adult immigrants to Brooklyn, the case group reported greater maternal cancers (13.26% vs. 4.73%, $p=0.003$) than did non-asthma/allergic rhinitis controls, with regression models confirming the above; a higher unadjusted odds of both asthma, $OR=2.69(CI:1.02-7.11)$, $p=0.045$ and rhinitis, $OR=3.09(CI:1.44-6.63)$, $p=0.004$ in those that had maternal cancer compared to controls. Adjusting for age, sex, ethnicity, years in NYC and country of origin predicted higher odds of rhinitis alone in those with maternal cancer, $OR=3.33(CI:1.43-7.74)$ $p=0.005$. In the study of FHC in families of Afro-Caribbean children in Brooklyn, we found a significantly increased odds of asthma in regression models associated with overall FHC, $OR=3.07(CI:2.01-4.69)$, $p<0.0001$. Adjusting for age, sex and ethnicity increased the likelihood of asthma, $OR=3.25(CI:2.06, 5.12)$, $p<0.0001$. In the NHIS, the average ages were 8.67 ± 5.3 years (children) and 38.0 ± 19.8 years (adults). We found greater childhood asthma in those with FHC (20.6% vs. 13.4%, $p<0.001$). FHC also significantly predicted asthma

in unadjusted models, OR=1.68(CI:1.47-1.91). This relationship persisted despite controlling for age, sex, race, family education, and family history of smoking, OR=1.41(CI:1.24-1.63), both $p<0.001$.

With these findings, we determine FHC to be independently and positively associated with childhood and adult asthma/allergic rhinitis evolution. These results provide evidence of a positive FHC-allergy relationship not only in NYC-based Hispanic, Asian, Black and Afro-Caribbean populations but in a nationally representative US sample as well. We believe these studies to be the first large-scale effort devoted to examining both the cross-sectional (NHIS) and retrospective associations (the two institutional studies) between FHC and asthma/allergic rhinitis. A possible limitation of these studies is the use of questionnaire data, which may involve recall bias. Future studies will further examine the sex- and type-specific associations of different cancers in relation to childhood asthma risk and investigate the longitudinal association between these factors. Clinicians should be aware that a higher prevalence of asthma was found in those with positive family histories of cancer, and this relationship was consistent in both NYC-based minorities and a nationally representative US sample. Interested primary care physicians/specialists may wish to make case-by-case clinical decisions to screen such individuals for asthma based on the presentation of the child/adult in question.

Taken together, these results strongly suggest a possible heritable factor common to both cancer and the primordial evolution of allergic rhinitis/asthma in offspring. One such mechanism might be the role of memory CD8⁺ T cells in allergic disease by promoting Th1 responses(7) or epigenetic changes in memory/naïve CD8 T cell ratios(8). Indeed, heritable changes in key

70 immune pathways may in later adult life confer the allergic individual protection against cancer.
71 Although the exact underlying mechanism is yet to be determined, our preliminary studies
72 suggest a heritable factor may play a role both in tumor protection/surveillance as well as
73 allergy- asthma pathogenesis.

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Table 1. The Relationship Between Allergic Rhinitis/Asthma and a Family History of Cancer

	Lutheran			SUNY Downstate			NHIS		
	Controls	Asthma/AR*	P	Healthy Controls	Asthma/AR*	P	Healthy Controls	Asthma	P
N	190	196	-	256	165	-	49383	7767	-
Age	39.9 ± 12.5	39.1 ± 11.4	0.5	9.4 ± 5.7	10.6 ± 4.8	0.08	8.35 ± 5.36	10.67 ± 4.48	<0.001
Female	123 (65%)	129 (65%)	0.8	129 (50.4%)	86 (52.1%)	0.72	24763 (50.1%)	4601 (59.2%)	<0.001
White	0 (0%)	1 (0.5%)	0.08				36375 (73.7%)	5121 (65.9%)	<0.001
Black	0 (0%)	3 (1.6%)		236 (94.1%)	133 (80.6%)	0.84 ^a	6404 (13.0%)	1611 (20.7%)	
Asian	124 (60.8%)	125 (68.7%)					3249 (6.6%)	334 (4.3%)	
Hispanic	67 (32.8%)	42 (23.1%)		10 (4.0%)	25 (15.2%)		n/a	n/a	
Positive FHC	9 (4.7%)	26 (13.2%)	0.003	62 (10.35%)	91 (16.06%)	<0.001	1183 (3.1%)	307 (5.0%)	<0.001
Regression									
<i>Univariate</i>		AR OR = 3.09 (1.44, 6.63)	0.004		Asthma OR = 3.07 (1.99, 5.02)	<0.001		Asthma OR = 1.68 (1.47, 1.91)	<0.001
		Asthma OR = 2.69 (1.02, 7.11)	0.045						
<i>Multivariate</i>		AR OR = 3.33 (1.43, 7.74)	0.005		Asthma OR = 3.25 (2.06, 5.12)	<0.001		Asthma OR = 1.41 (1.24, 1.63)	<0.001
		Asthma OR = 1.79 (0.56, 5.80)	0.32						

Results showing chi-square or Student's t-tests as applicable, bolded values are significant at $\alpha=0.05$ level. *Allergic Rhinitis

^aInsufficient numbers (n<10) of White and Asian subjects in the SUNY Downstate study; they were treated as missing for these analyses.

**Covariates: Lutheran (age, sex, race, years in NYC, country of origin); SUNY Downstate (age, sex, race); NHIS (age, sex, race, family education and smoking)

Note: NHIS statistics shown for children only. Information on Hispanic ethnicity collected separately from mainstream race variable in the NHIS

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