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A history of allergies is associated with reduced risk of oral squamous cell carcinoma

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Abstract

Purpose—A history of allergies is associated with a decreased risk of several types of cancers. Potential mechanisms include enhanced immune surveillance against tumor cells early in disease development and/or carcinogenic infectious agents. We tested whether allergies are inversely associated with oral squamous cell carcinoma (OSCC), accounting for factors that may modify the association, such as tumor site, stage, and HPV infection.

Methods—We estimated odds ratios (OR) and 95% confidence intervals (CI) for the association between allergy history (including different types of allergies) and OSCC, adjusted for potential confounders, among 400 cases and 613 controls. Analyses were also stratified by site, stage, and measures of HPV infection.

Results—We observed a weak inverse association between history of any allergy and OSCC (OR=0.81, 95% CI, 0.61–1.08). This association was present only for allergies to airborne allergens (dust/pollen/mold); OR=0.67; 95% CI, 0.48–0.93. The inverse associations with airborne allergies were slightly stronger for oropharyngeal SCC (OR=0.56; 95% CI, 0.35–0.90) than for oral cavity SCC (OR=0.71; 95% CI, 0.49–1.05), and present only for later stage cancers (OR=0.42; 95% CI, 0.26–0.66) as opposed to earlier stage cancers (OR=0.98; 95% CI, 0.66–1.46). Inverse associations were not particularly present or stronger among HPV-16 seropositive individuals or for HPV DNA positive OSCC.

Conclusions—There is an inverse association between history of allergies to dust, pollen or mold and OSCC. Whether the inverse association involves heightened immune surveillance, increased immune response to HPV or other antigen, or other carcinogenic mechanism, remains to be determined in more definitive studies.

Keywords

allergies; oral squamous cell carcinoma; HPV; HSV

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Conflict of Interest
The authors declare that they have no conflict of interest.

Introduction

History of any type of allergy, or allergy-related condition such as asthma, is associated with a decreased risk of multiple types of cancers, including colorectal [1, 2], cervical [3, 4], esophageal [2, 5], laryngeal [2, 3, 6], pancreatic [7, 8], and stomach [9], as well as leukemia [10, 11] and glioma [12]. However, some studies report that history of allergies may increase the risk of certain other types of cancers, such as bladder [6] and prostate [13] cancer. Results are conflicting for breast [9, 13] and lung cancer [6, 14, 15].

Multiple theories have been proposed to explain an inverse relationship between allergies and cancer. First, having a history of allergies may be indicative of enhanced immune surveillance against nascent tumors, and/or infectious agents [16–20]. Second, according to the “prophylaxis hypothesis”, allergy symptoms physically rid exposed tissues of potentially mutagenic toxins, pathogens, and foreign particles before carcinogenesis is initiated [21, 22]. Third, allergy symptoms may provide an indication as to which antigens should be avoided, leading to behavioral changes that may result in diminished exposure to carcinogens [22–24].

Michaud et al. recently reported a lower risk of head and neck squamous cell carcinoma (HNSCC) associated with history of allergies [25]. Previous hospital-based studies also suggested an inverse association between history of allergies and oral cancer risk [2, 3]. An increasing proportion of oral cancers, those arising in the oropharynx, are attributable to oncogenic HPV infection. If a history of allergies represents, in part, an immune status capable of countering an HPV infection, we would expect that the association between allergies and oral cancer would be strongest for oropharyngeal cancers and in particular for persons with exposure to oncogenic HPV. Associations with allergies were observed to be slightly stronger for oropharyngeal SCC; but HPV-16 serology status did not confound or modify the association between allergies and HNSCC [25].

We tested the hypothesis that the risk of oral squamous cell carcinoma (OSCC) is associated with history of allergies in a population-based study, accounting for tumor site and HPV-16 serology status as well as HPV DNA status. Prior studies have not examined the association between OSCC and multiple categories of allergens, such as pollen or mold, in detail. If allergies to particles that are in direct contact with the oral mucosa, such as allergies to airborne molecules, are particularly protective, this could provide support for mechanisms involving behavioral changes or prophylaxis. We thus stratified associations by several different allergen categories. To explore whether an association between allergies and OSCC is related to tumor progression or promotion, we tested whether associations differed by disease stage. We hypothesized that a stronger association between late stage cancers compared with early stage cancers would suggest that allergies are a marker of enhanced immune surveillance and greater response to tumor antigens.

Methods

Study Population and Interview Data

We used data and biological specimens from two population-based case-control studies that investigated the association between HPV infection and risk of OSCC [26, 27]. Cases were 18–65-year-old residents of Washington State diagnosed with incident histologically confirmed OSCC in 1985–1989 and 1990–1995. We identified cases, and determined age, stage, site, and histologic type through the Cancer Surveillance System (CSS), a participant in the National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) Program. Cancer sites included the tongue, gum, floor of mouth, other and unspecified part of the mouth, tonsils, and oropharynx. We used ICD-O codes to classify tumors according to

site and histology. The case participation proportions were 54% and 63% for the first and second study respectively.

Controls were 18–65-year-old Washington State residents with no history of oral cancer between 1985–1989 and 1990–1995, and were recruited by random-digit telephone dialing (RDD). Controls were frequency matched on age group and sex. The overall response proportions for control subjects were 63% and 61% for the first and second study respectively. The protocols for recruitment of, and data collection from, cases and controls in both studies were approved by the institutional review board of the Fred Hutchinson Cancer Research Center.

As previously described [27], following written informed consent, we interviewed study participants using a structured questionnaire eliciting demographic characteristics, medical and lifestyle history, for the time period prior to their reference date. The reference date for cases was the month and year of diagnosis, and the reference date for controls was randomly assigned from among case subject diagnosis dates prior to the recruitment of that control subject. Participants were asked if they had ever had allergies prior to the reference date and, if allergies were reported, the specific allergens, corresponding to 54 possible allergy codes, were recorded under five general headings: (1) foods, (2) pollens, plants, grasses, trees, (3) medications, drugs, immunizations, (4) inhalants, molds, dust, animals, tobacco, (5) other. Cigarette smoking data included whether a person had ever smoked >100 cigarettes, and details regarding continuous periods during which smoking habits (e.g., packs per day) were relatively unchanged. Episodes were delineated according to the ages at which each subject reported major changes in smoking habits, and these data were used to calculate average number of cigarettes smoked per day, total years of smoking, and total pack years of cigarette smoking. We ascertained alcohol consumption using a similar approach, and calculated lifetime average number of alcoholic beverages consumed per week.

Out of a total of 412 cases and 615 controls across both studies, 400 cases and 613 controls had data on age, sex, race, education, pack years of smoking, average alcoholic drinks per week, and history of allergies.

Biologic Specimens and Laboratory Methods

For this analysis, we used previously published data on HPV-16 and HSV serologic antibody response in cases and controls as well as HPV DNA typing in tumor tissue from cases in the second study (tumor tissue was not obtained in the first study) [27, 28]. An antibody capture enzyme-linked immunosorbent assay (ELISA) was used to test sera for antibody response to HPV type 16 L1 protein capsids (virus-like particles) and a Western blot method was used to test sera for HSV antibody status. We used oligonucleotide primers (MY09/MY11) complementary to highly conserved sequences in the L1 region of HPV to amplify HPV DNA from tumor tissue using the polymerase chain reaction (PCR). Specimens positive for the HPV L1 consensus probes were typed by sequential hybridizations with probes for HPV types 6, 11, 16, 18, 31, 33, and 35. We also used primers complementary to the respective E6 regions of HPV DNA types 6, 11, 16, and 18 in the second study. Blood samples were obtained from 85% of cases and 85% of controls in the first study, and 92% of cases and 94% of controls in the second study. HPV DNA status was determined for 226 of the 300 cases from the second study.

Data Analysis

We classified cases and controls as to whether or not they reported any allergy, as well as allergies to common reported allergens: pollens, dust, mold, penicillin, sulfa drugs, cats, dogs, and bee stings. No individual food (milk, chocolate, shellfish, wheat, citrus, eggs,

seafood, yeast, and miscellaneous food) was commonly reported as an allergen, so these were grouped together as "Food allergies." Associations were also estimated for airborne allergies combined (pollen, dust, or mold), antibiotic allergies combined (penicillin, sulfa drugs, or unspecified), and animal allergies combined (cats, dogs, bee stings, horses, cows, rabbits, or other or all animals). The groupings selected were similar to those used in similar studies [4]. For each allergy or group of allergies, the unexposed comparison group included all subjects without that specific allergy. We repeated these analyses with the unexposed comparison group comprised of subjects who reported no allergies of any type.

We estimated the odds ratio (OR) and 95% confidence intervals (CI) for the association between history of any allergies (yes/no) and OSCC by fitting unconditional adjusted logistic regression models. We adjusted for age (continuous), sex, race, educational attainment (categorical), pack years of smoking (continuous), smoking status (ever/never), and average alcoholic drinks per week (continuous). We repeated these analyses for a subset of subjects with data on HPV-16 serology, and additionally estimated ORs after adjusting for HPV-16 serology status. To explore differences by tumor site, we estimated ORs for oral cavity cancers and oropharyngeal cancers separately using polytomous logistic regression.

To determine whether the presence of allergies was associated with HPV-16 seropositivity, we investigated the independent association of a history of allergies with HPV-16 seropositivity for cases and controls separately. Although HPV seropositivity is a dynamic result of seroconversion and seroreversion, persistent HPV-16 infection is associated with greater likelihood of being HPV-16 seropositive [29, 30]. If enhanced immunity results in rapid clearance of any HPV infections, we might expect allergic individuals to be less likely to be HPV-16 seropositive.

We compared oncogenic HPV DNA-positive cases with controls and compared HPV DNA-negative cases with controls, repeating these analyses for oropharyngeal cancers separately. We explored effect modification by sex, cigarette smoking, and alcohol consumption. We also stratified by HPV-16 and HSV-1 serology, comparing all cases with controls, as well as oropharyngeal cases only with controls. To statistically assess departures from multiplicative effects, we included product terms in stratified analyses, and used a log-likelihood ratio test to compare logistic models with and without the product terms. We used polytomous logistic regression to explore differences by stage (in-situ/local versus regional/distant). We used Stata statistical software (version 11.0, Stata Corp.) for all analyses.

Results

Approximately 62% of case subjects had oral cavity SCC and 38% had oropharyngeal SCC. Case subjects were less likely to have attended college and tended to report lower incomes than control participants (Table 1). Cases had higher levels of cigarette smoking and alcohol consumption compared with controls. Case subjects were more likely to be HPV-16 seropositive: 59.4% of oropharyngeal SCC and 48.9% of oral cavity SCC subjects with serology data were HPV-16 seropositive, compared with 34.7% of controls.

Approximately 42% of cases and 50% of controls reported a history of any allergy. The most common allergies were to airborne agents (dust, pollen and mold), reported by 21% of cases and 33% of controls. Among controls, airborne allergies were not associated with household income or educational attainment. Controls with airborne allergies smoked less: 27% of those with airborne allergies had greater than 20 pack years of smoking, compared with 37% of those without allergies (chi-squared p=0.003). Airborne allergies were not associated with alcohol consumption (chi-squared p=0.19).

We observed a weak inverse association between history of any allergy and OSCC (OR=0.81, 95% CI, 0.61–1.08; Table 2). This inverse association appeared to be primarily driven by airborne allergies; i.e., allergies to dust (OR=0.69; 95% CI, 0.42–1.12), pollen (OR=0.72; 95% CI, 0.51–1.02) and mold (OR=0.34; 95% CI, 0.14–0.83). Repetition of analyses using subjects with no history of any allergies as the comparison group did not materially change the estimates for each allergy category. There was no inverse association for those with allergies that did not include airborne allergies (OR for any allergies other than airborne relative to those with no history of allergies: 1.06; 95% CI, 0.72–1.56). Additional adjustment for HPV-16 seropositivity did not materially affect the estimates. There was no evidence of effect modification by sex, cigarette smoking, or alcohol consumption (data not shown).

Estimates of the association between history of any allergies and oropharyngeal cancer (OR=0.84; 95% CI, 0.57–1.25; Table 3) were similar to estimates for oral cavity cancer (OR=0.76; 95% CI, 0.54–1.07). However, we observed somewhat stronger associations between airborne allergies and oropharyngeal cancer (OR=0.56; 95% CI, 0.35–0.90) than between airborne allergies and oral cavity cancer (OR=0.71; 95% CI, 0.49–1.05). Nevertheless, a polytomous regression model did not suggest heterogeneity by site for all allergies (p=0.53) or airborne allergies (p=0.50).

A history of allergies was not associated with HPV-16 seropositivity in controls (OR=0.96; 95% CI, 0.67–1.38) or cases (OR=0.95; 95% CI, 0.61–1.47). We observed little departure from multiplicativity of effects for allergies and HPV-16 serology for oral cavity SCC (likelihood ratio p=0.76) or oropharyngeal SCC (likelihood ratio p=0.61). Similarly, there was little evidence of interaction for airborne allergies and HPV-16 serology for oral cavity SCC (likelihood ratio p=0.48). Although the association between airborne allergies and oropharyngeal cancer was stronger among HPV-16 seronegative subjects (OR=0.43; 95% CI, 0.19–0.95; Table 4) versus HPV-16 seropositive subjects (OR=0.70; 95% CI, 0.36–1.35), there was little evidence of a meaningful interaction (likelihood ratio p=0.34). There was no evidence of effect modification by HSV-1 seropositivity (data not shown).

For case subjects with HPV DNA results, we observed an inverse association between airborne allergies and oropharyngeal cancer, albeit with very wide confidence intervals (OR=0.69; 95% CI, 0.39–1.24). The association with airborne allergies was near null for oncogenic HPV DNA-positive oropharyngeal cancer (OR=0.85; 95% CI, 0.38–1.92; Table 4) and inverse for oncogenic HPV DNA-negative oropharyngeal cancer (OR=0.54; 95% CI, 0.24–1.21).

Twelve case subjects were missing data on stage of tumor. The association between airborne allergies and OSCC, excluding these twelve subjects, was similar to primary results (OR=0.66; 95% CI, 0.47–0.92). Out of a total of 388 patients, 182 had in-situ/local disease and 206 had regional/distant cancer. We observed a strong inverse association between history of airborne allergies and regional/distant cancer (OR=0.42; 95% CI, 0.26–0.66) and no association with in-situ/local cancer (OR=0.98; 95% CI, 0.66–1.46). The polytomous regression model indicated significant heterogeneity by stage (p=0.001).

Discussion

We observed a weak inverse association between history of any allergy and OSCC. The inverse association was strongest for airborne agents (dust, pollens or mold), and there was no association between other allergies and OSCC.

Pollens made up the largest proportion of airborne allergens. Allergy to pollens was also the strongest driver of an observed inverse association between allergies and cervical cancer [4].

Similarly, pancreatic cancer was inversely associated with dust, plant, mold, and cat allergic reactions, but not other allergens [8]. We also observed inverse associations with cat allergies; however confidence intervals were too wide to meaningfully interpret the estimates. Other studies have examined specific allergic reactions such as hay fever, asthma, eczema, and hives, associated with various cancers. Hay fever is most commonly reported in association with reduced risk of cancers, although this finding is not entirely consistent (see Merrill et al. [31] and Turner et al. [32] for a review).

Three prior studies have investigated the association of allergies with oral cancer. In a hospital-based case-control study using questionnaire data, Vena et al. observed inverse associations with oral cancer in males who reported asthma (OR=0.82), hay fever (OR=0.49, $p<0.05$), hives (OR=0.60), or other allergies (OR=0.53, $p<0.05$) [3]. In a hospital-based investigation pooling data from several case-control studies, Bosetti et al. observed an inverse association between conditions such as allergic rhinitis, asthma, and atopic dermatitis and oral/pharyngeal cancer (OR=0.44; 95% CI, 95% CI 0.26–0.75); results for specific allergies were not reported [2]. In a recent population-based study of 1,014 cases and 1,193 controls, Michaud et al. observed an inverse association between self-reported history of allergies and HNSCC (OR=0.81; 95% CI, 0.67–0.98) [25]. It is notable that we observed the same association estimate, but with wider confidence intervals (OR=0.81, 95% CI, 0.61–1.08). In contrast to our results, they did not observe a difference in association by type of allergy. However, they did not have detailed allergen data, and categorized type of allergy as “food”, “seasonal” or “drug” allergies, whereas we recorded specific allergens, corresponding to 5 categories and 54 possible codes, such as pollens, mold, cats, etc.

We hypothesized that enhanced immune function associated with allergies may be a surrogate for other immune functions that lead to reduced risk of OSCC by inducing clearance of oncogenic HPV before infection becomes established, thereby reducing the incidence of a proportion of oropharyngeal SCC. However, as was also observed by Michaud et al [25], associations stratified by HPV-16 serostatus did not provide support for this hypothesis. There was some indication of a stronger inverse association between airborne allergies and oropharyngeal cancer among HPV seronegative subjects compared with HPV seropositive subjects; however, this was likely due to chance because of very small numbers of subjects.

The association with airborne allergies was near null for oncogenic HPV DNA-positive oropharyngeal SCC and stronger for oncogenic HPV DNA-negative oropharyngeal SCC. However, due to the relatively small number of oropharyngeal cases, our study lacked power to detect differences by HPV status if they exist. Unmeasured confounding factors or imperfect adjustment for confounders, such as pack years of smoking, might also explain why a stronger association was observed for oncogenic HPV DNA-negative oropharyngeal SCC. Cases with HPV-negative oropharyngeal cancer were much more likely to be heavy smokers (87% with >20 pack years of smoking) than cases with HPV-positive oropharyngeal cancer (40% with >20 pack years of smoking), but subjects with allergies were less likely to be heavy smokers, which may increase the relative influence of confounding in associations between allergies and HPV-negative oropharyngeal cancer.

We previously reported an increased risk of OSCC, and oropharyngeal cancer in particular, associated with seropositivity to HSV-1 [28], and examined these data as part of testing our hypothesis regarding the possible role of oncogenic infections in the relationship between allergies and oropharyngeal cancer. We found no evidence that the association between oropharyngeal cancer risk and allergy history depended on HSV-1 serostatus. Importantly, other investigators have not observed positive associations between HSV-1 and oral cancer, whether overall or by site [33, 34].

We observed a slightly stronger inverse association between airborne allergies and oropharyngeal cancer, compared with oral cavity cancer; however results from a polytomous regression analysis suggest that this could be due to chance. Michaud et al. noted an association between allergies and oropharyngeal cancer (OR = 0.73, 95 % CI = 0.57–0.92), but no association with oral cavity cancer (OR = 0.98, 95 % CI = 0.76–1.26) [25]. An inverse association that was particularly apparent for oropharyngeal SCC would be consistent with heightened immune surveillance in people with allergies, as the oropharynx contains a large collection of lymphatic tissue, which plays an important role in immune surveillance. Also partially in support of the hypothesis of enhanced immune surveillance and greater response to tumor antigens, we observed a strong inverse association between airborne allergies and later stage OSCC (regional/distant), and no association with earlier stage OSCC (in-situ/local). This suggests that characteristics associated with the presence of allergies play a role in protection against tumor progression/promotion.

The “prophylaxis” theory, whereby allergy symptoms expel carcinogenic agents from exposed tissues, remains a possible mechanism for an inverse association between airborne allergies and OSCC. The oral mucosa interacts directly with the external environment, and inverse relationships between allergies and various cancers have been more frequently observed for sites in direct contact with the environment [22]. In addition, inverse relationships with cancers have more frequently been reported for hay fever and animal allergies than drug allergies [22].

A final possibility that may account for our results is that allergies affect lifestyle choices [23, 24]. Avoidance of certain allergy triggers, including air pollutants or dietary constituents, may produce a self-selective reduction in exposure to environmental carcinogens. This may be particularly relevant for smoking, which is a major risk factor for OSCC. If this is the case, since smoking status is directly affected by the presence of allergies, and is a strong risk factor for OSCC, estimates without adjustment for smoking may be appropriate. However, associations with airborne allergies that are adjusted for all other potential confounders are similar with (OR=0.67; 95% CI, 0.48–0.93) and without (OR=0.63; 95% CI, 0.46–0.87) adjustment for pack years of smoking and smoking status (ever/never).

A limitation of this study is that we were only able to examine self-reported allergy history. Nevertheless, the prevalence of allergies among controls (50% for any allergy and 33% for airborne allergies) is in line with data from the NHANES III study, which reported a 54%-positive skin prick test for “any allergy” and a 40%-positive skin prick test for “outdoor” allergens [35]. However, it is possible that non-airborne allergies may have been overreported. Allergies to pollen, mold and dust are the most common allergies reported, and given that reactions to airborne allergens such as allergic rhinitis are overt and generally unmistakable, these allergies may be less likely to be confused with non-allergic conditions. However, conditions such as food intolerances may mistakenly be considered to be allergies. Such nondifferential misclassification would bias results for food allergies closer to the null, raising the possibility that underlying true inverse associations may be of similar magnitude as allergies to airborne agents. Recall bias may be a possibility if cases were more likely to report allergies; however, we then would be less likely to observe inverse associations with OSCC.

The participation proportions were fairly low (54.4% and 63.3% of cases and 63% and 61% of controls for the first and second study respectively). Although there is a possibility that participants may differ from non-participants in their exposure history, this is likely to be non-differential based on case-control status for an exposure such as allergies; and thus results would likely be biased toward the null. If a bias does exist, there is a possibility that

true estimates may in fact be stronger than those observed. A reason for the low participation rate in the first study is that almost one fourth of eligible cases died before recruitment [26]. Thus, case participants may have been less likely to have later stage disease than non-participants, and we observed a stronger association between airborne allergies and later stage disease compared with earlier stage disease.

Our ability to accurately assess the relevance of HPV infection with respect to the association between allergies and OSCC was hindered by limitations of both HPV serology and HPV DNA measurement. PCR amplification of HPV DNA may often yield false positive results [36], or merely reflect a transient infection, with no involvement in the carcinogenic process [37]. On the other hand, measurement of paraffin-embedded tissue, as was used in the present study, may underestimate the proportion of tumors containing HPV DNA because of degradation of specimens [38]. In addition, the dynamics of HPV seroconversion and the extent of antibody response to HPV type 16 capsids resulting specifically from oral HPV infection is unknown. We measured HPV-16 L1 antibodies, but not E6/E7 antibodies because L1 antibodies are markers of prior infection while E6/E7 antibodies are indicative of the presence of HPV-related cancer [39–41]; however sensitivity of HPV L1 antibodies is estimated to be only 50–70% [39]. Measurement issues are not expected to differ between cases and controls; however, misclassification of HPV status by serology or DNA measures would impact the ability to accurately categorize subjects, and thus limit the ability to detect any hypothesized heterogeneity by HPV status.

Conclusions

In this population-based case-control study, we observed a weak inverse association between a history of allergies and OSCC, adjusted for potential confounders. The association with OSCC was particularly strong for allergies to dust, pollen and mold. Large-scale prospective studies, including biomarkers such as skin-prick testing and IgE levels [32, 42] are needed to better characterize the association and provide insight into potential biological mechanisms.

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Table 1

Characteristics of oral squamous cell carcinoma cases and controls, Seattle metropolitan area, 1985–1989 and 1990–1995.[a]

Characteristic	Cases (n=400)		Controls (n=613)	
	n	%	n	%
Age (years)				
18–39	28	7.0	62	10.1
40–49	82	20.5	141	23.0
50–59	147	36.8	215	35.1
60–65	143	35.8	195	31.8
Sex				
Men	286	71.5	439	71.6
Women	114	28.5	174	28.4
Race				
White	375	93.8	578	94.3
Other	25	6.3	35	5.7
Income				
<$15,000	91	23.2	35	5.8
$15,000 to <$30,000	100	25.5	124	20.6
$30,000 to <$45,000	98	25.0	154	25.6
≥$45,000	103	26.3	289	48.0
Education				
High school or less	178	44.5	178	29.0
College or technical school	184	46.0	337	55.0
Graduate school	38	9.5	98	16.0
Pack-years of cigarette smoking				
Never	60	15.0	217	35.4
>0 to <10	28	7.0	115	18.8
10 to <20	29	7.3	72	11.8
20 to <30	42	10.5	75	12.2
30 to <40	76	19.0	51	8.3
40 to <50	58	14.5	32	5.2
≥50	107	26.8	51	8.3
Number of alcoholic drinks per week				
Never	16	4.0	45	7.3
>0 to <7	128	32.0	362	59.1
7 to <14	67	16.8	96	15.7
14 to <28	76	19.0	68	11.1
≥28	113	28.3	42	6.9
HPV-16 Seropositivity				
Positive	190	52.8	195	34.7
Negative	170	47.2	367	65.3

[a] Percentages have been rounded and may not total 100.

Table 2

Association of oral squamous cell carcinoma with self-reported history of allergies, Seattle metropolitan area, 1985–1989 and 1990–1995.[a]

	Cases (n=400)		Controls (n=613)			
Allergy History	**n**	**%**	**n**	**%**	**OR**	**95% CI**
Any allergy	166	41.5	306	49.9	0.81	(0.61–1.08)
Airborne allergies	84	21.0	202	33.0	**0.67**	**(0.48–0.93)**
Pollens	73	18.3	170	27.7	0.72	(0.51–1.02)
Dust	29	7.3	79	12.9	0.69	(0.42–1.11)
Mold	6	1.5	39	6.4	**0.34**	**(0.14–0.83)**
Antibiotic allergies[b]	44	11.0	65	10.6	1.12	(0.71–1.76)
Penicillin	35	8.8	39	6.4	1.37	(0.81–2.31)
Sulfa drugs	9	2.3	25	4.1	0.76	(0.32–1.77)
Food allergies[c]	31	7.8	67	10.9	0.84	(0.52–1.37)
Animal allergies[d]	22	5.5	56	9.1	0.88	(0.51–1.52)
Cats	12	3.0	40	6.5	0.76	(0.38–1.51)
Dogs	5	1.3	20	3.3	0.69	(0.25–1.91)
Bee stings	8	2.0	10	1.6	1.20	(0.44–3.28)

[a] Adjusted for age, sex, race, education, pack years of smoking, smoking status (ever/never), and average alcoholic drinks per week.

[b] Includes allergies to peniciliin, sulfa drugs and other antibiotics (unspecified).

[c] Includes allergies to milk, chocolate, shellfish, wheat, citrus, eggs, seafood, yeast, and miscellaneous food.

[d] Includes allergies to cats, dogs, horses, cows, rabbits, bee stings, and responses of “other” or “all animals.”

Table 3

Association of oral squamous cell carcinoma with self-reported history of allergies stratified by tumor site, Seattle metropolitan area, 1985–1989 and 1990–1995.[a]

	Oral cavity						Oropharynx					
	Cases (n=249)		Controls (n=613)				Cases (n=151)		Controls (n=613)			
Allergy status	**n**	**%**	**n**	**%**	**OR**	**95% CI**	**n**	**%**	**n**	**%**	**OR**	**95% CI**
Any allergies	100	40.2	306	49.9	0.76	(0.54–1.07)	66	43.7	306	49.9	0.84	(0.57–1.25)
Airborne allergies[b]	54	21.7	202	33.0	0.71	(0.49–1.05)	30	19.9	202	33.0	**0.56**	**(0.35–0.90)**

[a] Adjusted for age, sex, race, education, pack years of smoking, smoking status (ever/never), and average alcoholic drinks per week.

[b] Includes allergies to pollens, dust and mold.

Table 4

Association of oral squamous cell carcinoma with self-reported history of allergies stratified by site and HPV status, Seattle metropolitan area, 1985–1989 and 1990–1995.[a]

	Oral cavity						Oropharynx					
	Cases exposed		Controls exposed				Cases exposed		Controls exposed			
Allergy and HPV status	**N**	**%[b]**	**n**	**%[b]**	**OR**	**95% CI**	**n**	**%[b]**	**n**	**%[b]**	**OR**	**95% CI**
Any allergies												
HPV-16 Serology												
positive	44	39.6	98	50.3	0.78	(0.46–1.32)	35	44.3	98	50.3	0.85	(0.48–1.51)
negative	50	43.1	191	52.0	0.69	(0.43–1.10)	24	44.4	191	52.0	0.68	(0.36–1.29)
HPV DNA[c]												
positive	6	54.6	306	49.9	0.99	(0.28–3.45)	17	56.7	306	49.9	1.27	(0.59–2.72)
negative	58	41.7	306	49.9	0.78	(0.52–1.18)	23	50.0	306	49.9	0.84	(0.43–1.63)
Airborne allergies[d]												
HPV-16 Serology												
positive	20	18.0	64	32.8	0.58	(0.31–1.10)	18	22.8	64	32.8	0.70	(0.36–1.35)
negative	30	25.9	127	34.6	0.77	(0.46–1.29)	10	18.5	127	34.6	**0.43**	**(0.19–0.95)**
HPV DNA[c]												
positive	5	45.5	202	33.0	1.93	(0.54–6.93)	10	33.3	202	33.0	0.85	(0.38–1.92)
negative	29	20.9	202	33.0	0.65	(0.40–1.06)	10	21.7	202	33.0	0.54	(0.24–1.21)

[a] Adjusted for age, sex, race, education, pack years of smoking, smoking status (ever/never), and average alcoholic drinks per week.

[b] Percentages reflect the proportion of the whole in each category made up by the "n" to the left of each"%." Unexposed percentages are the complement of percentages shown.

[c] HPV types 16, 18, 31, 33, or 35. No HPV DNA data were available for controls.

[d] Includes allergies to pollens, dust and mold.