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A new questionnaire to determine the frequency and severity of symptoms caused by inhaled odors, chemicals and irritants in normal subjects and their relation to health-related quality of life

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A New Questionnaire to Determine the Frequency and Severity of Symptoms Caused by
Inhaled Odors, Chemicals and Irritants in Normal Subjects and Their Relation to Health-
Related Quality of Life

by

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A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Science in Public Health
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A New Questionnaire to Determine the Frequency and Severity of Symptoms Caused by Inhaled Odors, Chemicals and Irritants in Normal Subjects and Their Relation to Health-Related Quality of Life

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ABSTRACT

Individuals may develop symptoms in response to inhaled odors, chemicals, and irritants. This may affect their quality of life. Little is known about the prevalence and severity of symptoms that result from exposure to odors, chemicals and irritants. This study demonstrates the development of a new respiratory questionnaire to detect the prevalence and severity of symptoms experienced upon exposure to chemicals, odors, and irritants, and relates these symptoms to quality of life. This questionnaire was submitted to 96 volunteers at the University of South Florida College of Public Health who responded to items regarding symptoms developed in response to exposure to automobile exhaust, cigarette smoke, strong smells, cologne, perfumes or scented candles, or fresh paint vapors or fumes. Health-related quality of life was assessed using a subscale included with the questionnaire. The number and severity of symptoms developed in response to exposure to odors, chemicals, and irritants showed a strong negative correlation with health-related quality of life, consistent with intuitive estimates of the direction of this relationship. Also, it was shown that in normal populations, males and females develop statistically similar prevalence and severity of symptoms in response to exposure to odors, chemicals, and irritants.

Hypothesis and Specific Aims

Hypothesis

The frequency and severity of symptoms reported by those who are exposed to inhaled odors, chemicals and irritants can be determined by a self-administered questionnaire, and these symptoms affect their reported quality of life.

Specific Aims

I: To develop a self-administered questionnaire and demonstrate that it detects the frequency and severity of symptoms reported by normal individuals on their experience with odors, chemicals, and irritants.

II: To determine the relationship between self-reported quality of life and severity of reported symptoms in normal individuals' experience with inhaled odors, chemicals, and irritants.

Introduction

Questionnaires are an important and powerful tool to explore occupational health problems. They are easy to apply, inexpensive to administer, and readily interpretable. The proper use of a questionnaire is dependent on careful design, subsequent verification of validity and reproducibility, and the close monitoring of its application.¹ Here, we will demonstrate the creation of a questionnaire and its use to determine the effects of inhaled substances on normal individuals with regard to symptoms they experience and the effect of their symptoms on quality of life.

Many airborne chemical substances with an odor may produce sensory irritation in the eyes, nose and throat, as well as acute neurotoxic symptoms. Such symptoms are dose related and all persons experience them. Some persons who sense the odor from certain chemical substances may feel ill, although this reaction is not experienced by others with the same exposure. Irritant symptoms may arise in environments in which inhaled substances are at levels lower than regulation levels,² and some say that chemical sensitivity is due to inadequate exposure limits for chemicals.³ Only a few epidemiologic studies from different work places have been performed to study this phenomenon.⁴ It is important to understand this phenomenon to protect workers properly.

Individuals may incur great personal costs in order to ease their symptoms, whatever the cause or the current term for their symptoms or whether they incur the symptoms at home or work. Studies have shown that workers have had to change jobs⁴ or are perhaps drawn or pushed into other jobs⁵ because they could not tolerate the symptoms they sustain when exposed to odors and irritants at work.

The field of odor and irritant sensitivity requires understanding the contributions of many authors in the fields of anatomy, physiology, pathophysiology, and psychology. The literature covering this phenomenon is huge. A basic problem facing the study of sensitivity to inhaled substances is determining if the symptoms occur due to psychological factors or physiological factors. Broadly, areas of investigation include olfactory physiology, respiratory physiology, and psychology.

People are exposed to airborne substances at home and at work. Many of these substances not only produce an odor but can evoke ocular, nasal and throat irritation, as well as neurotoxic symptoms. It is useful to define the airborne substances of interest as odors or irritants. Briefly, odors stimulate the olfactory nerve (cranial nerve I). Irritants cause inflammatory effects.⁶ Lateralization testing demonstrates this difference. Single nostril stimulation with an irritant causes lateralization. That is, one can tell into which nostril the

stimulus is applied in the case an irritant, such as ammonia. An odor, however, infused into one nostril is sensed bilaterally.⁷ Many substances have odorous and irritant properties, but not all substances that are irritating are odorous (NO₂),⁸ and not all odorous substances are irritating (phenyl ethyl alcohol).² Irritant substances may be a simple molecule, such as acrolein and ozone or a complex mixture, such as tobacco smoke.⁹ However, inhaled odors and irritants can elicit complaints of eye, nose, and throat irritation, headache, nausea, diarrhea, hoarseness, sore throat, cough, chest tightness, nasal congestion, palpitations, shortness of breath, stress, drowsiness, and alterations in mood.⁸ The number of individuals who suffer from these symptoms is not known accurately, as estimates of the prevalence of this chemical sensitivity range from about 11 million¹⁰ to 90 million¹¹ individuals. The difference in prevalence is likely due to different case definitions.

The field studying sensitivity to inhaled substances suffers from the lack of a consistent case definition or the name for phenomenon of sensitivity to inhaled substances,⁴ therefore, the results of studies are difficult to compare. Odor perception is highly idiosyncratic, and this variability affects subjective responses. Numerous factors, including adaptation, medications, aging, nutritional status, pregnancy, and a variety of diseases and disorders can affect odor perception. Also, disorders of the olfactory system affect over 2.7 million Americans.⁷ Some of the symptoms of diseases such as asthma and allergic rhinitis overlap those symptoms developed after exposure to odors and irritants. Furthermore, allergic symptoms can be exacerbated by non-allergenic inhaled substances.^{10, 12}

Although it may appear to be straightforward to expose individuals to a chemical and ask them to report on the level of irritation they experience, the potential for confusion between olfactory and irritant modalities has produced extreme variability in direct scaling of upper airway irritant sensations by individuals with intact olfactory and trigeminal systems. This confusion is exacerbated when chemicals present in the air at levels that stimulate only odor sensation can prompt exposed individuals to report 'irritation', even if the perception is largely mediated through the psychological discomfort incurred by smelling the odor of an unfamiliar or unpleasant chemical, or even from misattributions of unrelated symptoms that happen to coincide with chemical exposure.² More simply, subjects may report to researchers "irritation" by odors that are merely unpleasant or unfamiliar, so this study design yields confusing results.

Psychologically, hypotheses have focused on psychiatric disorders, personality traits^{13, 14} and mass hysteria.¹⁵ Responses to inhaled chemicals are subjective, variable, and subject to suggestibility bias. Suggestion and/or suggestibility bias effects were demonstrated in a study in which people given positive information about odors to which they were exposed had less perceived irritation compared to people given negative information.⁷ In another study, reports of sensory irritation in the workplace were influenced by the reactions of co-workers and other bystanders to an odor.¹⁶ Instructing persons to attend to evidence of "nasal obstruction" as they breathed induced more symptoms than instructing them to attend to the "free passage of air." A significant amount of the variation in irritant and symptom perception in normal, healthy individuals can be attributed to differences in personality orientations. Positive affective orientations appear to lower individuals' expectancies of

becoming ill, while negative orientations appear to heighten those same expectancies.² Although psychiatric causes may be an important source for symptoms, studies of patients with multiple chemical sensitivity showed no psychiatric diagnosis in up to 50%.¹³

Demographic studies have shown that women, persons of relatively higher socioeconomic status, and in office rather than heavy industry positions are more likely to report symptoms from inhaled irritants.¹⁷ It is not understood why workers in heavy industry, who intuitively would have greater exposure to airborne chemicals, have less reported symptoms.

Physiology affects irritant and odor perception. Irritants typically obey a sigmoid dose-response relationship with a threshold under which no irritation reaction occurs. Many toxicological irritants show reversible effects – the inflammation disappears after exposure to the irritant ceases, however, acute exposures to high levels of some irritants can result in irreversible effects.^{9, 18} Human physiology can also affect this perception, as experiments have shown that odor intensity depends on the effort associated with inspiration.¹⁹ Interestingly, research shows that odors are perceived to be more pleasant and odor identification is more accurate when smelled with the right nostril than with the left.²⁰

Study limitations aside, there are at least three mechanisms by which ambient odors may produce health symptoms. First, symptoms can be induced by exposure to odorants at levels that also cause irritation or other toxicological effects. That is, irritation, rather than the odor is the cause of the health symptoms, and odor, the sensation, simply serves as an exposure marker. Second, health symptoms from odorants at nonirritant concentrations can be due to innate (genetically coded) or learned aversions. Third, symptoms may be due to a copollutant (such as endotoxin) that is part of an odorant mixture.⁴ A problem has developed, however, as there is a group of patients who have been given a diagnosis most commonly called Multiple Chemical Sensitivity. The incidence of Multiple Chemical Sensitivity is said to be increasing.^{3, 17} It has been defined as, "an acquired disorder characterized by recurrent symptoms, referable to multiple organ systems, occurring in response to demonstrable exposure to many chemically unrelated compounds at doses far below those established in the general population to cause harmful effects. No single widely accepted test of physiological function can be shown to be correlated with the symptoms."²¹ Media sources have sensationalized some aspects of this sensitivity by reporting on "sick buildings" and "20th Century Disease." Once the media and legal system have reinforced to the general public that a product is dangerous, scientific evidence that comes after this process is not likely to be reassuring, and the misperception endures.²² Waddell's comments in 1992 are still true. "The salient problem with MCS is that there is no consistent and specific effect from exposure to any specific chemical. This does not allow for any objective test for any disease entity that might be caused by the chemicals as indicated by the theory of MCS. The effects of exposure to chemicals as defined today by MCS are subjective, and no report is available to convincingly demonstrate that these effects would not have occurred merely by chance."²³

To summarize, odor and irritant perception is a complicated field of study, with disagreement about case definition, prevalence, and methodological problems that exist on

physiological and psychological levels. It is obvious that this field needs more study in order to answer the question, "... is it the agents or the responder?" To that end, we have created a questionnaire to identify normal individuals who seem to develop more severe symptoms from inhaled environmental odors, chemicals, and irritants. These individuals may be suitable for further physiological studies in the Breath Laboratory at the University of South Florida. Hopefully, this and further studies in this laboratory will help determine the cause of symptoms in this troubled population.

Methods

The Institutional Review Board of the University of South Florida reviewed the study proposal and exempted the study from further review.

This study describes the development and implementation of a self-administered questionnaire to demonstrate the frequency and severity of symptoms a normal adult population recalls when queried about their experience with exposure to four commonly encountered airborne odors and irritants -cigarette smoke, perfumes, automobile exhaust, and paint fumes - and relates these responses to their responses to quality of life queries.

The questionnaire was presented to volunteers as part of a packet contained in a self-addressed University of South Florida interoffice envelope from February 1, 2007, to February 28, 2007. The envelope contained a cover letter (Appendix B), a 23 item demographic and medical questionnaire (Appendix C), and a two page 42 item symptom and quality of life questionnaire (Appendix D).

The symptom questionnaire was created with input from consultants of the College of Industrial and Organizational Psychology at the University of South Florida, who have reviewed the questionnaire for readability and structure. Quality of life items are derived from intuitive queries in addition to selected items from the Centers for Disease Control Prevention Health-Related Quality of Life 14 Item Measure's "Healthy Days Core Module."²⁴ These items were included since they have been validated in other studies and increase the information contained in the data from ordinal to the interval level. The medical questionnaire was used to define the study population after the results were returned. It contained items concerning smoking history and medical and psychological conditions that could cause interference with normal olfaction and irritant sensation, all of which were used as exclusion criteria. The demographic portion of the questionnaire obtained sex and age information. No personally identifiable information was obtained. Information on age was used to study adults from 18 to 80 years old. The entire questionnaire took about 10 minutes to present and complete.

The questionnaire itself asked respondents to rate their likelihood of agreement with statements relating to symptoms they experienced when they encountered cigarette smoke; strong smells; cologne, perfumes or scented candles; automobile exhaust; or paint fumes in the past year. The responses were scored on a 5-point Likert scale (1 = almost never; 5 = almost always). The questionnaire contained subscales for ear, nose, and throat, lower respiratory, general, gastrointestinal, and neuropsychological symptoms. To simplify symptom scoring, the form of the statements is such that agreement with the experience of

symptoms results in a higher Likert score. In that way, more agreement with the statements resulted in higher raw symptom scores. In this questionnaire, two formats were compared to each other to quantify quality of life. In one format, four items were on a Likert scale, and in the other format based on the CDC items, 3 items were in a fill in the blank format, which will be referred to henceforth as “CDC styled” items.

Volunteers were obtained by submitting the questionnaire to male and female staff and students of the College of Public Health at the University of South Florida during business hours, personally delivered by the Principal Investigator. A kiosk in the College of Public Health was also used to attract volunteers from student and staff traffic in the lobby of the College of Public Health, also attended by the Principal Investigator. A flyer on the kiosk was used to attract attention and provide initial information to potential volunteers. Professors allowed the questionnaire to be distributed to a class in two cases.

Using standard deviation from the mean to define "high" and "low" scores, Magnavita¹⁵ was able to demonstrate a significant difference ($p < 0.001$) in total symptom scores between cacosmic and noncacosmic patients in a population of 47 subjects. We proposed, then, to obtain 50 included subjects by submitting 100 questionnaires, expecting to exclude about half of the returned questionnaires.

Volunteers were asked to respond to the questionnaire and mail their results via inter-office mail to the College of Public Health inbox, addressed to the principal investigator. The subjects completed the questionnaire privately in order to minimize social acceptability bias. A new pencil with the USF logo (value \approx \$0.50) was enclosed in the envelope with the questionnaire to compensate respondents for their time to complete the questionnaire.

In order to protect the privacy of participants, exclusion from analysis was performed after the questionnaires were returned. Responses were excluded if any of the items were answered positively in the medical questionnaire, except for one item, #3, which asked if the respondent considered themselves a healthy person. Items that were left blank on the Medical and Demographic portion of the questionnaire were considered a positive response and resulted in exclusion from the normal group. All raw data has been dated and filed in a locked cabinet in the Respiratory Laboratory in the College of Public Health for two years, and then destroyed. Respiratory Laboratory personnel will hold the key.

Quality of life was measured by 4 questions with Likert scales and with 3 questions using CDC styled items. The responses on the Likert format were summed to achieve a quality of life score, and the CDC styled questions were added to obtain another quality of life score. The possible range of values for summed Likert responses is 4 to 20. The possible range of values for the CDC styled scores was 0 to 90. Each of these scores were compared to total symptom scores to determine the relationship between quality of life scores and total symptom scores in response to inhaled odors, chemicals, and irritants, using simple linear regression.

Statistical calculations were performed using Microsoft Excel 2003. A symptom score with a possible range of 29-145 was obtained by summing the symptom ratings for each included subject. Scores for the five symptom groups were obtained by selecting the items corresponding to each system and summing the responses by system.

Results

Ninety-six questionnaires were submitted to volunteers, and 82 were returned. Fifty respondents identified themselves as female, and 28 identified themselves as male. Four respondents did not specify age or sex. Median age for all respondents was 31 years, ranging from 17 to 73. (Table 1) For reference, all items were numbered from the first demographic item, through the medical exclusion items, through the symptom items, and through the final quality of life items. These numbers appear in the far left column in the appended questionnaires.

Table 1: Demographic Summary for All Respondents

	n	Lowest Age	Median Age	Highest Age
All	82	17	31	73
Males	28	18	33.5	73
Females	50	17	29	61
Unspecified	4			

The intended group of respondents for this study, the inclusion group, were obtained by using the responses given on the Medical and Demographic Information page (Appendix C) to obtain a population without major physiological or psychological disease between the ages of 18 and 80. Four responses had data of such poor quality they were excluded on this basis alone. Exclusion criteria removed 55 more responses, leaving 23 responses included for further statistical analysis, which was called the normal sample. The inclusion group consisted of 13 females, 9 males and one unspecified age and sex. The median age for all normal respondents for which data was specified was 26, ranging from 18 to 47. (Table 2)

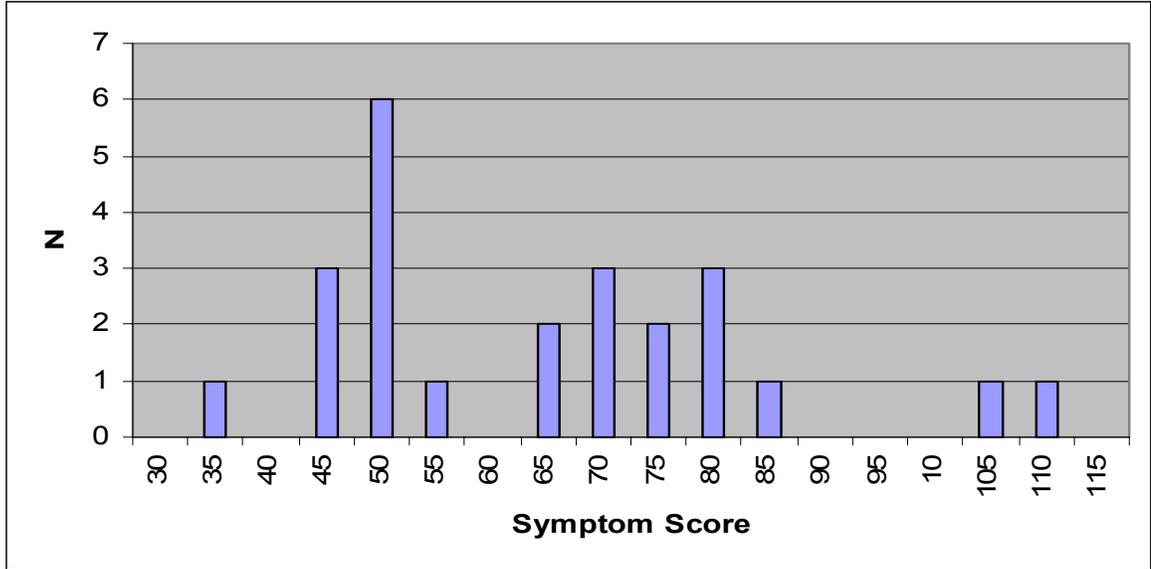
Table 2: Demographic Summary for Normal Respondents

	n	Lowest Age	Median Age	Highest Age
All	23	18	26	47
Males	9	18	28	38
Females	13	19	27	47
Unspecified	1			

Total symptom scores for the inclusion group were derived from a Likert scale and thus treated as ordinal variables. These scores ranged from 35 to 106, representing the sum of all

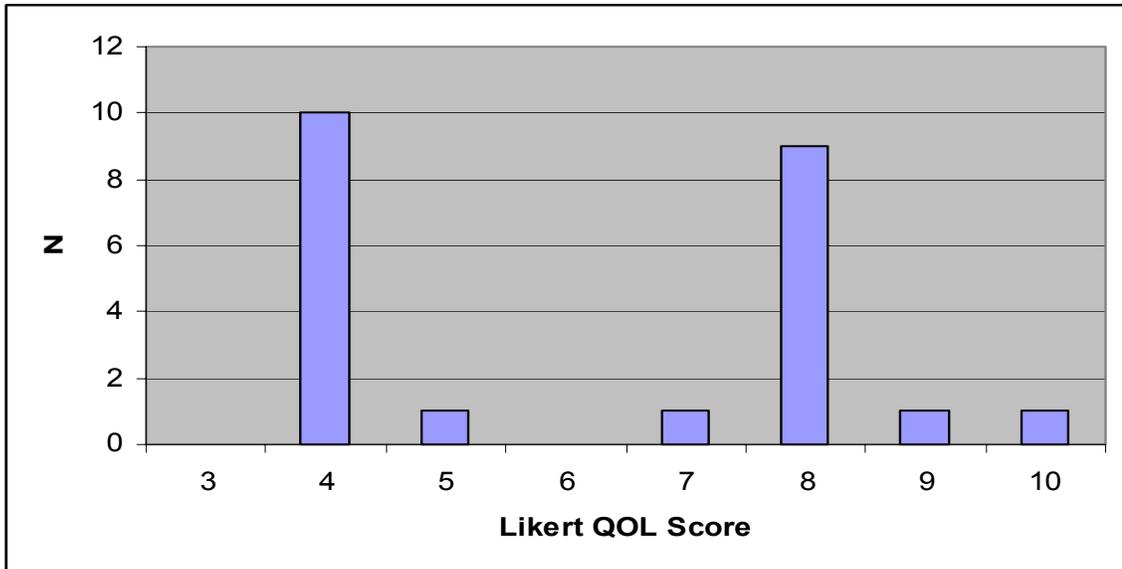
Likert responses to specific symptom queries. The median score is 63.5. The frequency distribution of symptom scores is shown in Figure 1.

Figure 1: Histogram of Total Symptom Scores in Normal Respondents



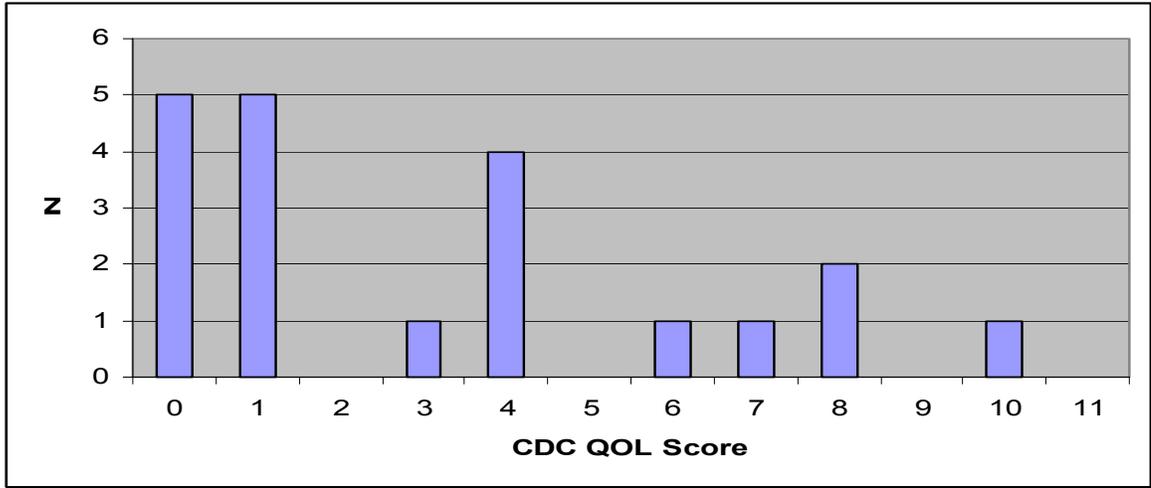
The quality of life scores for the inclusion group ranged from 4 to 10 on the Likert scaled items, out of a possible range of 4 to 20, representing the sum of responses to each of the 4 Likert items. A histogram of the quality of life scores on the Likert scale is shown in Figure 2. Increasing values on the Likert scale represented diminishing quality of life.

Figure 2: Histogram of Likert Quality of Life Scores in the Inclusion Group



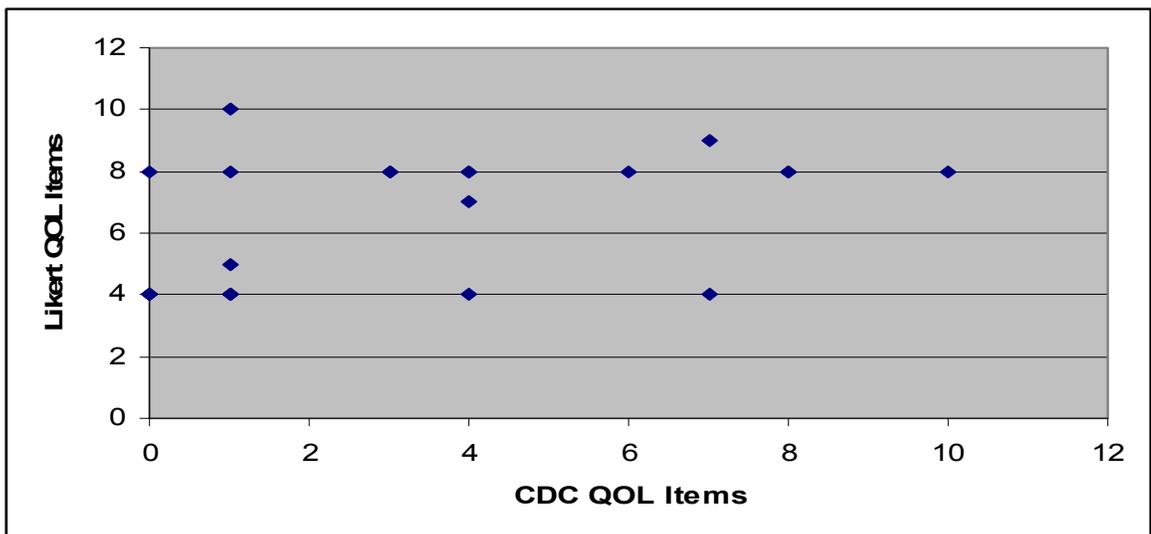
The histogram in Figure 3 shows the frequency of responses to the fill in the CDC styled quality of life scores in the inclusion group. Three responses from the above group of Likert respondents were not included in Figure 3 due to missing data. Increasing QOL score is in the direction of more days of disability.

Figure 3: Histogram of CDC Styled Quality of Life Scores



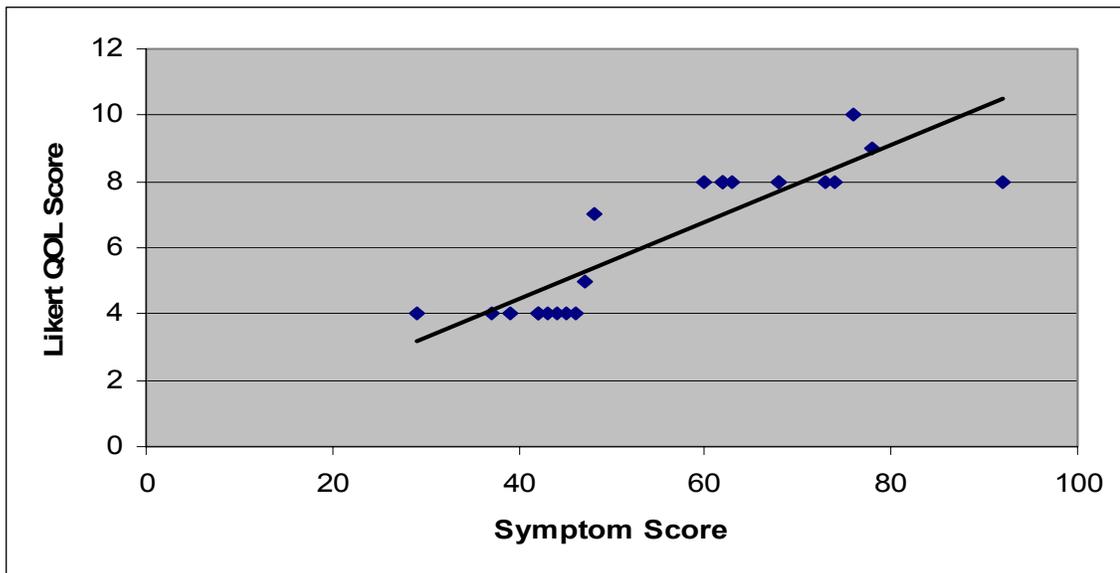
The adjusted Spearman rank correlation = .463 for the relationship between Likert-type items and the CDC styled items in the inclusion group. The scatter plot of the raw quality of life scores is represented in Figure 4.

Figure 4: Scatter Plot of Likert versus CDC Styled Responses



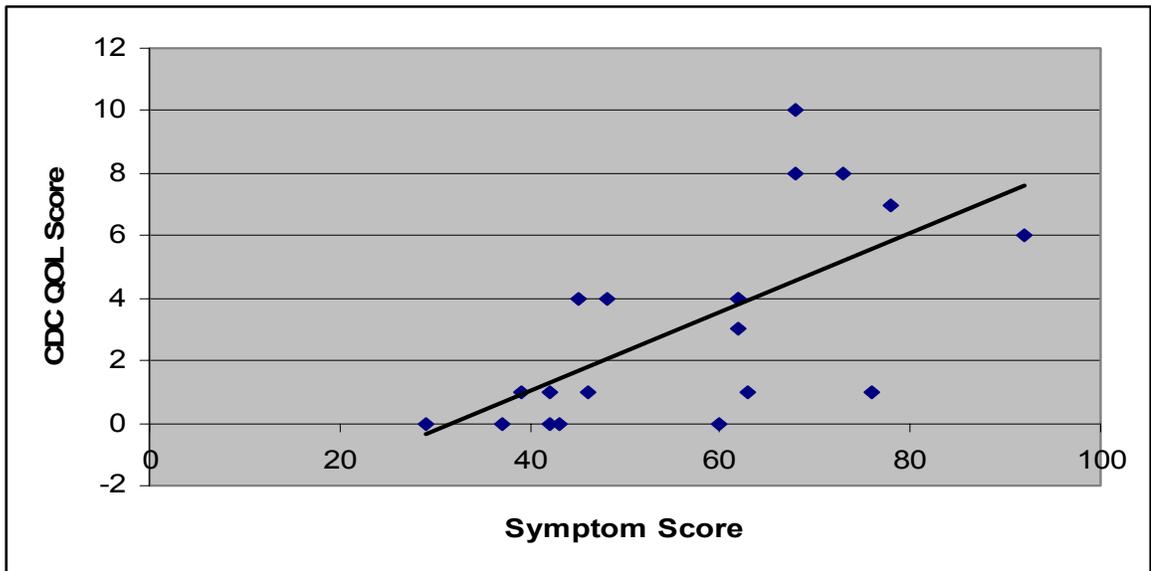
To show the relationship between quality of life score and symptom score, each of the two types of quality of life (Likert and CDC styled) scores were compared to total symptom scores in the normal patients. Again, there are three less comparisons in the CDC styled comparison than the Likert formatted items due to missing data. The relationship between the Likert styled items and symptom scores in normal patients yields an adjusted Spearman rank correlation = .916. The scatter plot and the best fit regression line for these points are in Figure 5.

Figure 5: Scatter Plot of Symptom Score versus Likert Quality of Life Scores



When the CDC styled quality of life scores are compared with the symptom scores, the regression function gives an adjusted Spearman rank correlation = 0.725. These data are represented in Figure 6 with a trendline showing the best fit for the regression function between the variables.

Figure 6: Scatter Plot of Symptom Score versus CDC Styled Quality of Life Score



The responses in each symptom group were averaged to give a system score, and the sum of these averages gave an adjusted symptom score that adjusted for the number of items in each symptom group, which ranged from 4 to 9 items. This controlled for the different weights given to the total symptom score due to the different number of items in each symptom group. The unadjusted and adjusted total symptom scores were very similar, with adjusted Spearman correlation coefficient between the two scores = 0.99. The possible adjusted symptom score ranged from 5 to 25. The 5 symptom groups were compared by relating their average score to the adjusted symptom score. This was done for several subsets of the responses, including the inclusion group, the excluded group, an “atopic group”, and smokers. These populations are not necessarily exclusive. The excluded group consisted of all responses between the ages of 18 and 80 that are not in the inclusion group. The “atopic group” consists of all excluded responses that would have been in the inclusion group but for a positive response to the items, “Do you get hay fever, seasonal allergies, or allergic rhinitis?” or “Do you have eczema or hives?” Smokers were defined as those excluded, but which would have been in the inclusion group except for a positive response on the items, “Are you a smoker?” or “Have you smoked in the last 10 years?”. Adjusted Spearman correlation coefficients for these relationship between the system symptom score and the total adjusted symptom score are presented in Table 3. LoResp represents the lower respiratory system, and NeuroP represents neuropsychological symptoms.

Table 3: Correlation Coefficients of Symptom Group with Adjusted Symptom Score

	Normal	Excluded	Atopic	Smokers	Average
General	0.86	0.87	0.75	0.73	0.80
ENT	0.92	0.83	0.90	0.91	0.89
GI	0.93	0.76	0.24	0.89	0.71
LoResp	0.66	0.91	0.48	0.95	0.75
NeuroP	0.80	0.44	0.81	0.62	0.67
Average	0.83	0.76	0.64	0.82	0.76

The symptom scores of these patient groups were compared to the Likert and CDC styled quality of life scores. The adjusted Spearman correlation coefficients for the Likert styled items appear in Table 4, and for the CDC styled items in Table 5.

Table 4: Correlation Coefficients of Symptom Group with Likert Styled Quality of Life Items

	Normal	Excluded	Atopic	Smokers	Average
General	0.84	0.79	0.43	0.81	0.72
ENT	0.89	0.86	0.07	0.85	0.67
GI	0.88	0.70	0.64	0.82	0.76
LoResp	0.49	0.90	0.52	0.82	0.68
NeuroP	0.80	0.77	0.48	0.77	0.70
Average	0.78	0.80	0.43	0.81	0.71

Table 5: Correlation Coefficients of Symptom Group with CDC Styled Quality of Life items

	Normal	Excluded	Atopic	Smokers	Average
General	0.65	0.11	-0.31	0.26	0.18
ENT	0.72	-0.05	-0.33	0.00	0.09
GI	0.60	0.04	-0.13	0.00	0.13
LoResp	0.35	0.04	-0.46	0.07	0.00
NeuroP	0.65	-0.19	-0.30	0.26	0.11
Average	0.59	-0.01	-0.31	0.12	0.10

The Mann-Whitney U test was used to determine the probability that the distributions of the different symptom groups in the different patient groups were different than that of the inclusion group. The p values are presented in Table 6:

Table 6: Probability of Difference from Inclusion Group

	Excluded	Atopic	Smokers
General	0.00	0.23	0.08
ENT	0.01	0.01	0.19
GI	0.31	0.25	0.73
LoResp	0.10	0.49	0.07
NeuroP	0.27	0.22	0.07

Items # 25 – 28 asked about respondents' reaction to cigarette smoke, automobile exhaust, strong smells, cologne, perfumes or scented candles, and fresh paint vapors or fumes (the substances in the table below). These responses were summed and compared with the symptom scores of the different patient groups. The adjusted Spearman correlation coefficients are shown in Table 7:

Table 7: Correlation Coefficients of Substances with Patient Groups

	Normal	Excluded	Atopic	Smokers
Cigarette	0.21	0.49	0.48	0.27
Exhaust	0.12	0.40	0.23	0.17
Scents	0.11	0.50	0.60	0.52
Paint	0.18	0.50	0.47	0.27

General health was queried twice, using two different formats. The first format gave a yes/no choice, and the second gave a 5 level Likert range of responses. In all cases, items answered "yes" to the query whether the respondent considered themselves a healthy person were answered from 1-3 in the Likert scale, representing excellent, very good, and good health. All "no" answers in the yes/no format were answered from 4 to 5 in the Likert representation of the query, representing fair or poor health. The adjusted Spearman correlation coefficient of this relation = .363.

There was a group of 15 respondents who were labeled "atopic", as they were excluded from the normal group only by their positive response to the items on the medical portion of the questionnaire relating to asthma, antihistamine use, hay fever, and eczema. The median symptom score for this "atopic" group was 65 ($n = 15$), and it was 54 ($n = 23$) for the normal group. Wilcoxon's two group rank-sum method²⁵ was used to test the hypothesis that the means of the groups were the same. The difference in the groups was significant for the two tailed test at $\alpha = 0.1$, with obtained $t = 3.53$ and critical $t = 2.673$.

The Mann-Whitney U test was used to determine the likelihood that patient groups' distribution of symptom scores and quality of life scores (on the two different quality of life styles) differed from the inclusion group scores. These are presented in Tables 8 and 9.

Table 8: Probability of Different Distribution from Inclusion Group Symptom Scores

Excluded	0.23
Atopic	0.16
Smokers	0.03

Table 9: Probability of Different Distribution from Inclusion Group Quality of Life Scores

	LQOL	CQOL
Excluded	0.40	0.37
Atopic	0.30	0.39
Smokers	0.12	0.28

Symptom scores for males were significantly less than those for females only in the inclusion group, with a one tailed $p = 0.048$. This same test shows that the mean symptom scores are not significantly different for males and females in the normal group, where $p = 0.5$ for the difference.

The adjusted Spearman's rank correlation coefficient relating age with total symptom scores = .239 in the normal group and = -.054 in the excluded group.

Item # 24 asked respondents to identify their agreement with the statement, "I am more sensitive to inhaled chemicals, irritants, odors, or strong fragrances than the average person." The adjusted Spearman's rank correlation coefficients relating the response to this single item to the symptom groups in the different patient groups in Table 10.

Table 10: Correlation coefficients between Item 24 and Symptom Group in Various Patient Groups

	Normal	Excluded	Atopic	Smokers	Average
General	0.30	0.41	0.47	-0.03	0.29
ENT	0.54	0.39	0.43	0.36	0.43
GI	0.38	0.27	-0.04	0.42	0.26
LoResp	0.09	0.45	0.42	0.47	0.36
NeuroP	0.36	0.46	0.69	0.17	0.42
Average	0.33	0.40	0.40	0.28	0.35

Discussion

Demographic comparison showed a similar age distribution between males and females, but female respondents numbered twice those of males, reflecting the student population of the College of Public Health at the University of South Florida.

The statistical analysis of the data in this cross-sectional study show that there is a bimodal distribution of symptom scores that adults between the ages of 18 and 80 without confounding disease states (the inclusion group) reports on their experience with cigarette smoke, automobile exhaust, strong smells, cologne, perfumes or scented candles or fresh paint vapors or fumes. This could represent a physiologic difference in individuals in the two groups, the normal individuals without symptoms and the normal individuals with symptoms. The nadir of the curve between modes provides a good point to divide "normal - asymptomatic" and "normal - symptomatic" responses. This point would be a total symptom score somewhere between 65 and 70, as this score seems to discriminate between the groups on gross inspection of the histogram of symptom scores.

The quality of life scores obtained from the Likert scale items in this included group correlate fairly well with symptom scores, whereas the quality of life scores from the fill in the blank items correlate less well with symptom scores. Also, the quality of life scores from the two different item formats correlate poorly with each other. None of the system subscores agreed well with the CDC styled quality of life in any patient group other than the inclusion group.

The hypothesis that increasing symptoms affects the health-related quality of life was supported, as shown in Figures 5 and 6, where the regression slope is not zero, but is positive in this case. This shows that increasing symptoms result in decreased health related quality of life perceptions.

On average, of all the symptom categories, ear, nose, and throat symptoms correlated best with total symptom scores, and neuropsychological symptoms correlated least well. High correlation of the total symptom score with ENT symptoms may result from the fact that this system is likely evolved to detect inhaled odors, chemicals, and irritants.

Interestingly, the quality of life scores for the atopic individuals was very poorly correlated with quality of life. Perhaps the symptoms of atopy have incorporated into the background sensations of these individuals to the point that these symptoms are not perceived as severe enough to report.

The only patient group system scores that differed at the 0.05 level of significance from the inclusion group was the General and ENT scores in excluded respondents and ENT scores in the atopic group.

Item # 24, regarding the overall question regarding one's perceived sensitivity to odors, chemicals, and irritants correlated fairly well with final symptom scores in all groups.

Magnavita, in his study of odor sensitivity in healthy workers, asked food store workers to rate the likelihood that each of 10 substances were able to cause them symptoms of physical illness. He found that self-identified odor intolerance was significantly associated with the frequency of physical symptoms. Pearson product-moment calculations in the present study agree with this conclusion, finding a coefficient = 0.55 between the item asking if an individual considered himself sensitive to odors, chemicals, and irritants, and their total symptom score. He also found that females developed symptoms more frequently than males without regard to preexisting disease. A similar analysis of our data shows the same effect when exclusions in this study are not applied, similar to his method. Comparisons between similar information asked at different points or asked a different way are useful to assess internal validity. There was agreement in direction of the answers to the items. All those who felt they were generally healthy also agreed that they enjoyed good to excellent health. All those who felt they were not generally healthy later agreed that they suffered fair or poor health.

Biases in this questionnaire implementation include a severe selection bias. This study sample represents a mostly young, ambulatory, healthy, educated population. This reflects the environment in which it was distributed. Males and females are not represented equally. The ethnic characteristics of this sample are not quantitatively known, but qualitatively, it can be said that the respondents were of several different ethnicities, including African, Caucasian, Hispanic, Black American, and Asian, with Caucasian representing the great majority of respondents. This will affect external generalization. As experience with the questionnaire grows, and the population to which it is submitted broadens, external generalizability will become more possible.

The Final Questionnaire

This questionnaire was a pilot study to create a final questionnaire to inexpensively identify normal respondents who may suffer from symptoms when exposed to inhaled odors, chemicals, and irritants in a stronger way than other normal individuals. This is to select those for physiological testing that are more likely to demonstrate a physiological difference when tested by inhalation challenge, which satisfies in part the ethical duty to minimize risks to those not likely to benefit from investigation.

After analysis of this pilot questionnaire, it can be simplified and it needs modification.

Several respondents reflected the teaching in the College of Public Health that sex does not equal gender, and the more appropriate question in this item would be gender.

Item # 3, asking, "Do you consider yourself a healthy person?", can be dropped, as it is such a general query it should not result in inclusion or exclusion in the normal group; that is, a volunteer's responses should not be segregated into the exclusion group if this were the only item answered positively on the medical questionnaire of exclusion criteria.

Only one respondent reported an abnormal sense of taste and a normal sense of smell. All other cases would have been excludable on the basis of abnormal sense of smell only. Also, the sense of taste is not critical to sensations of odors, chemicals, and irritants, so it (Item # 11) can be dropped.

Consideration should be given to dropping the item on heart disease (Item # 14). The item asking about heart medication should be more specific, as some respondents may consider antihypertensive medication to be "heart medication", yet hypertension *per se* does not indicate heart disease. This problem is magnified by the relatively high prevalence of antihypertensive treatment compared to the prevalence of significant heart disease. If Item # 14 is kept, it should be preceded by an item asking about hypertension, such as "Do you take medicine for high blood pressure?". Also, it is not critical that persons with heart disease are excluded from the normal group, as there is no known link between heart disease and perception of inhaled odors, chemicals, and irritants. Excluding respondents on the basis of this disease may be too restrictive.

The item regarding psychiatric disorders (Item # 19) should be more specific to definitely include those suffering from depression, which has been shown to influence responses to inhaled odors. Antidepressant therapy could be used as a proxy for the diagnosis of significant depression. It would be more accurate than self-diagnosis of depression without

developing another questionnaire to merely establish this point. The proposed items for this medical item are A: "Do you take medicine for depression?" and B: "Do you suffer from any other psychiatric disorder?" A positive response to either should result in exclusion from the normal group.

Near-identical responses to similar symptoms can be simplified by throwing out one or the other. These are the burning (Item # 31) and tingling (Item # 32) of the face items. They elicited identical responses, and therefore one is predictive of the other 100% of the time, so either can be discarded. As few agreed with either statement, both could be dropped.

Item # 61 is moved upward in the item bank to follow the other symptoms and allow the quality of life items to finish the section in order to ease analysis and scoring.

Two scales were tested to indicate quality of life. The Likert styled items, as they correlated more closely with symptom scores than the CDC styled items, should be used if quality of life is to be measured in the future. Therefore, in the final version, Items # 62-65 are dropped.

(Appendix E) The final exclusion panel changes are shown in gray. It will consist of 20 items, including age and gender. The final symptom questionnaire, excluding quality of life items, will consist of 33 items. It is expected that, using the considerations above, this simpler questionnaire will retain the ability of the pilot questionnaire to detect the frequency and severity of symptoms reported by normal individuals on their experience with odors, chemicals, and irritants, and relate that with their quality of life.

As the items that were excluded from the symptom queries were mostly removed due to low prevalence of positive responses, the dividing symptom score between normal and responsive normal subjects can continue to be somewhere between 65 and 70 until the distributions are better defined for the symptom scores.

List of References

1. Merchant J. Occupational Respiratory Diseases. U.S. Department of Health and Human Services, 1986.
2. Dalton P. Upper airway irritation, odor perception and health risk due to airborne chemicals. *Toxicol Lett* 2003; 140-141:239-48.
3. Ziem G, McTamney J. Profile of patients with chemical injury and sensitivity. *Environ Health Perspect* 1997; 105 Suppl 2:417-36.
4. Moen BE. Chemical sensitivity and the work place environment: research needs. *Psychoneuroendocrinology* 2005; 30(10):1039-42.
5. Cullen MR. Epidemiologic methods for the study of occupational asthma. Current problems and solutions. *Chest* 1996; 109(3 Suppl):51S-54S.
6. Nowak D. Chemosensory irritation and the lung. *Int Arch Occup Environ Health* 2002; 75(5):326-31.
7. Chrostowski P, Foster S. Odor Perception and Health Effects. Water Environment Federation 2003 Annual Technical Exhibition and Conference. Los Angeles, California: CPF Associates, Inc., 2003.
8. Schiffman SS, Williams CM. Science of odor as a potential health issue. *J Environ Qual* 2005; 34(1):129-38.
9. Bascom R. The upper respiratory tract: mucous membrane irritation. *Environ Health Perspect* 1991; 95:39-44.

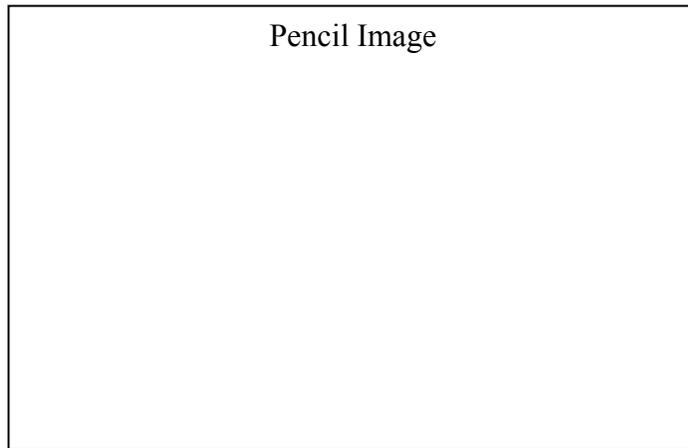
10. Meggs WJ, Dunn KA, Bloch RM, et al. Prevalence and nature of allergy and chemical sensitivity in a general population. *Arch Environ Health* 1996; 51(4):275-82.
11. Kreutzer R, Neutra RR, Lashuay N. Prevalence of people reporting sensitivities to chemicals in a population-based survey. *Am J Epidemiol* 1999; 150(1):1-12.
12. Shim C, Williams MH, Jr. Effect of odors in asthma. *Am J Med* 1986; 80(1):18-22.
13. Caccappolo-van Vliet E, Kelly-McNeil K, Natelson B, et al. Anxiety sensitivity and depression in multiple chemical sensitivities and asthma. *J Occup Environ Med* 2002; 44(10):890-901.
14. Dalton P. Odor, irritation and perception of health risk. *Int Arch Occup Environ Health* 2002; 75(5):283-90.
15. Magnavita N. Cacosmia in healthy workers. *Br J Med Psychol* 2001; 74(Pt 1):121-7.
16. Dalton P. Cognitive influences on health symptoms from acute chemical exposure. *Health Psychol* 1999; 18(6):579-90.
17. Miller CS. The compelling anomaly of chemical intolerance. *Ann N Y Acad Sci* 2001; 933:1-23.
18. Alberts WM, Brooks SM. Reactive airways dysfunction syndrome. *Curr Opin Pulm Med* 1996; 2(2):104-10.
19. Landis BN, Hummel T, Hugentobler M, et al. Ratings of overall olfactory function. *Chem Senses* 2003; 28(8):691-4.
20. Lledo PM, Gheusi G, Vincent JD. Information processing in the mammalian olfactory system. *Physiol Rev* 2005; 85(1):281-317.
21. Cullen MR. The worker with multiple chemical sensitivities: an overview. *Occup Med* 1987; 2(4):655-61.

22. Nanagas KA, Kirk MA. Perceived poisons. *Med Clin North Am* 2005; 89(6):1359-78.
23. Waddell WJ. The science of toxicology and its relevance to MCS. *Regul Toxicol Pharmacol* 1993; 18(1):13-22.
24. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention Health-Related Quality-of-Life 14-Item Measure. 2005.
25. Blair RC, Taylor RA. *Biostatistics for the Health Sciences*: Prentice Hall, 1999.

Appendices

Appendix A: Flyer.
Formatting altered to fit format constraints.

A Questionnaire and 15 minutes could
score you a shiny new
USF pencil!



Details here

(813) 943-7960

Appendix B: Cover Letter

To the volunteer:

I am inviting you participate in a research project to study symptoms that one develops after exposure to airborne irritants. Along with this letter is a short questionnaire that asks a variety of questions about this. I am asking you to look over the questionnaire and, if you choose to do so, complete it and send it back to me using the interoffice envelope in which it came. It should take you about 15 minutes to complete.

The results of this project will be used to refine this questionnaire so it can be used to identify subjects for further study. Through your participation, I hope to identify those questions that are most and least useful. The development and results of this study will be used as the subject of my Masters Thesis in the College of Public Health.

I do not know of any risks to you if you decide to participate in this survey, and I guarantee that your responses will not be identified with you. I promise not to share any information that identifies you with anyone. You should not volunteer to put your name or any other information on the questionnaire other than that which is requested. If you do not feel comfortable completing the survey, discard it.

The survey should take you about 15 minutes to complete. I hope you will take the time to complete this questionnaire and return it. Your participation is voluntary, and there is no penalty if you do not participate. Regardless of whether you choose to participate, the results will be on file at the University of South Florida Shimberg Health Sciences Library after April 7, 2007.

If you have any questions or concerns about completing the questionnaire or about being in this study, you may contact me at (813) 943-7960. Alternatively, if you have questions about your rights, general questions, complaints, or issues as a person taking part in this study, you may also call the Division of Research Integrity and Compliance of the University of South Florida at (813) 974-9343.

Sincerely, and thank you,

signature

Stephen E. Williamson, M.D.
Chief Investigator

Appendix C: Medical and Demographic Information.
 Formatting altered to fit format constraints.

Demographics and History

1	Sex _____	
2	Age _____	

Please place an "X" in the appropriate box below

		Yes	No
3	Do you consider yourself a healthy person?		
4	Do you take antihistamines?		
5	Do you get hay fever, seasonal allergies, or allergic rhinitis?		
6	Do you cough every day?		
7	Do you suffer from respiratory problems?		
8	Do you have asthma?		
9	Are you a smoker?		
10	Do you have a normal sense of smell?		
11	Do you have a normal sense of taste?		
12	Have you smoked in the last 10 years?		
13	Have you received systemic steroids or antibiotics within the past 4 weeks?		
14	Do you have congestive heart failure, cardiomyopathy, valvular heart disease, angina, cardiac arrhythmia, or had a myocardial infarction within the last 6 months?		
15	Are you taking heart medication?		
16	Do you have hepatitis or cirrhosis?		
17	Do you suffer from renal failure?		
18	Do you suffer from any neurologic disorder?		
19	Do you suffer from any psychiatric disorder?		
20	Are you pregnant or think you might be?		
21	Do you have eczema or hives?		
22	Do you have arthritis?		
23	Has a doctor ever told you that you have fibromyalgia, chronic fatigue syndrome, or multiple chemical sensitivity?		

Appendix D: Symptom and Quality of Life Questionnaire.
 Formatting altered to fit format constraints.

Chemical, Odorant And Irritant Sensitivity Questionnaire

This questionnaire asks about how you feel now and over the past year.

Please check the box that most closely describes how you feel.

	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree
24 I am more sensitive to inhaled chemicals, irritants, odors, or strong fragrances than the average person					

	Nothing unusual	I am bothered	A mild reaction	Become somewhat ill	Become very ill
25 If I am around the following I get this reaction: Cigarette smoke					
26 Automobile exhaust					
27 Strong smells, cologne, perfumes or scented candles					
28 Fresh paint vapors or fumes					

If I am exposed to cigarette smoke, automobile exhaust, strong smells, perfumes or colognes, or fresh paint vapors:

	Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree
29 I suffer discomfort					
30 I become sick					
31 I develop burning in the skin of my face					
32 I develop tingling in the skin of my face					
33 I develop a funny sensation of the skin of my face					
34 I develop eye irritation					
35 I develop eye pain					
36 I develop eye itching					
37 I develop sore or burning nasal					

	passages					
38	I develop burning in my nasal passages					
39	I develop a sore throat					
40	I feel nauseated					
41	I develop indigestion					
42	I develop diarrhea					
43	I get gas					
44	I may cough					
45	I may cough phlegm up					
46	I feel like I can't get my breath.					
47	I start wheezing					
48	I feel tightness or pressure in my chest					

Continued on next page

If I am exposed to cigarette smoke, automobile exhaust, strong smells, perfumes or colognes, or fresh paint vapors:

		Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree
49	I develop aching joints					
50	I develop trouble sleeping					
51	I develop numbness or tingling in my hands or feet					
52	My body feels hot or cold					
53	I become emotional					
54	I get a headache					
55	I become anxious					
56	I have trouble concentrating					
57	I miss work					
58	I miss social or business appointments					
59	I feel stress at home or work					
60	I find it hard to interact with other persons					
61	My symptoms ease if I can get away					

		Excellent	Very good	Good	Fair	Poor
62	Would you say that in general your health is:					

63	Now thinking about your physical health, which includes physical illness and injury, for how many days during the past 30 days was your physical health not good?	
64	Now thinking about your mental health, which includes stress, depression, and problems with emotions, for how many days during the past 30 days was your mental health not good?	
65	During the past 30 days, for about how many days did poor physical or mental health keep you from doing your usual activities, such as self-care, work, or recreation?	

Appendix E: Proposed Revised Medical and Demographic Information

Demographics and History

1	Sex Gender	
2	Age	

Please place an "X" in the appropriate box below

	Yes	No
3	<input type="checkbox"/>	<input type="checkbox"/>
4	<input type="checkbox"/>	<input type="checkbox"/>
5	<input type="checkbox"/>	<input type="checkbox"/>
6	<input type="checkbox"/>	<input type="checkbox"/>
7	<input type="checkbox"/>	<input type="checkbox"/>
8	<input type="checkbox"/>	<input type="checkbox"/>
9	<input type="checkbox"/>	<input type="checkbox"/>
10	<input type="checkbox"/>	<input type="checkbox"/>
11	<input type="checkbox"/>	<input type="checkbox"/>
12	<input type="checkbox"/>	<input type="checkbox"/>
13	<input type="checkbox"/>	<input type="checkbox"/>
14	<input type="checkbox"/>	<input type="checkbox"/>
15	<input type="checkbox"/>	<input type="checkbox"/>
16	<input type="checkbox"/>	<input type="checkbox"/>
17	<input type="checkbox"/>	<input type="checkbox"/>
18	<input type="checkbox"/>	<input type="checkbox"/>
19	<input type="checkbox"/>	<input type="checkbox"/>
20	<input type="checkbox"/>	<input type="checkbox"/>
21	<input type="checkbox"/>	<input type="checkbox"/>
22	<input type="checkbox"/>	<input type="checkbox"/>
23	<input type="checkbox"/>	<input type="checkbox"/>

Appendix F: Proposed Revised Symptom and Quality of Life Questionnaire

Chemical, Odorant And Irritant Sensitivity Questionnaire

This questionnaire asks about how you feel now and over the past year.

Please check the box that most closely describes how you feel.

		Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree
24	I am more sensitive to inhaled chemicals, irritants, odors, or strong fragrances than the average person					

	If I am around the following I get this reaction:	Nothing unusual	I am bothered	A mild reaction	Become somewhat ill	Become very ill
25	Cigarette smoke					
26	Automobile exhaust					
27	Strong smells, cologne, perfumes or scented candles					
28	Fresh paint vapors or fumes					

If I am exposed to cigarette smoke, automobile exhaust, strong smells, perfumes or colognes, or fresh paint vapors:

		Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree
29	I suffer discomfort					
30	I become sick					
31	I develop burning in the skin of my face					
32	I develop tingling in the skin of my face					
33	I develop a funny sensation of the skin of my face					
34	I develop eye irritation					
35	I develop eye pain					
36	I develop eye itching					
37	I develop sore or burning nasal passages					
38	I develop burning in my nasal passages					

39	I develop a sore throat					
40	I feel nauseated					
41	I develop indigestion					
42	I develop diarrhea					
43	I get gas					
44	I may cough					
45	I may cough phlegm up					
46	I feel like I can't get my breath.					
47	I start wheezing					
48	I feel tightness or pressure in my chest					

Continued on next page

If I am exposed to cigarette smoke, automobile exhaust, strong smells, perfumes or colognes, or fresh paint vapors:

		Strongly Disagree	Disagree	Uncertain	Agree	Strongly Agree
49	I develop aching joints					
50	I develop trouble sleeping					
51	I develop numbness or tingling in my hands or feet					
52	My body feels hot or cold					
53	My symptoms ease if I can get away	Moved from item 61 to new position				
54	I become emotional					
55	I get a headache					
56	I become anxious					
57	I have trouble concentrating					
58	I miss work					
59	I miss social or business appointments					
60	I feel stress at home or work					
61	I find it hard to interact with other persons					

Delete the following if quality of life is assessed. Use above Likert styled items, # 58-61

		Excellent	Very good	Good	Fair	Poor
62	Would you say that in general your health is:					

63	Now thinking about your physical health, which includes physical illness and injury, for how many days during the past 30 days was					
----	--	--	--	--	--	--

	your physical health not good?		
64	Now thinking about your mental health, which includes stress, depression, and problems with emotions, for how many days during the past 30 days was your mental health not good?		
65	During the past 30 days, for about how many days did poor physical or mental health keep you from doing your usual activities, such as self-care, work, or recreation?		