The Spectrum of Irritant-Induced Asthma*

Sudden and Not-So-Sudden Onset and the Role of Allergy

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A retrospective investigation of 86 asthmatic subjects defined clinical features of irritant-induced asthma and assessed the contributory role of an allergic predisposition. Three categories of asthma were evaluated: (1) occupational asthma due to a sensitizer (11 subjects, 13%); (2) irritant-induced asthma (54 persons, 63%); and (3) not occupational/environmental exposure-related asthma (21 subjects, 24%). Two distinct clinical presentations of irritant-induced asthma emerged: the first was sudden onset (29 subjects) and the second was not so sudden in onset (25 subjects). Sudden-onset, irritant-induced asthma was analogous to the reactive airways dysfunction syndrome. Clinical manifestations began immediately or within a few hours (always within 24 h) following an accidental, brief, and massive exposure. In contrast, for the not-so-sudden-onset asthma subjects, the causative irritant exposure was not brief, usually not massive, continued for >24 h, and the initiation of asthma took longer to evolve. Eighty-eight percent of individuals with not-so-sudden irritant-induced asthma displayed an atopy/allergy status (p<0.01). Some of the atopy/allergy subjects with presumed new-onset asthma were found to have suffered preexisting asthma that had been clinically quiescent for at least 1 year before the triggering exposure (16 persons). We conclude that preexisting allergic/atopy and/or preexisting asthma were significant contributors to the pathogenesis of not-so-sudden, irritant-induced asthma and emphasizes a critical interaction between environmental and host factors in the pathogenesis of asthma.

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Key words: airway hyperresponsiveness; irritant-induced asthma; occupational asthma; reactive airways dysfunction syndrome; workplace asthma

Abbreviations: PC_{20}=provocative concentration causing a 20% fall in FEV\(_1\); RADS=reactive airways dysfunction syndrome; RAST=radioallergosorbent test; USF=University of South Florida

Brooks and colleagues,\(^1\) in 1985, described the clinical and pathological features of the reactive airways dysfunction syndrome (RADS), \(\text{ie, the sudden onset of asthma following a high-level irritant gas, vapor, or fume exposure. The diagnosis of RADS required that asthma begins within 24 h of an exposure that was characteristically single, high level, and brief.}\)\(^1\) Several subsequent publications modified the original diagnostic criteria of RADS to include asthma after exposures lasting >24 h. Exposures were sometimes repetitive and occurred over >1 day. A restrictive pattern on pulmonary function testing was noted in some cases, and exposures were occasionally "low level."\(^2\)\(^-\)\(^12\)

The disparate clinical issues regarding RADS were elucidated by designing a retrospective analysis of occupationally and environmentally induced cases of asthma to accomplish several objectives: (1) to better define the clinical features of irritant-induced bronchial asthma, and (2) to evaluate the contributing role of such host factors as allergic/atopy in its pathogenesis.

**Materials and Methods**

**Study Population**

The patient population consisted of subjects with diagnosis of occupationally or environmentally induced asthma who had been
evaluated at the University of South Florida (USF) Occupational and Environmental Medical Clinic during the 3½-year period between June 1989 and December 1992.

The initial study population consisted of 136 subjects who were believed to suffer from asthma. After examination, 50 cases were deemed ineligible for consideration. Of the 50 excluded cases, 9 subjects had asthma associated with significant past asbestos exposure, often with evidence of asbestos-related disease. There were 17 subjects who lacked the diagnostic criteria for asthma and were considered not to suffer from asthma. The remaining 24 subjects were excluded because their information was incomplete or lacked the specific predefined information requirements necessary for data analysis in this investigation. When the information base of the three excluded groups (ie, asthma/asbestos; not asthma; and insufficient information) was compared to the study population, there were no statistically significant differences in age, gender, or other demographic characteristics. There were 86 subjects in the final study population.

Medical Evaluation at USF

Each subject completed a standardized respiratory questionnaire, underwent direct medical history, and had a physical examination (all performed by S.M.B.). The subject’s medical records were examined for completeness, breadth of information, validity of lung function tests, diagnosis of asthma, criteria establishing “allergic” or atopic status, assessment of exposure considered causative of the asthmatic condition; and, survey of analytical, toxicologic, and environmental data of the exposure, including its duration, nature, and intensity. The clinical, exposure, and toxicologic information for each subject was examined independently by two physicians experienced in occupational medicine (J.G., K.J.).

Clinical Definitions

Exposure event was a specific workplace or environmental exposure to an irritant and/or sensitizing agent believed to be responsible for asthma. The exposure information was reviewed by an industrial hygienist (Y.H.) and the toxicologic details were assessed by a toxicologist (I.R.).

Time to onset was the span of time of continued or repeated exposure before the patient first developed asthma symptoms. Allergic or atopic status (allergy/atopy) was established by one or more of the following criteria: (1) at least one positive radioallergosorbent test (RAST) to a battery of common aeroallergens for southeastern United States (by Smith-Kline Laboratories; Alternaria, Bermuda grass, cat dander, Cladosporium herbarum, common ragweed, Dermatophagoides farinae, dog dander, June grass, oak, rough pigweed); and/or (2) at least two positive skin prick and/or intradermal (≥2+ ) skin tests to a battery of common aeroallergens; and/or (3) total serum IgE concentration of ≥250 U/mL in the absence of other known causes of elevated IgE; and/or (4) reported personal history of an allergic disorder (ie, allergic rhinitis, conjunctivitis, hay fever, or asthma); and/or (5) reported presence of an allergic disorder (ie, allergic rhinitis, conjunctivitis, hay fever, or asthma) in a close family member (parents, sibling, child).

Asthma diagnosis required that three essential clinical features be present:13-15 (1) presence of at least three of four typical asthmatic manifestations: (a) episodic cough and/or sputum production; (b) wheezing; (c) nocturnal episodes of cough, wheezing, and breathlessness; and (d) “bronchial irritability,” the patient experiencing respiratory complaints after exposures to various nonspecific irritants, physical factors, and odors; (2) spirometric evidence of the following: (a) variable airflow limitation or (b) a positive response to an inhaled bronchodilator and/or (c) the confirmation of nonspecific airway hyperresponsiveness by provocation testing; and (3) corroboration that a diagnosis and/or treatment of bronchial asthma had been made by a physician before the USF evaluation. For the provocation testing, a methacholine (or histamine) challenge testing procedure employed the protocol of Juniper et al19 and Cockcroft et al20 aerosolizing increasing concentrations (0.03 mg/mL to 16 mg/mL) of the test solution using a nebulizer (Wright; S & M Instruments Co Inc; Doylestown, Pa) driven by a compressed air source. Methacholine or histamine challenges were not performed in subjects with significant impairment of lung function.

Asthma Classification

The 86 patients were classified into one of the three following categories.23

1. Allergic occupational asthma (11 patients) criteria consisted of the following: (1) initiation of asthma caused by exposure in the workplace to a sensitizing agent known to cause allergic-type asthma; (2) cases of asthma occurring after a latent period of exposure lasting at least 4 months; and (3) cases with a consistent temporal relationship between attacks of asthma and workplace exposures.

2. Irritant-induced asthma (54 patients) criteria required the following: (1) initiation of asthma was temporally related to an irritant exposure; (2) asthma symptoms developed during the time period that an irritant exposure was taking place; (3) exposures could be either intermittent or continuous in nature; and (4) subjects were excluded if the irritant exposure lasted >16 weeks (4 months) before initiation of asthma. Subjects with preexisting asthma in remission were included if asthma recurred after remission had been present for at least 1 year before the exposure event.

3. Not occupational/environmental exposure-related asthma (21 patients) was characterized by (1) the absence of a consistent exposure history, and (2) the lack of suitable temporal relationship between asthma initiation and a workplace or environmental exposure.

Analysis of Data

Yates’ corrected values were used in χ² analyses, and Mantel-Haenzel method and Fisher’s Exact Test were used to test and to explore associations.21,22 Odds ratios and the Cornfield 95% confidence limit for the odds ratios were calculated.21,22 Relative risks with Taylor series 95% confidence limits for relative risk were estimated and Student’s t tests compared group differences.21,22

RESULTS

Demographics

The final study population consisted of 86 subjects. The group demographics, atopic/allergic status, FEV₁%, and provocative concentration causing a 20% fall in FEV₁ (PC₂₀) values are summarized in Table 1. Of 86 asthmatic subjects, 54 (63%) suffered asthma from an irritant exposure while 11 (13%) were diagnosed as having asthma caused by a sensitizer. There were 21 subjects (24%) determined not to suffer occupational/environmental exposure-re-
lated asthma. There was excellent consistency of the diagnoses made by the three different investigators; a discordance usually centered on whether there was sufficient information to include a subject in the final study population. No case was excluded because of a disagreement with the diagnosis.

The age distribution of the 86 subjects ranged between 17 and 71 years; there were 40 men and 46 women. Forty-six of the 86 (53%) were current or former cigarette smokers. Most nonsmokers appeared among the irritant-induced asthma group (73% of total). Subjects with asthma caused by an allergic sensitizer exhibited lower lung function values. The 16 subjects presumed to have new-onset irritant-induced asthma but who were suffering from an exacerbation of preexisting asthma in remission showed higher results of lung function tests than the 38 new-onset asthma patients; findings of both of the latter two groups were statistically significantly different as shown in Table 1. There were no statistically significant differences in PC20 values among the four groups (Table 1).

**Types of Irritant-Induced Asthma**

Two clinical presentations were appreciated. Among the 54 persons with irritant-induced asthma, 38 (70%) were specified as having new-onset irritant-induced asthma; a preexisting asthmatic disorder, occurring before the exposure event, could not be substantiated for this group.

Alternatively, 16 (30%) subjects who had been presented as having new-onset irritant-induced asthma had suffered an exacerbation of a preexisting asthmatic state that had been in remission. Usually, the remission was present for years before the exposure occurred, during which time the person was asymptomatic and did not require medications. Subjects in this group, when carefully questioned, recalled previous episodes of asthma, often occurring during childhood or they recalled having been diagnosed as asthmatic by a physician. In other subjects in this group, a strong suspicion of a past asthmatic condition was recognized during the USF examination. Usually, these subjects described an asthma-like process during childhood or early adulthood (frequent wheezing with infections, wheezing with pet animal exposures, "repeated bouts of bronchitis," "allergies with wheezing," etc) but no actual asthma diagnosis was confirmed by a physician. These latter cases were considered to represent preexisting asthma. In order for subjects with preexisting asthma to qualify for the study, there must have transpired a remission of asthma lasting for at least 1 year (and usually for many years); during this time, the patient experienced no asthma manifestations. In these patients, the available medical records documented that no asthma medications were taken and no physicians were consulted during the remission period.

**Allergic/Atopy**

The allergy/atopy status was documented for the 86 subjects as follows: 46 (53%) persons were decided by either allergen skin testing or RAST; for 12 (14%) individuals, a personal history of an allergic disease was noted; in one (1%) subject, there was an elevated total IgE level. Finally, there were 27 (31%) persons in whom atopy/allergy status was based solely on a family history of allergy.

For the 86 subjects in the study population, allergy/atopy occurred in 46 persons. Of these 46 allergic/atopic individuals, 37 (80%) subjects suffered irritant-induced asthma (p<0.01); one (2%) individual had allergic occupational asthma; and eight (17%) subjects were considered to have asthma that was not of occupational/environmental origin.

For the 37 subjects with irritant-induced asthma who were considered to be allergic/atopic persons,
the allergy/atopy status was established by the following: allergic skin testing/RAST battery in 27 (73%); personal history of a known allergic disorder in three (8%); elevated total IgE in one (3%); and family history in six (16%).

Information relating the allergic/atopic status to the different types of irritant-induced asthma for 54 cases of irritant-induced asthma showed that 25 of 38 (66%) subjects with new-onset irritant-induced asthma possessed an allergic/atopy predisposition. Of the remaining 16 who suffered an exacerbation of preexisting asthma that was in remission, 12 of 16 (75%) were positive for allergy/atopy (Fig 1).

There was an increased odds ratios (±95% confidence limits) for “allergic/atopy” presence of 7.3 (2.5 to 22.2) (p<0.001) for the irritant-induced asthma group as a whole. The odds ratio for “allergic/atopy” was 15.9 (2.0 to 339.67) for irritant-induced asthma occurring in the preexisting asthma in remission group (p<0.001). The odds ratio was 1.92 (0.73 to 5.09) for new-onset irritant-induced asthma (p=0.14). A lower odds ratio was observed for both the allergic occupational asthma (0.06 [0.0 to 0.47]) (p<0.001) and not occupational/environmental exposure asthma groups (0.40 [0.12 to 1.10]) (p=0.07). The finding of allergic/atopy, by itself, was not a reliable predictor of asthma occurrence; sensitivity was 66% and the specificity was 29%; the positive predictive value was 68% and the negative predictive value was 28% (p was not significant).

**Exposure Event**

There were 65 exposure events: 54 persons were exposed to irritants and 11 persons were exposed to sensitizers. There was a multiplicity of exposures for irritant-induced asthma; SO₂ and pesticide spraying in four circumstances each; chlorine gas and ammonia/bleach/caustic soda in three cases each; solvent vapors/mist and paint vapors/spray in two persons each; there were also other exposures as noted in Table 2. Occupational asthma was caused by disocyanates in five cases, acrylates in four cases, and flour exposure (“baker’s asthma”) in the two remaining subjects (Table 2).

**Time to Onset**

Table 3 summarizes this information (duration of exposure before asthma symptoms began) for all 54 irritant-induced asthma cases. For 29 (54%) subjects, the onset of asthma was sudden or immediate (≤24 h). In contrast, for 25 subjects (46%), asthma evolved from irritant exposures that were repeated and continued for >24 h (not so sudden).

Among the 29 subjects with sudden-onset irritant-induced asthma (≤24 h), two subcategories were recognized: the first consisted of 23 (79%) subjects with documented RADS. The second group included six (21%) persons with apparent RADS who had suffered a recurrence of preexisting asthmatic state exacerbated by the irritant exposures.

![Figure 1. Schematic representation of the numbers of subjects assigned to various irritant-induced asthma groups. The two classifications of new-onset and preexisting asthma were further subcategorized into (1) sudden (≤24 h) and (2) not-so-sudden onset (>24 h) irritant-induced asthma. The numbers of atopic and nonatopic subjects identified for the two subcategories are shown. A significant prevalence of atopy/allergy is noted for the not-so-sudden group (p<0.01).](https://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21757/)
Preexistent asthma

Asthma

New-onset and not-so-sudden vs subcategory of asthma. Figure only included asthma of month disqualifying in asthma individuals 8 months. massive induced asthma repeated. The duration of irritant-induced asthma was >24 h, because of the enormity of the exposure, extensive airway damage ensues that induces bronchial mucosal inflammation leading to airways hyperresponsiveness and clinical asthma. An atopic status was not deemed operative in the pathogenesis of RADS, which exemplified the extreme end of the spectrum of an irritant effect on the airways.

A second type of irritant-induced asthma was not so sudden in onset and embodied features differing from RADS. The causative exposure persisted >24 h, was not brief, and asthma took longer to develop, sometimes days or weeks after repeated exposures.

The prevalence of atopy among subjects with the first type (sudden-onset irritant-induced asthma) who were considered to have RADS was 15 of 29 (52%), which though high was not statistically significant. Consistent with our findings is the rate of allergy/atopy reported for clinical facilities evaluating pulmonary patients with asthma. Atopic prevalence might well be lower if other populations, such as orthopedic patients, were examined. Our investigation found that allergy/atopy prevalence was not

Table 2—Exposure Events

<table>
<thead>
<tr>
<th>Exposures</th>
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<tr>
<td>Irritant exposures</td>
</tr>
<tr>
<td>Pesticide spraying</td>
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<tr>
<td>Cement sealant</td>
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<tr>
<td>Mixed solvent vapors and mist</td>
</tr>
<tr>
<td>Household bleach vapors</td>
</tr>
<tr>
<td>Spray paint</td>
</tr>
<tr>
<td>Sulfur dioxide gas</td>
</tr>
<tr>
<td>Titanium tetrachloride mist</td>
</tr>
<tr>
<td>Volatile organic vapors from poor indoor air quality</td>
</tr>
<tr>
<td>Ammonia vapors</td>
</tr>
<tr>
<td>Muratic acid spill</td>
</tr>
<tr>
<td>Welding fumes</td>
</tr>
<tr>
<td>Chlorine gas</td>
</tr>
<tr>
<td>Burned freon fumes</td>
</tr>
<tr>
<td>Fire retardant aerosol</td>
</tr>
<tr>
<td>Caustic soda aerosol</td>
</tr>
<tr>
<td>Sensitizer exposures</td>
</tr>
<tr>
<td>Diphenylmethane diisocyanate</td>
</tr>
<tr>
<td>Hexamethylene diisocyanate</td>
</tr>
<tr>
<td>Toluene diisocyanate</td>
</tr>
<tr>
<td>Flour dust</td>
</tr>
<tr>
<td>Acrylates-methacrylate and cyanoacrylate ester</td>
</tr>
</tbody>
</table>

For the 25 individuals with not-so-sudden irritant-induced asthma (≥24 h), 10 had a history of preexisting asthma. Characteristically, the irritant exposures of the not-so-sudden asthma case were not massive or single (as for RADS) but were moderate and repeated. Data of 25 subjects with not-so-sudden asthma were as follows: in 9 subjects (36%), asthma developed within 1 week of repeated exposures; in 8 persons (32%), asthma appeared within a month of repetitive exposures; and in the remaining 8 individuals (32%), the irritant exposure persisted >1 month before asthma began. Patients were included only if asthma began during the irritant exposure; asthma appearing >24 h after the exposure disqualified the diagnosis of irritant-induced asthma. Figure 1 depicts the distribution of cases in each subcategory of irritant-induced asthma (new onset vs preexisting) and the number of atopic and nonatopic subjects in the subcategories of sudden and not-so-sudden asthma.

Table 4 and Figure 2 correlate the relation between time to onset and the presence of atopy/allergy for subjects with irritant-induced asthma. The prevalence of atopy/allergy was increased as the time to onset increased. Of 29 subjects with sudden-onset (≥24 h) asthma, 15 (52%) evidenced allergy/atopy status, not significantly increased (p>0.05). In contrast, of 25 individuals with not-so-sudden asthma (≥24 h), there were 22 (88%) found to be atopic (p<0.004). Of 16 individuals with an onset time of >1 week, 15 were atopic (p<0.01).

DISCUSSION

Sudden-onset, irritant-induced asthma (clinically manifests within 24 h) corresponds to the previously described RADS. Affected individuals are immediately ill and require prompt medical care. RADS was a sudden response to a brief but massive exposure to an irritant gas, vapor, or fume. Because of the enormity of the exposure, extensive airway damage ensues that induces bronchial mucosal inflammation leading to airways hyperresponsiveness and clinical asthma. An atopic status was not deemed operative in the pathogenesis of RADS, which exemplified the extreme end of the spectrum of an irritant effect on the airways.

A second type of irritant-induced asthma was not so sudden in onset and embodied features differing from RADS. The causative exposure persisted >24 h, was not brief, and asthma took longer to develop, sometimes days or weeks after repeated exposures.

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Table 3—Duration of Exposure Before Asthma Onset Among Subjects With Irritant-Induced Asthma

<table>
<thead>
<tr>
<th>Asthma Category</th>
<th>Sudden, h</th>
<th>New-Onset Asthma</th>
<th>Preexisting Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤24 h</td>
<td>1-7 d</td>
<td>1-4 wk</td>
</tr>
<tr>
<td>New-onset asthma</td>
<td>23</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Preexisting asthma</td>
<td>6</td>
<td>5</td>
<td>2</td>
</tr>
</tbody>
</table>

*p<0.004 (25 subjects with asthma occurring ≥24 h).

Table 4—Time to Onset and Presence of Atopy Among Subjects With Irritant-Induced Asthma

<table>
<thead>
<tr>
<th>Duration</th>
<th>No.</th>
<th>Atopy</th>
<th>No.</th>
<th>Atopy*</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤24 h</td>
<td>22</td>
<td>12</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>1-7 d</td>
<td>4</td>
<td>3</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>1-4 wk</td>
<td>6</td>
<td>5</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>1-4 mo</td>
<td>5</td>
<td>5</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>25</td>
<td>16</td>
<td>12</td>
</tr>
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</table>

*Clinical Investigations
increased among other asthma categories (38% for not occupational/environmental asthma and 9% for asthma due to sensitizer groups). The lower prevalence found for asthma due to an occupational sensitizers is in agreement with reported observations of asthma caused by low molecular weight chemical agents.29-32

Some subjects with new-onset irritant-induced asthma were actually in remission from a preexisting asthmatic state. Usually the remission had been present for years before the irritant exposure, during which time the person remained asymptomatic and did not require medications.33-35 It is reasonable to conclude that the irritant exposure exacerbated asthma in these individuals. We infer that such subjects, if studied prior to the occurrence of the irritant exposure, would manifest distinct pathologic airway changes,36,37 nonspecific airways hyperresponsiveness,33-35 and/or other biochemical abnormalities.38,39

Persons with a history of asthma who were asymptomatic and considered themselves “normal” might demonstrate respiratory physiologic abnormalities that could become clinically evident as asthma after an irritant exposure.11,33,40 Nonspecific airway hyperresponsiveness has been found to be common among atopic persons with rhinitis, asymptomatic asthmatic subjects, and presumably, some “normal” persons.34,41-43 Individuals in this investigation, with preexisting asthma in remission, who developed a sudden-onset asthma after a high-level irritant exposure, would not be considered to have RADS or to have suffered newly acquired asthma.

For the not-so-sudden asthma cases, it is difficult to explain why a low-level, moderate-irritant exposure would provoke persistent airway inflammation and hyperresponsiveness. These irritant exposures were adjudged not to be of the magnitude described for subjects with RADS and there was a longer onset time (eg, >24 h) because the subjects could tolerate a lower-level exposure.1,25

The fact that a moderate-level irritant exposure could initiate asthma requires consideration of mechanisms other than airway damage alone to induce the asthmatic attack. Preexisting host susceptibility, such as asthma or atopy, with its associated inherent biochemical and pathologic consequences is one possibility. There was no greater prevalence of allergy/atopy among subjects with RADS. However, 88% of individuals with not-so-sudden onset (p<0.01) exhibited an allergy/atopy status and 30% of subjects with new-onset irritant-induced asthma were really manifesting an exacerbation of a preexisting asthmatic state. Therefore, allergy/atopy status and preexisting asthma are important risk factors for developing asthma from irritant exposures and there may be other risk factors for irritant-induced asthma not addressed by this investigation.

Figure 2. Graphic presentation showing the relationship between the prevalence of allergy/atopy (percent) and the time to onset for asthma initiation. As the irritant exposure time became longer, the prevalence of allergy/atopy was found to be higher. It approached 100% for exposures that were >1 week duration (p<0.01).
As to other possible mechanisms to initiate irritant-induced asthma in an atopic individual, it is possible that atopic persons have a unique response to irritants. Atopic individuals are known to be at an increased risk for developing asthma, show accelerated declines in lung function, and display exaggerated responses to irritants. Furthermore, IgE, a hallmark of atopy, has been linked to bronchial hyperresponsiveness.

Bronchial epithelial cells of atopics might react differently to irritant exposures because high-affinity IgE is bound to their surfaces. Another possibility is that a preceding irritant exposure enhances bronchial mucosal permeability that has been demonstrated to increase bronchial sensitization. Such enhanced bronchial mucosal permeability leads to greater penetration of the airway mucosa by common airborne environmental aeroallergens. In an atopic person previously sensitized to these aeroallergens, the increased allergen penetration might cause more pronounced allergic response and mediator release, eventuating into clinically new-onset asthma. An irritant exposure may lead to mediator release from various airway cells (eg, mast cells, bronchial epithelial cells) inducing airway inflammation and hyperresponsiveness. Alternatively, airway sensitivity to an allergen may be augmented by an irritant exposure, supported by the findings of Molfino et al and Jorres and colleagues whose investigations demonstrated enhanced specific bronchial airway responsiveness to aeroallergens after preexposure to low levels of ozone.

CONCLUSIONS

The present investigation defined the clinical features of irritant-induced asthma and described some cases that were not so sudden in onset. A preexisting allergic diathesis was identified as a host factor consequential to the development of not-so-sudden irritant-induced asthma. This resembles the findings of adult-onset asthma after a viral respiratory infection. The present study suggests that an irritant exposure of a susceptible person may initiate the onset of asthma in a manner similar to a viral respiratory infection in an atopic individual or a large allergen load in a sensitized person. The importance of not-so-sudden, irritant-induced asthma as a public health issue is that it underscores a critical interaction between environmental and host factors in initiating the onset of asthma. Not-so-sudden, irritant-induced asthma must be differentiated from occupational asthma due to workplace sensitizers and sudden-onset asthma (RADS) from massive workplace irritant exposures.

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