Background: There is a paucity of lung function data in patients, both before and after episodes of near-fatal asthma (NFA), requiring transient endotracheal intubation and mechanical ventilation.

Methods: Lung function was initially measured in 43 asthmatic patients (age range, 16 to 49 years), who were observed and treated in a tertiary referral asthma clinic and were clinically stable at the time of study. Subsequently, clinical and physiologic follow-up studies were obtained over >5 years. The primary outcomes were to determine (1) the integrity of lung elastic recoil and (2) the severity of expiratory airflow limitation, and (3) to correlate these outcomes with adverse clinical complications.

Results: Fourteen of 26 asthmatic patients (54%) [age range, 30 to 49 years] had significantly reduced lung elastic recoil pressures at all lung volumes compared to 3 of 17 asthmatic patients (18%); p < 0.02 [χ² test and Fisher exact test] [age range, 16 to 26 years]. In asthmatic patients between the ages of 30 and 49 years, significant loss of lung elastic recoil was noted in 4 of 10 patients with mild reduction in FEV₁ (FEV₁, > 79% predicted), 6 of 12 patients with moderate reduction in FEV₁ (FEV₁, 61 to 79% predicted), and all 4 patients with severe reduction in FEV₁ (FEV₁, < 61% predicted). In asthmatic patients between the ages of 16 and 26 years, significant loss of lung elastic recoil was noted in 0 of 11 patients with mild reduction in FEV₁, 2 of 5 patients with moderate reduction in FEV₁, and 1 of 1 patient with severe reduction in FEV₁. A subgroup of 10 asthmatic patients (7 men) [mean (± SD) age, 37 ± 11 years] were studied when clinically stable, both before and after an episode of NFA in 8 cases and only after an episode of NFA in 2 additional cases. In 1 of 10 cases, the FEV₁ was mildly reduced, in 4 cases it was moderately reduced, and in 5 cases it was severely reduced, both before and after an episode of NFA. The sensitivity was 90%, the specificity was 61%, the positive predictive value was 41%, and the negative predictive value was 95% for NFA with an FEV₁ < 79% predicted or FEV₁/FVC ratio of < 75%. Prior to an episode of NFA, all 8 asthmatic patients had significant loss of lung elastic recoil pressure, and afterward all 10 had significant loss of lung elastic recoil pressure (ie, less than the predicted normal mean minus 1.64 SD at a total lung capacity [TLC] of 100 to 70% predicted). The sensitivity was 100%, the specificity was 79%, the positive predictive value was 59%, and the negative predictive value was 95% for NFA with an FEV₁ ≤ 79% predicted or FEV₁/FVC ratio of < 75%. Prior to an episode of NFA, all 8 asthmatic patients had significant loss of lung elastic recoil pressure, and afterward all 10 had significant loss of lung elastic recoil pressure [ie, less than the predicted normal mean minus 1.64 SD at a total lung capacity [TLC] of 100 to 70% predicted]. The sensitivity was 100%, the specificity was 79%, the positive predictive value was 59%, and the negative predictive value was 95% for NFA with the loss of lung elastic recoil. The mean TLC measured with a plethysmograph in 10 patients with NFA was 7.2 ± 1.41 (124 ± 16% predicted). The sensitivity for TLC of > 115% predicted was 70%, the specificity was 70%, the positive predictive value was 88%, and the negative predictive value was 41% for NFA.

Conclusion: A persistent reduction in FEV₁ of ≤ 79% predicted or an FEV₁/FVC ratio of < 75%, and, especially, the loss of lung elastic recoil and hyperinflation at TLC are risk factors for NFA. The loss of lung elastic recoil in asthmatic patients was associated with increased age, duration of disease, and progressive expiratory airflow limitation.

Key words: lung elastic recoil; lung function; near-fatal asthma

Abbreviations: NFA = near-fatal asthma; sGaw = specific airway conductance; TLC = total lung capacity

While the majority of asthmatic patients respond well to therapy, there is now greater concern over the mounting health-care needs and services required for a rapidly increasing population of difficult-to-manage asthmatic patients.1–3 Furthermore, there is mounting evidence that outcomes in adult asthma may be determined primarily in early childhood.4 These observations appear to be paradoxical with the increasing knowledge of asthma pathogenesis and treatment that is currently available.1–3,5,6 It has been proposed5,6 that the recurrent or persistent presence of cytokines and mediators of inflammation in asthma patients eventually leads to pathologic remodeling of both the large and small airways.
Despite seemingly optimal medical therapy, these airway alterations presumably lead to bronchoconstriction and airway hyper-responsiveness, causing increased intrinsic airway resistance.\textsuperscript{1,2,5,6} Airway remodeling is currently suspected but has not been proven to be primarily responsible for persistent clinical symptoms as well as chronic expiratory airflow limitation in patients with refractory asthma.\textsuperscript{1,2,5,6}

Maximum expiratory airflow at effort-independent lung volumes is proportionate to the product of lung driving pressure, \(\text{ie}^{*}\), lung elastic recoil, and airway conductance or inversely proportionate to intrinsic airway resistance.\textsuperscript{7,8} We have reported on\textsuperscript{9} an unsuspected and unexplained marked loss of lung elastic recoil that was not due to emphysema in nonsmoking, stable, treated asthmatic patients with chronic asthma (\(\text{ie}^{*}\) mean \([\pm \text{SD}]\) duration of asthma, 40 \pm 10 years) with a mean age of 59 \pm 15 years, who had a mean postbronchodilator \(\text{FEV}_1\) of 55 \pm 11\% predicted. The loss of lung elastic recoil accounted for 25 to 39\% of the expiratory airflow limitation.\textsuperscript{9} Furthermore, a longitudinal spirometry study\textsuperscript{10} suggested the possibility of early, unsuspected significant loss of lung elastic recoil in asthmatic patients with chronic, persistent, moderate, and severe asthma. These two studies\textsuperscript{9,10} did not report adverse clinical consequences.

The present study prospectively explores the integrity of lung elastic recoil and the severity of expiratory airflow limitation. We also attempted to correlate these outcomes with adverse clinical consequences, including near-fatal asthma (NFA) in stable, nonsmoking, treated asthmatic patients with chronic asthma who were between the ages of 16 and 49 years. We suspected that a loss of lung elastic recoil with decreased driving pressure during expiration and less extramural support of the small airways would lead to premature airway closure. This would have an adverse physiologic and clinical impact on asthmatic patients who already were experiencing large and small airway bronchial hyper-reactivity and spasmodic bronchoconstriction.

\textbf{Materials and Methods}

\textbf{Patient Selection}

Lung function was initially measured in 43 asthmatic patients (age range, 16 to 49 years), who were observed in a tertiary referral asthma clinic for patients with difficult-to-treat asthma. The diagnosis of difficult-to-treat asthma in asthmatic patients required at least three hospitalizations for asthma over 2 years or receiving three or more courses of tapering corticosteroids in 1 year. Asthmatic patients were evaluated with lung function studies prior to 1998, and then were prospectively observed for 5 years. All asthmatic patients were clinically stable at the time of study.

All asthmatic patients studied had given informed consent for participation in the study. This study was approved by the Institutional Review Board. Outpatient treatment included combinations of short-acting aerosolized \(\beta_2\)-agonists and/or long-acting \(\beta_2\)-agonists, aerosolized ipratropium bromide, oral and/or inhaled corticosteroids, leukotriene inhibitors, and antibiotics, as needed. No asthmatic patient was maintained on long-term oral corticosteroids for \(>1\) month. Optimal medical therapy was confirmed by evaluating clinical status and serial spirometry findings obtained during routine outpatient clinic visits every 1 to 2 months.

All patients satisfied the criteria for at least partial reversibility with an increase in \(\text{FEV}_1\) of \(>12\%\) following therapy with 180 \(\mu\text{g}\) aerosolized albuterol sulfate when they had not received any long-acting and short-acting \(\beta_2\)-agonists for 48 and 6 h, respectively. Chronic bronchitis was never diagnosed, and only two asthmatic patients were former mild cigarette smokers (\(\text{ie}^{*}, <10\) pack-years). The other patients never had smoked. The results obtained in the present study have not been previously published.

\textbf{NFA}

NFA was defined as an episode of asthma requiring temporary intubation and mechanical ventilation due to deteriorating clinical status and progressive acute respiratory acidosis. The decision to intubate was made solely by emergency department physicians, none of whom participated in the present study.

\textbf{Lung CT Scan Studies}

A high-resolution, thin-section CT scan of the lung was obtained in 13 of 17 patients with loss of lung elastic recoil (4 patients refused), including 8 of 10 patients who had experienced an episode of NFA, and was scored by a radiologist (Mark J. Schein, MD) on a scale of 0 to 100 (with 100 being the worst) using picture templates, as has previously been validated.\textsuperscript{11} We chose not to obtain lung CT scans in asthmatic patients who had no loss of lung elastic recoil.

\textbf{Lung Function Studies}

When asthmatic patients had been clinically stable for at least 2 months, they were instructed to continue treatment with all of their medications, only withholding the use of inhaled albuterol sulfate and ipratropium bromide 6 h prior to testing. Lung function, including lung volumes, single-breath diffusing capacity, airway resistance, and static lung elastic recoil pressures, was
measured using similar techniques and equipment, including the use of a pressure-compensated flow plethysmograph (model 6200 Autobox; SensorMedics, Yorba Linda, CA) to avoid artifacts of gas compression, as has been reported.9,10 A panting frequency of ≤ 1 Hz was used to avoid the underestimation of alveolar pressure, as measured at the mouth, which could lead to a spurious increase in thoracic gas volume. The reciprocal of airflow resistance (ie, airway conductance) was determined and divided by the corresponding thoracic gas volume, at which point it was measured and specific airway conductance (sGaw) was reported.

The severity of post-treatment and postbronchodilator expiratory airflow limitations was evaluated using FEV1 as the signal, and it was scored, as previously reported,3 with the above-noted modifications. The term mild refers to an FEV1 of > 79% predicted, moderate refers to an FEV1 of 61 to 79% predicted, and severe refers to an FEV1 of < 61% predicted. The FEV1/FVC ratio of < 75% also was scored as abnormal.

Seventeen clinically stable asthmatic patients, including 8 with prospectively observed NFA, agreed to be restudied when clinically stable, within 1 to 3 years subsequent to the initial testing, to evaluate the reproducibility of the static lung elastic recoil pressures and maximum expiratory airflow measurements. If the difference between the measurements of the initial and subsequent lung recoil pressures were within 10% at the same lung volume (ie, 100 to 70% predicted total lung capacity [TLC]), they were designated as being similar. This value represents the range for reproducibility in healthy subjects in our laboratory when three to five separate deflation static lung elastic recoil pressure curves were obtained.

For a comparison of lung elastic recoil in asthmatic patients aged 30 to 49 years with normal control values, we used our previously published normal results.9,10,12 And for asthmatic patients aged 16 to 26 years, we obtained normal values from 11 nonsmoking healthy volunteers, who had normal findings for spirometry, diffusing capacity, and lung volumes. All control subjects had similar gender, race, and ethnicity characteristics as the asthmatic patients currently being studied. A significant loss of lung elastic recoil was defined as a value less than the predicted normal mean, −1.64 SD at 100 to 70% predicted of TLC.

**Transdiaphragmatic and Muscle Pressures and Neuromechanical Coupling**

Transdiaphragmatic pressures were measured, and the net total diaphragmatic neuromechanical coupling was determined, as previously described.9 Overall muscle strength was evaluated by measuring maximal inspiratory and expiratory pressures.9

**Statistical Analysis**

The distribution of data was analyzed for normality, and if homogeneity of variance was present, standard parametric tests were used to detect differences between two groups of asthmatic patients. Otherwise, nonparametric tests were used. The χ2 test was used to evaluate the distribution of a discrete variable in a 2 × 2 contingency table. Standard definitions for sensitivity, specificity, positive predictive values, and negative predictive values were used. A p value of < 0.05 was considered to be statistically significant.

**RESULTS**

We prospectively studied 43 clinically stable asthmatic patients. The mean (± SD) postbronchodila-
Therefore, asthmatic patients were divided into two groups, above and below age 30 years. Normal values for patients aged 30 to 49 years were previously obtained. At 100%, 90%, 80%, and 70% predicted TLC, the mean static lung elastic recoil pressures were 21 ± 1.6, 17 ± 4.5, 10.6 ± 2.1, and 7.5 ± 1.8 cm H₂O, respectively. The values in 11 healthy subjects aged 16 to 26 years were 25 ± 7, 20 ± 8, 12.6 ± 3.4, and 8.9 ± 2.6 cm H₂O, respectively. Lung elastic recoil pressure was significantly reduced in 17 of 43 asthmatic patients when first studied, especially in older asthmatic patients with moderate and severe reductions in expiratory airflow. Fourteen of 26 asthmatic patients aged 30 to 49 years had significantly reduced lung elastic recoil pressures at all lung volumes compared to 3 of 17 asthmatic patients aged 16 to 26 years (p = 0.02 [χ² test and Fisher exact test]). There was significant correlation between the loss of lung elastic recoil and decreasing FEV₁ percent predicted at 80% and 70% predicted TLC (r = 0.5; p < 0.02). In asthmatic patients aged 30 to 49 years, a significant loss of lung elastic recoil was noted in 4 of 10 patients with mild reduction in FEV₁ percent predicted, in 6 of 12 patients with moderate reduction in FEV₁ percent predicted, and in all 4 patients with severe reduction in FEV₁ percent predicted. In asthmatic patients aged 16 to 26 years, a significant loss of lung elastic recoil was noted in 0 of 11 patients with mild reduction in FEV₁ percent predicted, in 2 of 5 patients with moderate reduction in FEV₁ percent predicted, and 1 of 1 patient with severe reduction in FEV₁ percent predicted. All asthmatic patients who had an episode of NFA experienced a significant loss of lung elastic recoil when clinically stable (prior to NFA episode, 8 patients; after NFA episode, all 10 patients).

### Table 1—Results of Lung Function Studies in 43 Patients With Chronic Persistent Asthma Separated by Presence (Group A, 26 Cases) or Absence (Group B, 17 Cases) of Normal Lung Elastic Recoil and a Subgroup of 10 Patients With NFA, All of Whom Had Loss of Lung Elastic Recoil (Group C)*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Normal Lung Elastic Recoil (Group A)</th>
<th>Abnormal Lung Elastic Recoil (Group B)</th>
<th>p Value †</th>
<th>NFA (Group C)</th>
<th>p Value ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>25 ± 3 (16–26)†</td>
<td>33 ± 6 (19–49)†</td>
<td>&lt; 0.04</td>
<td>37 ± 11 (19–49)†</td>
<td>0.02</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>17</td>
<td>12</td>
<td></td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>9</td>
<td>5</td>
<td></td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>FVC, L</td>
<td>4.3 ± 0.7 (104 ± 19)</td>
<td>3.7 ± 0.8 (98 ± 14)</td>
<td>0.09</td>
<td>3.8 ± 0.9 (91 ± 14)</td>
<td>NS</td>
</tr>
<tr>
<td>FEV₁, L</td>
<td>3.2 ± 0.6 (92 ± 17)</td>
<td>2.5 ± 0.6 (82 ± 20)</td>
<td>&lt; 0.03</td>
<td>2.2 ± 0.7 (66 ± 22)</td>
<td>0.002</td>
</tr>
<tr>
<td>FEV₁/FVC, % predicted</td>
<td>74 ± 10</td>
<td>69 ± 12</td>
<td>NS</td>
<td>58 ± 14</td>
<td>0.005</td>
</tr>
<tr>
<td>FRC, L</td>
<td>3.1 ± 0.9 (114 ± 27)</td>
<td>3.8 ± 1.0 (148 ± 32)</td>
<td>&lt; 0.04</td>
<td>4.2 ± 1.2 (138 ± 23)</td>
<td>0.02</td>
</tr>
<tr>
<td>RV, L</td>
<td>2.1 ± 0.6 (134 ± 43)</td>
<td>2.7 ± 0.7 (173 ± 37)</td>
<td>&lt; 0.04</td>
<td>3.2 ± 0.5 (177 ± 39)</td>
<td>0.000</td>
</tr>
<tr>
<td>TLC, L</td>
<td>6.3 ± 1.1 (109 ± 15)</td>
<td>6.6 ± 1.4 (121 ± 9)</td>
<td>&lt; 0.03</td>
<td>7.2 ± 1.4 (124 ± 16)</td>
<td>0.02</td>
</tr>
<tr>
<td>DLCO, mL/min/mm Hg</td>
<td>25 ± 5 (101 ± 13)</td>
<td>25 ± 6 (106 ± 11)</td>
<td>NS</td>
<td>31 ± 7 (116 ± 15)</td>
<td>NS</td>
</tr>
<tr>
<td>sGaw, L/cm H₂O/L</td>
<td>0.11 ± 0.07 (52 ± 47)</td>
<td>0.11 ± 0.07 (45 ± 26)</td>
<td>NS</td>
<td>0.10 ± 0.07 (33 ± 21)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Values given as mean ± SD (postbronchodilator mean ± SD, mean percent prediction ± SD), unless otherwise indicated. NS = not significant; FRC = functional residual capacity; RV = residual volume; DLCO = diffusing capacity of the lung for carbon monoxide.
†Values in parentheses are age range.
‡Group A vs group B.
§Group A vs group C.

**Subsequent Measurement of Lung Elastic Recoil Pressure in 17 Patients**

Repeat static lung elastic recoil pressure-lung volume curves were obtained in 11 clinically stable asthmatic patients 1 to 3 years after the initial study demonstrated a significant loss of lung elastic recoil. Despite markedly variable FEV₁ percent predicted values on the second study, similar lung elastic recoil pressures (ie, ≤ 10% difference at same lung volume at 70 to 100% predicted TLC) were observed subsequently in all 11 asthmatic patients. This included all eight asthmatic patients who had experienced an initial loss of lung elastic recoil, and had been studied both before and after an episode of NFA. One asthmatic patient, who had experienced a loss of lung elastic recoil pressure prior to an episode of NFA, refused to be restudied after the episode. However, abnormal spirometry findings, elevated lung volumes, and normal diffusing capacity were similar before and after the episode of NFA. When lung volume was expressed as the percent observed TLC rather than the percent predicted TLC, as shown in Figures 1 and 2, the results were similar, since hyperinflation was mild and the mean TLC was 120 ± 14% predicted. In addition, the repeat static lung elastic recoil pressure measurements vs repeat lung volume curves were similar in six asthmatic patients (FEV₁ between 65% and 85% predicted) who had not experienced an initial loss of lung elastic recoil (data not shown).
Muscle Pressures

The mean (± SD) values for transdiaphragmatic pressures in 10 patients prior to an episode of NFA using the sniff and occlusion technique were 128 ± 23 cm H₂O and 120 ± 23 cm H₂O, respectively, and they were in the normal range, despite the presence of hyperinflation at functional residual capacity. The mean results of neuromechanical coupling were normal or mildly reduced (0.96 ± 0.24). When restudied in eight patients after an episode of NFA, the mean values of sniff and occlusion, transdiaphragmatic pressure, and neuromechanical coupling index were similar at 114 ± 27, 107 ± 20, and 0.93 ± 0.37, respectively (difference not significant).

In six patients prior to an episode of NFA, the mean maximal inspiratory and expiratory pressures were

![Figure 1. Lung elastic recoil pressure, Pstat (l), at 100%, 90%, 80%, and 70% predicted TLC in 17 stable patients with chronic, persistent asthma aged 16 to 26 years (left) and in 26 stable patients with chronic asthma aged 30 to 49 years (right) with mild, moderate, and severe reductions in FEV₁ percent predicted. Solid line = each of 33 patients without an episode of NFA; dashed line = NFA in 10 patients; bars = mean for normal Pstat (l) ± 1.64 SD. There was a significantly higher incidence of the loss of static lung elastic recoil in the asthmatic patients aged 30 to 49 years compared to those aged 16 to 26 years (p = 0.02 [x² test and Fisher exact test]). There was significant correlation between the loss of lung elastic recoil and decreasing FEV₁ percent predicted at 80% and 70% predicted of TLC (r = 0.5; p < 0.02). An abnormal loss of lung elastic recoil was demonstrated in 0 of 11 asthmatic patients aged 16 to 26 years with mild obstruction, 2 of 5 patients with moderate obstruction, and 1 of 1 patient with severe obstruction. An abnormal loss of lung elastic recoil also was demonstrated in 4 of 10 asthmatic patients aged 30 to 49 years with mild obstruction, 6 of 12 patients with moderate obstruction, and 4 of 4 patients with severe obstruction.

Clinical Investigations
and 5 others have had repeated emergency department visits and hospitalizations for exacerbation of asthma after >5 years follow-up. In the 26 asthmatic patients without significant loss of lung elastic recoil, no episodes of NFA were found, and only 2 patients had required hospitalization and emergency department visits after >5 years of follow-up. The difference in hospitalizations between the two groups was significant (p < 0.001 [Fisher exact test and χ² test]).

Clinical Consequences of Loss of Lung Elastic Recoil

In the 17 asthmatic patients who had loss of lung elastic recoil, 10 had one or more episodes of NFA, and 5 others have had repeated emergency department visits and hospitalizations for exacerbation of asthma after >5 years follow-up. In the 26 asthmatic patients without significant loss of lung elastic recoil, no episodes of NFA were found, and only 2 patients had required hospitalization and emergency department visits after >5 years of follow-up. The difference in hospitalizations between the two groups was significant (p < 0.001 [Fisher exact test and χ² test]).
Risk Factors for NFA

In NFA patients, the sensitivity for the presence of moderate and/or severe obstruction was 90%, the specificity was 61%, the positive predictive value was 41%, and the negative predictive value was 95%. The sensitivity for an abnormal loss of lung elastic recoil (i.e., less than the predicted normal mean – 1.64 SD) was 100%, the specificity was 79%, the positive predictive value was 59%, and the negative predictive value 100% for NFA patients.

Using TLC percent predicted as a surrogate for elastic recoil, the sensitivity for TLC of > 115% predicted was 70%, the specificity was 70%, the positive predictive value was 88%, and the negative predictive value was 41% for NFA patients. Using the ratio of FEV1 percent predicted to TLC percent predicted of ≤ 0.70, the sensitivity was 90%, the specificity was 78%, the positive predictive value was 56%, and the negative predictive value was 96% for NFA patients.

Discussion

The unexpected loss of lung elastic recoil in patients with chronic persistent asthma and its significant physiologic contribution to adverse clinical complications, including NFA, are novel prospective observations. This loss of lung elastic recoil was associated with increasing age, duration of asthma, and severity of expiratory airflow limitation, using postbronchodilator FEV1 percent predicted as the signal. Additionally, normal transdiaphragmatic pressures, despite the presence of hyperinflation in patients with NFA, extend similar observations about asthmatic patients without NFA.9 The loss of lung elastic recoil due to unknown mechanisms9,10 remains a physiologic burden in asthmatic patients and limits their defenses when challenged with superimposed bronchoconstriction.

Pathologic airway remodeling, as well as other indexes of inflammation, have not always correlated closely with chronic expiratory airflow obstruction in asthma patients,1,2,5,6,13–22 especially with the thickening of the reticular basement membrane.15,20–22 Mansud et al16 noted that structural abnormalities in the elastic fiber integrity was limited to the large airways. Moreover, Carroll et al15 concluded that elastic fiber abnormalities surrounding both the large and small airways were not responsible for excessive airway narrowing. Benayoun et al17 reported that fibroblast accumulation and airway smooth muscle hypertrophy in proximal airways were selective determinants of severe persistent asthma. Alternatively, other investigators18,19 have suggested that mast-cell infiltration of airway smooth muscle was responsible for abnormal airway function.

All asthmatic patients in the present study, as well as in our previous studies,9,10 had normal diffusing capacities. This is a surrogate for normal alveolar-capillary surface area, which is consistent with no or trivial emphysema.23 Additionally, high-resolution, thin-section lung CT scan-scored parenchyma as essentially normal in all 13 asthmatic patients tested in the present study who had a loss of lung elastic recoil that was similar to that found in our previous studies in other asthmatic patients.9,10 Furthermore, autopsies in patients who have had fatal attacks of asthma have noted the absence of emphysema.13–16 Therefore, it would be unlikely that emphysema was responsible for any loss of lung elastic recoil noted in the present study as well as in our previous studies.9,10

Investigators have previously reported reversible loss of lung elastic recoil and hyperinflation at TLC during acute attacks of asthma that were spontaneous,24–28 or were induced by exercise27,29 or by antigen challenge.31,32 However, while the loss of lung elastic recoil in patients with chronic, persistent asthma has been suspected,33 or documented in patients fixed obstructions,9,10 partial obstructions,25,26,28 or reversible obstructions,34 the clinical correlation with hospitalization and episodes of NFA has not been reported, as in the present study. The loss of lung elastic recoil due to unknown mechanisms is not specific for patients with acute and chronic persistent asthma. We have previously reported36 the loss of lung elastic recoil with only mild expiratory airflow limitation (i.e., normal FEV1 percent predicted) in long-term smokers with proven moderate-to-severe emphysema,35 and in patients with unexplained severe intrinsic small airway disease without asthma or emphysema.

It is important to identify and study acute attacks of NFA as a surrogate for fatal asthma attacks. Attacks of NFA may occur precipitously over several hours in 10 to 20% of cases, or they may progress over several days.37–43 Clinical risk stratification for NFA include the worsening of asthma despite therapy, often requiring emergency department visits in patients with known difficult-to-manage asthma.37–43 Alternatively, other investigators have reported that one third of pediatric episodes of NFA occurred in presumed mild or trivial cases.44 Previous life-threatening allergic reactions and a history of prior NFA episode or ICU admission for severe asthma are additional risk factors.37–44 Furthermore, a decreased perception of dyspnea during acute asthma attacks has also been identified as a risk factor.49,45,46 Inner-city settings with reduced socioeconomic stan-

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standards, and home and environmental pollution also have been cited, especially among African Americans.\textsuperscript{38,47} Despite these observations, precipitating triggers were not apparent in half of the cases of NFA.\textsuperscript{40} This is consistent with our data. While the current data do not answer the question, the role of therapy with oral corticosteroids during exacerbations of severe asthma in preventing NFA remains speculative.

The diagnosis of NFA has been associated with a poor prognosis post-hospital discharge. Marquette et al\textsuperscript{48} noted that the mortality rate due to subsequent respiratory failure was 10\% at 1 year, 14\% at 3 years, and 22\% at 6 years, whereas Strunk et al\textsuperscript{49} noted a mortality rate of 15\% at \textgreater{} 10 years.

Unfortunately, for a variety of reasons, lung function studies have not been obtained in most patients when they were clinically stable before and after episodes of NFA. In short-term follow-up studies, previous investigators also have reported abnormal spirometry findings\textsuperscript{39,40} and increased airway hyper-responsiveness to methacholine challenge.\textsuperscript{39,40,50} The present results demonstrated a loss of lung elastic recoil in 10 of 10 asthmatic patients with histories of NFA when they were clinically stable. In addition, a persistent FEV\textsubscript{1} of \textless{} 75\% predicted or an FEV\textsubscript{1}/FVC ratio of \textless{} 75\% in 9 of 10 cases were risk factors for NFA, and complement the previously described clinical risk factors for NFA.\textsuperscript{37–47} Measurements of airway resistance require the use of a plethysmograph, and calculated values of airway conductance and sGaw do not distinguish between intrinsic airway obstruction and extrinsic airway obstruction secondary to the loss of lung elastic recoil or a combination of both, as shown in the present study. While spirometry has similar physiologic limitations, it is easy to obtain and readily available to clinicians.

Despite the construct of the present study with potentially biased selection criteria, the physiologic loss of static lung elastic recoil and the resultant persistent abnormal spirometry findings have important clinical and physiologic consequences in patients with chronic persistent asthma. Identification should alert clinicians to the potential risks and need for aggressive therapeutic intervention when indicated to potentially avoid asthma-related hospitalization and especially catastrophic episodes of NFA.

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