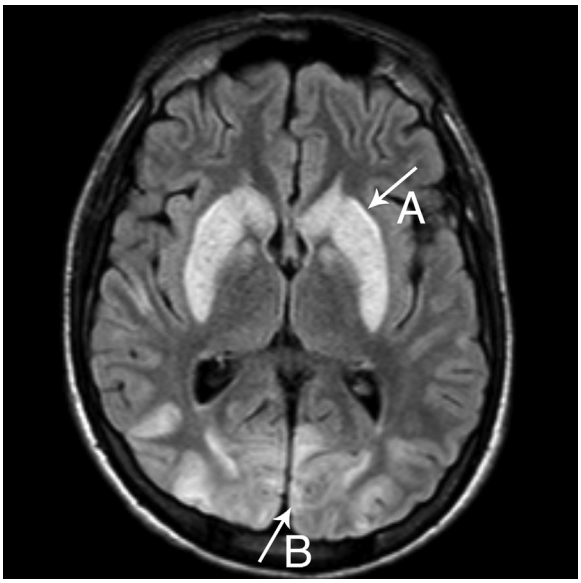

Figure 1. Magnetic resonance imaging of patient 2. Signs of diffuse hypoxic ischemia. Fluid-attenuated inversion recovery sequence: high-signal intensity (damaged tissue) in basal ganglia (caudate nucleus, striatum) (arrow A) and occipital lobe (visual cortex) (arrow B).

avoid the hypoxic brain damage. At the time of the described attacks, the diagnosis of HAE-C1-INH was unknown in patient 1 and known in patient 2.

Laryngeal attacks represent only approximately 1% of attacks in patients with HAE-C1-INH. The course of laryngeal attacks may include a predyspnea phase, a dyspnea phase, and a loss-of-consciousness phase.[4] Complete recovery and death by asphyxiation have been reported in treated and untreated patients with HAE-C1-INH. Complete recovery without any residual impairment was reported for 324 untreated laryngeal attacks in 24 patients.[5] Furthermore, complete recovery was reported in numerous laryngeal attacks of many patients treated on demand with various drugs.[5–7] Death by asphyxiation in untreated, delayed treated, or inadequately treated patients has been reported many times and in numerous patients. One case was already mentioned in one of the earliest descriptions of HAE.[8]

We report a third kind of outcome, survivors of far advanced laryngeal attacks having irreversible disabilities as sequelae of brain damage after cardiac arrest and hypoxemia. Until now there have been no reports of patients with HAE-C1-INH who have survived a severe laryngeal attack that required reanimation measures and who subsequently remained permanently disabled because of hypoxic brain damage. The short course of the laryngeal attacks in the patients described here underlines the necessity of an early diagnosis, a disease documentation, and an optimal treatment plan for laryngeal attacks in patients with HAE-C1-INH, including treatment with drugs that can rapidly counter the laryngeal attack.[9,10]

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High exhaled nitric oxide levels correlate with nonadherence in acute asthmatic children

Nonadherence to asthma controller medication is associated with an increased number of acute exacerbations, increased asthma-related emergency department visits and childhood hospitalizations, and high health care costs.[1] The average medication adherence rate in children with asthma tends to be poor (<50%). Improving patient adherence is essential to achieving optimal outcomes.[2]

Measurement of fractional exhaled nitric oxide (FeNO) has been suggested as a sensitive, noninvasive indicator for monitoring

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Table 1
Frequencies of Responses for Each Item of the Hill-Bone Medication Adherence Scale Short Form in Patients Hospitalized for Asthma

Hill-Bone Medication Adherence Scale	Response categories (N = 102), %			
	None of the time (1 point)	Some of the time (2 points)	Most of the time (3 points)	All of the time (4 points)
How often do you forget to take your asthma controller?	42	52	6	0
How often do you decide not to take your asthma controller?	73	18	7	2
How often do you forget to refill your prescription?	89	8	3	0
How often do you run out of asthma controller?	92	7	1	0
How often do you skip your controller before you go to your physician?	85	10	5	0
How often do you miss taking your controller when you feel better?	68	22	7	3
How often do you miss taking your controller when you feel sick?	89	5	6	0
How often do you take someone else's asthma controller?	92	6	2	0
How often do you miss taking your controllers when you are careless?	70	26	4	1

T-helper cell type 2 (T_H2)-mediated airway inflammation in children with asthma.[3,4] Nonadherence to daily use of inhaled corticosteroids (ICSs) has been implicated as a key contributor to acute asthma exacerbation.[5] Using the FeNO measurement in clinical practice is beneficial to predict future exacerbations and can be used to identify poor adherence to anti-inflammatory therapy in patients with allergic asthma.[6] Feedback of FeNO findings during an acute asthma exacerbation offers a chance of improving parental knowledge of ICS characteristics by health providers. However, the feasibility and usefulness of FeNO as a diagnostic tool for identifying nonadherence to ICS in children with acute asthma exacerbation has not been established.

Identifying nonadherent patients with asthma is difficult and electronic monitoring is the only reliable method to assess ICS adherence, but this is not routinely available in clinical practice.[5] The Hill-Bone Medication Adherence Scale (HBMAS) is a well-validated instrument for determining adherence to hypertension medications.[7] In this study, a modified short-form HBMAS for asthma control was administered to assess the behavioral domains of asthma control treatment, taking medication, and keeping appointments. The availability of short screening tools can increase awareness and identify barriers of adherence to asthma control medication.[8]

The characteristics of the 102 subjects are shown in the eMethods section and eTable 1. Their median Childhood Asthma Control Test scores[4] were 19.0 (18.4–20.1) and 30% had a previous emergency department visit, including 22% with a history of hospitalization in the past year. For asthma control treatment, 68% were prescribed an ICS, 13% were prescribed an ICS and a long-acting β_2-adrenergic agonist, and 80% were prescribed leukotriene modifiers. The HBMAS was used to dichotomize the responses as "perfect adherence" (9 points) and "imperfect adherence" (>9 points; Table 1), and only 32 patients (31%) with asthma reported perfect adherence (eTable 1).

The FeNO levels were significantly increased in the group with moderate to severe persistent compared with the groups with intermittent and mild persistent asthma ($P < .05$; eFig 1). The 102 hospitalized children with acute asthma were categorized as having a normal FeNO (<20 ppb; n = 39), an intermediate FeNO (20–35 ppb; n = 30), and a high FeNO (>35 ppb; n = 33) based on the American Thoracic Society (ATS) FeNO guidelines (Table 2). Patients in the intermediate and high FeNO groups had significantly higher total asthma attack rates, more emergency department visits in the past year, and higher *Dermatophagoides pteronyssinus*–specific immunoglobulin E levels compared with the normal FeNO group ($P < .05$; Table 2).

Based on the responses to the 9 items of the short-form HBMAS, 69% of enrolled patients had less than perfect adherence (>9 points) to asthma control. Approximately 5% to 10% of subjects had high scores for each question (>3 points), indicating that some patients needed more reinforcement with asthma education (Table 1). The high FeNO (>35 ppb) group had less than perfect HBMAS scores compared with the normal and intermediate FeNO groups ($P < .01$; Table 2).

We examined the FeNO levels 1 month after hospital discharge for high (n = 70) vs normal (n = 32) HBMAS scores based on the time of enrollment. The FeNO levels were decreased after a course of steroid treatment compared with during acute exacerbation ($P < .01$; eFig 2A). The group with high HBMAS scores for asthma control had persistently high FeNO levels ($P < .05$; eFig 2A). The log

Table 2
Characteristics of Asthma Severity in Different FeNO Groups[a]

	Normal FeNO (<20 ppb)	Intermediate FeNO (20–35 ppb)	High FeNO (>35 ppb)
Subjects	39	30	33
C-ACT scores	23.0 (20.3–22.9)	19.5 (17.9–21.0)	17.0 (15.3–17.5)[b,c]
ICS (equivalent to daily fluticasone)	100.0 (41.4–74.3)	100.0 (53.2–108.1)	100.0 (95.2–211.0)[b,c]
Days hospitalized in past year	4.0 (3.5–3.9)	4.0 (3.4–3.9)	4.0 (3.9–4.7)[b,c]
Total asthma attacks	0.0 (0.0–0.3)	1.0 (0.8–1.5)[b]	1.0 (0.5–3.5)[b]
Previous ED visit	0.0 (0.0–0.3)	0.0 (0.2–0.7)[b]	0.0 (0.3–0.9)[b]
Previous hospitalization	0.0 (0.0–0.2)	0.0 (0.0–0.7)	0.0 (0.1–1.0)[b]
PEFR % predicted	64.0 (59.8–66.1)	61.5 (57.1–63.6)	55.0 (48.6–57.6)[b,c]
Total IgE (IU)	354.5 (384.2–905.2)	574.0 (545.5–1001.5)	954 (832.9–1582.7)[b,c]
Der p (IU/ml)	51.2 (34.3–61.8)	100.0 (62.6–94.1)[b]	100.0 (53.5–84.5)[b]
Eosinophils (n/μL, %)	0.8 (1.2–3.3)	3.1 (2.6–4.9)	5.0 (3.5–6.1)[b]
HBMASSF	9.0 (9.5–10.3)	10.0 (10.1–11.7)	13.0 (13.0–15.8)[b,c]

Abbreviations: C-ACT, Childhood Asthma Control Test; Der p, *Dermatophagoides pteronyssinus*; ED, emergency department; FeNO, fractional exhaled nitric oxide; HBMASSF, Hill-Bone Medication Adherence Scale Short Form; ICS, inhaled corticosteroid; IgE, immunoglobulin E; PEFR, peak expiratory flow.
[a]Data are presented as median (95% confidence interval).
[b]$P < .05$ vs normal FeNO (<20 ppb) group.
[c]$P < .05$ for high FeNO (>35 ppb) vs intermediate FeNO (20–35 ppb) group.