



# Interference of psychological factors in difficult-to-control asthma <sup>☆</sup>

Laurence Halimi<sup>a</sup>, Isabelle Vachier<sup>a</sup>, Muriel Varrin<sup>a</sup>, Philippe Godard<sup>a</sup>,  
G rard Pithon<sup>b</sup>, Pascal Chanez<sup>a,\*</sup>

<sup>a</sup>Clinique des Maladies Respiratoires, H pital Arnaud de Villeneuve, 371 Av. du Doyen Gaston Giraud 34295 Montpellier Cedex 5, France

<sup>b</sup>Laboratoire de Psychologie Sociale, Universit  Paul Val ry, Montpellier, France 34295 Montpellier Cedex 5, France

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## KEYWORDS

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## Summary

**Background:** Most patients with asthma can be controlled with suitable medication, but 5–10% of them remain difficult to control despite optimal management.

**Objective:** We investigated whether patients with difficult-to-control asthma (DCA) or controlled asthma (CA) differ with respect to psychological factors, such as general control beliefs on life events.

**Methods:** DCA was defined as an absence of control despite optimal management. Recent control was measured using the Asthma Control Questionnaire. General control beliefs were investigated using a Locus of Control scale (LOC).

**Results:** Patients with DCA had a significantly higher external LOC as compared to patients with CA ( $P = 0.01$ ). In the DCA group, the hospital admission rate was highly significant in association with the external LOC ( $P = 0.004$ ) as compared to the internal LOC trend.

**Conclusion:** This study showed that patients with DCA had different general control beliefs which might have hampered their management and interfered with their therapeutic adherence. The present findings could enhance management of DCA in a clinical setting.

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## Introduction

Asthma can induce medically and socially expensive respiratory handicaps<sup>1</sup> but it can also be a life-threatening condition. Although most patients with asthma can be controlled with suitable medication,

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\*Corresponding author. Tel.: +33 4 67 33 61 26;  
fax: +33 4 67 52 18 48.

E-mail address: [chanez@montp.inserm.fr](mailto:chanez@montp.inserm.fr) (P. Chanez).

epidemiological studies have indicated that about 5–10% of patients remain difficult to control despite optimal management with high doses of inhaled corticosteroids, long-acting  $\beta_2$  agonists and sometimes long-term treatment with oral corticosteroids.<sup>2</sup> Difficult-to-control asthma (DCA) is defined as a failure to achieve control when maximal doses of inhaled therapeutic drugs are prescribed.<sup>3</sup> Different factors could be involved in this type of asthma, e.g. differential diagnosis, comorbidity, inappropriate therapy, behavioral, psychological or social factors, and therapeutic adherence.<sup>4,5</sup>

Lack of adherence to an asthma medication regime is a significant problem that can lead to poor control and functional limitations—and it has been established that only half of patients take their medication as prescribed.<sup>6</sup> Adherence does not simply concern medication use; it also involves the inhalation technique, peak flow meter use, allergen avoidance, and the patient's relationship with the physician—factors which also have to be optimal for asthma control.<sup>7</sup> Health providers have implemented various methods in attempts to enhance adherence, but each technique has limitations. The physician's clinical assessment was shown to be unreliable when detailed and accurate data are necessary, due to overestimation of adherence degree, poor communication skills, and preconceived beliefs about patients or patient adherence.<sup>8</sup>

International guidelines underline the urgent need to better understand patients with DCA, with acute severe episodes and near-fatal asthma.<sup>9</sup> Recent findings have shown that psychological disturbances contribute to increased health care utilization independently of asthma severity.<sup>10</sup> Several psychosocial factors have been associated with poor control, including depression, anxiety, denial, skills and coping strategies, which might in turn influence therapeutic adherence.<sup>11</sup>

The definition of psychological characteristics of patients with DCA and those with controlled asthma (CA) could highlight factors that would differentiate these patient groups. Health providers are increasingly interested in patients-oriented outcomes and in better understanding patients' expectations and beliefs.<sup>12</sup> Consequently, we focused on general control beliefs on life events using the Locus of Control concept (LOC).<sup>13</sup> In chronic disease, the internal LOC is considered to be a favorable factor for better adaptation, active research and use of medical information, and the adoption of behaviors such as therapeutic adherence.<sup>14,15</sup>

Several psychosocial factors have been described in asthma,<sup>16</sup> but no single study has tried to relate DCA to patients' way of life and behavior. This

study was designed to assess LOC in patients with a difficult-to-control form of asthma in comparison to patients with CA. Unexpected results were obtained that related LOC orientation to therapeutic adherence.

## Methods

### Participants

Seventy-three non-smoking asthmatic patients were consecutively recruited through a chest physicians network in our area during a 6-month period. Asthma was defined according to ATS standards. Asthma severity was classified according to GINA guidelines<sup>9</sup> and patients received treatments according to their severity stage during the last year before enrollment. Severe asthmatic patients were treated with a high dose of inhaled corticosteroids and long-acting  $\beta_2$  agonists with, for some of the most severe cases, a dose of oral corticosteroids on top of this treatment. This oral corticosteroid supplement was administered to patients who had a high frequency of acute exacerbation following at least two attempts to wean them in the past 2 years. There was no modification in treatments for any patients during the year preceding the study in order to maintain the best potential control. All data concerning asthma history, symptoms, clinical features and medication requirement were obtained and documented during an initial interview conducted according to a structured computerized questionnaire.<sup>17</sup>

All patients who were approached accepted to participate in the study. Our local ethics committee approved the study and participants signed an informed consent form before the screening visit.

The same physician assessed overall asthma control (rate of exacerbations and brief symptoms) during the previous year and recent control (last week) was assessed using the Asthma Control Questionnaire (ACQ French version for France).<sup>18</sup>

DCA was defined by the absence of control despite a 1-year follow-up by a chest specialist and optimal management according to the GINA guidelines. Patients with CA had the same prior follow-up and asthma management as DCA patients.

### Locus of Control (LOC)

Some people think they can control life events. This is based on the belief that personal objectives can be reached and negative events avoided through one's own behavior, i.e. personal actions, efforts,

capacities, abilities, and skills. The LOC orientation is considered as internal when the person feels that he/she can control later events via personal actions. However, the LOC is considered to be external when the person believes that life events are due to luck, chance, fate, or powerful others.

We assessed LOC using Rotter's scale on the day of the screening visit, after the medical visit and in the presence of a psychologist. This general unidimensional scale has been fully validated for investigating this concept. It involves a forced-choice response format and does not include items specific to expectations about health.<sup>13,19,20</sup> Internal LOC was considered for scores of  $\leq 11$ . Individuals with a high score were considered as "external" (score  $> 11$ ). We used the French version which has been fully validated ( $n = 210$ ; mean = 10.5;  $SD = 3.8$ ).<sup>21</sup>

### Physician's adherence assessment

In this study, with the help of a visual analogical scale, the physician clinically assessed patient adherence rather than using more expensive or invasive approaches. General and specific therapeutic adherence criteria (asthma disease awareness, appropriate use of medication, mastery of practical aspects such as the inhalation technique, self-monitoring skills, regular visits to health care providers, environment control, and peak flow meter use) were investigated by the same physician through a question-and-answer interchange and an unstructured interview. The accuracy of the physician's clinical assessment was maximized by questions concerning the regimen follow-up: a patient was considered as non-adherent when he/she stated that the regimen had not been followed.<sup>22</sup>

### Data analysis

Descriptive statistics were used to characterize the asthmatic sample in terms of psychological and

medical characteristics. When the distribution was skewed, comparisons were analyzed using non-parametric Mann-Whitney  $U$  and  $\chi^2$  analyses.  $T$ -test was used for normally distributed data (Tables 1 and 3). In the DCA group, odds ratios for external versus internal LOC were obtained by multiple logistic regression analysis. All statistical analyses were performed with StatView F-4.2 and SAS-6.12.  $P$  values of less than 0.05 were considered significant.

## Results

### Patient characteristics

The characteristics of the DCA and CA groups are shown in Table 2. The patients were mostly female (57%; mean 48.5 years of age). There were no differences between the two groups with respect to demographic characteristics, but clear significant differences were noted concerning the clinical parameters (oral corticosteroid use at entrance, exacerbation rate, hospital admission rate, severity, recent control, and  $FEV_1$ ). Significant differences were noted in the LOC scores and consequently in the internal and external orientation. In the DCA group, the mean LOC score on the  $I-E$  scale was 12.5, and 73% of the patients were considered to have an external orientation. The CA group was distributed differently, with a mean LOC score of 10.8, and only 41% of the subjects had an external orientation. There were significant differences in the physician's clinical assessment, i.e. 71% of the patients with DCA were perceived as non-adherent as compared to patients with CA (45%) (See also Table 3).

### Differences in LOC orientation among patients with CA

There were no significant differences between patients with an internal or external LOC orientation

**Table 1** Shapiro-Wilks's test for normality: clinical characteristics (CA Versus DCA group).

	CA	DCA	Statistical tests
Age (yr)	0.54	0.04	MW*
ACQ	0.06	0.01	MW
Oral corticosteroids at entrance (mg)	$< 0.0001$	$< 0.0001$	MW
Hospital admissions last year	—	$< 0.0001$	MW
Exacerbations last year	$< 0.0001$	0.0006	MW
$FEV_1$ , % predicted	0.47	0.02	MW
LOC score	0.09	0.09	$T$ -test

\*Non-parametric Mann-Whitney  $U$ -test.

**Table 2** Clinical characteristics of the controlled asthma group (CA) Versus the difficult-to-control asthma group (DCA).

	CA N = 24	DCA n = 49	P value
Sex (M/F)	11/13	20/29	0.68*
Age (yr)**	50 (38–62)	47 (34–60)	0.63 <sup>†</sup>
ACQ** (1–β) = 1	9 (5–11)	22 (15–24)	<0.0001 <sup>†</sup>
Oral corticosteroids at entrance (mg)** (1–β) = 0.99	0 (0–0)	0 (0–26)	0.0023 <sup>†</sup>
Hospital admissions last year** (1–β) = 1	0 (0–0)	0.5 (0–1)	<0.0001 <sup>†</sup>
Exacerbations last year** (1–β) = 1	0 (0–2)	4 (3–6)	<0.0001 <sup>†</sup>
Mild moderate/severe**	10/14	0/49	<0.0001*
FEV <sub>1</sub> , % predicted** (1–β) = 0.98	79 (70–93)	66 (53–79)	0.0028 <sup>†</sup>
Clinical assessment: adh./non adh.	13/11	14/35	0.02*
LOC E/I	10/14	36/13	0.01*
LOC score*** (1–β) = 0.95	10.8 (3.03)	12.5 (2.58)	0.014 <sup>††</sup>

\*Chi<sup>2</sup>.

\*\*Median (25th–75th percentiles).

\*\*\*Mean (SD).

<sup>†</sup>P value for nonparametric Mann-Whitney U-test.<sup>††</sup>P value for parametric T-test. E, external; I, internal.**Table 3** Shapiro–Wilks' test for normality: clinical parameters (internal Versus external patients).

	External	Internal	Statistical tests
<i>Controlled Asthma group</i>			
Oral corticosteroids at entrance (mg)	<0.0001	<0.0001	MW*
Exacerbations last year	0.007	0.0003	MW
FEV <sub>1</sub> , % predicted	0.72	0.70	T-test
ACQ	0.04	0.13	MW
<i>Difficult-to-control Asthma group</i>			
Oral corticosteroids at entrance (mg)	<0.0001	0.0009	MW
Hospital admissions last year	<0.0001	<0.0001	MW
Exacerbations last year	0.0009	0.38	MW
FEV <sub>1</sub> , % predicted	0.04	0.05	MW
ACQ	0.04	0.58	MW

\*Non-parametric Mann–Withney U-test.

concerning clinical parameters (severity, oral corticosteroid use at entrance, exacerbation rate, recent control, and FEV<sub>1</sub>) (Table 4). However, there were significant differences in the physician's clinical assessment, i.e. 78% of patients with internal orientation were perceived as adherent as compared to only 20% of those with an external orientation.

### Differences in LOC orientation among patients with DCA

There were no significant differences between patients with an internal or external LOC orienta-

tion concerning clinical parameters (oral corticosteroid use at entrance, exacerbation rate, recent control, and FEV<sub>1</sub>) (Table 4). The predominance of females with DCA was higher in the external orientation (66%), but this difference was not significant. The hospital admission rate was highly significant with the external orientation (one admission) as compared to the internal orientation (no admission). There were significant differences in the physician's clinical assessment, i.e. 61% of patients with an internal orientation were perceived as adherent as compared to only 16% of those with an external orientation. Externally oriented patients with DCA had an almost 13-fold increased risk of non-adherence, along with an

**Table 4** Clinical parameters among internal and external patients.

	External	Internal	P value
Controlled asthma group	<i>n</i> = 10 (41%)	<i>n</i> = 14 (58%)	
Sex (M/F)	3/7	8/6	0.18*
Mild moderate/severe	3/7	6/8	0.52*
Oral corticosteroids at entrance (mg)**	0 (0–0)	0 (0–0)	0.55†
Exacerbations last year**	0.5 (0–2)	0 (0–2)	0.59†
FEV <sub>1</sub> , % predicted***	77.8 (13.55)	83 (16.06)	0.41††
ACQ**	10 (9–12)	6 (2–10)	0.16†
Clinical assessment: adh./non adh. (Fisher p)	2/8	11/3	0.01
<i>Difficult-to-control Asthma group</i>	<i>n</i> = 36 (73%)	<i>n</i> = 13 (26%)	
Sex (M/F)	12/24	8/5	0.076*
Oral corticosteroids at entrance (mg)**	0 (0-30)	0 (0-20)	0.68†
Hospital admissions last year**	1 (0-2)	0 (0-0)	0.004†
Exacerbations last year**	5 (3-6)	3 (2-6)	0.18†
FEV <sub>1</sub> , % predicted**	68 (59-79)	56 (48-77)	0.21†
ACQ**	21 (15-25)	22 (12-23)	0.56†
Clinical assessment: adh./non adh.	6 / 30	8/5	0.002*

\*Chi<sup>2</sup>.

\*\*Median (25th-75th percentiles).

\*\*\*Mean (SD).

†P value for nonparametric Mann-Whitney U-test.

††P value for parametric t-test.

**Table 5** Odds ratios for adherence and hospitalizations of internal versus external patients with difficult asthma.

	OR†	(95% CI)‡	P value
Adherence (N/external)*	12.8	(2.1–77.5)	0.002
Hospitalizations (≥ 1/external)	21.6	(1.9–245.3)	0.003

Concordance = 74.4%; Hosmer Lemeshow test: *P* = 0.84.

\*N = Non adherent.

†OR = Odds Ratios.

‡CI = Confidence Interval.

almost 21-fold increased risk of one or more hospitalizations during the previous year as compared to patients with an internal orientation (Table 5).

## Discussion

The aim of this study was to identify psychological factors associated with asthma control and our findings revealed a link between asthma control and the LOC orientation. An internal orientation was a characteristic of CA patients, while the DCA group generally had an external orientation. Our aim was not to accurately measure patients'

adherence, but we did integrate the physician's clinical assessment of this adherence and obtained an unexpected result. Between the two groups, asthmatic patients with an external orientation were considered to have poor adherence (real or supposed) in comparison to asthmatic patients with an internal orientation. Moreover, in the DCA group, external individuals had a higher hospital admission rate. Consequently, a psychological factor was related to both asthma control and the physician's clinical adherence assessment.

The first finding suggested that asthma, as a life event, could probably be considered as out of personal control. In our experience, we have noted

that patients with DCA often discuss asthma, using terms such as “accident”, “heredity”, “allergy”, “weather”, and “environment”. This illustrates the way asthmatic patients “externalize” illness, evoking an etiology that is out of their control. Concerning hospital admissions in the DCA group, externality was also associated with poor asthma control and thus with more hospitalizations. This latter correlation could be explained by the need for more powerful external support from the hospital and physicians, etc. Inversely, internal patients in the DCA group could have been focused on their own efforts, i.e. developing abilities to gain control over their situation and avoiding hospitalization. Moreover, the lack of perceived control in past situations—specific to externality—could induce external patients with asthma to feel helpless and to give up making efforts, thus influencing their adherence to treatment. This could partially explain the poor asthma control and high hospitalization rate in the DCA group. In this respect, previous studies reported a clear association between poor adherence and risk of hospital admission.<sup>23</sup>

To our knowledge, few studies have been published about asthma control and LOC. A recent study revealed that the health LOC orientation could differentiate patients with mild and severe asthma. External health LOC and less trust in medication were found among severe asthmatic patients.<sup>16</sup> Either chronic disease severity makes a person more fatalistic and less confident in treatment (if LOC is considered as a learned behavior), or severity is partially due to externality (if LOC is considered as a personality trait). Our study demonstrated that the general LOC orientation differentiated mild from severe asthmatics, but also DCA from CA within severe patients.

In our study, there were significant differences in the physician’s clinical adherence assessment, i.e. 71% of patients in the DCA group and almost 50% in the CA group were assessed as having poor therapeutic adherence. A physician has to assess therapeutic adherence in order to enhance the asthma assessment and to understand why the patient’s asthma continues to be difficult to control.<sup>24</sup> In the absence of clear guidelines for detecting adherence, a physician usually relies his/her clinical assessment to estimate patient adherence.<sup>25</sup> It is known that the medical situation has an influence on physicians’ estimates of adherence.<sup>26</sup> In our study, patients with CA could have been incorrectly classified as adhering to medical instructions because the medical situation was good, while some DCA patients could have been considered as non-adherent. However, there

were also differences in physicians’ clinical assessment of the internal–external orientation among patients with CA and DCA—externality was linked to perceived non-adherence (Table 2). The clinical judgment was based on clinical observations and expert opinions, but also on the physician’s feelings or presuppositions concerning the patient’s efforts to take care of him/herself and comply to the prescription—a physician might inadvertently be evaluating patient internality or externality when actually wanting to assess the patient’s therapeutic adherence.

Measuring LOC was a major problem, so we opted to use Rotter’s scale despite some critiques.<sup>27</sup> Nearly all existing scales have been discussed in the literature, but most have not been fully validated or they do not really assess the LOC concept, as defined by Rotter, or the wording is not adapted to the situation. Many investigators focusing on health LOC or specific medical conditions such as cancer or asthma have developed their own scales.<sup>28–30</sup> However, we deliberately opted for this well-validated general scale because we wanted to assess a general belief and not the LOC perception in a disease-related situation. Items of health scales could make it difficult for subjects with a difficult-to-control chronic health status to respond, i.e. “I control my health”<sup>28</sup> and determining the general LOC does not imply that specific expectancies are absent.<sup>31</sup> In our study, a recent asthma control assessment with ACQ during the same visit provided another argument in favor of using a general scale, i.e. too many terms concerning “health control” could confuse patients. Moreover, the LOC structure is always discussed and the notion of dimensionality is ambiguous. Most health LOC scales have split externality into two dimensions (Chance and Powerful Others), with the C factor implying a worse physical and mental health condition, and the P factor implying perceived and adapted control.<sup>19,20</sup> This three-factor structure has been supported by the results of many studies and with samples of patients with chronic illnesses, and internality and powerful others were found to be slightly positively correlated.<sup>29</sup> For other researchers, internality is linked to a beneficial impact on health, and the two factors P and C are slightly interrelated and negatively correlated with health.<sup>32</sup>

In short, psychological factors are considered to be a major factor in the development of severe asthma.<sup>33</sup> Greater health care utilization was noted in patients with asthma and comorbid psychological disorders, irrespective of the degree of severity.<sup>10</sup> In many studies, the results indicated

that non-adherence to asthma therapy was implicated in the risk of hospital admission or in the development of severe asthma.<sup>23,34</sup> The present study, involving patients with DCA, revealed that the general LOC was related to asthma control, hospital admission and perceived adherence. Consequently, general control beliefs should not be overlooked in case of DCA, and we thus recommend that two new strategies be implemented in asthma management. First, patients should be managed in the same department and medical and psychological specialists should be jointly involved when asthma is difficult-to-control—indeed, current guidelines recommend referring a patient to professionals.<sup>35</sup> The results of this study also highlighted the difficulty for any physician to accurately assess patient adherence in asthma control. All national and international guidelines stress the importance of enhancing the awareness of asthmatic patients on their condition, but denial based on a feeling of not being in control might be a potential barrier to this educational process.<sup>36</sup> The present findings question the nature of the LOC and researchers have divergent opinions about it (personality trait or learned behavior?).<sup>19,20</sup> When an asthma problem is related to a personality trait in the patient, rather than trying to overcome this trait, the medical system should be flexible so that treatments can be specifically tailored to each patient's condition. In cases where adherence to therapy is actually involved, these results could be discussed in terms of their implications for specific and original clinical interventions.

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