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## Psychosocial Factors and Behavioral Medicine Interventions in Asthma

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### Abstract

**Objective**—This review examines the evidence for psychosocial influences in asthma and behavioral medicine approaches to its treatment.

**Method**—We conducted a systematic review of the literature on psychosocial influences and the evidence for behavioral interventions in asthma with a focus on research in the past 10 years and clinical trials. Additional attention was directed at promising new developments in the field.

**Results**—Psychosocial factors can influence the pathogenesis and pathophysiology of asthma, either directly through autonomic, endocrine, immunological, and central nervous system mechanisms, or indirectly through lifestyle factors, health behaviors, illness cognitions, and disease management including medication adherence and trigger avoidance. The recent decade has witnessed surging interest in behavioral interventions that target the various pathways of influence. Among these, self-management training, breathing training, and exercise or physical activation programs have proven particularly useful, whereas other essential or promising interventions, such as smoking cessation, dietary programs, perception and biofeedback training, and suggestive or expressive psychotherapy, require further more rigorous evaluation. Given the high comorbidity with anxiety and mood disorders, further evaluation of illness-specific cognitive behavior therapy is of particular importance. Progress has also been made in devising community-based and culturally tailored intervention programs.

**Conclusion**—In concert with an essential medication treatment, behavioral medicine treatment of asthma is moving closer towards an integrated biopsychosocial approach to disease management.

### Keywords

Behavioral medicine; asthma; psychosocial factors; treatment

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## Definition, epidemiology and pathophysiology

Asthma is a chronic inflammatory disease of the airways that is characterized by excessive bronchoconstriction, mucus production, airway edema and remodelling of the airway walls. Patients suffer from periodic exacerbations with symptoms of shortness of breath, wheezing, and coughing (National Heart, Lung, and Blood Institute/National Asthma Education and Prevention Program [NHLBI/NAEPP], 2007; Global Initiative for Asthma [GINA], 2010). The prevalence of asthma has increased markedly in the last few decades, now affecting an estimated 300 million individuals worldwide and 30 million in the US alone (Braman, 2006). Asthma is now among the most common chronic diseases in adult populations, whereas in children it is the most common chronic disease and is among the most frequent reasons for hospital admissions. With an estimated US\$16 billion in health care and lost productivity cost, the economic costs are substantial, as is the burden to the sufferers' well-being.

In patients suffering from asthma, the airways are hyperresponsive to a variety of endogenous and environmental trigger factors, including a variety of allergens, exercise, cold and/or dry air, air pollution or irritants, infections, or gastric reflux (NHLBI/NAEPP, 2007; GINA, 2010). Whereas the role of such triggers is well described in the literature and recognized in the clinical management of established asthma, the knowledge on risk factors for the pathogenesis of asthma is still limited. Factors such as genetic predisposition for atopy (excessive production of immunoglobulin E), prenatal or early life exposure to cigarette smoke, high allergen levels, and viral respiratory tract infections have been described (NHLBI/NAEPP, 2007; Martinez, 2011). In this context, the hygiene hypothesis (Strachan, 2000) has achieved particular prominence, which postulates that a lack of confrontation with bacterial or viral infections in early life results in overexpression of T helper (Th) cell Type 2 lymphocyte populations that favor an allergic response. In recent years, it has become apparent that the exclusive focus on the allergic process is a limitation of this hypothesis, as is the simplicity of Th cell Type 1/Type 2 balance paradigm (El Biaze et al., 2003; Salvi, Babu, & Holgate, 2001). More complex models of pathogenesis have been discussed including the sedentary Westernized lifestyle (Platts-Mills, Erwin, Heymann & Woodfolk, 2005) and alternative inflammatory pathways (Holgate, 2008).

Asthma has been viewed as a heterogeneous disease category for some time (e.g. extrinsic allergic vs. intrinsic infectious asthma, Rackemann & Edwards, 1958), but recent years have seen large scale efforts to identify a limited number of asthma phenotypes using a combination of clinical or physiological features (e.g., frequency of exacerbations, persistence of airway obstruction, resistance to steroids, age of onset), trigger factors (e.g., allergens, aspirin, exercise, occupational allergens or irritants) or inflammatory processes (e.g. recruitment of eosinophils or neutrophils) (Wenzel, 2006). The various asthma syndromes overlap partially and are probably determined by a number of different underlying pathophysiological mechanisms (endotypes, Lötvall et al., 2011). This research is still in its infancy, but a better understanding of clinical subsyndromes and their pathophysiological differences can be expected to improve patient care by greater individualization of therapy (see also, for occupational asthma, Lavoie, Joseph, & Bacon, 2009). Further diagnostic challenges remain for early childhood asthma and the overlap of

asthma with vocal cord dysfunction (Wamboldt & Balkissoon, 2008). The primary treatment of asthma involves anti-inflammatory controller medication, mostly inhaled, but in severe cases or exacerbations, oral corticosteroids, combined with beta-adrenergic inhaler medication that relieves acute bronchoconstriction. Despite substantial progress in the medication treatment of asthma and efforts to improve awareness of the disease and standardization of its diagnosis and management (NHLBI/NAEPP, 2007; GINA, 2010), the overall control of this chronic disease remains unsatisfactory.

## **Psychosocial influences on asthma: Psychobiology and health behavior**

Psychosocial factors have long been suspected to influence the onset and course of the disease (for earlier reviews, see e.g., Weiner, 1977; Lehrer, Isenberg & Hochron, 1993). Both direct influences on pathophysiological processes and indirect influences through self-management of the disease have been described.

### **Direct psychosocial influences on asthma**

Progress has been made in the past decade in elucidating direct psychosocial influences on the pulmonary system, autonomic and endocrine regulation, as well as inflammatory and immune processes. Acceptance of such direct influences is also increasing in the traditional biomedical field (Douwes, Brooks & Pearce, 2011). Studies have shown that emotional arousal constricts the airways in adult asthma patients, with stronger effects often observed for negative emotional states in both laboratory and field settings (for review, see Ritz & Kullowatz, 2005). Vagal excitation seems to be the key mechanism underlying these airway constrictions (Ritz et al., 2010). Longitudinal diary studies have also linked adverse life events to asthma exacerbations in children (Sandberg et al., 2004). A bias towards parasympathetic activation has been observed in children with asthma exposed to sadness-inducing film stimuli (Miller et al., 2009), which may be a mechanism contributing to the association between childhood deaths from asthma and depression (Miller & Strunk, 1989). Induction of sadness or depressed mood can also elicit airway constriction associated with vagal activity in adults with asthma in the laboratory (Ritz, Thoens, Fahrenkrug & Dahme, 2005).

Given the central role of airway inflammatory processes in asthma, research has also begun elucidating immune and endocrine pathways of psychosocial influences. Low levels of endogenous cortisol or reduced cortisol reactivity to stress have been observed in children and adolescents with asthma or allergies (e.g., Buske-Kirschbaum et al., 2003; Wamboldt, Laudenslager, Wamboldt, Kelsay, & Hewitt, 2006), which has been linked to elevated airway inflammation (Ritz et al., 2011). A greater propensity of stimulated Type 2 Th cells of the immune system to produce cytokines such as IL-4, IL-5, or IL-13 in asthmatic children and adults has been shown in response to academic or examination stress (Kang et al., 1997; Liu et al., 2002) or life events and chronic stress (Chen et al., 2006). Gene expression of adrenergic and glucocorticoid receptor mRNA in children with asthma has also been shown to be diminished by life events or chronic stress (Miller & Chen, 2006). Studies demonstrating adverse effects of aversive experimental stressors on inflammation and airway hyperreactivity in animal models of asthma and allergy (for reviews, see Quarcoo, Pavlovic

& Joachim, 2009; Wright, 2010) have confirmed the tight association between psychosocial processes and asthma pathophysiology, but also highlighted the need for more systematic distinctions of acute and chronic stress effects (Kang & Weaver, 2010). Thus, discrepancies can be found in humans with asthma between effects of acute negative affect versus chronic daily hassles on airway inflammation and lung function (Kullowatz et al., 2008), or effects of acute versus the combination of acute and chronic stress on cytokine production of stimulated Th cells (Marin et al., 2009).

The scepticism towards early psychoanalytical models of asthma psychogenesis (for review see, Weiner, 1977) has more recently given way to a renewed interest in the etiological role of psychosocial factors. Epidemiological studies have linked psychopathology to subsequent asthma disease onset (e.g. Hasler et al., 2005) and have demonstrated a link between the psychosocial environment and subsequent inflammatory processes (Wright, Mitchell, et al., 2004). The psychosocial aspects of the prenatal and perinatal environment are now also thought to play a key role in priming the immune system towards atopy (Cookson, Granell, Joinson, Ben-Shlomo, & Henderson, 2009; Wright, 2010). Integrating the multiple systems, levels of influence, and stages of transformation will be a future challenge for research devoted to the fascinating question of how the various psychosocial challenges “invade” the airways and alter their biological make-up. This task is even more daunting given the heterogeneity of asthma and the continuing expansion of our knowledge of relevant etiological factors and pathophysiological processes (Holgate, 2008).

### **Indirect psychosocial influences on asthma outcomes**

Another pathway for influences of psychosocial factors on asthma morbidity and mortality is through self-management and health behaviors.

**Medication adherence**—Asthma poses special challenges as a chronic disease because the underlying inflammation requires in most cases daily treatment with anti-inflammatory medication despite symptom-free periods. Consequently, patients’ have developed beliefs that “no symptoms” mean “no asthma”, which then results in poor asthma control (Halm, Mora, & Leventhal, 2006). Typically, around 50% of patients are nonadherent to inhaled corticosteroid medication across studies and nonadherence is linked to poor asthma outcomes (Bender, Milgrom, & Apter, 2003). Mastery of inhaler technique is another aspect of self-management that is often lacking, with adverse consequences for asthma control, including increase in emergency visits and hospitalizations (Melani et al., 2011).

**Perception of airway obstruction**—Given the variability of asthma, accurate perception of airway obstruction is an important patient skill that is needed to initiate adequate changes in management and thereby avoid exacerbations (Barnes, 1992). Perception of symptoms is also a key factor in patients’ communication of their symptoms to health care professionals and thus is central to success in treatment. Both underperception and overperception of symptoms are frequently observed among child and adult asthma patients (Janssens, Verleden, De Peuter, Van Diest, & Van den Bergh, 2009) and can have adverse consequences for asthma management (e.g., Magadle et al., 2002). Overperception is linked to an exaggerated use of medication and health care resources, resulting in an increase in

medication side effects and an unnecessary burden to patients and health care systems. Underperception of symptoms can lead to insufficient adherence with anti-inflammatory medication, delayed physician visits, and an elevated risk of life threatening states (for review, see Janssens et al., 2009).

Recent studies have demonstrated that irrespective of ventilatory changes, several psychosocial factors can considerably impact asthma symptom perception including affective states, learning processes, focus of attention, social comparison style, and contextual cues (Janssens et al., 2009; Petersen & Ritz, 2010). Similar to pain, a sensory and an affective component of dyspnea can be distinguished, which may be influenced differently by psychosocial factors as well as contribute differentially to asthma management behavior (Lansing et al., 2009; von Leupoldt, Seemann et al., 2007). Progress has been made in recent years to elucidate neural circuitries involved in dyspnea. Emotional stimuli or state anxiety can alter activity of these pathways (von Leupoldt, Chan et al., 2011; von Leupoldt et al., 2010). Neuroimaging studies have demonstrated that brain areas with high relevance to emotion processing such as the insular cortex, anterior cingulate cortex and amygdala play an important role in the processing of dyspnea, presumably for its affective aspects (Evans, 2010; von Leupoldt, Sommer et al., 2008). There is evidence that negative affective quality of dyspnea can habituate in some asthma patients, which is accompanied by insular cortex down-regulation as well as functional and structural up-regulation in the brainstem periaqueductal grey (von Leupoldt et al., 2009, von Leupoldt, Brassens, Baumann, Klose & Büchel, 2011). First attempts have also been documented linking neural processing of asthma-relevant stimuli with airway and inflammatory responses to allergen challenge (Rosenkranz & Davidson, 2009)

**Illness beliefs**—Symptom perception itself is part of the patient’s illness belief system, which is critical in motivating and guiding self-management behaviors (Leventhal, Weinman, Leventhal, & Phillips, 2008). The influence of this belief system on chronic disease management has been detailed in many studies and its role in determining asthma management outcomes is well established (Kaptein, Klok, Moss-Morris, & Brand, 2010). Such beliefs or illness perceptions can address various aspect of the disease and its management, including temporal characteristics (transience versus chronicity, Halm et al., 2006), medication effects (Ponieman, Wisnivesky, Leventhal, Musumeci-Szabó, & Halm, 2009), or complementary and alternative medicine use (Koinis Mitchell et al., 2008).

**General health behaviors**—In addition to asthma-related cognitions and behaviors, general health behaviors can also shape clinical outcomes in asthma. Thus, lack of physical fitness may exacerbate exercise-induced symptoms (Fanelli, Cabral, Neder, Martins, & Carvalho, 2007), and smoking is a source of symptoms, airway irritation, and premature loss of lung function (Thomson & Chaudhuri 2009). A variety of potentially critical dietary factors for asthma patients have also been proposed, including vitamins, minerals, fatty acids, certain foods or complex diets (e.g., Mediterranean-style) (McKeever & Britton, 2004; Nurmatov, Devereux, & Sheikh, 2011). In addition, obesity is among the major contemporary challenges with an impact on the pathophysiology of asthma, with genetics,

diet, inflammation, oxidative stress, airway mechanics, and gastro-esophageal reflux among the primary candidates for underlying mechanisms (Lugogo, Kraft & Dixon, 2010).

## Comorbidity of asthma with psychological disorders

Many studies have documented that psychological disorders occur at elevated rates in patients with asthma. The strongest and most consistent associations have been found between asthma and anxiety disorders, in particular panic disorder, panic attacks, generalized anxiety disorder, and phobias (e.g., Goodwin, Jacobi, & Thefeld, 2003; Lavoie et al., 2011), with overall prevalence rates for anxiety disorders of up to 45% in some inner-city samples (Feldman et al., 2005). Part of this association is likely due to the frightening nature of asthma exacerbations, extreme dyspnea, chest tightness, or feelings of suffocation. Thus, rates of anxiety disorders are especially elevated for patients with severe asthma who suffer frequent life-threatening asthma episodes (Kolbe, Fergusson, Vamos, & Garrett, 2002). In young inner-city children with asthma entering school, those with persistent symptoms, as compared to intermittent or no symptoms, show the most behavioral disturbances including both externalizing and internalizing behaviors (Haltermann et al., 2006). A higher prevalence of depression is also frequently found in patients with asthma, although findings are less consistent (for review, see Opolski & Wilson, 2005), in particular with regard to a longitudinal association between depression and asthma onset (Slattery & Essex, 2011). However, additional adverse effects on asthma control, quality of life, and management may be found for depression only, or over and above anxiety (e.g., Lavoie et al., 2006; Kullowatz, Kanniss, Dahme, Magnussen, & Ritz, 2007). Asthma has also been linked to a higher incidence rate of subsequent suicide mortality but not natural death in adolescents in Taiwan (Kuo et al., 2010), but a potential mediation by anxiety and/or depression has not been explored. In addition, recent population-based studies suggest an elevated comorbidity of asthma with schizophrenia (e.g., Pedersen, Benros, Agerbo, Børghlum, & Mortensen, 2012).

Asthma and psychopathology can exacerbate each other. For example, asthma exacerbations lead to symptoms greatly feared by panic disorder patients, thus exacerbating panic attacks (Carr, 1998). Child anxiety patients that are referred to behavioral treatment are likely to suffer from greater psychopathology with an additional diagnosis of asthma (Meuret, Ehrenreich, Pincus, & Ritz, 2006). Anxiety and asthma comorbidity is also associated with mutual complications and errors in the diagnosis and management of both illnesses, leading to additional costs for the health care system (Carr, 1998; Greenberg et al., 1999).

The high comorbidity of psychological disorders with asthma is likely to be multifactorial, including common genetic risk factors (Mrazek, 2003). Findings from longitudinal studies of a bidirectional relationship between asthma and anxiety and/or depression (e.g., Hasler et al., 2005; Scott et al., 2008) seem to support the notion of a common diathesis. Once both illnesses are established, the pathways of influence on asthma control can again be directly through influences on asthma pathophysiology or indirectly through effects on asthma management. Given the evidence on bronchoconstrictive and airway inflammatory effects of negative affect and stress (Ritz & Kullowatz, 2005; Liu et al., 2002), exacerbations by frequent arousal of such states in psychological disorders appears likely. Reports of more

frequent psychological asthma triggers are associated with higher levels of anxiety and/or depression in adults (Ritz et al., 2008), adolescents (Feldman et al., 2005), and children (Wood et al., 2007). Phobias, such as blood-injection-injury phobia, involve particularly pronounced bronchoconstriction during exposure to feared stimuli (Ritz, Wilhelm, et al., 2011). Panic attacks have been linked to increases in ventilation, a factor known to play a role in asthma symptoms and exacerbations (Meuret & Ritz, 2010). Similarly, depression has been hypothesized to affect asthma through a variety of autonomic, endocrine, immune and cellular signaling pathways (e.g., Miller et al., 2009; Van Lieshout, Bienenstock & MacQueen, 2009). Elevated comorbidities of schizophrenia and asthma have also nurtured speculation about communalities in immune dysregulation, particularly in the Th1/Th2 cell balance (Müller & Schwarz, 2010).

With respect to indirect influences through asthma management, earlier research of Kinsman, Dirks, and colleagues demonstrated “psychomaintenance” of asthma by generalized panic-fear, a trait construct that incorporates features of panic and generalized anxiety disorder and is predictive of episodes of hospitalization (Kinsman, Dirks, Jones, & Dahlem, 1980). On the other hand, a certain amount of panic-fear about asthma symptoms is believed to motivate self-management behaviors, although higher levels have also been linked to frequent primary care provider use (Feldman et al., 2005) as well as higher corticosteroid intake (e.g., Hyland, Kenyon, Taylor, & Morice, 1993). The elevated use of medication, including short-acting beta<sub>2</sub>-agonists and oral corticosteroids, may work both ways, leading to secondary psychological symptoms, reducing asthma control, and increasing mortality risk. Anti-asthmatic corticosteroid medication, and possibly also leukotriene modifiers, could contribute to depressive symptoms (Opolski & Wilson, 2005; Van Lieshout et al., 2009). In addition to exacerbating psychopathology, long-term corticosteroid use could also lead to neurocognitive deficits (Brown et al., 2004; NHLBI/NAEPP, 2007). Depression and asthma could sustain each other by effects on asthma self-management adherence, medication effects, and the emotional toll of the chronic disease. In addition, some secondary symptom overlap (fatigue, sleep disturbance) may complicate diagnosis (Opolski & Wilson, 2005). Finally, a general problem that applies to more severe psychopathologies such as schizophrenia in particular are the potential disparities these patients face in receiving adequate health care for their chronic disease (Baxter, Samnaliev, & Clark, 2009).

## **Social, cultural and diversity aspects in asthma**

The past decade has seen a greater appreciation of the complexity of a biopsychosocial approach to asthma involving multiple levels including cultural, social, and family factors of influence (Canino, McQuaid, & Rand, 2009; Wright & Subramanian, 2007). Major minority populations in the US are disproportionately affected by asthma. African-Americans/Blacks, Puerto Ricans, and American Indians/Alaskan Natives have a higher prevalence of asthma than Whites. Hispanics/Latinos not of Caribbean origin have an overall lower prevalence, but similar to most other minorities, they are underserved in asthma care, show lower asthma control, fewer prescriptions of inhaled steroids, more frequent hospitalization or emergency department use, and are more likely to die from asthma (Leong, Ramsey, & Celedon, 2011), even after controlling for insurance or socioeconomic status.

Living conditions in inner cities contribute to higher asthma morbidity and mortality, with a greater impact of specific trigger factors such as house dust, rodent and cockroach allergens, air pollution, or viral infection (Cannino et al., 2009; Wright & Subramanian, 2007). Ethnic differences in asthma symptom perception or report (Fritz et al., 2010; Hardie et al., 2000), comorbidity with psychological disorders (Feldman et al., 2010), and management strategies that deviate from the traditional biomedical approach (Pachter et al., 1995; Koinis Mitchell et al., 2008;) have been reported. Ethnic or cultural variations in nutrition (e.g., vitamin D deficiency in African Americans; Hill, Graham & Divgi, 2011) and rates of obesity (Bender, Fuhlbrigge, Walders, & Zhang, 2007) need to be considered as factors. Genetic variation and/or its interaction with specific environments also contribute to disparities, such as altered responses to anti-asthmatic medications (Leong et al., 2011).

The critical role of family variables in affecting asthma particularly in children has been recognized for a long time (Kaugars, Klinnert & Bender, 2004). Factors such as the parent-child relationship, parenting difficulties, family conflicts, and family organization and responsibility have been shown to affect asthma management and clinical outcomes. Negative emotional family climate and relational insecurity are also associated with depression in children with asthma, which in turn affects asthma outcomes (Wood et al., 2006). Similarly, peer group attitudes and behavior can pose significant barriers to effective asthma management in adolescents (Rhee, Belyea, Ciurzynski, & Brasch, 2009). The dynamics of self-evaluation, stigmatization of asthma as a disease, and social comparison processes with their consequences for self-management and coping with the disease require further attention (Petersen & Ritz, 2010). Awareness of macro-level influences on asthma outcomes, such as social cohesion and violence in inner city neighborhoods, has also grown in recent years (Wright & Subramanian, 2007). Urban environments suffer from a multitude of adverse environmental and social stressors, including air pollution, pest infestation, poverty, high crime rates, domestic violence and disrupted family relationships that can interact with genetic factors to affect health outcomes in asthma. Exposure of caregivers of children with asthma to community violence by has been shown to affect pathogenesis, management, and exacerbation risk of their asthma (Apter et al., 2010; Wright, Finn, et al., 2004). Acute stress in children from lower socioeconomic backgrounds may also lead to more pronounced airway inflammatory responses (Chen et al., 2010). It is conceivable that the various levels of the social environment may affect asthma morbidity through different direct (biological) or indirect (management and health behavior) pathways, but research elucidating such pathways is still in its infancy (Chen et al., 2007; Wright, Finn, et al., 2004).

## Diagnostic assessments of asthma in behavioral medicine

The diagnosis of asthma typically comprises multiple components including experiential, behavioral, and biological markers. Central to the definition of asthma are symptom experience, variability of airway obstruction, hyperreactivity of the airways, and airway inflammation (Reddel et al. 2009). None of these components alone is sufficient to diagnose the disease and the empirical correlation of these components is only modest at best. In addition to general guidelines on diagnosis and treatment of asthma (NHLBI/NAEPP, 2007; GINA, 2010), various relevant consensus reports have been issued in recent years for the



assessment of dyspnea (Parshall et al, 2012), pulmonary function (Beydon et al., 2007; Ritz et al., 2002), airway hyperresponsiveness (Crapo et al., 2000), and airway inflammation by exhaled nitric oxide (Silkoff et al, 2006). A recent guideline report has also summarized the assessment domains with practical recommendations for clinical outcome studies (Reddel et al., 2009). A particularly promising development in monitoring biological markers are noninvasive techniques of measuring airway inflammation, particularly exhaled nitric oxide, which is also available in the form of light-weight, hand-held devices for patient self-monitoring (Alving, Jansson & Nordvall, 2006). The utility of such techniques for the diagnosis and medication management of asthma is currently the focus of intensive research efforts (e.g., Vijverberg et al., 2011).

As a major advance in diagnostic classification, more explicit definitions of asthma severity, control, and exacerbation have been proposed recently. Exacerbations are classified as severe or moderate (Reddel et al., 2009). A severe exacerbation is defined as an event requiring urgent action to avoid a serious outcome, such as hospitalization or death from asthma, whereas the moderate form is an event viewed as “troublesome” for the patient that diverges from the patient’s normal day-to-day range disease variation, requiring a change in management strategy. Systematic assessment of exacerbations is now recommended for clinical trials and routine practice. Classifying asthma severity as intermittent and mild, moderate, and severe persistent has long dominated clinical guidelines, but once treatment has been initiated this definition needs to be replaced by one referring to the level of treatment needed to control the disease well (NHLBI/NAEPP, 2007). Evaluation of asthma control has taken on a more central role in the clinical assessment of asthma (Taylor et al., 2008). Asthma control is defined by the extent to which the manifestations of the disease are removed or reduced through treatment (Reddel et al., 2009). Although control is thought to be comprised of two larger components, impairment and risk of future exacerbations, only the former is currently determined readily by validated questionnaires (e.g., the Asthma Control Test, Nathan et al., 2004) and the integration of both components to an overall index of control is not well solved. Similarly, the conceptual justification for scoring self-report and lung function as part of one dimension of asthma control (Juniper et al., 1999) is not very strong.

Quality of life is another clinical end-point that is frequently assessed. Both generic (e.g., Ware, 2000) and asthma-specific instruments have been included in treatment research (for review, see Apfelbacher, Hankins, Stenner, Frew, & Smith, 2011). Their common use constitutes a major advance in that it considers the patients’ perception as a criterion of clinical improvement. Typically, they incorporate multiple item domains covering symptoms, triggers, social and physical activity limitations, and emotional functioning. Whereas these questionnaire measures are useful in reflecting overall clinical status of the patient, they are rarely based on explicit conceptual models of quality of life and constitute a pragmatic blend of psychological concepts merging various aspects of illness perception and management behaviors. For more concept-oriented research, questionnaire measures that tap into distinct concepts such as symptom perception and distress elicited by symptoms (Kinsman et al., 1973; Steen et al., 1993), perceived triggers (Ritz, Steptoe, Bobb, Harris & Edwards, 2006; Wood et al., 2007), perceived control (Katz et al., 2002), or self-efficacy, attitudes, and knowledge (Wigal et al., 1993) may be preferable<sup>1</sup>. Generic instruments

capturing aspects of illness cognitions or perceptions have also been validated successfully in asthma patient populations (e.g., Broadbent, Petrie, Main, & Weinman, 2006).

Self-report measures are important in capturing the patients' perception of various aspects of the illness process and management, but limitations become apparent in domains such as the assessment of adherence to medication regimens and self-monitoring instructions (Bender et al., 2003). Both patients' self-report and physicians' clinical judgment frequently overestimate actual adherence. Alternative adherence indicators such as amount of quantity of medication used, obtained prescriptions, pharmacy refills, electronic monitoring of inhaler or spirometer use, and observation by family members or staff in institutional settings may yield more valid data, but have all their own inherent limits.

Among the general issues pertaining to questionnaire measures in the context of behavioral medicine treatment research are sensitivity to change, clinical significance of change, and cultural appropriateness. Questionnaires vary in the extent to which they reliably index current status versus measure change sensitivity, implying different approaches to their psychometric validation. Sensitivity to change cannot be assumed unless demonstrated by longitudinal studies. Because statistical change in a questionnaire measure does not necessarily coincide with clinically relevant change, efforts have also been made to determine "minimal important change" using patients' global ratings of improvement as anchors (for review, see Turner et al., 2010). Adaptations in various languages are available for a number of asthma-related questionnaires (e.g., Mora et al., 2009), which is a first step to reduce disparities in behavioral medicine asthma research and care, but more work is needed to adapt assessment tools in order to capture unique cultural aspects of asthma perception and management.

Diagnostic assessments are also likely to become more complex, with an increasing focus on distinct subpopulations of asthma patients (phenotypes), which may require different management approaches. One study has shown that a limited number of distinct patient subpopulations can probably be identified by the combination of a number of standard assessments, including baseline and post-bronchodilator lung function and symptom report (Moore et al., 2010). Further validation of such approaches is needed. Given the high comorbidity of asthma with psychological disorders and the ensuing effects on clinical asthma outcomes, diagnosis in behavioral medicine also needs to incorporate assessment of the psychological status of patients. Because elaborate diagnostic interviews are often not feasible in this context, brief and conceptually sound screening instruments are needed, such as the Hospital Anxiety and Depression Scale, which avoids the inflation of scores by the organic disease symptomatology through omission of physical symptom items (Zigmond & Snaith, 1983). A number of generic stress measures have been reviewed recently by Kopp et al. (2010). Stress assessments need to be increasingly precise about definitions of and distinctions between acute and chronic stress, different forms of acute stress, such as active or passive coping challenges, and various types of chronic stress, such as life events with lasting consequences, bereavement, loneliness, burn-out, or daily hassles.

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<sup>1</sup>For a more extensive list of relevant questionnaire measures please consult the web site of the American Thoracic Society's Behavioral Science Assembly (<http://qol.thoracic.org/sections/instruments/ko/index.html>).

## Behavioral medicine treatment approaches for asthma

The multitude of psychosocial influences on asthma disease activity and the lack of optimal control of asthma in clinical practice form the backdrop for efforts to improve asthma control by methods of behavior change or psychotherapy. The status of these interventions is supportive or adjunctive with respect to the necessary medical treatment of asthma (e.g., fostering adherence with anti-inflammatory medication or adding to the reduction in symptom burden). In the following, we will briefly outline the rational, existing empirical evidence, and promising new developments for psychophysiological control interventions, lifestyle interventions and rehabilitation, asthma self-management and education, individualized psychotherapy, and psychosocial interventions on the family and community level. A summary evaluation of the current status of these interventions is provided in Table 1.

In analogy to a basic distinction, which is customary for anti-asthmatic medication treatment, behavioral approaches that target pathophysiological processes of asthma directly could be classified as “rescue” or “maintenance” measures. Some psychophysiological control interventions, such as specific biofeedback techniques, relaxation, breathing training, or suggestive techniques, have originally been conceptualized more as rescue measures in that they aimed to achieve short-term dilatory effects on the airways. However, with increasing realization of the importance of anti-inflammatory treatment, potential maintenance benefits of behavioral interventions are now increasingly explored, with the idea that these measures can counteract adverse psychological influences on airway inflammation. A further number of behavioral interventions, such as self-management education or complex psychosocial interventions, cannot be conveniently subsumed under the rescue vs. maintenance paradigm, in particular when interventions are supportive of all aspects of asthma self-management.

On a practical level, there are multiple roles for psychologists in contributing to patient care in a multi-disciplinary team. Besides a key role in the diagnostic assessment of experiential and behavioral patient characteristics, psychologists will administer individualized and family psychotherapies as well as psychophysiological control interventions, and will contribute in various functions to lifestyle interventions and rehabilitation, asthma self-management and education, and psychosocial community level interventions. These functions include developing individualized treatment plans in a team with other health care professionals, implementing treatment plans with patients on an individual basis or in collaboration with their families, schools, or workplaces, as well as directly administering and supervising intervention modules. In addition, psychologists contribute to promotional and motivational work and design new interventions based on accepted scientific principles of behavior change.

### Psychophysiological control interventions

A number of behavioral interventions have been devised with the aim of targeting specific aspects of the asthma pathophysiology directly or indirectly. Often, such techniques have been developed with a specific interaction between pathophysiological, experiential and/or behavioral processes in mind. Although psychophysiological rationales are a particular

strength of these interventions, these rationales have rarely been tested in the treatment context. Also, some studies have combined some of these techniques (e.g. breathing training with relaxation techniques, biofeedback with certain breathing techniques), which makes it more difficult to determine effects of individual techniques.

**Breathing training**—Exercises that alter aspects of the breathing pattern have been variously combined into intervention techniques for asthma patients, altering speed, volume or regularity of breathing, the balance between nasal versus oral route or abdominal versus chest compartments, or training of breathing in against resistances for improving inspiratory muscle strength or breathing out against resistances such as pursed lips to avoid airway collapse. The rationale for some of these techniques is well founded in respiratory physiology (Ritz & Roth, 2003), but larger clinical trials testing their efficacy are still rare. Among the most widely used techniques are slow, abdominal, and nasal breathing, which have been at the core of recent trials that showed improvements in quality of life, mood, and symptoms, but not in pulmonary physiology (Holloway & West, 2007; Thomas et al., 2009). However, hyperventilation (low CO<sub>2</sub> levels) is common in asthma (Thomas et al., 2005) and these techniques do not target low CO<sub>2</sub> levels directly. Slow abdominal breathing may actually make hyperventilation worse because deep breaths can result in a loss of CO<sub>2</sub> (Meuret et al., 2003). Based on the claim that low CO<sub>2</sub> levels contribute to asthma pathophysiology, a breathing technique developed by a Russian physician, Vladimir Buteyko, aims at raising CO<sub>2</sub> levels by slow breathing training with breath-holding (Bruton & Holgate, 2005). Indeed, basic research has confirmed that low CO<sub>2</sub> is linked to bronchoconstriction (van den Elshout, van Herwaarden, & Folgering, 1991) and airway hyperreactivity (Osborne, O'Connor, Lewis, Kanabar, & Gardner, 2000). Although a number of treatment trials have shown reductions in medication and improving quality of life following hypoventilation training (Bruton & Thomas, 2011), demonstration of the critical role of CO<sub>2</sub> levels in treatment outcome is still lacking. In fact, clinical trials of the Buteyko method have rarely included PCO<sub>2</sub> measurements and have so far failed to demonstrate increases in this key parameter. A recently developed breathing training that teaches slow, abdominal, and shallow breathing guided by assessments of CO<sub>2</sub> with a capnometer showed improvements in asthma symptoms and asthma control, including lung function variability, in a pilot-study (Meuret et al., 2007). Overall, breathing training is currently viewed as a promising adjunctive treatment for asthma (Bruton & Thomas, 2011).

**Biofeedback training**—A number of biofeedback techniques have been devised with the aim of improving lung function in asthma patients (Ritz, Dahme & Roth, 2004), including incentive spirometry, respiratory resistance feedback, frontal muscle relaxation, heart rate and heart rate variability (HRV) biofeedback. Each of these approaches has its own specific set-up of sensors and follows a different psychophysiological rationale. Findings with direct feedback of respiratory resistance (controlled for hyperinflation of the lungs, which can reduce resistance), one of the most relevant parameters of asthma pathophysiology, were disappointing (Mass, Dahme & Richter, 1993). Similarly, electromyography-supported facial muscle relaxation that has been promoted in earlier research has been found questionable in its rationale and empirical outcome (Ritz, 2004). More recently, a larger clinical trial demonstrated positive effects of a HRV biofeedback on medication needs and

exacerbation frequency in asthma (Lehrer et al., 2004). The method aimed at enhancing baroreflex function, which is hypothesized to improve autonomic and airway regulation in general (Lehrer et al., 2003), but no lasting baroreflex changes were observed. Thus, the mechanisms of action remain unknown, but could resemble those responsible for some of the positive effects of slow breathing training that may be linked to improvements of gas exchange (Giardino, Glenny, Borson & Chan, 2003) or bronchodilation and bronchoprotection through deep breath-induced airway smooth muscle stretch (Krishnan et al., 2008).

*Relaxation training* has long been proposed as an adjunctive intervention for asthma patients, however, studies that convincingly demonstrate favorable outcomes have remained rare. Most reviews concur that there is not enough evidence to recommend one of the various techniques of relaxation for asthma patients (Ritz, 2001; Huntley, White & Ernst, 2002). The main problem lies in the unclear psychophysiological rationale of relaxation, because the desired decrease in sympathetic activity and/or increase in parasympathetic activity should in fact lead to bronchoconstriction (Lehrer et al., 1997; Ritz, 2004). Studies demonstrating the utility of relaxation skills for reducing emotion-induced bronchoconstriction or coping with stronger symptom episodes or exacerbations are missing. More recent studies by one team indicated improvements in lung function following progressive muscle relaxation training, functional relaxation and/or guided imagery (Nickel et al., 2005; Lahmann et al., 2009). However, the significance of findings remains unclear due to a number of methodological problems, such as use of a motivation-dependent index of lung function, lack of patients' expectancy and plausibility monitoring, and lack of medication monitoring. Most recently, a larger trial of mindfulness-based stress reduction found intervention effects only on quality of life and perceived stress at 12-month follow-up, while lung function and asthma control remained unchanged (Pbert et al., 2012).

The status of the evidence for yoga therapy has also remained disappointing and the quality of studies is mostly poor (Posadzki & Ernst, 2011; Ritz, 2001), although conceptualization of yoga as relaxation therapy is not fully appropriate because it can also contain elements of breathing training and lifestyle advice. Research that isolates one element of yoga training, the pranayama breathing technique that aims to reduce respiration rate and increase expiratory duration, has not consistently yielded positive effects over placebo control (Cooper et al., 2003). Another recent trial of a more comprehensive yoga intervention found improvements in spirometric lung function compared to wait-list control (Vempati, Bijlani, & Deepak, 2009), but suffered from methodological shortcomings similar to recent relaxation studies. In summary, given the long history of mixed results, larger studies with the most rigorous standards of evidence-based medicine are now needed in this area.

**Training of perception of airway obstruction**—Improving perception of airway obstruction may be another route to better self-management, avoiding dangerous over- or undertreatment of asthma symptoms and thus unwanted medication side effects or life-threatening emergencies. Two earlier studies used external resistive load detection with feedback of success to train interoception of resistance, either by signal detection of critical resistances (Harver, 1994) or by comparison tasks of resistance pairs to identify increasingly smaller differences between resistance levels (Stout, Kotses & Creer, 1997). Both forms of

training showed short-term improvements in perceptual accuracy, but the translation of such improvements into asthma self-management outcomes has not been studied. Diaries of estimated and actually measured lung function (peak flow) over weeks have also been employed to improve perception of obstruction, with some evidence of increasingly closer associations between self-measured lung function and estimations (Schandry, Leopold & Vogt, 1996). However, it cannot be ruled out that these associations reflect purely cognitive changes in that patients become more familiar with typical levels of their lung function and thus become better at guessing their actual values (Dahme, Richter & Mass, 1996). More recent research also showed little association between perception quantified by added resistive loads and peak flow diaries (Fritz et al., 2007). This lack of associations between methods of measuring interoceptive abilities reflects typical findings from interoception research in general (Pennebaker, Gonder-Frederick, Cox & Hoover, 1985). There is yet no consensus on how to define inaccurate perception (e.g., Rhee, Belyea & Halterman., 2011, Fritz et al., 2007) and the ecological validity of an approach purely informed by psychophysics is probably limited. Because cognitive factors (lay theories, beliefs) and situational or environmental cues (Pennebaker et al., 1985) and affect (Janssens et al., 2009) are thought to contribute substantially to patients' perceptions of their symptoms, approaches that incorporate monitoring of patients' implicit attitudes (Petersen & Ritz, 2010), focus of attention (von Leupoldt et al., 2007), current mood state (von Leupoldt, Riedel & Dahme, 2006), or perceived asthma triggers (Ritz et al., 2006) may substantially improve patients' predictions of their asthmatic status. Overall, although these approaches are clinically important and promising, research on the potentials of perception training for asthma management is still at an early stage.

### Lifestyle interventions and rehabilitation

**Physical activity and exercise**—Exercise is one of the best known triggers of asthma symptoms (McFadden & Gilbert, 1992). Therefore, it is not surprising that patients have an unfavorable attitude toward more demanding physical activity (Millard, 2003). The consequence is a sedentary lifestyle that results in deconditioning. Paradoxically, skeletal muscle activation leads to an initial bronchodilation by vagal withdrawal, as demonstrated by animal, exercise, and muscle tension biofeedback studies (Ritz, 2004). Only later stages of exercise or stronger exhaustion lead to symptoms that are known as exercise-induced asthma. Interestingly, physical activity in daily life is linked to better lung function, but it is also related to reports of stronger symptoms in asthma patients (Ritz, Rosenfield & Steptoe, 2010). Controlled studies suggest that overall, asthma patients benefit from exercise training by an increase in cardiopulmonary fitness without side effects (Ram, Robinson, Black, & Picot, 2005). There is also evidence for a reduction in exercise-induced constriction, improvements in quality of life (Fanelliet al., 2007) and inflammatory status of the airways (Mendes et al., 2011). However, standard prescription for exercise in asthma is pre-training bronchodilator use, which implies that exercising patients are encouraged to use their rescue inhalers more often, although the goal of optimal asthma control is to reduce the need for this medication (NHLBI/NAEPP, 2007). A solution to this dilemma could be provided by a specific warm-up training with brief bouts of exercise, which dilate the airways, reduce bronchoconstriction, and make the airway smooth muscles less responsive to subsequent longer exercise challenges (e.g., McKenzie, McLuckie, & Sterling, 1994). This behavioral

strategy has not yet been implemented widely. Overall, exercise is clearly indicated for a substantial segment of the asthma patient population. Utilizing bronchodilatory properties of physical activity and potential anti-inflammatory effects by increasing antioxidant levels (Gomez-Cabrera, Domenech, & Viña, 2008) provide promising perspectives for future study.

**Nutrition and diet**—The worldwide epidemics of obesity have also drawn attention to complications in asthma (Eneli, Skybo, & Carmago, 2008). Although epidemiological and longitudinal studies suggest an association between both conditions, the reasons for this relationship are not yet fully understood (Lugogo et al., 2010). Weight loss intervention with patients suffering from both asthma and obesity have generally yielded improvement in asthma outcome measures, but have mostly used surgical methods or were uncontrolled (Eneli et al., 2008). One clinical trial using caloric restriction in a 14-week intervention group compared with asthma and allergy education achieved a 14.5% reduction in weight, improvements in symptoms, lung function, and rescue medication needs (Stenius-Aarniala et al., 2000). More comprehensive intervention concepts of life-style change including gradual dietary restriction, physical activity increase, and methods of behavior change based on Social Cognitive Theory and the Transtheoretical Model of Behavior Change may be more promising (Ma et al., 2010).

Effects of a variety of nutrients on asthma pathophysiology have been identified in cross-sectional studies, however, evidence from controlled trials of supplementation is less encouraging (McKeever & Britton, 2004). Promising new angles of intervention include supplementation of magnesium (Kazaks et al., 2010) and Vitamin D (Brehm et al., 2010). Significant but weak effects of various nutrients, fruit, vegetables and Mediterranean diet were also reported for primary prevention of allergy and asthma (Nurmatov et al., 2011). Some studies have specifically focused on effects of supplementation with probiotic bacteria that colonize the gut, such as *Bifidobacterium spp.* and *Lactobacillus spp.* typically found in yogurt. This could up-regulate Th1 cells and thus may confer protection against allergies or reduce their severity (Singh & Ranjan Das, 2010). Findings of dietary intervention studies in asthma and allergies have remained mixed though, with some positive treatment outcomes for children with allergic asthma (Chen, Jan, Lin, Chen, & Wang, 2010). Future research will need to address these dietary supplements as part of a complex network of developmental, pathophysiology and lifestyle factors that may have additive or interactive effects on asthma control.

**Smoking cessation**—Smoking in asthma is associated with more symptoms, reduced asthma control, more health care utilization, reduced sensitivity to corticosteroids, and an accelerated decline in lung function and transition into more chronic obstruction (Tomson & Chaudhuri 2009). Nevertheless, the prevalence of smoking is equal to the general population, as are age of smoking initiation, smoking patterns, readiness to quit smoking, and history of quit attempts (Wakefield, Ruffin, Campbell, Roberts, & Wilson, 1995; Zimmerman et al., 2004). Even more worrisome are reports of more favorable attitudes towards cigarettes and smoking in asthmatic than nonasthmatic adolescents (Brook & Shiloh, 1993).

Despite these urgent problems, few attempts have been made to study smoking cessation in asthma patients or to adapt cessation programs systematically to the challenges in this population. Two intervention studies combined oral or inhaled corticosteroid treatment with encouragement to quit smoking using unspecified or no aids, nicotine replacement, or acupuncture (Chaudhuri et al., 2006; Jang et al., 2010). Quitting success after 6–12 weeks was identical in both studies (31.3%) and both showed improvements in lung function in quitters compared to continuing smokers. A third study observed reductions in symptoms, medication needs, and airway hyperreactivity as well as improvement in quality of life in a larger group of quitters using nicotine replacement compared with continuing smokers over 4 months (Tonnesen et al., 2005).

More efforts have been directed recently at primary prevention of asthma through reducing environmental tobacco smoke (ETS), due to its adverse effects during pregnancy and early childhood on asthma development in children (NHLBI/NAEPP, 2007). However, smoking cessation trials for parents with asthmatic children have also demonstrated limited success (Priest et al., 2008) even when enhanced by feedback of blood cotinine levels (Wilson, Farber, Knowles & Lavori, 2011). Substantial barriers have to be overcome in reducing ETS exposure of inner-city children with asthma (Haltermann et al., 2007)

### **Asthma management and education**

Given the primary importance of medication treatment of asthma, in particular inhaled corticosteroids or other anti-inflammatory agents, patients need to participate in the management process by taking their maintenance medications regularly (in most cases daily). It is now well established that self-management training and education is essential for all asthma patients at all stages of care. The NHLBI/NAEPP (2007) guidelines summarize this evidence based on multiple clinical trials and recommend the following training elements as essential: self-monitoring (symptoms or self-assessment of lung function) as well as “asthma information and training in asthma management skills”, “written asthma action plans”, and “regular assessment by a consistent clinician” (p.97). The patient should be involved in the decision about the type of self-monitoring, and the asthma action plan should contain instructions on daily management, recognizing and handling the worsening of asthma, if necessary by self-adjustments of medication dosage. The consensus is that self-management programs should generally be provided for asthma patients (Gibson et al., 2003; NHLBI/NAEPP, 2007).

**Comprehensive education programs**—Education programs vary in their content, often include multiple components across multiple sessions and may also include individual psychophysiological control interventions (such as relaxation, breathing techniques) and/or life style interventions (exercise, diet) (Mühlig et al., 2002). Documentation of educational content was suboptimal in many of the earlier trials (Sudre, Jacquemet, Uldry, & Perneger, 1999). Where inpatient programs (in hospitals, specialized clinics) are offered, patients appear to prefer comprehensive in-patient training over shorter outpatient versions (ambulatory programs of hospitals, specialists, or primary care clinics), and particularly welcome additional psychological treatment components (coping, motivation, introspection) (de Vries, Mühlig, Waldmann & Petermann, 2008). Programs are mostly assembled in an



eclectic fashion and only sometimes based on a theoretical background in self-regulation and empowerment, learning theory, behavior modification and change (e.g., Bailey, Davis & Kohler, 1998; Put, van den Bergh, Lemaigre, Demedts, & Verleden, 2003). Detailed analysis of the process and enhancement of interventions by such principles may help improve patient adherence and management success (e.g., Creer, 2008).

**Limited or single component education interventions**—Problems with patient adherence and implementation of multiple-session programs in out-patient health care have motivated the exploration of limited, one-session education interventions or single components of education. Thus, an intervention limited to provision of information about asthma, its causes, and its treatment, has not been shown to improve asthma control in adults (Gibson et al., 2008). Limited, one-session allergen and general trigger avoidance advice in primary care by specialized asthma nurses can improve lung function at three months follow-up (Bobb, Ritz, Rowlands & Griffiths, 2010).

**Individualized tailoring of asthma education**—The need for individualized tailoring of longer programs is now well established (NHLBI/NAEPP, 2007). Structured asthma education programs in primary care settings have generally not been met with enthusiasm by patients, physicians, and nurses, as patients prefer more autonomy in management decisions (Jones, Pill & Adams, 2000). Indeed, written action plans allowing patient-directed vs. physician-directed adjustment of medication have yielded similar improvements in symptoms and health care utilization (Powell & Gibson, 2009). However, elimination of regular medical review by physicians resulted in more health center visits and sickness days. In addition, when using a written asthma action plan, versus not using it, does not seem to lead to better asthma control with all other things equal (Sunshine, Song, & Krieger, 2011). Particular self-management components also require more exploration regarding their benefits for specific patient subpopulations. For example, although self-monitoring of symptoms or lung function generally appear to be equally effective, lung function self-monitoring was particularly beneficial for patients with seasonal flu exacerbations (Janson, McGrath, Covington, Baron, & Lazarus, 2010).

**Self-management training in alternative settings**—More recent developments include the implementation of asthma self-management training outside the usual health care settings. A large number of intervention studies have explored the benefits of school-based education programs, which have the advantage of reaching a broad spectrum of children including urban minorities with equal levels of training. These programs increase asthma knowledge, self-efficacy, and self-management behaviors, but past findings on clinical outcomes including quality of life have been mixed or not studied (Coffman, Cabana & Yelin, 2009). The most convincing results to date come from a recent larger trial of mostly Hispanic and African American High school students participating in an 8-week intervention, which resulted in additional improvements on quality of life and a number of indicators of exacerbation risk. (Bruzzeze et al., 2011). The implementation of such programs face unique challenges including difficulties in developing and maintaining partnerships with school administrations, school-based health centers and nurses, parents, and primary care physicians. Some schools districts also do not allow children to carry

rescue medication and lack the on-site health care workers to support the implementation of these programs.

The internet has opened up new delivery modes of asthma self-management education outside of the traditional health care setting. Although this delivery form can also reach patients in rural and remote places, internet penetration is a critical factor in the success of such interventions, as is acceptance of the various forms of technologies for the specific patient population (Wade & Wolfe, 2005). A review of various interactive computerized asthma patient education programs found improvements in asthma knowledge and symptoms as well as less consistently some benefits on aspects of asthma control (Bussey-Smith & Rossen, 2007). Another review that also included remote telemedicine monitoring of illness parameters and telephone- or video-based consultation and reminder interventions concluded that no gain in quality of life was achieved, but a reduction in the rate of hospital admissions in more severe asthma patients was noted (McLean et al., 2011). However, given that patient interest and satisfaction appears to be high, further exploration of internet-based self-management interventions is indicated.

**Adherence training**—Although any self-management education includes information about the importance of adherence to prescribed medication, interventions have also targeted adherence to medication more selectively. A critical review of earlier research concluded that studies either had shown no effect on adherence or found no translation into substantial asthma treatment effects that would justify the efforts and expenses of such interventions (Bender et al., 2003). A number of methodological problems including inadequate assessment methods of adherence (most studies have relied on self-report of adherence) and the complexity of determinants of adherence (e.g., McQuaid, Kopel, Klein, & Fritz, 2003; Drotar & Bonner, 2009) may contribute to failures of this research. A recent larger trial using problem solving training to overcome barriers to adherence for adults did not show improvements in adherence over asthma education (Apter et al., 2011). More economic methods of adherence prompting, e.g. by interactive voice response systems (Bender et al., 2010) or cell phone messaging (Strandbygaard, Thomsen & Backer, 2010) have also been piloted, but their translation into improvements in asthma control awaits demonstration.

*Motivational interviewing* has recently been implemented to enhance asthma self-management, in particular medication adherence. Pilot research suggests that the technique can boost motivation to adhere in urban adolescents (Riekert, Borrelli, Bilderback, & Rand, 2011) and additional beneficial effects on symptoms, functional limitations, medication needs, exhaled nitric oxide, and perceived independence in asthma management were noted in another study (Haltermann et al., 2011).

### Individual psychotherapy

Psychotherapy interventions assume that asthma is accompanied by cognitive, emotional or behavioral problems that lead to suboptimal asthma control. Although the search for specific personality features that might distinguish patients from the rest of the population has not surprisingly been discouraging (Kaptain, 1998), there may be subpopulation of patients with distinct problems that could benefit from psychotherapy.

**Cognitive-behavior therapy (CBT) for comorbid asthma and anxiety**—CBT for anxiety disorders focuses on the repeated exposure to feared situations and sensations, supported by a set of control-based coping skills (Craske & Barlow, 2008). These skills typically aim to change catastrophic appraisals and/or somatic symptoms. CBT targeting anxiety within asthma patients has only been tested in two adult and one child study. In these studies, traditional CBT components (i.e., education, breathing retraining and progressive muscle relaxation, cognitive restructuring, and interoceptive and in-vivo exposure to feared bodily sensations) were combined with additional asthma-specific components. In a small study, Ross, Davis and McDonald (2005) found that an 8-week group treatment that combined CBT for panic disorder with asthma education (addressing asthma triggers and control, lung function and symptom monitoring, medication use, and side-effects) led to long-term reductions in panic and anxiety, and short term improvements in morning peak flow and asthma-related quality of life. Papneja and Manassis (2006) tested the effects of CBT in 36 children with comorbid anxiety and asthma. Results suggested decreases in anxiety and depression at post-treatment. An uncontrolled pilot study by Lehrer et al. (2008) compared 14-session and 8-session CBT protocols. Patients were educated in asthma symptoms and problem solving, proper medication use, smoking reduction, and assertiveness training. Additionally, CBT components relevant for asthma (such as breathing exercises) were expanded, whereas techniques with detrimental effect to the patients (e.g., hyperventilation exercises, which can induce bronchoconstriction) were eliminated. Both protocols were largely equivalent for reductions in panic and asthma symptoms, improvement in asthma quality of life, and decreased bronchodilator use, but drop out was high for the longer protocol with 50% compared to 17% for the shorter protocol. Finally, Parry et al. (2012) showed substantial reductions in catastrophizing thoughts and panic-fear in an adult asthma CBT intervention group compared to routine clinical care, but outcomes on asthma were not reported. Thus, although promising, larger clinical trials and additional efforts to determine the optimal combination of treatment components are needed. There is also a striking lack of clinical trials for clinically depressed asthma patients.

**Suggestive methods**—It is now well established that 20–40% of patients with asthma respond to specific suggestions with significant deterioration of their lung function (Isenberg, Lehrer & Hochron, 1992). In the most common paradigm, patients are told that they are inhaling a bronchoconstrictive substance, which in fact is an inert gas or room air. Patients that are more hypnotizable are more likely to show this effect (Leigh, MacQueen, Tougas, Hargreave & Bienenstock, 2003). The benefits of hypnotherapy for asthma have been explored for some time, with the weight of the evidence suggesting some improvement in self-report of clinical outcomes rather than lung function (Hackman, Stern & Gershwin, 2000). Better patient hypnotizability, more experienced therapists, and additional use of self-hypnotization techniques seem to yield better results. Overall, the potential of suggestive techniques for interventions has not been fully explored yet. Positive variations of the suggestion effect have also been observed in earlier studies, with smaller improvements in lung function due to bronchodilatory suggestions or reduced severity of exercise-induced asthma with hypnosis or placebo inhaler use (Isenberg et al., 1992). However, the extent to which experienced effects of suggestive interventions diverge from actual change in pathophysiology requires attention. A recent study demonstrated that despite only weak

improvements in lung function after two inert placebo treatments, substantial improvements in self-reported asthma symptoms were observed, which were similar to those after treatment with a real bronchodilator (Wechsler et al., 2011).

**Expressive methods**—Both theoretical psychodynamic accounts of asthma and empirical observations (Florin et al., 1993) have directed attention to potentially detrimental effects of emotional suppression or repression in asthma. Following earlier positive findings with emotional writing in asthma (Smyth, Stone, Hurewitz, & Kaell, 1999), in which patients typically write about negative life experiences in three 20-min sessions, a subsequent controlled trial with adults was not able to replicate these findings (Harris, Thoresen, Humphreys, & Faul, 2005), whereas a trial with children found improvements in symptoms, emotional and behavioral functioning, but not lung function (Warner et al., 2006). Nevertheless, the issue of emotional expression in asthma remains intriguing, because emotional facial muscle tension has been associated with improvements in lung function (Ritz, 2004), a logical consequence of the autonomic regulation of the airways, which are constricted mainly by vagal excitation.

### Psychosocial interventions

**Family therapy**—The extent to which family therapy as an adjuvant treatment leads to reductions in symptoms in children has been examined in three randomized controlled trials (see also Yorke & Shuldham, 2005, for a review of two of these). In the study by Lask and colleagues (1979), children with moderate to severe asthma received 6 hours of family treatment in addition to standard medical treatment. Children assigned to family therapy, as compared to standard care only, had significantly better day-wheeze scores and thoracic gas volumes. Gustafsson et al. (1986) examined the effect of family therapy in a small sample of children with severe, chronic bronchial asthma. Compared to the treatment as usual group, greater improvement in clinical assessment and number of functionally impaired days in the children receiving family therapy was observed. A more recent trial of 11-week family therapy for children asthma within the Chinese cultural context showed improvements in airway inflammation in the active group compared to wait-list control, a trend towards symptom reduction and improved adjustment to asthma for the child and improvements in parents' asthma-related self-efficacy (Ng et al., 2008). Although promising, among the study's limitations were a relatively small sample size, no control of medication effects, and lack of intent-to-treat analysis.

The latter study exemplifies that family therapy programs for asthma will most likely not only address emotional aspects of the family interaction but also general asthma management skills and their optimal implementation in the family, thus making it difficult to disentangle the effects of both components on asthma outcomes. Overall, there is some preliminary indication that family therapy may represent a valuable adjunct to medication in the management of childhood asthma.

**Community-based interventions**—Given the well-established disparities in asthma morbidity and disadvantages of inner city environments, efforts have also been directed at the community level with home visitations by community workers, nurses and specialists to

help improve the residential environment and thus asthma control (Persky et al., 2007). The Task Force on Community Preventive Services (2011) guidelines found these interventions to be cost effective due to the money saved through decreased use of emergency care and increased symptom-free days. Community multi-trigger, multi-component interventions help reduce asthma symptoms, daytime activity limitations, and emergency services use (see also, Crocker et al., 2011; Postma, Karr & Kieckhefer, 2009). Improvements in quality of life scores and a decrease in the days missed at school have also been observed, although more research on effects for adult patients with asthma is indicated. Inconsistent findings also remain on actual change in behaviors conducive to reduction of allergen exposure (Postma et al., 2009).

**Culturally sensitive interventions**—Many aspects of asthma care are shaped by cultural influences, including symptom perception and management (Hardie et al., 2000; Koinis-Mitchell et al., 2008). In a multicultural society, language barriers can make communication with health care providers challenging (Ortega & Calderon, 2000). However, there is only limited research on culture-specific interventions for children and adults with asthma. A review of the best available evidence suggested that culture-specific interventions do improve quality of life, education about asthma, asthma symptoms, asthma control, but not all asthma-related health outcomes (Bailey et al., 2009). These findings are based on the outcomes of four studies, so findings should be interpreted with caution. More studies are needed to effectively establish the effectiveness of culturally-sensitive interventions.

## **Conclusion: Recent progress in studying behavioral medicine treatment of asthma**

Substantial progress has been made in the past years to further elucidate the involvement of psychosocial factors in the pathophysiology and management of asthma. Nevertheless, there is still a considerable need for future research on the specific mechanisms and interactions that link psychosocial factors with this disease. Continued efforts to design and test interventions that address some of these influences have also managed to expand and fine tune some of the instrumentation available to the behavioral medicine interventionist. Progress has been most visible in areas of disease self-management, although stricter, conceptually-driven approaches informed by theories of behavior change and maintenance are still needed. Other areas of progress or consolidation are seen in breathing training and physical activity/exercise interventions for asthma (Table 1). Areas with mixed results that may require new creative approaches are life style interventions of smoking cessation and some aspects of nutrition, training of adherence to medication, relaxation training, and biofeedback training. Promising areas that are still lacking sufficient research initiative are training methods to improve interoception and psychotherapy protocols involving suggestive techniques, as well as cognitive behavioral interventions for comorbid anxiety and depression.

In contrast to the amount of evidence generated in recent years on emotion and stress effects in asthma, the general lack of interventions to address emotion-induced asthma is striking. Studies both testing the capability of existing interventions for addressing this problem as

well as developing new creative intervention methods are needed to tackle this issue. In particular, the development of simple behavioral rescue methods that target vagally induced bronchoconstriction, such as dynamic skeletal muscle activation or deep breaths, could be a promising avenue for future research.

On the other hand, an encouraging development is the increasing number of studies dedicated to social factors in asthma as well as community-level interventions and culturally adapted interventions. Nevertheless, much work remains to be done in these areas, including the elucidation of the multitude of factors that contribute to low asthma control in urban environments as well as cultural, ethnic and racial differences in asthma management and control.

Further collaboration across disciplines of psychology, social sciences, medicine, and other health care specialties is key to addressing these challenges adequately. Developments such as these will bring us closer to a transformation of asthma treatment in behavioral medicine that is true to Engel's (1980) vision of biopsychosocial care.

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**Table 1**

Overview of current site of research and clinical applicability of behavioral treatments for asthma

	<b>Further need for research</b>	<b>Potential for clinical practice</b>	<b>Current usefulness for clinical practice</b>	<b>Key references<sup>a</sup></b>
Psychophysical control interventions				
Breathing training	moderate	high	high	Bruton & Thomas (2011) Meuret et al. (2007)
Relaxation training and meditation	moderate	moderate	moderate	Lahmann et al. (2009); Posadzki & Ernst (2011)
Respiratory resistance biofeedback	low	low	low	Mass et al. (1993)
Frontal EMG biofeedback	low	low	low	Ritz et al.(2004)
Heart rate variability biofeedback	high	high	moderate	Lehrer et al. (2004)
Training of airway obstruction perception	high	high	low	Kotses et al. (1997)
Lifestyle interventions				
Nutrition and diet	high	moderate	moderate	Eneli et al. (2008); Nurmatov et al. (2011)
Physical activity and exercise	moderate	high	high	Ram et al. (2005) McKenzie et al. (1994)
Smoking cessation	high	high	moderate	Chaudhuri et al. (2006) Priest et al. (2008)
Asthma self-management and education				
Comprehensive education programs	moderate	high	high	Gibson et al. (2003)
Limited education interventions	high	high	moderate	Gibson et al. (2008) Bobb et al. (2010)
Individually tailored asthma education	moderate	high	high	Powell & Gibson (2009)
Self-management training in schools	moderate	high	high	Bruzzese et al. (2011)
Telehealth delivered self-management	high	high	moderate	McLean et al. (2011)
Adherence training	moderate	moderate	moderate	Bender et al. (2003) Drotar, & Bonner (2009)
Motivational interviewing	high	high	moderate	Riekert et al. (2011)
Individual psychotherapy				
Cognitive behavior therapy	high	high	low	Papneja & Manassis (2006) Lehrer et al. (2008)
Suggestive methods	high	moderate	low	Hackman et al. (2000) Wechsler et al. (2011)
Expressive methods	moderate	moderate	low	Warner et al. (2006) Harris et al. (2005)
Psychosocial interventions				
Family therapy	high	moderate	moderate	Yorke & Shuldham (2005) Ng et al. (2011)
Community-based interventions	high	high	moderate	Postma et al. (2009) Crocker et al. (2011)
Culturally sensitive interventions	high	high	moderate	Bailey et al. (2009)

*Note:*Labels „low“, „moderate“, and „high“ were assigned qualitatively taking into account the available evidence from clinical trials. *Further need for research* was high when none or few smaller trials were available and basic research and/or uncontrolled studies suggested that the intervention was promising; it was moderate when some trials were already available but findings were mixed; it was low when sufficient evidence from controlled trials was available or smaller trials and uncontrolled studies had been unsuccessful and the rationale was not well conceived. *Potential*

*for clinical practice* was high when controlled trials showed promise and the expected impact on asthma control was high; it was moderate when findings from trials were mixed and/or the expected impact on asthma control was limited; it was low when controlled trials or uncontrolled studies were unsuccessful and the rationale was not well conceived. *Current usefulness for clinical practice* was high when trials were supportive and intervention protocols were well-prepared for implementation; it was moderate when clinical trials were mixed and/or more work on preparing implementation was needed; it was low when evidence was mixed and major work on protocols was needed for implementation

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