

EXPERT
REVIEWSAcupuncture for allergic
disease therapy – the current
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Florian Pfab^{*1–3},
Peter C Schalock⁴,
Vitaly Napadow^{3,5,6},
Georgios I
Athanasiadis¹,
Johannes Huss-Marp^{7,8}
and Johannes Ring⁹

¹Department of Dermatology and
Allergy, Technische Universität
München, Munich, Germany

²Department of Prevention and Sports
Medicine, Technische Universität
München, Munich, Germany

³Martinos Center for Biomedical
Imaging, Massachusetts General
Hospital, Harvard Medical School,
Charlestown, MA, USA

⁴Department of Dermatology,
Massachusetts General Hospital,
Harvard Medical School, Boston, MA,
USA

⁵Department of Radiology, Logan
College of Chiropractic, Chesterfield,
MO, USA

⁶Department of Biomedical Engineering,
Kyunghee University, Yongin, Korea

⁷University Freiburg Medical Center,
Department of Exercise Medicine and
Sport, University of Freiburg, Freiburg,
Germany

⁸Thermo Fisher Scientific, Phadia
GmbH, Freiburg, Germany

⁹Department of Dermatology and
Allergy, Christine Kühne-Center of
Allergy Research and Education
(CK-CARE), Klinikum rechts der Isar,
Technische Universität München,
Munich, Germany

*Author for correspondence:
florian.pfab@lrz.tum.de

This review summarizes current evidence for acupuncture treatment of allergies. Several randomized controlled trials have demonstrated a specific effect of acupuncture for allergic rhinitis; while a few studies have shown positive effects for atopic dermatitis, asthma and itch. Specifically for allergic rhinitis and asthma, acupuncture may be cost-effective in terms of money spent per quality-of-life gained. Acupuncture plays an increasingly important role as an evidence-based therapy for allergy relief and can be recommended as adjunct therapy for allergic rhinitis. Future randomized controlled trials need to further explore acupuncture efficacy for the treatment of itch, atopic dermatitis and asthma. More experimental research is also needed to investigate mechanisms of action underlying acupuncture for allergy relief.

KEYWORDS: acupuncture • allergic rhinitis • allergy • asthma • atopic dermatitis

Complementary and alternative medicine (CAM) is an increasingly popular approach to treat allergic diseases for both patients and medical providers. It is defined as a group of diverse medical and healthcare systems, practices and products that are not generally considered part of conventional medicine [1]. Complementary medical practices are often grouped into broad categories, such as natural products, mind and body medicine and manipulative and body-based practices. Natural products include a variety of herbal medicines (also known as botanicals), vitamins and minerals. Mind-body medicine includes meditation techniques, yoga, acupuncture, deep breathing exercises, hypnotherapy, progressive relaxation, qigong and tai chi. Manipulative and body-based practices include osteopathy, chiropractic manipulation and massage therapy.

Acupuncture, derived from the Latin terms ‘acus’ (needle) and ‘pungere’ (pinch), is a popular treatment modality in many parts of the world. In the USA, an estimated 3 million adults and 150,000 children use acupuncture with a 50% increase from 2002 to 2007 [2,3]. In Canada, about 12% of the population have used acupuncture [4]. Use among specific patient populations, prevalence is frequently much higher (i.e., up to 47.5%) [5–8].

Traditionally, stimulation of acupuncture points is supposed to regulate Qi, sometimes translated as ‘energy’ flow, in the body, to dispel pathogenic factors and increase well-being. According to Traditional Chinese Medicine, the Qi flow occurs mainly through so-called channels or meridians, such as the lung, large intestine, stomach or spleen channel, that span the human body and effectively connect different acupuncture points (FIGURE 1). These points can be stimulated by needles, pressure, heat or other stimuli. However, the philosophical constructs noted above, may or may not correspond to biomedical physiological phenomena, an open and controversial avenue of research.

As a medical therapy, acupuncture has been used for thousands of years in various cultures to treat disease [9,10]. Despite this, its scientific basis has not been explored until the last several decades. There is growing evidence for a specific effect (relative to ‘sham’ acupuncture, broadly defined) for different kinds of pain conditions [11], such as knee, lower back, shoulder pain and headache, as well as for the treatment of nausea and vomiting [12]. Within the last several years, research has expanded to explore the effectiveness and mechanisms of action of acupuncture in allergic diseases. This article aims to summarize current evidence.

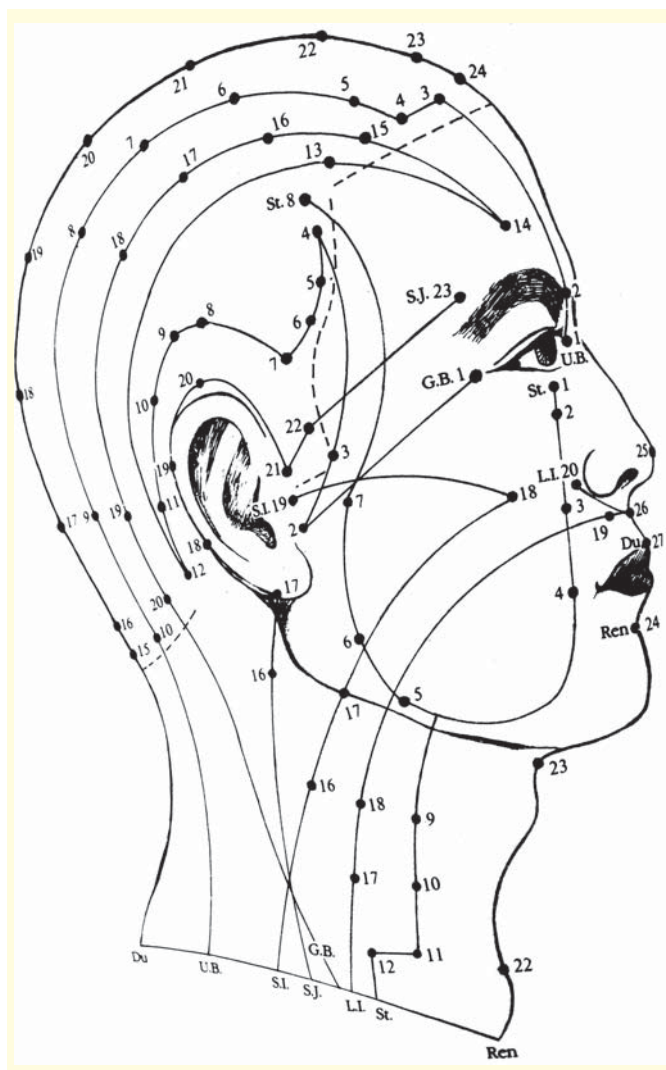


Figure 1. Schematic illustration of acupuncture points of the head. Points close to eyes and nose are typically used as local points for the treatment of allergic rhinoconjunctivitis.

Allergic rhinoconjunctivitis

Allergic rhinoconjunctivitis (AR) is an IgE-mediated inflammation and irritation of internal upper airways and the eyes accompanied by redness, itch and secretion. It affects an estimated 16% of the US children [13], and US\$1.2 billion is spent annually in the USA on medication and preventive measures [14]. AR is associated with asthma, atopic eczema, sinusitis and Eustachian tube dysfunction. Depending on the duration and timing of symptoms, AR can be divided into a seasonal/intermittent and a perennial/persistent type. Despite advances in treatment and consensus guidelines for management of the condition [15], many patients seek complementary and alternative therapies for their symptoms. The estimated lifetime prevalence of CAM use among patients with AR ranges from 27 to 46%, and acupuncture is used by about 18% of patients with AR [16–18].

Seasonal/intermittent allergic rhinitis

Although acupuncture is used by as many as 18% of patients with seasonal/intermittent allergic rhinitis (SAR) [17], it has not been until recently that the first large multi-center randomized controlled trial (RCT) on the effects of acupuncture on SAR was published. Brinkhaus *et al.* investigated the specific short- and long-term effects of acupuncture compared with sham acupuncture (SA) and rescue medication alone in disease-specific quality of life and demand for rescue medication in 422 patients suffering from SAR due to birch and grass pollen [19]. Acupuncture and SA consisted of 12 treatments within 8 weeks during pollen season. The main acupuncture points used in this study were LI4, LI11, LI20 and Yin Tang. Compared with SA or rescue medication alone, acupuncture was associated with a statistically significant improvement in Rhinitis-Quality of Life-Questionnaire score and lower rescue medication score directly after the treatment (8 weeks from baseline). These improvements may, however, not be clinically relevant. There were no differences after 16 weeks in the first year when the pollen exposure had dropped. After the 8-week follow-up phase in the second year during pollen exposure, small improvements favoring real acupuncture over the sham procedure were noted regarding Rhinitis Quality of Life Questionnaire as well as need for rescue medication.

One smaller trial also investigated the effect of acupuncture on SAR reporting a significant difference favoring acupuncture compared with sham (TABLE 1) [20].

Perennial/persistent allergic rhinitis

A recent multicenter RCT [21] in 238 adult patients with perennial/persistent allergic rhinitis compared acupuncture with SA (both three-times per week for 4 weeks) and a wait list control not receiving any acupuncture treatment. The main acupuncture points used in this study were LI4, LI20, ST2, ST36, GV23 and Yin Tang. After treatment, the total nasal symptom score was significantly reduced in the active acupuncture group compared with SA. Active acupuncture showed a significantly greater effect on symptoms of allergic rhinitis compared with either SA or no active treatment. Symptoms of allergic rhinitis decreased significantly after treatment in both acupuncture and SA groups. Two further smaller clinical trials in children [22] and adults [23] reported superiority of acupuncture compared with SA. Two smaller experimental studies evaluated the effect of a one-time treatment of acupuncture on perennial/persistent allergic rhinitis reporting mixed results (TABLE 1) [24].

Two trials included patients with both intermittent and persistent allergic rhinitis not differentiating their results: a large pragmatic trial (n = 981) reported that acupuncture in addition to routine care was beneficial and cost-effective for treating SAR symptomatology [25]. One smaller trial reported no significant differences between acupuncture and sham procedures (TABLE 1) [26].

Mechanisms of action

Studies investigating the mechanisms of action of acupuncture in allergic rhinitis are rare. In an allergic rhinitis mouse model,

acupuncture and moxibustion (applying heat to acupuncture points) were shown to exert their effects by reducing the expression of substance P, STAT6, NF- κ B and iNOS [27]. However, more experimental research, in both animal and human models is needed to better understand the specific effect underlying acupuncture efficacy.

Cost-effectiveness

A recent randomized multicenter study conducted in Germany (n = 364) evaluated costs and quality of life in a health economic evaluation [28]. Patients receiving acupuncture or SA produced higher costs than patients in the control group receiving only systemic antihistamines or corticosteroids. However, patients in the acupuncture group gained significantly more quality-adjusted life-years compared with the control group. Depending on the scenario, the incremental cost-effectiveness ratio (ICER) for acupuncture patients was between €31,241 (~US\$38,569) and €118,889 (~US\$146,777) from society's perspective and between €20,807 (~US\$25,688) and €74,585 (~US\$92,080) from a third-party payer's perspective. The authors concluded that acupuncture is an effective intervention that results in improved quality of life in patients with SAR. However, in times of limited resources for healthcare, acupuncture for AR may not be a cost-effective intervention. In a previous non-blinded study, acupuncture plus usual care versus usual care alone in Germany (n = 981) resulted in increased quality of life (50.1 vs 47.0) and total treatment cost (763 vs 332 Euros). Acupuncture resulted in 17,377 Euro per quality-adjusted life-year (women 10,155 Euro, men 44,871 Euro) [29].

Atopic dermatitis

Atopic dermatitis (AD) is a non-contagious, chronically relapsing, inflammatory and highly pruritic skin disease with a chance to occur during lifetime of up to 20.5% worldwide [30–33]. It commonly presents during early infancy or childhood, but can persist into adulthood or present for the first time in adults. In industrialized countries, the AD prevalence has increased by two- to threefold over the past several decades.

AD has a wide clinical spectrum, ranging from minor forms, such as pityriasis alba or hand eczema, to major forms with erythrodermic dermatitis [34]. The disorder imposes a considerable social and economic burden with overall costs similar to those for asthma treatment. AD is characterized by poorly defined erythema with edema, vesicles and weeping in the acute stage and skin thickening in the chronic stage. Of the major clinical features, pruritus and chronic or relapsing eczematous lesions with typical shape and distribution are essential for diagnosis [30]. The cardinal symptom of itch is defined as unpleasant sensation inducing the desire to scratch [35,36]. AD significantly impairs quality of life and is often accompanied by serious complications, such as bacterial, viral or fungal superinfection of the skin [37,38]. A remarkable number of AD patients in France (49%), Germany (46%), Australia (49%) and the USA (34%) have turned to CAM alternatives such as herbal medicine, probiotics and acupuncture for relief [39].

Acupuncture

Several experimental studies have investigated the effect of acupuncture on itch in healthy volunteers [40]. Three RCT investigated the therapeutic effects of acupuncture on histamine-induced itch, with stimulation mainly at acupoint LI11 (FIGURE 2). These studies found a point-specific effect compared with placebo point stimulation [41–43]. A further RCT evaluated the effect of electrical ear acupuncture on histamine-iontophoresis-induced itch, showing a point-specific effect of ear points (most pain sensitive points of the skin, reflection point of spinal cord dorsal root, thalamic point and sensitive spinal cord point of the corresponding body region) in comparison to placebo points on allodynia [44].

A recent study found that acupuncture at acupoints LI11 and SP10 produced a significant reduction of clinically relevant type I hypersensitivity itch sensation (induced by grass, birch pollen, cat or house dust mite dander) after verum acupuncture treatment compared with placebo-point treatment and no treatment in patients with AD [45]. Regarding the preventive influence, the specific acupuncture effect (difference between verum and placebo-point acupuncture) diminished with regard to subjective itch sensation, whereas it increased the suppression of skin prick reactions. A possible explanation of acupuncture action may be a neural suppression of the axonal process associated with the wheal and flare reaction. Studies investigating this possible effect are needed.

Electrical stimulation of acupuncture points LI11 and SP10 and cetirizine treatment both produced significant itch reduction when compared with respective placebos and no therapy in AD patients using a validated on-off experimental itch model [46,47]. While preventive acupuncture (i.e., acupuncture applied before itch provocation) was similarly effective to cetirizine, abortive acupuncture (i.e., acupuncture applied concurrent to itch provocation) was significantly more effective than preventive acupuncture, SA or cetirizine. In fact, abortive acupuncture was the only intervention to reduce itch below the clinically relevant scratch urge threshold. Interestingly, preventive acupuncture was the only therapy to significantly reduce skin reactions (flare size). In this study, cognitive side effects (specifically regarding attention) were less pronounced for acupuncture compared with cetirizine. Although antihistamines are still the first-line systemic antipruritic treatment in AD, their specific clinical effect may be questioned: in this study cetirizine significantly reduced itch compared with placebo.

Salameh *et al.* [48] investigated the effect of acupuncture treatment (individual selection of points) twice a week in combination with a Chinese herbal formula *Dictamnii cortex (baixianpi)*, *Lonicerae flos (jinyinhua)*, *Moutan cortex (mudanpi)*, *Polygoni multiflori caulis (yejiaoteng)*, *Rehmanniae radix (shengdihuang)*, *Sophorae radix (kushen)* three-times daily for 12 weeks, showing an improvement of itch intensity of nearly 50% in an uncontrolled trial. Lee *et al.* compared the effect of acupressure using a 1.2 mm acupellet at the LI11 point, applying pressure for 3 min, three-times per week for 4 weeks with

Table 1. Summarizing clinical studies on acupuncture and allergic diseases (PubMed search including English-written studies until 3/2014).

Study (year)	Atopic disease/ number of patients	Main outcome parameter	Result	Comment	Ref.
<i>Intermittent allergic rhinitis</i>					
Brinkhaus <i>et al.</i> (2013)	Seasonal allergic rhinitis (n = 422) Acupuncture vs Sham vs Rescue medication	RQLQ RMS	After treatment (after 8 weeks): Verum 0.5/1.1 points better than sham and 0.7/ 1.45 better than rescue medication group (RQLQ/RMS) 1 year post-treatment: Verum 0.3/1.1 points better than sham (RQLQ/RMS)	RQLQ ranked from 0 to 6 RMS: comprising the weekly sum of daily medication needed (cetirizine 10 mg = 1 point, cetirizine 20 mg = 2 points, systemic steroid = 3 points)	[19]
Xue <i>et al.</i> (2002)	Seasonal allergic rhinitis (n = 30) Acupuncture vs Sham	Subjective symptoms on 5-point scale and relief medication after 4 weeks of treatment	Nasal as well as non-nasal symptom score significantly lower in Acupuncture (0.7/0.4) vs Sham (1.3/0.9). No difference in relief medication	Five-point scale used: 0 = no symptoms; 1 = very slight symptoms but noticeable; 2 = moderate severity of symptoms; 3 = severe symptoms; 4 = very severe symptoms	[20]
<i>Persistent allergic rhinitis</i>					
Petti <i>et al.</i> (2002)	Persistent allergic rhinitis (n = 90) Acupuncture vs Sham vs Control	Subjective symptoms on 5-point scale 24 h after one single treatment compared with before treatment	Verum (19.3–8.6) with significantly greater reduction of symptom score compared with sham (19.5–16.4) and control (19.3–20.8)	IL-10 reduced in verum group	[24]
Choi <i>et al.</i> (2013)	Persistent allergic rhinitis (n = 238) Acupuncture vs Sham vs Control	TNSS difference after 8 weeks to baseline	Verum 1.03 points better than Sham Verum 2.5 points better than waitlist control	TNSS: sum of the 4 symptoms: rhinorrhea, nasal congestion, sneezing, nasal itching scored on 0–3 scale	[21]
Ng <i>et al.</i> (2004)	Persistent allergic rhinitis in children (n = 72) Acupuncture vs Sham	Daily rhinitis score, symptom free days	After 2 months acupuncture: Verum: VAS score 4.6/10; Daily rhinitis score 5.6/10 Sham: VAS score 6.1/10; Daily rhinitis score 6.7/10		[22]
Xue <i>et al.</i> (2007)	Persistent allergic rhinitis (n = 80) Acupuncture vs Sham	TNSS difference after 8 weeks to baseline	Verum 13.2 points better than Sham	TNSS: twice daily	[23]
<i>Mixed (no differentiation between intermittent and persistent allergic rhinitis)</i>					
Magnusson <i>et al.</i> (2004)	Allergic rhinitis (n = 40) Acupuncture vs Sham	Mean tendency (improvement, unchanged or worsening) in 12-month period including initial 3-month treatment period	No significant difference in clinical symptoms	No evaluation of direct treatment effect published, No differentiation between seasonal as well as persistent allergic rhinitis results	[26]

FEV(1): Forced expiratory volume in 1 s; FVC: Forced vital capacity; ICER: Incremental cost–effectiveness ratio; IHS: Inhaled steroids; IGA: Investigator's global assessment; PA: Placebo point acupuncture; PFV: Peak flow variability; QALYs: Quality-adjusted life-years; RMS: Rescue medication score; RQLQ: Rhinitis quality of life questionnaire score; STAIC: State-Trait Anxiety Inventory for Children; TNSS: Total nasal symptom score; VA: Verum point acupuncture.

Table 1. Summarizing clinical studies on acupuncture and allergic diseases (PubMed search including English-written studies until 3/2014) (cont.).

Study (year)	Atopic disease/ number of patients	Main outcome parameter	Result	Comment	Ref.
<i>Mixed (no differentiation between intermittent and persistent allergic rhinitis) (cont.)</i>					
Brinkhaus <i>et al.</i> (2008)	Allergic rhinitis (n = 981) Acupuncture vs Control	RQLQ after 3-month treatment	Improvement: post-treatment: Acupuncture 1.48 Control group no intervention 0.50	No differentiation between seasonal as well as persistent allergic rhinitis results	[25]
<i>Cost-effectiveness acupuncture for allergic rhinitis</i>					
Reinhold <i>et al.</i> (2013)	Seasonal allergic rhinitis (n = 364) Acupuncture vs Sham vs Rescue Medication	Costs and Health-related quality-of-life study by Choi <i>et al.</i> [21]	ICER for acupuncture patients was between €31,241 (~US \$38,569) and €118,889 (~US \$146,777) from society's perspective and between €20,807 (~US\$25,688) and €74,585 (~US\$92,080) from a third-party payer's perspective	ICER = mean total costs (acupuncture group-rescue medication group)/mean QALYs	[28]
Witt <i>et al.</i> (2009)	Allergic rhinitis (n = 981) Acupuncture vs Control	Quality of life (SF-36 Health Survey), cost and QALY at 3 months	Acupuncture plus usual care vs usual care: Quality of life: 50.1 vs 47.0 total treatment cost 763 vs 332 Euros 17,377 Euro per quality adjusted life year (women 10,155 Euro, men 44,871 Euro)		[29]
<i>Atopic eczema</i>					
Pfab <i>et al.</i> (2010)	Histamine itch atopic eczema (n = 30; cross-over design) Acupuncture vs Placebo vs Control	Mean itch intensity within 10 min after itch induction by VAS	Mean itch intensity was significantly lower in VA (35.7) compared with NA (45.9) and PA (40.4) regarding the direct effect; and significantly lower in VA (34.3) and PA (37.8) compared with NA (44.6) regarding the preventive effect	Scratch threshold defined at 33% of the VAS VA: Verum point acupuncture PA: Placebo point acupuncture NA: No intervention	[45]
Pfab <i>et al.</i> (2008, 2012)	Allergen itch atopic eczema (n = 20; cross-over design) Acupuncture vs Cetirizine vs Placebos vs Control	Mean itch intensity (VAS)	Mean itch intensity significantly lower following VAa (31.9) compared with all other groups (PAa: 36.5; VC: 36.8; VAp: 37.6; PC: 39.8; PAp: 39.9; NI: 45.7; p < 0.05)	NI: no-intervention control; PAp: Placebo acupuncture preventive; PAa: Placebo acupuncture abortive; PC: placebo cetirizine; VA: verum acupuncture; VC: Verum cetirizine	[46,49]
Lee <i>et al.</i> (2012)	Atopic eczema (n = 12) Acupressure vs control with no intervention; unblinded	Itch intensity (VAS) after 4 weeks compared with baseline, IGA and the Eczema Area and Severity Index	Significant decrease in VAS and IGA in Acupressure compared with control group	Low quality study, no precise results given	[49]
Pfab <i>et al.</i> (2011)	Atopic eczema (n = 10) Acupuncture vs control with no intervention; unblinded	Mean itch intensity (VAS) and <i>in vitro</i> basophil CD63 expression upon allergen stimulation after 15 and 33 days of therapy	Mean itch intensity significantly lower in the acupuncture group (~25% at day 15; ~24% at day 33) Acupuncture group showed less CD63 positive basophils than control group		[50]

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Table 1. Summarizing clinical studies on acupuncture and allergic diseases (PubMed search including English-written studies until 3/2014) (cont.).

Study (year)	Atopic disease/ number of patients	Main outcome parameter	Result	Comment	Ref.
Asthma					
Karlson and Bennicke (2013)	Asthma in children (n = 52) Acupuncture plus routine care vs routine care; unblinded	Symptom score and use of inhaled steroids at end of 3-month treatment and 8-month follow-up	Significant reductions were observed in subjective asthma symptoms and in use of IHS and $\beta(2)$ agonists in both groups at 3 months. Compared with the control group, the reduction in asthma symptoms ($p = 0.0376$) and use of IHS ($p = 0.0005$) was significantly larger in the intervention symptom scores and medication use were not different between the groups at 8 months after completion of acupuncture group		[64]
Scheewe <i>et al.</i> (2011)	Asthma in children (n = 93) Acupuncture plus routine care vs routine care; unblinded	Severity of symptoms, lung function, illness-specific quality of life (Paediatric Asthma Quality of Life Questionnaire) and general and asthma-specific level of anxiety (STAIC)	Peak expiratory flow variability and rehabilitation response at the time of discharge concerning perceived anxiety (STAIC-S). significantly better in acupuncture group. Lung function tests with no differences between groups		[65]
Stockert <i>et al.</i> (2007)	Asthma in children (n = 17) Laser acupuncture and probiotics vs placebo	PFV and FEV(1) and quality of life by questionnaire	Laser acupuncture and probiotics significantly decreased mean weekly PFV as a measurement of bronchial hyperreactivity by -17.4% in the TCM group vs 2.2% in the control group ($p = 0.034$). No significant effect was detected for FEV(1), quality of life criteria and additional medication		[69]
Yang <i>et al.</i> (2013)	Allergic asthma (n = 100) and chronic bronchitis (n = 74) Acupuncture vs No intervention control	Overall clinical efficacy and various experimental parameters	Overall efficacy of acupuncture on patients with allergic asthma and chronic bronchitis at the end of one course of treatment (after 5 weeks) was 85% (85/100) and 85.14% (63/74), respectively. 27 patients with allergic asthma and 25 with chronic bronchitis were followed-up. For patients with allergic asthma and chronic bronchitis, the efficacy was 37.04 and 28% after 1 year of treatment, respectively; after 3 years of treatment, the clinical control rates were 22.22 and 12%, respectively	Unclear definition of overall efficacy	[75]

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Table 1. Summarizing clinical studies on acupuncture and allergic diseases (PubMed search including English-written studies until 3/2014) (cont.).

Study (year)	Atopic disease/ number of patients	Main outcome parameter	Result	Comment	Ref.
<i>Asthma (cont.)</i>					
Ngai et al. (2009)	Exercise-induced asthma (n = 15; crossover design) Different Electrical acupuncture stimulation settings vs placebo	FEV(1) and FVC before, immediately after and at 20-min intervals post-exercise for 1 h	Immediately after exercise, FEV (1) and FVC rose in group 2 (1.3 and 0.6%), but decreased in group 1 (-5.1 and -1.8%), and more so in group 3 (-11.6 and -7.2%). The differences became even more pronounced at 20, 40 and 60 min post-exercise	Group 1: Acu-TENS over acupuncture points Lieque and Dingchuan for 45 min prior to a symptom-limited treadmill exercise test. Group 2: Acu-TENS similarly applied prior to and throughout the exercise test Group 3: mimicked group 1 but without any electrical output from the device	[72]
<i>Cost-effectiveness acupuncture for asthma</i>					
Reinhold et al. (2013)	Asthma	Cost-effectiveness, QALYs and ICER	Acupuncture with significantly higher costs compared with control patients (overall costs: €860.76 vs €518.80; p = 0.003; asthma-related costs: €517.52 vs €144.87; p < 0.001). Acupuncture with superior effectiveness in terms of QALYs. ICER between €23,231 (overall) and €25,315 (diagnosis-specific) per additional QALY. When using German acupuncture prices of year 2012, the ICER would improve to €12,810 (overall) vs €14,911 (diagnosis-specific) per QALY gained	Additional costs seem essentially driven by acupuncture costs themselves (€378.40)	[74]

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standard-of-care therapy alone showing an improvement in pruritus and lichenification [49]. However, large randomized, well-controlled clinical trials are still lacking (TABLE 1) [50].

Cost-effectiveness

To the authors' knowledge, there is no study evaluating cost-effectiveness of acupuncture in AD to date.

Mechanisms of action

Possible mechanisms for itch reduction of acupuncture in patients with AD include reduction of *in vitro* allergen-induced basophil activation [50] and modulation of brain areas that are involved in itch processing [51,52]. In a recent neuroimaging study, allergen itch was experimentally provoked in patients with AD [53]. Acupuncture reduced insula and striatum activation during an increasing itch phase and premotor activation

during a peak itch phase, when evoked itch sensation had reached a plateau. Neither anti-histamine nor SA reduced itch or altered brain response to evoked itch. Greater itch reduction following acupuncture was associated with greater reduction in putamen response to increasing itch, specifically implicating this region in acupuncture's anti-pruritic. Furthermore, other basic research studies have suggested that acupuncture may also modulate neurotransmitters and peripheral hormone levels, such as opioid peptides, adrenocorticotrophic hormone and somatostatin [54–57].

Asthma

Asthma is a chronically relapsing inflammatory disease of the respiratory tract, characterized by bronchial hyperreactivity and variable congestion. It is one of the most common chronic diseases with a prevalence of 10% in children and 5% in adults [58].



Figure 2. Acupuncture point LI11 (Quchi).

The prevalence of reported CAM use among children with asthma ranges between 13 and 65%, with vitamins, homeopathy and acupuncture being the most popular modalities [59–63].

Acupuncture

A randomized controlled non-blinded trial in 52 Danish pre-school children aged between 6 months and 6 years, reported a reduction in asthma symptoms and use of inhaled steroids in the acupuncture group (10 treatments within 3 months) compared with no intervention at the end of treatment [64]. Symptom scores and medication use, however, were not different between the groups at 8 months after completion of acupuncture. A further RCT in 93 children and adolescents with bronchial asthma compared the effect of 12 sessions of acupuncture plus add-on therapy (asthma sports, climate therapy and behavioral training) to add-on therapy alone [65]. After additional acupuncture, amelioration of peak expiratory flow variability and anxiety was reported, without any difference in objective lung function tests and quality of life between study groups.

A systematic review of laser acupuncture in childhood asthma included three RCTs with a total number of 176 patients [66]: one RCT with a parallel group design showed positive results, while two crossover RCTs generated negative results. The authors concluded that to date no compelling evidence exists to suggest that laser acupuncture is an effective treatment for childhood asthma. A few further small experimental and clinical studies point toward efficacy of acupuncture in asthma [67–72]. Large well-controlled RCTs are, however, still lacking (TABLE 1).

Sham acupuncture

Wechsler *et al.* [73] compared the effect of an albuterol inhaler, a placebo inhaler, SA or no intervention on maximum forced expiratory volume in 1 s (FEV(1) in 39 patients with asthma in a crossover design. Albuterol resulted in a 20% increase in FEV(1), as compared with approximately 7% with each of the other three control groups ($p < 0.001$). However, while patients' reports of improvement after the intervention did not differ significantly for the albuterol inhaler (50% improvement), placebo inhaler (45%) or SA

(46%), the subjective improvement with all three of these interventions was significantly greater than that with the no-intervention control (21%) ($p < 0.001$). This study showed that 'non-specific' effects, including those supporting SA, can be clinically meaningful and can rival the effects of active medication in patients with asthma. The definition of SA as a viable placebo control from acupuncture is fraught with difficulty and current research is aimed at understanding which aspects of acupuncture are important for clinical efficacy and thereby developing a better form of placebo acupuncture for future use.

Cost-effectiveness

Reinhold *et al.* [74] evaluated the resource consumption, costs and health-related quality of life at baseline, and after 3 and 6 months in 306 patients randomized to either acupuncture treatments or wait list control. Both groups were free to use routine care treatment. Acupuncture treatment was associated with significantly higher costs compared with control patients (overall costs: €860.76 vs €518.80; $p = 0.003$; asthma-related costs: €517.52 vs €144.87; $p < 0.001$). These additional costs seem essentially driven by acupuncture costs themselves (€378.40). However, acupuncture was associated with superior effectiveness in terms of quality-adjusted life-years (QALYs). Resulting ICER lay between €23,231 (overall) and €25,315 (diagnosis-specific) per additional QALY. When using German acupuncture prices of year 2012, the ICER would improve to €12,810 (overall) versus €14,911 (diagnosis-specific) per QALY gained. In this study, acupuncture in addition to routine care resulted in additional costs and better effects in terms of patients' quality of life and therefore seemed to be a cost-effective add-on treatment.

Mechanisms of action

Despite of the growing number of clinical studies, little is known regarding the biological basis of acupuncture treatment for asthma. Yang *et al.* [75] examined the immunomodulatory effects of a 5-week acupuncture treatment (GV14, BL12 and BL13; three-times per week) in 174 patients with allergic asthma and chronic bronchitis. After treatment, the concentrations of sIgA and total IgA in the saliva ($p < 0.01$, $p < 0.02$) and nasal secretions ($p < 0.02$, $p < 0.02$) were significantly decreased and the levels of total IgE in sera ($p < 0.001$), the counts of IL-2R + T lymphocytes ($p < 0.001$) and the absolute and differential numbers of eosinophils ($p < 0.01$, $p < 0.01$) in the peripheral blood were also significantly decreased. The numbers of CD3⁺, CD4⁺ and CD8⁺ T lymphocytes in the peripheral blood were significantly increased in the allergic asthmatics treated by acupuncture ($p < 0.001$, $p < 0.01$ and $p < 0.001$, respectively). The concentration of cortisol in the plasma of asthmatic patients did not change significantly after the acupuncture treatment ($p > 0.05$). A proteomic analysis of acupuncture-treated rats with asthma onset revealed downregulation of proinflammatory proteins (e.g., S100A8, RAGE and S100A11) and upregulation of anti-inflammatory proteins (e.g., CC10, ANXA5 and sRAGE). However, further functional

investigation of these potentially acupuncture-specific effector proteins should be carried out to verify these results [76].

Side effects

In general, significant side effects of conventional electro- or manual acupuncture are rare. A large prospective observational study (n = 229,230) adverse effects in patients who received acupuncture treatment for chronic osteoarthritis pain of the knee or hip, low back pain, neck pain or headache, allergic rhinitis, asthma or dysmenorrhea were documented; 8.6% reported experiencing at least one adverse effect. Common adverse effects were bleedings or hematoma (6.1% of patients, 58% of all adverse effects), pain (1.7%) and vegetative symptoms (0.7%). Two patients experienced a pneumothorax (one needed hospital treatment, the other observation only) [77]. In the hand of well-trained therapists, acupuncture is considered a relatively safe therapy [78].

Conclusion

The authors feel that acupuncture plays an increasingly important role in evidence-based treatment of allergies. There are several randomized clinical trials supporting the use of acupuncture in allergic rhinitis as well as the symptom of itch. Experimental studies point to an effect of acupuncture in atopic eczema and asthma; however, large RCTs are lacking. Acupuncture for the treatment of other allergic diseases such as contact eczema, drug rashes or anaphylaxis cannot be recommended to date. Further research is needed to more clearly identify clinical effects above and beyond placebo and mechanisms of action.

Expert commentary

Growing evidence for its effectiveness and limited side effects in the treatment of atopic diseases and their main symptom of itch characterize acupuncture as a tempting intervention in a hospital and private setting. Further large-scale well-controlled clinical as well as experimental studies, however, are much needed to further elucidate the quantity of a clinical effect, the cost-effectiveness and included mechanisms of action. The role of acupuncture in further allergological diseases has so far not been thoroughly studied.

Five-year view

Further large-scale multi-center randomized and well-controlled trials as well as experimental trials will clarify the role of acupuncture in atopic diseases in the healthcare system. Smaller studies will intend to approach evaluation of acupuncture in diseases that have so far been neglected.

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Key issues

- High percentage of patients use acupuncture for treatment of allergies.
- Two large multi-center randomized controlled trial (RCTs) show acupuncture effects on allergic rhinitis.
- Smaller RCTs and experimental studies point toward effect on itch, atopic dermatitis and asthma. However, so far no large RCTs have been carried out.
- Acupuncture for the treatment of allergic rhinitis and asthma seems cost-effective.
- Lack of scientific data on treatment of other allergic diseases.
- Modest side effects.

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