

Complementary and alternative medicine for allergic rhinitis

Li-Xing Man

Department of Otolaryngology, University of Pittsburgh
School of Medicine, Pittsburgh, Pennsylvania, USA

Correspondence to Li-Xing Man, MD, MSc,
Department of Otolaryngology, University of Pittsburgh
School of Medicine, 203 Lothrop Street, Suite 500,
Pittsburgh, PA 15213, USA
Tel: +1 412 647 4789; fax: +1 412 648 6300;
e-mail: manl@upmc.edu

Current Opinion in Otolaryngology & Head and Neck Surgery 2009, 17:226–231

Purpose of review

Otolaryngologists and other physicians who diagnose and treat allergic rhinitis encounter patients who use complementary medicine and alternative remedies. This article reviews the recent literature regarding complementary and alternative therapies for the treatment of allergic rhinitis.

Recent findings

There are a myriad of modalities for treating allergic rhinitis. Few are studied with rigorous randomized, double-blind, placebo-controlled trials for clinical efficacy. Often, the biological mechanisms and adverse effects are even less well understood. A few therapies, including spirulina, butterbur, and phototherapy hold some promise. Thus far, complementary and alternative therapies have not been integrated into the general treatment armamentarium of allergic rhinitis.

Summary

Several studies report beneficial effects of certain alternative treatments for allergic rhinitis. Additional insight into the mechanisms of action, short-term and long-term effects, and adverse events is needed.

Keywords

allergy, alternative medicine, complementary medicine, rhinitis

Curr Opin Otolaryngol Head Neck Surg 17:226–231
© 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins
1068-9508

Introduction

Complementary and alternative medicines (CAMs) are frequently used to treat allergic rhinitis worldwide. The percentage of adults who are using or have used CAM treatments ranges from 25 to 50% in France and Australia [1,2]. Among adults in the United States, over one-third report using CAM treatments [3], and up to one-half with asthma or rhinosinusitis have tried such treatments [4]. The use of CAM therapies has increased over the past several decades, and trends indicate that use will continue to increase [2,3].

Given the increasing prevalence of allergic diseases, it is essential that otolaryngologists and other physicians treating allergic rhinitis understand the array of CAM therapies used by their patients. Knowledge of the clinical efficacy as well as adverse effects of these treatments is necessary so that healthcare practitioners can appropriately guide their patients, especially because over 50% of those using CAM therapies do not disclose their use to their physicians [2,5]. This article reviews the current literature regarding various CAM treatments for allergic rhinitis.

Acupuncture

Developed from traditional Chinese medicine techniques, acupuncture involves the stimulation of specific

points located along lines of meridians corresponding to the flow of energy through the body. Traditionally, these acupoints were stimulated using fine needles. Modern acupuncture has evolved to include the application of pressure, the use of electric currents, and the use of low-intensity lasers to stimulate the acupoints.

Acupuncture is the third most common CAM treatment for allergies in Germany [6]. Acupuncture is thought to modulate levels of cytokines and other inflammatory mediators, and one recent study showed decreased expression of interleukin (IL)-1 receptor- α up to 4 weeks after therapy [7]. Rigorous evidence on the scientific basis and clinical efficacy of acupuncture is lacking [8,9].

Most clinical studies are nonrandomized and poorly designed. A recent systematic review identified only seven randomized placebo-controlled trials, with only two of high methodological quality [10^{••}]. Meta-analysis failed to show benefits of acupuncture as measured by symptom severity scores or serum IgE measure titers. Two additional randomized controlled trials (RCTs) have been subsequently published. One large study [11] comparing acupuncture and conventional treatment with conventional therapy alone showed significantly improved symptom scores at the end of a 3-month treatment period. The benefit persisted at 6 months, but the symptom scores of the control group approached those of the treatment groups. This study was not placebo-controlled by either

sham or inactive acupuncture. The second study [12^{*}] evaluated the use of acupuncture versus sham acupuncture in 80 patients with perennial allergic rhinitis over an 8-week treatment and 12-week follow-up period. The active acupuncture group had significantly decreased total nasal symptom score and rhinorrhea at the end of both treatment and follow-up periods compared with the sham group. This was not correlated with any significant reduction in the use of antihistamines, nasal decongestants, or intranasal steroids in the active acupuncture group. Based on the current evidence, there is insufficient proof to substantiate or refute the use of acupuncture in allergic rhinitis.

Dietary and nutritional supplements

There is an increase interest in dietary and nutritional supplements for the treatment of allergic rhinitis.

Capsaicin

Capsaicin (8-methyl-*n*-vanillyl-6-nonenamide), the pungent component of chili peppers, is used topically as an ointment for pain relief in peripheral neuropathy. Capsaicin is thought to block neuropeptides, especially substance P, via the capsaicin [transient receptor potential vanilloid subfamily 1 (TRPV1)] receptor, which is expressed in various nasal mucosal cells [13]. Nasal mucosal nerve fibers immunoreactive to substance P have been found to be increased in patients with allergic rhinitis [14], and stimulation of the TRPV1 receptor with capsaicin has been shown to induce the production of IL-6 [15]. A recent Cochrane Systematic Review of capsaicin for allergic rhinitis identified only one RCT meeting study criteria [16]. In this study, capsaicin was not effective in treating symptoms of perennial allergic rhinitis to dust mites [17].

Fish oil and ω -3 polyunsaturated fatty acids

Fish oil contains eicosapentaenoic and docosahexaenoic acids, which are ω -3 polyunsaturated fatty acids (ω -3 PUFA). They have anti-inflammatory effects *in vitro* and have a wide range of beneficial health effects in various chronic inflammatory diseases [18]. Epidemiologic evidence suggests a link between declining consumption of ω -3 PUFA and a rise in the prevalence of allergic diseases [19^{*},20]. Meta-analyses of RCTs evaluating fish oil supplementation in adults for allergic diseases such as asthma and atopic dermatitis have shown limited benefit [18]. There are few data on allergic rhinitis. One older double-blind, placebo-controlled trial of fish oil supplementation in adults showed no significant differences in nasal symptoms between groups [21]. On the other hand, there is recent evidence in cross-sectional studies [22,23^{*}] that the intake of eicosapentaenoic and docosahexaenoic acids may be associated with a reduced prevalence of allergic rhinitis. Maternal perinatal consumption of fish

oil and ω -3 PUFA has been postulated to prevent the development of allergic disease in infants [19^{*}].

Spirulina

Spirulina, the dried biomass of the blue-green algae *Arthospira platensis*, has a long history as a food source. It is believed to have been a food source for the Aztecs in 16th-century Mexico and the Kanem Empire in 9th century Chad. Spirulina is rich in protein (up to 70% by dry weight), containing all essential amino acids. It also contains essential fatty acids, vitamins, minerals, and β -carotene. The supplement is considered to be safe for human consumption by the US Food and Drug Administration. Spirulina is thought to inhibit histamine release from mast cells [24^{*},25]. In one RCT, patients taking spirulina for 12 weeks had a significant reduction in blood IL-4 levels [26]. More recently, a double-blind, placebo-controlled study [27^{**}] demonstrated a significant reduction in nasal symptom scores in clinically diagnosed allergic rhinitis patients taking spirulina daily for 6 months. Although the preliminary data are promising, additional studies are needed to determine both the efficacy and the active pharmacologic agent of spirulina.

Herbal medicines

There are numerous herbal remedies for allergic rhinitis, due in part to their history of use in the traditional Indian Ayurvedic and Chinese medical systems. A well written systematic review of herbal medicines for the treatment of allergy has recently been published [28^{**}]. Recent updates to the literature for some of the most well known herbal medicines are discussed below.

Ayurvedic medicine

Aller-7 is a formulation of seven Indian herbal extracts that has shown some efficacy in relieving symptoms of allergic rhinitis [28^{**},29]. It is thought to act through antioxidant and anti-inflammatory pathways [30–32]. Tinofend (Verdure Sciences, Noblesville, Indiana, USA), *Tinospora cordifolia*, is an Indian herbal tablet that has also been shown to offer symptom relief compared with placebo [33]. There have been no recent data to support the use of these formulations, although a review of Tinofend has been published recently [34].

Butterbur

Butterbur (*Petasites hybridus*) is a perennial shrub native to Europe, southwestern Asia, and North America. The leaf and root extracts contain sesquiterpenes (petasins) as pharmacologically active compounds that have been used to treat asthma, migraine headaches, and smooth muscle spasms. Preclinical studies suggest that petasins may inhibit leukotriene and histamine synthesis [28^{**}] as well as mast cell degranulation [35]. Raw butterbur extract

contains pyrrolizidine alkaloids that are hepatotoxic and carcinogenic [36[•]]. Petasin (Ze 339), an extract of butterbur leaves with the alkaloids removed, was approved in 2003 in Switzerland for the treatment of seasonal allergic rhinitis (Tesalin; Zeller AG, Romanshorn, Switzerland). A postmarketing survey found side effects were mainly nonspecific gastrointestinal complaints occurring at a rate of 4% [37].

In randomized, double-blind, placebo-controlled studies, Ze 339 was found to significantly improve symptom scores compared with placebo [38] and to be comparable in efficacy with cetirizine [39] and fexofenadine [40,41]. However, another double-blind, placebo-controlled crossover study [42] demonstrated no difference in symptom scores and peak nasal airflow compared with placebo. There have been no newer trials published.

The long-term effects of butterbur are unknown. Moreover, the therapeutic mechanism remains uncertain. In a study comparing Ze 339 with an antihistamine and placebo in skin-prick tests [43], Ze 339 did not inhibit skin-test reactivity to the allergens tested, raising the question of whether Ze 339 has any antihistaminic effect. Although preliminary data suggest butterbur may be effective in allergic rhinitis, additional studies are needed to better elucidate the efficacy, safety, and pharmacologic mechanism.

Traditional Chinese medicine

Laboratory studies suggest the Chinese herbal remedy Shi-bi-lin may inhibit the release of IL-4 and tumor necrosis factor- α (TNF- α) [44]. Shi-bi-lin was found to decrease sneezing, nasal scratching, and thromboxane B2 levels in a guinea pig model [45,46]. A human safety and efficacy study has been recently completed [47]. Patients with perennial allergic rhinitis confirmed with skin-prick tests were randomized to low-dose Shi-bi-lin or placebo in a double-blind trial. Symptoms scores and quality-of-life indicators improved in both treatment and placebo groups and there was no statistically significant difference between groups. However, symptoms remained improved 2 weeks after the completion of Shi-bi-lin treatment, whereas symptoms returned to baseline in the placebo group.

Xiao-qing-long-tang, better known as Sho-seiryu-to (TJ-19) in Japanese, an extract of eight traditional Chinese herbs is used to treat the common cold, asthma, and allergic rhinitis. It is marketed in Japan but is not available in the United States as ephedra is one of the ingredients. It was tested in patients with perennial allergic rhinitis with efficacy for nasal symptoms [28^{••}]. Sho-seiryu-to has recently been found to inhibit histamine signaling and IL-4 and IL-5 gene expression in a rat model [48].

Biminne [49], an 11-herb formulation, and RCM-101 [50], an 18-herb formulation, have been found to improve symptom scores when compared with placebo in older, single-study trials, but these results have not been replicated. Recent research has focused on the mechanisms of RCM-101. In animal models, RCM-101 inhibited histamine release [51], prostaglandin E2 production [51,52], and nitric oxide synthesis [52,53].

Other herbal remedies

Single randomized, controlled trials for *Urtica dioica* (stinging nettle), grape seed extract, and *Perilla frutescens* for the treatment of allergic rhinitis have been recently reviewed [28^{••},54[•]]. There have been no recent new data to support their use.

Homeopathy

Homeopathy is based on the premise that diseases can be cured if the same substances that provoke the symptoms of the disease are given in ultra diluted form. Homeopathic treatments are selected on the basis of symptoms and prepared with repeated dilution and 'potentiation'.

There are several controlled studies for homeopathy and allergic rhinitis. In the most recent randomized, double-blind controlled trial, investigators compared a homeopathic preparation of grass, tree, and weed allergens with placebo and found significantly better quality-of-life questionnaire scores in patients in the active treatment group [55]. Studies showing positive results for homeopathy are counterbalanced with a comparable number of negative studies [56,57]. Some homeopathic preparations actually exacerbated symptoms [58,59].

Although the published literature suggests homeopathy has some effect, there is controversy on whether the results of homeopathy are actually placebo effects [60]. A recent study [61] comparing placebo-controlled trials of homeopathy matched 1:1 to conventional allopathic treatment by disease and outcome concluded that the evidence for specific beneficial effects of homeopathic treatments is weak after controlling for biases and confounding factors. Overall, there is inadequate evidence to recommend homeopathy for the treatment of allergic rhinitis.

Phototherapy

Phototherapy with ultraviolet (UV) light is used for the treatment of immune-mediated dermatologic conditions such as psoriasis. The therapeutic mechanism of UV light is attributed to its immunosuppressive effects, including the reduction of antigen presentation by dendritic cells, inhibition of pro-inflammatory cytokine synthesis and release, and induction of apoptosis in immune cells

[62**]. One group in Hungary has studied the use of narrow-band UV light as intranasal therapy for allergic rhinitis. Early uncontrolled studies using a 308 nm UV-B laser [63] and UV-A light and psoralen [64] showed improvement in nasal symptom scores. A randomized, double-blind controlled trial using a combination of low-dose UV-B, low-dose UV-A, and visible light in patients with ragweed-induced allergic rhinitis resulted in decreased nasal symptom scores and reduced levels of eosinophils and IL-5 [65]. The researchers then found the combination phototherapy to be superior to fexofenadine in the reduction of rhinorrhea, nasal obstruction, and total symptom score [66]. The only side effect of intranasal phototherapy in these studies was dryness of the nasal mucosa. These investigators have developed a phototherapeutic device (Rhinolight; Rhinolight Ltd., Szeged, Hungary) for the intranasal delivery of combination of low-dose UV-B, low-dose UV-A, and visible light that is approved and marketed in Hungary [62**].

UV light induces DNA damage and, at high doses, is associated with carcinogenesis. A recent study of nasal cytology samples from patients undergoing intranasal phototherapy [67*] demonstrated UV-specific markers of photodamage 10 days after treatment to be similar to baseline. Another study [68] suggested markers of DNA damage found elevated immediately after phototherapy were not present within several days of treatment. Nevertheless, the long-term effect of phototherapy on nasal mucosa is unknown.

Physical techniques and other complementary treatments

Physical techniques (biofeedback, breathing control, chiropractic manipulation, and yoga) have not been studied in allergic rhinitis. One recent cross-sectional study of children in western Europe [69] found the prevalence of allergies was lower in children from anthroposophic families. Anthroposophy is a spiritual philosophy based on a belief that an objective spiritual world is accessible through inner development. The anthroposophic lifestyle includes avoiding antibiotics, antipyretics, and vaccinations. No RCTs on allergic rhinitis have been performed with other complementary treatments, including anthroposophy, aromatherapy, Bach's flowers, chromotherapy, clinical ecology, Hopi candles, hydrocolon, iridology, reflexology, and urine therapy.

Conclusion

Evidence on the therapeutic efficacy of CAM treatments for allergic rhinitis is limited. None of the therapies reviewed was superior to existing standard allopathic treatments, although some beneficial effects compared with placebo. The data on acupuncture are mixed, with

some RCTs demonstrating efficacy while others showed no effect. Fish oil and ω -3 PUFA intake is associated with decreased prevalence of allergic rhinitis in epidemiological studies, but not corroborated by RCTs. Spirulina and butterbur are two herbal remedies that show promise and may eventually prove to be useful when used in combination with established treatments. Phototherapy is a new modality for allergic rhinitis that is grounded in scientific and clinical data from the dermatology literature. Additional data on the mechanisms, clinical efficacy, drug interactions, and side effects of CAM treatments are needed.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 247–248).

- 1 Fisher P, Ward A. Complementary medicine in Europe. *BMJ* 1994; 309:107–111.
- 2 MacLennan AH, Myers SP, Taylor AW. The continuing use of complementary and alternative medicine in South Australia: costs and beliefs in 2004. *Med J Aust* 2006; 184:27–31.
- 3 Tindle HA, Davis RB, Phillips RS, Eisenberg DM. Trends in use of complementary and alternative medicine by US adults: 1997–2002. *Altern Ther Health Med* 2005; 11:42–49.
- 4 Blanc PD, Trupin L, Earnest G, *et al.* Alternative therapies among adults with a reported diagnosis of asthma or rhinosinusitis: data from a population-based survey. *Chest* 2001; 120:1461–1467.
- 5 Gardiner P, Graham R, Legedza AT, *et al.* Factors associated with herbal therapy use by adults in the United States. *Altern Ther Health Med* 2007; 13:22–29.
- 6 Schafer T, Riehle A, Wichmann HE, Ring J. Alternative medicine in allergies – prevalence, patterns of use, and costs. *Allergy* 2002; 57:694–700.
- 7 Shiue HS, Lee YS, Tsai CN, *et al.* DNA microarray analysis of the effect on inflammation in patients treated with acupuncture for allergic rhinitis. *J Altern Complement Med* 2008; 14:689–698.
- 8 Ernst E. Acupuncture – a critical analysis. *J Intern Med* 2006; 259:125–137.
- 9 Ernst E. The recent history of acupuncture. *Am J Med* 2008; 121:1027–1028.
- 10 Roberts J, Huissoon A, Dretzke J, *et al.* A systematic review of the clinical effectiveness of acupuncture for allergic rhinitis. *BMC Complement Altern Med* 2008; 8:13.
- This meta-analysis reviews the biological plausibility of acupuncture and summarizes the RCT data on acupuncture for allergic rhinitis.
- 11 Brinkhaus B, Witt CM, Jena S, *et al.* Acupuncture in patients with allergic rhinitis: a pragmatic randomized trial. *Ann Allergy Asthma Immunol* 2008; 101:535–543.
- 12 Xue CC, An X, Cheung TP, *et al.* Acupuncture for persistent allergic rhinitis: a randomised, sham-controlled trial. *Med J Aust* 2007; 187:337–341.
- This RCT is one of the most well conducted studies evaluating acupuncture for allergic rhinitis. Total symptom score and rhinorrhea symptom score were significantly improved by the use of acupuncture (versus sham), but other individual symptom scores and rescue medication use with conventional therapies were not statically affected. This study highlights the difficulties in interpreting conflicting results.
- 13 Seki N, Shirasaki H, Kikuchi M, *et al.* Expression and localization of TRPV1 in human nasal mucosa. *Rhinology* 2006; 44:128–134.
- 14 O'Hanlon S, Facer P, Simpson KD, *et al.* Neuronal markers in allergic rhinitis: expression and correlation with sensory testing. *Laryngoscope* 2007; 117:1519–1527.
- 15 Seki N, Shirasaki H, Kikuchi M, Himi T. Capsaicin induces the production of IL-6 in human upper respiratory epithelial cells. *Life Sci* 2007; 80:1592–1597.
- 16 Cheng J, Yang XN, Liu X, Zhang SP. Capsaicin for allergic rhinitis in adults. *Cochrane Database Syst Rev* 2006; CD004460.

- 17 Gerth Van Wijk R, Terreehorst IT, Mulder PG, *et al*. Intranasal capsaicin is lacking therapeutic effect in perennial allergic rhinitis to house dust mite. A placebo-controlled study. *Clin Exp Allergy* 2000; 30:1792–1798.
- 18 Dunstan JA, Prescott SL. Does fish oil supplementation in pregnancy reduce the risk of allergic disease in infants? *Curr Opin Allergy Clin Immunol* 2005; 5:215–221.
- 19 Blumer N, Renz H. Consumption of omega3-fatty acids during perinatal life:
 - role in immuno-modulation and allergy prevention. *J Perinat Med* 2007; 35 (Suppl 1):S12–S18.
 This review summarizes the evidence for immunomodulatory effects of ω -3 PUFA supplementation during the perinatal period on the developing immune system of the child.
- 20 Hwang I, Cha A, Lee H, *et al*. N-3 polyunsaturated fatty acids and atopy in Korean preschoolers. *Lipids* 2007; 42:345–349.
- 21 Thien FC, Mencia-Huerta JM, Lee TH. Dietary fish oil effects on seasonal hay fever and asthma in pollen-sensitive subjects. *Am Rev Respir Dis* 1993; 147:1138–1143.
- 22 Hoff S, Seiler H, Heinrich J, *et al*. Allergic sensitisation and allergic rhinitis are associated with n-3 polyunsaturated fatty acids in the diet and in red blood cell membranes. *Eur J Clin Nutr* 2005; 59:1071–1080.
- 23 Miyake Y, Sasaki S, Tanaka K, *et al*. Fish and fat intake and prevalence of allergic rhinitis in Japanese females: the Osaka Maternal and Child Health Study. *J Am Coll Nutr* 2007; 26:279–287.
- Data from a prospective cohort study, if mothers and their children intended to assess risk factors for maternal and child health problems, showing an association between increased eicosapentaenoic and docosahexaenoic acids and decreased prevalence of allergic rhinitis after adjustment for potentially confounding factors (multivariate odds ratio 0.56, 95% confidence interval 0.32–0.96, *P* for trend = 0.03).
- 24 Karkos PD, Leong SC, Karkos CD, *et al*. Spirulina in clinical practice:
 - evidence-based human applications. *Evid Based Complement Alternat Med* 2008 [Epub ahead of print].
 A review of the current evidence for spirulina in the treatment of chronic fatigue, allergic rhinitis, hypercholesterolemia, and diabetes mellitus.
- 25 Karkos PD, Leong SC, Arya AK, *et al*. 'Complementary ENT': a systematic review of commonly used supplements. *J Laryngol Otol* 2007; 121:779–782.
- 26 Mao TK, Van de Water J, Gershwin ME. Effects of a spirulina-based dietary supplement on cytokine production from allergic rhinitis patients. *J Med Food* 2005; 8:27–30.
- 27 Cingi C, Konk-Dalay M, Cakli H, Bal C. The effects of spirulina on allergic
 - rhinitis. *Eur Arch Otorhinolaryngol* 2008; 265:1219–1223.
 The second published randomized, double-blind, placebo-controlled trial on spirulina for allergic rhinitis. Spirulina consumption significantly improved both symptoms including sneezing, rhinorrhea, congestion, and nasal itching, and subjective physical findings compared with placebo.
- 28 Guo R, Pittler MH, Ernst E. Herbal medicines for the treatment of allergic
 - rhinitis: a systematic review. *Ann Allergy Asthma Immunol* 2007; 99:483–495.
 A good systematic review of specific herbal remedies for allergic rhinitis. This article examines the literature in greater detail but is limited to herbal treatments only.
- 29 Saxena VS, Venkateshwarlu K, Nadig P, *et al*. Multicenter clinical trials on a novel polyherbal formulation in allergic rhinitis. *Int J Clin Pharmacol Res* 2004; 24:79–94.
- 30 D'Souza P, Amit A, Saxena VS, *et al*. Antioxidant properties of Aller-7, a novel polyherbal formulation for allergic rhinitis. *Drugs Exp Clin Res* 2004; 30:99–109.
- 31 Pratibha N, Saxena VS, Amit A, *et al*. Anti-inflammatory activities of Aller-7, a novel polyherbal formulation for allergic rhinitis. *Int J Tissue React* 2004; 26:43–51.
- 32 Amit A, Saxena VS, Pratibha N, *et al*. Mast cell stabilization, lipoxygenase inhibition, hyaluronidase inhibition, antihistaminic and antispasmodic activities of Aller-7, a novel botanical formulation for allergic rhinitis. *Drugs Exp Clin Res* 2003; 29:107–115.
- 33 Badar VA, Thawani VR, Wakode PT, *et al*. Efficacy of *Tinospora cordifolia* in allergic rhinitis. *J Ethnopharmacol* 2005; 96:445–449.
- 34 Panchabhai TS, Kulkarni UP, Rege NN. Validation of therapeutic claims of *Tinospora cordifolia*: a review. *Phytother Res* 2008; 22:425–441.
- 35 Shimoda H, Tanaka J, Yamada E, *et al*. Anti type I allergic property of Japanese butterbur extract and its mast cell degranulation inhibitory ingredients. *J Agric Food Chem* 2006; 54:2915–2920.
- 36 Sadler C, Vanderjagt L, Vohra S. Complementary, holistic, and integrative
 - medicine: butterbur. *Pediatr Rev* 2007; 28:235–238.
 This article summarizes the evidence regarding butterbur for allergic rhinitis and is useful for the reader seeking more in-depth information on this specific treatment.
- 37 Kaufeler R, Polasek W, Brattstrom A, Koetter U. Efficacy and safety of butterbur herbal extract Ze 339 in seasonal allergic rhinitis: postmarketing surveillance study. *Adv Ther* 2006; 23:373–384.
- 38 Schapowal A. Butterbur Ze339 for the treatment of intermittent allergic rhinitis: dose-dependent efficacy in a prospective, randomized, double-blind, placebo-controlled study. *Arch Otolaryngol Head Neck Surg* 2004; 130:1381–1386.
- 39 Schapowal A. Randomised controlled trial of butterbur and cetirizine for treating seasonal allergic rhinitis. *BMJ* 2002; 324:144–146.
- 40 Schapowal A. Treating intermittent allergic rhinitis: a prospective, randomized, placebo and antihistamine-controlled study of butterbur extract Ze 339. *Phytother Res* 2005; 19:530–537.
- 41 Lee DK, Gray RD, Robb FM, *et al*. A placebo-controlled evaluation of butterbur and fexofenadine on objective and subjective outcomes in perennial allergic rhinitis. *Clin Exp Allergy* 2004; 34:646–649.
- 42 Gray RD, Haggart K, Lee DK, *et al*. Effects of butterbur treatment in intermittent allergic rhinitis: a placebo-controlled evaluation. *Ann Allergy Asthma Immunol* 2004; 93:56–60.
- 43 Gex-Collet C, Imhof L, Brattstrom A, *et al*. The butterbur extract petasin has no effect on skin test reactivity induced by different stimuli: a randomized, double-blind crossover study using histamine, codeine, methacholine, and aeroallergen solutions. *J Investig Allergol Clin Immunol* 2006; 16:156–161.
- 44 Zhao Y, van Hasselt CA, Woo JK, *et al*. Effects of the Chinese herbal formula Shi-Bi-Lin on cytokine release from the human mast cell line. *Ann Allergy Asthma Immunol* 2005; 95:79–85.
- 45 Zhao Y, van Hasselt CA, Woo JK, *et al*. Effect of a Chinese herbal formula, Shi-Bi-Lin, on an experimental model of allergic rhinitis. *Ann Allergy Asthma Immunol* 2006; 96:844–850.
- 46 Zhao Y, Woo JK, Leung PC, *et al*. Symptomatic and pathophysiological observations in a modified animal model of allergic rhinitis. *Rhinology* 2005; 43:47–54.
- 47 Zhao Y, Woo KS, Ma KH, *et al*. Treatment of perennial allergic rhinitis using Shi-Bi-Lin, a Chinese herbal formula. *J Ethnopharmacol* 2008 [Epub ahead of print].
- 48 Das AK, Mizuguchi H, Kodama M, *et al*. Sho-seiryu-to suppresses histamine signaling at the transcriptional level in TDI-sensitized nasal allergy model rats. *Allergol Int* 2009; 58.
- 49 Hu G, Walls RS, Bass D, *et al*. The Chinese herbal formulation biminne in management of perennial allergic rhinitis: a randomized, double-blind, placebo-controlled, 12-week clinical trial. *Ann Allergy Asthma Immunol* 2002; 88:478–487.
- 50 Xue CC, Thien FC, Zhang JJ, *et al*. Treatment for seasonal allergic rhinitis by Chinese herbal medicine: a randomized placebo controlled trial. *Altern Ther Health Med* 2003; 9:80–87.
- 51 Lenon GB, Xue CC, Story DF, *et al*. Inhibition of release of inflammatory mediators in primary and cultured cells by a Chinese herbal medicine formula for allergic rhinitis. *Chin Med* 2007; 2:2.
- 52 Lenon GB, Li CG, Xue CC, *et al*. Inhibition of release of vasoactive and inflammatory mediators in airway and vascular tissues and macrophages by a Chinese herbal medicine formula for allergic rhinitis. *Evid Based Complement Alternat Med* 2007; 4:209–217.
- 53 Lenon GB, Li CG, Xue CC, *et al*. Inhibition of inducible nitric oxide production and iNOS protein expression in lipopolysaccharide-stimulated rat aorta and Raw 264.7 macrophages by ethanol extract of a Chinese herbal medicine formula (RCM-101) for allergic rhinitis. *J Ethnopharmacol* 2008; 116:547–553.
- 54 *Urtica dioica*; urtica urens (nettle). Monograph. *Altern Med Rev* 2007;
 - 12:280–284.
 This article summarizes the evidence regarding *U. dioica* for allergic rhinitis and is useful for the reader seeking more in-depth information on this specific treatment.
- 55 Kim LS, Riedlinger JE, Baldwin CM, *et al*. Treatment of seasonal allergic rhinitis using homeopathic preparation of common allergens in the southwest region of the US: a randomized, controlled clinical trial. *Ann Pharmacother* 2005; 39:617–624.
- 56 Passalacqua G, Bousquet PJ, Carlsen KH, *et al*. ARIA update: I – Systematic review of complementary and alternative medicine for rhinitis and asthma. *J Allergy Clin Immunol* 2006; 117:1054–1062.
- 57 Resnick ES, Bielory BP, Bielory L. Complementary therapy in allergic rhinitis. *Curr Allergy Asthma Rep* 2008; 8:118–125.
- 58 Aabel S. No beneficial effect of isopathic prophylactic treatment for birch pollen allergy during a low-pollen season: a double-blind, placebo-controlled clinical trial of homeopathic Betula 30c. *Br Homeopath J* 2000; 89:169–173.

- 59 Aabel S, Laerum E, Dolvik S, Djupesland P. Is homeopathic 'immunotherapy' effective? A double-blind, placebo-controlled trial with the isopathic remedy Betula 30c for patients with birch pollen allergy. *Br Homeopath J* 2000; 89: 161–168.
- 60 Jonas WB, Kaptchuk TJ, Linde K. A critical overview of homeopathy. *Ann Intern Med* 2003; 138:393–399.
- 61 Shang A, Huwiler-Muntener K, Nartey L, *et al.* Are the clinical effects of homeopathy placebo effects? Comparative study of placebo-controlled trials of homeopathy and allopathy. *Lancet* 2005; 366:726–732.
- 62 Kemeny L, Koreck A. Ultraviolet light phototherapy for allergic rhinitis. •• *J Photochem Photobiol B* 2007; 87:58–65.
This article summarizes the scientific basis of understanding and clinical trials regarding phototherapy for allergic rhinitis.
- 63 Csoma Z, Ignacz F, Bor Z, *et al.* Intranasal irradiation with the xenon chloride ultraviolet B laser improves allergic rhinitis. *J Photochem Photobiol B* 2004; 75:137–144.
- 64 Csoma Z, Koreck A, Ignacz F, *et al.* PUVA treatment of the nasal cavity improves the clinical symptoms of allergic rhinitis and inhibits the immediate-type hypersensitivity reaction in the skin. *J Photochem Photobiol B* 2006; 83:21–26.
- 65 Koreck AI, Csoma Z, Bodai L, *et al.* Rhinophototherapy: a new therapeutic tool for the management of allergic rhinitis. *J Allergy Clin Immunol* 2005; 115:541–547.
- 66 Koreck A, Csoma Z, Boros-Gyevi M, Kemeny L. Comparison of the efficacy of intranasal phototherapy and fexofenadine hydrochloride for the treatment of seasonal allergic rhinitis. *Clin Immunol* 2005; 115 (Suppl 1): S50.
- 67 Koreck A, Szechenyi A, Morocz M, *et al.* Effects of intranasal phototherapy on nasal mucosa in patients with allergic rhinitis. *J Photochem Photobiol B* 2007; 89:163–169.
One of the first articles exploring safety issues regarding phototherapy.
- 68 Mitchell D, Paniker L, Sanchez G, *et al.* Molecular response of nasal mucosa to therapeutic exposure to broad-band ultraviolet radiation. *J Cell Mol Med* 2008; [Epub ahead of print].
- 69 Alfven T, Braun-Fahrlander C, Brunekreef B, *et al.* Allergic diseases and atopic sensitization in children related to farming and anthroposophic lifestyle – the PARSIFAL study. *Allergy* 2006; 61:414–421.