

## Respiratory illness: a complementary perspective

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In the UK there were 13 million visits to practitioners of complementary and alternative medicine (CAM) in 1981, a third of the number of visits made to general practitioners.<sup>1</sup> The use of CAM has grown substantially over the last 10 years; between 1986 and 1991 the proportion of *Which* readers using CAM increased by 70%,<sup>2</sup> and a more recent *Which* survey of 9000 readers in 1995 revealed that 25% had seen a CAM practitioner over the last year with 75% claiming benefit.<sup>3</sup> Eisenberg *et al* noted a similar situation in the United States, estimating that the US public spent \$13.7 billion out of pocket in 1990 on CAM,<sup>4</sup> a figure no doubt substantially increased by recent interest. Similar data document the rise and importance of CAM in Australia to much the same levels of interest and expenditure as those in the USA and the UK.<sup>5</sup>

As yet we have no definite answers as to why people seek CAM. We know that the public perceives these treatments as often being more successful for chronic illness than conventional medicine.<sup>6</sup> It also seems that patients who attend CAM practitioners feel more empowered by the process and therefore more in control of their illness.<sup>7-8</sup> Thomas *et al* found that 40% of general practices offered access to at least one complementary therapy.<sup>9</sup>

This growing interest in complementary medicine is not confined to the general public; in 1983 80% of trainee general practitioners wished to receive training in CAM,<sup>10</sup> and by 1987 this had risen to 92%.<sup>11</sup> In 1986 it was reported that 38% of general practitioners in Avon and 31% in Oxfordshire had received training in complementary therapy.<sup>12-13</sup>

One area of concern to respiratory physicians is the increased incidence of asthma which is estimated to be rising by 10% per annum in some populations, suggesting that there may be 2-3 million asthmatic subjects in the UK.<sup>14</sup> It is estimated that the disease costs the NHS approximately £400 million per annum, £80 million of which is due to hospital care.<sup>15</sup> This literature review will look primarily at asthma and chronic obstructive pulmonary disease (COPD). The evidence for the use of CAM in COPD and terminal breathlessness is limited, but it is important to note that lack of evidence does not mean that treatment is ineffective—simply that it has not been adequately investigated. This article is based on a non-systematic review that involved searching Medline, CISCOP (the Research Council for

Complementary Medicine's database), and a number of non-Medline journals on CAM.

### Asthma

#### ACUPUNCTURE

Acupuncture has been widely used in the treatment of asthma, and in some countries nearly a quarter of general practitioners believe it to be efficacious.<sup>16</sup> There are a number of uncontrolled trials assessing the use of acupuncture in the treatment of asthma,<sup>17-18</sup> however this review will concentrate on the controlled studies. These fall into two classes: (1) those of an experimental nature where only a single or small number of sessions of acupuncture was given and the short term effects monitored, and (2) trials where a course of acupuncture was given and both short and long term effects were assessed.

Tashkin and colleagues compared classical acupuncture, sham acupuncture (needle insertion at incorrect sites), isoprenaline, saline, and no treatment in methacholine induced bronchospasm in 12 patients with chronic stable asthma.<sup>19</sup> On a wide range of objective measures of lung function (specific airway resistance, thoracic gas volume, and forced expiratory flow volume) the authors showed a significantly greater effect for real acupuncture over sham and saline, though isoprenaline was the most effective treatment. Similarly, Virsik and colleagues showed a significant increase in peak flow and forced expiratory flow volume and a decrease in airway resistance after a single session of acupuncture in patients with chronic stable asthma.<sup>20</sup> Takishima and colleagues<sup>21</sup> and Yu *et al*<sup>22</sup> also reported significant improvement in lung function in patients with acute asthma immediately after a single acupuncture treatment with no further follow up. Two controlled studies have monitored the short term effect after each of a series of treatments; positive results were reported by Berger and Nolte<sup>23</sup> but negative findings by Dias and colleagues,<sup>24</sup> and again neither of these studies addressed the question of long term benefits.

While acupuncture has been shown to be beneficial in acute asthma in the short term, it has proven more difficult to demonstrate its efficacy in the management of chronic symptoms. Tashkin compared eight sessions of acupuncture with eight sessions of sham acupuncture in 25 chronic asthmatic subjects, interspersing each group of treatments with a four week washout period.<sup>25</sup> He failed to show a significant short term benefit for symptoms,

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medication use, or lung function with either form of acupuncture.

Christensen and colleagues conducted a similar study in which the effects of 10 twice weekly sessions of acupuncture in 17 patients with stable asthma were compared with 10 sessions of minimal sham acupuncture.<sup>26</sup> Outcomes involved daily self-ratings, measures of lung function, and serum IgE. The results of the study indicated an effect, albeit modest, of acupuncture on both subjective and objective measures of asthma compared with sham treatment, but a significant decrease in medication use in those receiving real acupuncture (53%), a conclusion supported by Sternfeld *et al.*<sup>27</sup> The brief follow up period (four weeks) did not permit any conclusions about the value of acupuncture in reducing medication in the long term. In contrast, a double blind placebo controlled crossover study involving 15 chronic stable asthmatic subjects treated twice weekly for five weeks failed to find any subjective or objective improvement in pulmonary function.<sup>28</sup>

All these studies must be interpreted with caution since they involved relatively small numbers of patients, a wide variety of experimental paradigms, and shared a number of methodological weaknesses.<sup>29-30</sup> Very few of the published trials have specifically assessed immunological end points, although reduced "leucocyte responsiveness" has been reported in one study following acupuncture.<sup>31</sup> In addition, it is important to realise that in traditional Chinese medicine acupuncture would normally be used in conjunction with a wide range of herbal preparations for the treatment of asthmatic patients and this may explain why studies from China have reported a much greater degree of success than those in the West.<sup>32</sup>

The evidence to date suggests that acupuncture almost certainly improves airway obstruction acutely, but its long term efficacy has yet to be established. In addition, acupuncture may be more effective in certain subgroups such as drug induced or allergic asthma rather than in those with exercise induced asthma.<sup>33</sup>

#### HOMOEOPATHY

There are three different homoeopathic approaches to the management of asthma. The first is classical homoeopathy in which the toxic symptoms of a particular herb or animal remedy are matched against the patient's symptoms and then the remedy is given in a very dilute form. This is single or classical homoeopathy and involves a detailed history and a good memory in order to match the patient's symptoms to the key symptoms of a particular remedy.<sup>34</sup>

The second approach utilises complex homoeopathy which involves medicines containing a mixture of a variety of different herbal and homoeopathic products. There is a large volume of descriptive evidence that looks at both complex and classical homoeopathy, and many claims are made for the use of homoeopathy as a treatment of asthma in a wide variety

of materia medicas. However, there is virtually no clinical trial evidence to substantiate these claims.

The third homoeopathic approach involves isopathy, which is a much simpler system. Isopathic theory suggests that someone suffering from hay fever should be treated with a homoeopathic dilution of pollens, treating like with like.<sup>35</sup> This is also called homoeopathic immunotherapy (HIT).<sup>36</sup> A number of studies have been published on the use of homoeopathy in rhinitis, probably one of the most widely reported being that by Reilly which demonstrated symptomatic improvement and a 50% reduction in antihistamine requirements.<sup>37</sup> A recent review of five double blind randomised controlled trials involving the treatment of 350 patients suggested that HIT was effective in the treatment of rhinitis.<sup>35</sup>

Based on the evidence in rhinitis we can hypothesise that an isopathic approach—for instance giving a small amount of house dust mite to house dust mite sensitive asthmatics—might have some real validity in the management of asthma. Reilly has now provided some preliminary evidence to support this hypothesis.<sup>37-38</sup> In a meta-analysis combining data from his rhinitis and two asthma studies, Reilly *et al* argued that the evidence to support HIT was unequivocal.<sup>38</sup> Detractors have argued that, although the second larger asthma study was a rigorously controlled and very carefully performed double blind study, its power was limited by the small number of patients involved and the major outcome was the patient's own perception of their asthma rather than any objective measurements of lung function.

#### FOOD ALLERGY AND INTOLERANCE

Wraith argues strongly that food allergy is a very important cause of asthma and is often overlooked.<sup>39</sup> Certainly there is good evidence that tartrazine can provoke asthma in those with aspirin sensitivity<sup>40</sup> in addition to the well established bronchoconstricting effects of acetylsalicylic acid.<sup>41</sup> Similarly, the preservative sodium metabisulphite and biogenic amines such as occur in yeast and cheeses have been shown to provoke bronchoconstriction.<sup>42-43</sup> Wraith suggests that individuals showing multiple symptoms, such as associated eczema or urticaria, a family history of allergy or food intolerance and other atopic symptomatology, may well have a food intolerance and that food avoidance can significantly reduce the use of oral steroids and bronchodilators.<sup>44</sup> He argues that approximately 65% of patients with asthma will give a positive skin prick test (SPT) for inhalants and 39% for foods. However, some individual's breathlessness may be precipitated by food intolerance rather than food allergy, and therefore have a negative SPT and serum radioallergen absorbent test (RAST).<sup>44</sup> Far and away the most common food sensitivity isolated in asthmatic patients is milk, closely followed by egg, artificial colourants, and wheat. Wheat is more common in older patients than in young asthmatic subjects.<sup>39</sup> There are four studies, all using slightly differ-

ent methodology, which suggest that food sensitivities might be relevant in asthma,<sup>41 44-46</sup> but none of these studies involved double blind food challenge. Wraith has suggested that food preservatives and colourants in particular can have a dramatic effect on asthma, which is reversible if these substances are avoided.<sup>39</sup>

Radcliffe describes how food sensitivity may be diagnosed and food avoidance diets developed while recognising both the need and the difficulty of designing studies with double blind food challenges.<sup>47</sup> Wraith *et al* have suggested that the use of oral sodium cromoglycate in asthmatic patients may well be having its clinical effect by modifying the immune response to food in the gastrointestinal tract which, in turn, may modify the patient's asthmatic symptoms. While the evidence for implicating house dust mite in asthma is overwhelming, the case for food allergy or sensitivity is currently scientifically weak and requires more research.

#### NUTRITIONAL THERAPIES

Nutritional therapies involve the use of a variety of vitamin and mineral supplementation regimes. Some general guidelines in relation to nutritional therapies and bronchial asthma have emerged over the last decade.<sup>48</sup> Two studies by Burney, one in 1986 and one in 1989, showed that a high sodium intake correlates closely with an increased bronchial responsiveness to histamine,<sup>49 50</sup> suggesting that sodium restriction may be of value in some asthmatics.

Schwartz and Weiss suggested that increased vitamin C intake might be associated with a 30% lower incidence of active bronchitis and wheezing,<sup>51</sup> and this assertion has received support from two double blind crossover trials.<sup>52 53</sup> However, some authors have found the opposite effect.<sup>54</sup>

Fantidis *et al* have clearly shown that intracellular white cell (polymorphonuclear) magnesium concentrations are very low in asthmatic subjects<sup>55</sup> and suggests that this may have important implications; indeed, intracellular magnesium may be implicated in the severity of asthma through a number of possible mechanisms that include a direct effect on smooth muscle contraction, an effect on the histamine release of mast cells, through its interaction with calcium ions and also, possibly, through a change in acetylcholine from nerve cells.<sup>56</sup>

Britton *et al* have shown that bronchial hyperreactivity, as measured by forced expiratory volume in one second (FEV<sub>1</sub>) after methacholine challenge, is directly related to dietary intake of magnesium.<sup>57</sup> Furthermore, high magnesium dietary intake is also associated with a reduction in self-reported wheeze. Britton *et al* concluded that adequate levels of dietary magnesium are independent and directly related to bronchial hyperactivity. Low magnesium intake may therefore be involved in the aetiology of asthma and also possibly COPD. Britton *et al* suggest that low magnesium intake is related to our current diet which involves more cooked and refined foods and, as a consequence, a decrease in both magnesium

and other oxidants.<sup>57</sup> A number of studies also suggest that intravenous magnesium sulphate has a clear effect on acute asthma attacks.<sup>56 58</sup> Skobeloff *et al* noted a dramatic and significant improvement in peak flow in a double blind, randomised, placebo controlled trial involving 38 patients with acute asthma.<sup>58</sup> While the role of magnesium in asthma would appear to be clearly an important one, there has still been no prospective study to demonstrate that magnesium supplementation will improve lung function in the long term in patients with both asthma and other respiratory diseases.

#### MIND BODY THERAPIES (YOGA AND HYPNOTHERAPY)

The use of yoga in asthma has been investigated and two studies are worthy of note. The first by Nagarathna involved 53 patients with asthma who were trained over two weeks in an integrated set of yoga exercises, including breathing, physical postures and breath slowing techniques, as well as training in meditation.<sup>33</sup> Patients in the treatment and control groups were equally motivated to take up yoga at randomisation. Those randomised to the treatment arm were instructed to practise these techniques for 65 minutes every day and were compared with a control group of 53 patients with asthma, matched for age, sex and severity, who continued to take their usual drugs. Patients were followed up over a period of six weeks. There was a significantly greater improvement in the yoga group with respect to the number of asthma attacks per week, the use of asthmatic medication, and the peak expiratory flow rate (PEFR).

A further double blind, randomised, controlled trial by Singh *et al* came to a similar conclusion.<sup>59</sup> This trial assessed the effects of two pranayama yoga breathing exercises (the Pink City lung exercise) on airway reactivity, airway calibre, symptom scores, and medication usage in patients with mild asthma. Following a one week run in period the 18 patients with mild asthma practised slow deep breathing for 15 minutes twice daily for two weeks. During the control period subjects were provided with a matched placebo device. Mean FEV<sub>1</sub>, PEFR, symptom score, and inhaler use over the last three days of each treatment period were assessed in comparison with the baseline assessment. All patients improved more with the Pink City lung exerciser than with the placebo device, but the differences in this small study did not reach statistical significance. However, there was a statistically significant increase in the dose of histamine needed to provoke the 20% reduction in FEV<sub>1</sub> (PD<sub>20</sub>) during pranayama breathing, but not with the placebo device. This study suggests that a simple device which effectively imposes a yoga breathing technique may help asthma. Whether these effects were brought about by the effect of yoga on endogenous glucocorticoid production<sup>60</sup> or autonomic function<sup>61</sup> is unknown.

A range of other techniques which affect the mind/body interface such as hypnosis may also be of real value in asthma. For example,

Isenberg *et al* suggested that 35–40% of asthmatics may bronchoconstrict to suggestion or stress.<sup>62</sup> Brown and Fromm have explored the mechanisms by which hypnosis may affect airway calibre.<sup>63</sup> While stress and hypnosis can induce bronchoconstriction, the evidence that hypnosis can promote bronchodilation is less convincing. The early uncontrolled work in this area suggested that hypnosis could produce a reduction in morbidity and steroid usage in asthmatics.<sup>64–65</sup> This has been supported by a more recent controlled study which demonstrated the effectiveness of hypnosis in reducing the hospital admission rate, duration of stay, and need for systemic steroids in 16 subjects with inadequately controlled asthma.<sup>66</sup> However, a larger multicentre study conducted by the British Thoracic Society was unable to confirm any subjective or objective benefit of hypnosis in 91 asthmatics.<sup>67</sup> A number of hypnosis studies have reported improvements in airway calibre and blunting of the response to hypercapnia with hypnosis,<sup>68–69</sup> although this is less apparent in those with low susceptibility to hypnosis.<sup>70</sup>

The overall benefit of hypnosis may be related to providing patients with a greater sense of control and involvement in their disease in much the same way as patients have been encouraged to take responsibility for their medication.<sup>71</sup>

#### HERBAL MEDICINE

A number of herbal medicines have been used in asthma, and some of these have been evaluated in controlled trials. *Coleus forskholii* is a herb used in Ayurvedic medicine and contains a molecule which has been shown to increase intracellular levels of cyclic AMP.<sup>72</sup> Two studies have been published over the last decade which suggest that it may have a powerful bronchodilating effect<sup>73–74</sup> with fewer side effects than fenoterol.

*Ginkgo biloba* has also been investigated; it contains several unique terpene molecules which have been shown to antagonise platelet activating factors (PAF), hence limiting bronchial hyperreactivity. Studies with ginkgolides show that oral administration improves pulmonary function and protects against exercise induced asthma.<sup>74</sup> A small double blind controlled study by Guinot also showed decreased bronchial hyperreactivity to nebulised house dust mite.<sup>75</sup> *Tylophora asthmatica* is another commonly used Ayurvedic herb. Studies in animals and in large controlled double blind crossover studies in humans all show positive results from this herb.<sup>31 76–78</sup>

The effect of Saiboku-to (TJ-96) on bronchial asthma has also been studied in some depth. Nakajima reported clinical benefit and steroid sparing effects of this herbal preparation in 40 patients who took the remedy regularly for 6–24 months,<sup>79</sup> and these findings have been confirmed by Homma *et al*.<sup>80</sup>

A number of other herbs have been used in the treatment of asthma but research on these has been poorly controlled, of low quality, and is consequently of limited value. It is of interest that the studies by Shivpuri *et al* on *Tylophora*

*asthmatica*, while demonstrating clinical benefit, reported that 17–53% of those taking the remedy experienced some adverse reaction.<sup>31–78</sup> This suggests that natural medicines are not necessarily always safe and free from side effects, a fact emphasised by a recent letter to the *BMJ* which suggests that steroids are being used in some so-called “herbal preparations” for the treatment of eczema.<sup>81</sup>

#### Cancer-related breathlessness

This distressing symptom all too often presents a major challenge to those involved in palliative care. Filshie *et al* reported a rigorous but descriptive and uncontrolled study of the impact of simple acupuncture techniques in this condition.<sup>82</sup> They noted that 14 of the 20 patients studied reported marked improvement 90 minutes after acupuncture, and this was associated with a statistically significant reduction in respiratory rate. The therapeutic value of acupuncture in this condition would appear to be significant but the phenomenon requires further investigation.

#### Chronic obstructive pulmonary disease (COPD)

The literature for the use of CAM in chronic obstructive lung disease is limited. It is part of the accepted (and not unreasonable) “wisdom” of most CAM therapies that they are rarely of real value in illness where tissue repair is either impossible or likely to be very limited by the nature of the pathology involved.

#### ACUPUNCTURE

The report by Jobst *et al* of disabling breathlessness is of great interest.<sup>48</sup> He evaluated, on a single blind randomised controlled basis, real acupuncture according to traditional Chinese principles as compared with sham acupuncture. The results significantly favoured real acupuncture in the short term but the study did not involve long term follow up.

Maa *et al* reported a single blind crossover study of 31 patients with COPD who received either acupressure or sham acupressure as part of a pulmonary rehabilitation programme<sup>83</sup>; real acupressure was found to be far more effective than sham acupressure in reducing dyspnoea. Sliwinski *et al* reported a long term descriptive study of 51 patients with COPD who were also taking oral steroids; 64% of the patients were able to eliminate their use of steroids entirely during this period and the remainder reduced their steroid use significantly.<sup>84–85</sup> The authors suggest that prolonged acupuncture has an immunoregulatory effect which tends to normalise leucocyte migration.<sup>84</sup>

#### HERBAL MEDICINES

Castiglioni and Gramolini have looked at the long term effect of Sobrerol, a herbal remedy, on acute exacerbations in 706 patients with chronic bronchitis.<sup>86</sup> The study was double blind, placebo controlled, and multicentred. Seventy six percent of those receiving the herbal remedy and 58% receiving placebo did not experience acute exacerbations over a three



month period. The use of bronchodilators was significantly lower in the Sobrerol group and lung function, as measured by FEV<sub>1</sub>, was significantly higher. Interestingly, Medici *et al* in a smaller study involving only 23 patients suggested that Sobrerol had no such effect.<sup>87</sup> Ferley *et al* conducted a placebo controlled trial looking at acute exacerbations in 182 patients with chronic bronchitis in order to evaluate "Goutes aux Essences", a widely used herbal aromatherapy mixture.<sup>88</sup> They suggested that the incidence of acute infections was not modified by the treatment, although the infections that did occur resolved more swiftly and were less likely to relapse in the active treatment group. While other studies using herbal remedies in patients with COPD have claimed these preparations to be of benefit, the study design and outcomes are of poor quality.<sup>89, 90</sup> Kong *et al* suggested that herbal remedies are of substantive value in acute bronchitis in children, reducing the duration of symptoms by 25% and appearing to be superior to antibiotics.<sup>91</sup>

#### HOMOEOPATHY

The literature on homoeopathy in COPD is sparse, uncontrolled, and of limited value. Linde *et al* reported on 15 good quality randomised placebo controlled trials of the treatment of upper respiratory infections, including cough, otitis media and sinusitis.<sup>92</sup> These studies, taken as a group, substantially favour homoeopathy over placebo in line with the overall conclusions of Linde *et al*.

#### NUTRITIONAL THERAPIES

Skorodin reported a randomised double blind controlled study involving 72 patients with acute exacerbations of COPD who received either placebo or intravenous magnesium sulphate and mirrored the suggestions made for the use of magnesium in asthma (see above).<sup>93</sup>

Fata *et al* reported an impaired antibody response to a pneumococcal polysaccharide vaccine in elderly patients with low serum vitamin B<sub>12</sub> levels; indeed, serum vitamin B<sub>12</sub> appeared to be an independent and valid predictor of antibody response after vaccination.<sup>94</sup> Woo *et al* analysed the nutritional status of elderly patients recovering from a chest infection who received at random either a broad spectrum liquid nutritional supplement or no supplement.<sup>95</sup> Not surprisingly, a variety of measures of biochemical status improved in those receiving the supplements, but recovery from the acute infection was not affected by supplementation.

#### MIND BODY THERAPIES

A meta-analysis of 65 studies by Devine and Percy in 1966 looked at the effects of education, exercise, and psychosocial support in adults with COPD and found that relaxation alone had a significant effect on both dyspnoea and well being. Education alone also had a benefit on the accuracy of performing inhaler skills, and pulmonary rehabilitation itself was not as beneficial as either relaxation techniques

or educational programmes. The authors reported that the research base had quite substantial methodological weaknesses, but concluded that mind body techniques are of significant benefit in the management of chronic and disabling breathlessness.<sup>96</sup>

#### Conclusion

Complementary and alternative medicine is a broad subject and can probably be best defined as therapeutic interventions not usually taught as part of the undergraduate medical school curriculum. A number of popular therapies have not been discussed in this review, partly because the evidence base for their use is very sparse (aromatherapy and reflexology) and partly because of the constraints of space. Overall, there is inadequate evidence for the use of CAM in the major respiratory diseases that confront us; however, there is probably far more evidence than many respiratory physicians might at first realise.

The increase in popularity of CAM demands that conventional respiratory physicians understand a little about the therapies and the evidence base that underpins them. From the literature presented, it is quite clear that an evidence based integration of CAM into conventional respiratory disease is at present inappropriate. Many CAM therapies have very limited evidence of efficacy and almost no research looking at relative effectiveness. There are, however, some encouraging areas that may be of value to conventional respiratory physicians in the future. Mind body therapies and acupuncture appear to be safe, and it is reasonable to think that, on an empirical basis, these two approaches could be integrated into conventional care. The preliminary evidence for homoeopathy is encouraging, but there is a clear need for larger and more definitive studies before we can come to any clear conclusion. Herbal remedies should be used with caution, particularly as adverse drug reactions appear to be more likely with these preparations than with other CAM treatments and interactions with conventional therapies are both more likely and at present completely undefined. Nutritional supplementation, particularly in asthma, may offer benefits that could help both prophylactically and therapeutically in controlling the increasing number of asthmatic subjects in the UK, but again more research is required.

CAM is a fledgling discipline and, while the evidence in some areas is promising, it is far from definitive. However, increasing numbers of patients wish to use CAM in conjunction with, or instead of, conventional medical intervention. It would be wise for respiratory physicians to listen to their patients and work with them. Providing the patient's management is safe, then it would seem reasonable to consider the use of CAM on an empirical basis and evaluate each individual's response to their preferred approach to the management of their respiratory disease.

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