

## 28 Complementary and alternative medicine

Since the earliest of times, humans have endeavoured to enhance their physical and emotional wellbeing by selectively choosing botanicals, minerals and extracts of animal, avian and reptilian tissues, and physical measures such as massage. Powerful medical systems such as Ayurvedic and Traditional Chinese Medicine were developed from these essential ingredients.

Complementary and Alternative Medicines (CAM) are now being used more frequently in both general medical care and in association with cancer.<sup>1-3</sup> The increasing employment of CAM is due to clinicians perceiving some value in CAM therapy as outlined in a meta-analysis by Ernst, Resch and White.<sup>3</sup> After a wide literature search aimed at retrieval of all recent surveys (1983–2004) of CAM, the search was extended beyond the common databases. The overall results were highly heterogeneous. To achieve the aim of using a uniform grading system to determine whether physicians perceive CAM as useful and/or effective, six CAM experts (medical and non-medical) assessed 12 surveys using a scale of 0% (neither useful nor effective) to 100% (optimal usefulness and effectiveness). There was significant variability between the 12 surveys. Physicians rated CAM as moderately effective,  $46 \pm 16$  on the proposed scale, with younger physicians proving more accepting than their more experienced seniors. There was no trend to endorse CAM as useful or effective and the data do not confirm whether physicians see CAM as a non-specific powerful placebo or as specifically effective. The conclusion is that CAM may be useful but is in need of randomised controlled trials (RCTs) if it is to be further embraced.

Given the increasing patient interest in CAM it is proposed that clinicians pay more attention to accruing data that will provide reliable evidence and identify approaches that will ameliorate the patients' lot rather than do harm. Governments are alert to public need and demand and some, together with their instrumentalities, are seeking a better 'fit' for CAM in an environment of conventional therapy. Maha,<sup>4</sup> in a recent exploratory and qualitative paper outlining the views of academic doctors towards CAM and its role in the United Kingdom's National Health Service, concludes that while CAM is unlikely to be incorporated on a wholesale basis into NHS practice, it could be adopted and applied more widely to 'enhance overall quality of care and even increase doctors' fulfilment in their practice'.

Clinicians are very observant and must evaluate information both observed and provided. Some CAM modalities can be involved in situations where claims made for treatments lead to demand for their assessment. In just such a situation, an NIH Consensus conference<sup>5</sup> adjudged acupuncture to be effective in managing nausea and vomiting associated with chemotherapy and in controlling pain associated with surgery.

The consensus meeting also referred to a wide range of possibilities for the use of acupuncture as well as to the wide range of difficulty in conducting evidentiary-oriented studies.<sup>5</sup>

A major difficulty in evaluating CAM relates to the lack of a unifying definition for CAM, although Sollner<sup>6</sup> derives a useful approach from outlines suggested by Eisenberg<sup>7</sup> and Ernst and Cassileth.<sup>1</sup>

A review of CAM in PubMed leads to an extensive list of interventions, very few of which apply specifically to melanoma in a clinical sense. Among the modalities available are the following:

- music
- religion
- colour therapy
- relaxation
- acupuncture
- homeopathy
- massage
- hypnosis
- systematic management (vitamins, hormones, mistletoe)
- diet.

This list, which is not in itself exhaustive, clearly outlines the task ahead to properly evaluate each declension of CAM.

## 28.1 CAM – what patients find worthwhile

A significant number of patients employ CAM initiatives while undergoing conventional care.

Downer and colleagues<sup>8</sup> aimed to assess the CAM treatments most used in cancer and the motivation for using them. The study was conducted using a postal screening questionnaire and a semi-structured interview. Six hundred (600) unselected oncology patients were approached; 415 (69%) responded; 16% had used CAM in a variety of forms (see list above), with dietary therapies, however, often causing difficulties. Of the 48 patients (74%) interviewed, 36 (75%) commenced CAM during conventional therapy, 28 derived greater hope from CAM than from conventional therapy, and 20 were attracted to the holistic, non-toxic nature of the treatments. Twelve wanted therapies allowing greater involvement with their treatment, eight said the relationship with their doctor was important, while 12 were said to be incurable in spite of conventional treatment, prompting them to turn to CAM.

Patients using CAM tended to be younger, higher social class and female. Their satisfaction with CAM other than dietary therapies was high and they found psychological benefits, including hope and optimism.<sup>8</sup>

Another study by Sollner<sup>6</sup> examined CAM correlation with psychological disturbance, coping with illness and compliance with standard treatment. The study involved 172 participants answering 205 questionnaires, an 83.9% response rate, in which 24.4% used CAM and 31.4% showed interest in CAM. Logistic regression analysis observing demographic and psychological factors as independent variables provided three useful predictors: younger age ( $p=0.004$ ), progressive cancer ( $p=0.064$ ) and active coping ( $p=0.16$ ). CAM did not involve greater psychological disturbance, decreased psychological disturbance, decreased social support, or less trust in conventional medicine. CAM can be seen as prompting coping, and avoiding passivity and feelings of hopelessness (see also Chapter 16 *Psychosocial issues* and Chapter 17 *Palliative care*).

Evidence summary	Level	References
There are clear indications that patients embrace CAM for a range of physical and emotional reasons, with many hoping for cure, many hoping for help to cope, many looking to avoid passivity, and many wishing for their treating doctors' involvement in their care	IV	1–8

Recommendation	Grade
1. Patients be encouraged to share with their treating clinician(s) their wishes to embark on either a complementary or alternative therapy	C

## 28.2 Comparing CAM and conventional therapies for melanoma

Searches resulted in one randomised control trial in which melanoma is directly addressed in a selective treatment arm. Another trial in a systematic review of mistletoe<sup>6</sup> was not further considered due to methodological limitations.

The EORTC 18871/DKG 80-1 randomised phase III adjuvant trial<sup>9</sup> addresses evaluation of the efficacy and toxicity of low-dose recombinant interferon – alpha 2b (rIFN-alpha 2b) (IMU) or recombinant interferon gamma (rIFN-gamma) (0.2mg – given subcutaneously every other day for 12 months and compared with an untreated control group.

The German Cancer Society (DKG) added a fourth arm, using Iscador M on a special schedule (p=391). This popular mistletoe product is the CAM most widely used against cancer in Eastern Europe.

The study subjects were all high-risk melanoma patients who had either stage II (thickness > 3mm) and stage III patients (positive lymph nodes) without distant metastases. They were randomised and followed to first progression or death, and were subjects of an intention to treat analysis.

From 1988–1996, 830 patients were randomised into a four-arm trial. Stage II patients were treated by primary tumour resection with a > 2cm free margin and regional lymph node metastases were resected in the manner of Karakousis.<sup>10</sup> There were 423 patients in a three-arm EORTC trial and 407 in the DKG arm. Median follow-up was 8.2 years.

The disease-free interval rate at eight years was 32.4% and overall survival 40%. The 95% confidence intervals (CIs) for rIFN-alpha 2b versus control was 1.04 (0.84, 1.30), for rIFN-gamma CI versus control was 0.96 (0.77, 1.20), and for Iscador M versus controls CI was 1.32 (0.93, 1.87). For overall survival in the three arms, the CI was 0.96 (0.76, 1.21), 0.87 (0.69, 1.10) and 1.21 (0.84, 1.75) respectively. 'No adjustment for multiple comparisons was done. The trials were stopped once the planned sample size was reached to provide sufficient power to answer the IFN-question. To assess the efficacy of Iscador, it was impossible to continue the randomisation after an eight-year recruitment period. An interim evaluation at that time showed an approximately 10% lower two-year DFI (Disease Free Interval) rate in the Iscador® arm compared with the control group.'<sup>9</sup>

There was no clinical benefit for adjuvant treatment in this study with low-dose recombinant interferon, rIFN-alpha 2b or rIFN gamma or with Iscador M in high-risk melanoma patients. The data supported but did not prove a negative effect of mistletoe extracts in melanoma patients, since the observations did not reach significance.<sup>9</sup> There was no demonstrated efficacy in reducing toxicity of conventional therapy.

A retrospective study compared 153 white adult patients, aged 25–72 years, with superficial-spreading nodular melanoma to rates in the medical literature.<sup>11</sup> The patients were treated with Gerson’s diet therapy – this is a lactovegetarian, low sodium, low fat and (temporarily) protein, high potassium, fluid and nutrients (hourly raw vegetable and fruit juices). Metabolism increased by thyroid hormone administration, calorie supply was limited to 2600–3200 calories/day. Coffee enemas as needed for pain and appetite. Comparison of conventional results from literature seem favourable, the number of patients is small, retrospective and non-randomised.

Evidence summary	Level	Reference
A well-conducted randomised phase III trial yielded no benefit for adjuvant treatment with low-dose recombinant interferon rIFN-alpha 2h or rIFN gamma or with Iscador M (mistletoe) in high-risk melanoma patients. The Iscador M arm of the trial was discontinued after eight years of recruitment, as interim review revealed approximately 10% lower two year DFI when compared to control groups  The evidence accrued on Iscador M supported but did not statistically prove a negative effect on patients with melanoma	II	9

Recommendation		Grade
2. There is no available evidence to recommend CAM over conventional therapy for adjuvant management of melanoma		C

### Key point

- There is level IV evidence suggesting patients may derive emotional benefit from CAM therapy

## 28.3 Value for money and CAM therapies

No evaluations specific to melanoma were located. MacLennan, Wilson and Taylor<sup>12</sup> reported a 1993 survey on the use of CAM by a South Australian population aged 15 or over, and using correlations with demographics and medical variables, they extrapolated modelling of the costs to the Australian population in 1993 of \$621 million and for CAM therapists \$309 million. In 1992/1993 the Australian people spent \$360 million on CAM. Users of CAM were primarily post-menopausal females, of normal weight, better educated, more likely to be employed, and having greater alcohol intake than non-users.

A question is raised as to the size of expenditure in comparison to the paucity of sound safety and efficacy available for CAM products.

A further paper by MacLennan, Myers and Taylor<sup>13</sup> surveyed a similar population in South Australia and found the extrapolated cost of CAM and CAM therapists to be \$1.8 billion, falling from \$2.3 billion in 2000.

It was reported that CAM users had lower quality of life scores and that 57.2% did not inform their doctors of their use. Most believed the drugs were tested by The Therapeutic Goods Administration (TGA), but testing for safety and efficacy is not done at this time.

Evidence summary	Level	References
While the dollar value of CAM in Australia is large, there is little or no control of either product content or the clinical competence of CAM practitioners	IV	12,13

Recommendation	Grade
3. Patients are advised to discuss planned CAM therapy with their clinician, to ensure the safety of their action	C

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