

# Unconventional therapies for cancer and cancer-related symptoms

Andrew J Vickers and Barrie R Cassileth

**A significant proportion of cancer patients try unconventional therapies and many use 'complementary' therapies, as adjuncts to mainstream care, for management of symptoms and to improve quality of life. A smaller proportion use 'alternative' therapies, which are typically invasive, biologically active, and commonly promoted as replacements for, rather than adjuncts to, mainstream therapy. Many alternative therapies, including high-dose vitamin C, the Di Bella regimen, and laetrile have been shown not to be effective. For others, such as metabolic therapy, evidence is extremely limited. Conversely, most complementary therapies are well studied and of proven benefit. There is evidence from randomised trials supporting the value of hypnosis for cancer pain and nausea; relaxation therapy, music therapy, and massage for anxiety; and acupuncture for nausea. Such complementary therapies are increasingly provided at mainstream cancer centres.**

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Complementary and alternative medicine is a highly visible part of contemporary health care. No longer restricted to the lay sector and the medical fringe, such practices can be found in mainstream hospitals and cancer centres. In the USA, and in other more-developed countries, many millions of patients spend billions of dollars each year on complementary and alternative therapies.

In this review, we discuss the terminology and usage of complementary and alternative medicine, report on the major alternative approaches in current use by patients with cancer, along with any relevant data, and describe complementary therapies useful in cancer medicine according to the clinical problems they benefit. Research issues are noted and sources of further information provided.

## Terminology

The general term 'complementary and alternative medicine' is used to describe techniques as diverse as chiropractic and yoga (Figure 1), iridology and meditation, colonic irrigation and spiritual healing. As such, it defies simple definition. Most published terminologies define complementary and alternative medicine simply as anything that is not conventional medicine.<sup>1,2</sup>

An advantage of the phrase 'complementary and alternative' is that it offers the opportunity to make important distinctions between the two. 'Alternative' therapies typically are invasive and biologically active and



Figure 1. Yoga – a popular method of improving relaxation and well being.

are commonly promoted for use instead of, rather than as an adjunct to, mainstream therapy. Conversely, 'complementary' therapies are used together with mainstream care for management of symptoms and to improve quality of life.

This distinction is especially important in oncology, in which alternative methods are promoted as literal alternatives to conventional care. As a result, some patients select unproven methods instead of mainstream treatments after diagnosis; most of these methods involve much travel and expense. A particularly important point is that many alternative therapies are associated with significant risks of adverse events.

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### Use of complementary and alternative medicine by patients with cancer

A review of relevant published international data identified 26 surveys of cancer patients from 13 countries, including five from the USA.<sup>3</sup> The average prevalence of use of these therapies across all studies was 31%. Those most commonly used included dietary treatments, herbs, homoeopathy, hypnotherapy, imagery and visualisation, meditation, megadose vitamins, relaxation, and spiritual healing. Subsequent investigations have reported similar findings, although prevalence approached 50% in several.<sup>4-6</sup> There is some indication of growth in the use of complementary and alternative medicine by patients with cancer in recent years.<sup>3</sup>

### Complementary therapies for control of pain

#### Mind-body medicine

A wide variety of complementary therapies are claimed to relieve stress and increase quality of life by producing relaxation. One popular technique, progressive muscle relaxation, involves sequential tensing and relaxing of muscles. Another is hypnosis, the induction of a deeply relaxed state, with increased suggestibility and suspension of critical faculties. Once in this state, sometimes called a hypnotic trance, patients are given therapeutic suggestions to encourage changes in behaviour or symptom relief. Visualisation and imagery techniques involve the induction of a relaxed state followed by use of a visual image, such as a pleasant scene that enhances the sense of relaxation. Several randomised trials have shown effects of hypnosis on both procedural and malignant pain. A recent systematic review and a National Institutes of Health technology assessment panel have both supported the use of hypnosis for cancer-related pain.<sup>7,8</sup> There is also evidence from a randomised trial that relaxation and imagery decrease cancer pain.<sup>9</sup>

#### Acupuncture

The details of practice may differ between individual schools, but all traditional Chinese medical theory is based on the Taoist concept of yin and yang and the flow of Qi (energy) along hypothesised channels in the body (Figure 2).

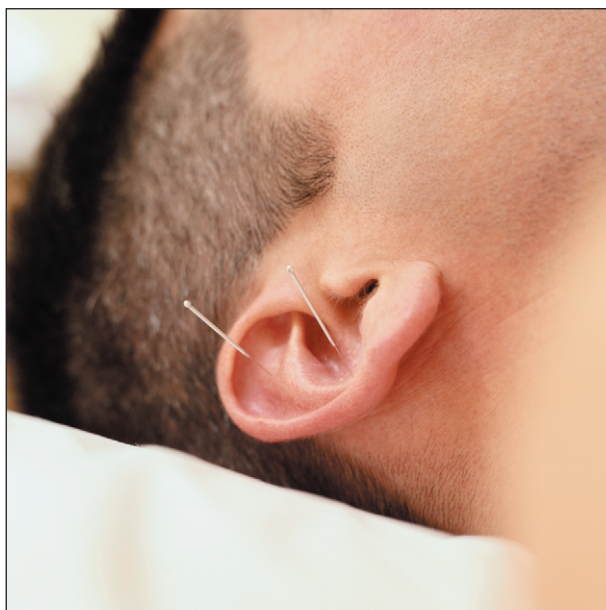


Figure 2. Acupuncture – trials have shown beneficial effects for relief of pain, nausea, and vomiting.

Many health professionals who practise acupuncture dispense with such traditional concepts. Instead, they view acupuncture points as corresponding to physiological and anatomical features such as peripheral nerve junctions, and diagnoses are developed in purely conventional terms. Many randomised trials have examined, and largely support, the use of acupuncture for acute pain, such as dental surgery,<sup>10</sup> and chronic pain, such as migraine.<sup>11</sup> As yet, there has been no controlled study in the western literature on use for cancer-related pain. Several uncontrolled trials (eg ref 12) have shown promising results, but the value of acupuncture in reducing cancer pain remains to be sufficiently evaluated.

#### Music therapy

Music can be used in a controlled way to effect clinical benefit. It is ideally provided live by trained therapists, but

### Recommended sources of information

#### Websites

American Cancer Society: [www.cancer.org](http://www.cancer.org)

National Center for Complementary and Alternative Medicine, National Institutes of Health, USA: [nccam.nih.gov](http://nccam.nih.gov)

Integrative Medicine at Memorial Sloan-Kettering Cancer Center: [www.mskcc.org/patients\\_n\\_public/patient\\_care\\_services/outpatient\\_services\\_and\\_facilities/integrative\\_medicine\\_service/index.html](http://www.mskcc.org/patients_n_public/patient_care_services/outpatient_services_and_facilities/integrative_medicine_service/index.html)

Quackwatch: [www.quackwatch.com](http://www.quackwatch.com)

HealthTel Corp Links: [www.medmatrix.org/index.asp](http://www.medmatrix.org/index.asp)

#### Books

Duke JA. *The green pharmacy*. New York: Rodale Press, 1997.

Duke JA. *Handbook of medicinal herbs*. Boca Raton: CRC Press, 1987.

Cassileth BR. *The alternative medicine handbook: the complete reference guide to alternative and complementary therapies*. New York: WW Norton and Company, 1998.

Fetrow CW, Avila JR. *Complementary and alternative medicines*. Springhouse, Pennsylvania: Springhouse Corp, 1999.

Tyler VE. *Herbs of choice: the therapeutic use of phytomedicinals*. London: Pharmaceutical Press, 1994.

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Zollman C, Vickers A. *ABC of complementary medicine*. London: BMJ Publishing, 2000.

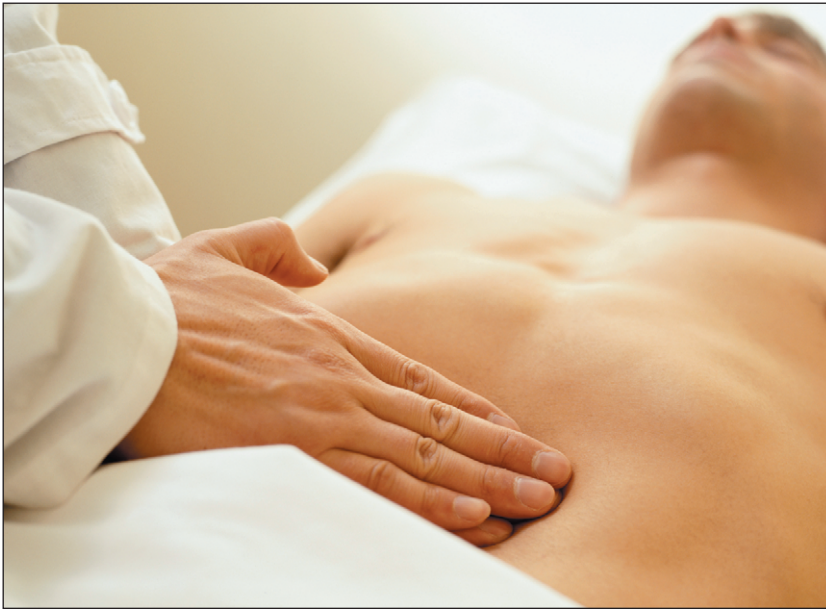


Figure 3. Massage – improves relaxation and reduces anxiety.

music therapy commonly takes the form of recorded music, particularly in the research setting. There is evidence from a randomised trial that music therapy is beneficial for acute pain, such as postoperative pain.<sup>13</sup> However, there are insufficient data specifically for cancer-related pain. In a small trial of 15 patients, improvements in cancer pain scores taken during music therapy were twice those found with non-music sound.<sup>14</sup>

#### **Massage**

Therapeutic massage (Figure 3) involves manipulation of the soft tissue of the whole body or specific areas to induce general improvements in health, such as relaxation or improved sleep, or particular physical benefits, such as relief of muscular aches and pains. Despite many anecdotal reports that massage reduces pain, current research evidence is limited. Only two small randomised pilot trials have provided preliminary evidence of the effectiveness of massage<sup>15</sup> and reflexology (foot massage)<sup>16</sup> for pain in cancer patients.

#### **Complementary therapies for anxiety and depression**

##### **Mind-body medicine**

Several randomised trials have examined the effects of relaxation therapy on anxiety, depression, or mood in cancer patients. Bindemann and colleagues, for example, randomly assigned patients with newly diagnosed cancer to relaxation training or control groups.<sup>17</sup> Anxiety and psychiatric morbidity increased significantly more in controls than in treated patients. There was also a positive effect on depression scores in women. In studies with similar designs in breast cancer, relaxation training led to better mood<sup>18</sup> and general quality of life.<sup>19</sup> Relaxation training and hypnosis had an effect on anxiety during treatment procedures, such as chemotherapy or bone-marrow aspiration, in most<sup>20,21</sup> but not all<sup>22</sup> randomised trials.

#### **Massage**

There is evidence from some randomised trials that massage (Figure 3) reduces anxiety, in the short term at least, in groups as varied as adolescent psychiatric patients, intensive-care-unit patients, elderly people in residential care, and children with post-traumatic stress disorder. A high-quality trial of massage for patients undergoing autologous bone-marrow transplantation found clinically and statistically significant improvements in anxiety compared with controls. There were also improvements in nausea, fatigue, and general well-being.<sup>23</sup> Similarly, a crossover trial of reflexology<sup>16</sup> reported statistically significant improvements in anxiety during treatment phases compared with control phases.

#### **Music therapy**

In a study of the effects of music therapy on the mood of patients with cancer, 50 hospital inpatients were randomly assigned either a live music therapy session or tape-recorded music. Patients receiving live music reported significantly lower anxiety scores than the other group.<sup>24</sup>

#### **Complementary therapies for nausea and vomiting**

##### **Mind-body medicine**

Hypnosis has been found effective for the treatment of anticipatory nausea in children.<sup>25</sup> Trials have also generally found hypnosis and relaxation training to be beneficial against chemotherapy-induced nausea in adults,<sup>26,27</sup> although some studies found no differences between groups.<sup>28</sup> One of the more effective methods seems to be 'systematic desensitisation'. Patients describe situations that cause anticipatory nausea and place these in a hierarchy (for example, driving to the hospital is placed lower than sitting in the treatment room). A relaxed state is then induced, and the patients are asked to imagine the nausea-inducing situations, which are presented in ascending order of intensity, while remaining relaxed.<sup>27</sup> Hypnosis and relaxation techniques do not seem to be effective for reducing nausea associated with bone-marrow transplantation.<sup>29</sup>

##### **Acupuncture**

There is good evidence that acupuncture reduces nausea and vomiting. A systematic review of acupuncture-point stimulation for nausea and vomiting related to chemotherapy, pregnancy, or anaesthetics reported that 11 of 12 placebo-controlled, randomised, double-blind studies favoured acupuncture.<sup>30</sup> Of 16 trials published since the review, 11 also found significant differences or trends in favour of acupuncture. A recently published randomised trial compared acupuncture with sham acupuncture and

with antiemetic medication only in women undergoing myeloablative chemotherapy. The mean numbers of vomiting episodes in the three groups were 6.3, 10.7, and 13.4 respectively; the differences between the acupuncture and sham groups were highly significant.<sup>31</sup>

### **Music therapy**

Music has been investigated for the treatment of nausea and vomiting in patients undergoing bone-marrow transplantation, who receive particularly high doses and emetogenic regimens. Patients assigned antiemetic drugs plus music distraction reported significantly less nausea and vomiting than those assigned antiemetics alone.<sup>32</sup>

### **Complementary therapies for other symptoms**

There are some uncontrolled data suggesting positive effects for acupuncture against vasomotor symptoms in patients with prostate<sup>33</sup> and breast cancers.<sup>34</sup> These results require confirmation in a randomised trial.

In an uncontrolled study,<sup>35</sup> 14 of 20 patients treated for cancer-related breathlessness reported substantial symptomatic improvement. Subjective feelings of breathlessness decreased by about a third within 5 minutes of needle insertion. These results suggest that further hypothesis-testing research would be valuable.

### **Alternative (unproven) treatments for cancer**

A large number of unproven treatments have been recommended for the treatment of cancer. Many of these are promoted as alternatives to conventional care. Below are described a small selection of some of the more popular alternative cancer treatments.

#### **Burzynski**

Some alternative remedies for cancer are the invention of a single individual and are offered at a single site. An example is antineoplastons, developed by Stanislaw Burzynski. Clinical trials have either failed to accrue patients or have been uninterpretable. Nonetheless, this remains a popular alternative therapy, especially for children with brain tumours.

#### **Di Bella**

The Di Bella regimen, consisting of melatonin, bromocriptine, retinoids, and either somatostatin or octreotide, generated intense public interest in Italy in the late 1990s. In a rare example of strategically planned and rapidly implemented research in alternative medicine, two studies were completed. Neither showed any benefit for this treatment.<sup>36,37</sup>

#### **Laetrile**

Laetrile is an interesting 'alternative' cancer medicine because, like many conventional chemotherapeutics, it consists of a single compound isolated from a natural substance (in this case, apricot pits or almonds). Yet unlike, for example, paclitaxel, it is promoted as natural, the invented 'vitamin B17'. Proper use of this substance, proponents claim, could eradicate cancer entirely ([www.worldwithoutcancer.com](http://www.worldwithoutcancer.com); [www.sumeria.net/health/laetrile.html](http://www.sumeria.net/health/laetrile.html)). However, a phase II trial showed no benefit, and some toxicity, with laetrile.<sup>38</sup> Although the product waned in popularity after that study, it was revived recently by new promoters who dismiss the study, along with the general efforts of conventional regulatory bodies, as the result of pressure exerted by vested interests trying to protect their profits in the cancer industry.

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#### **Livingston-Wheeler**

Alternative cancer treatments appear subject to fashion, and they commonly rise and fall in popularity. A therapy that was popular in the 1980s but is less so now is the Livingston-Wheeler regimen. On the basis of a hypothesis tested and discarded in the 1930s, Virginia C Livingston-Wheeler believed that cancer is caused by a bacterium, *Progenitor cryptocides*, an entity that has not been described outside of her work. The cancer treatment offered at the Livingston-Wheeler clinic in San Diego, California, USA, consisted of efforts to strengthen the immune system by 'detoxification' through diet and enemas and by the administration of special vaccines. A case-control study matched patients with advanced cancer treated at the Livingston-Wheeler clinic with those who received treatment at a conventional cancer centre. No difference in survival was found between the two sites, and Livingston-Wheeler patients had poorer quality of life.<sup>39</sup>

#### **Macrobiotics**

Many diets have been suggested as cancer cures, with different diets popular in different countries. The macrobiotic diet, which is a common cancer diet in the USA, has three features that make it typical of many alternative cancer diets: first, unless followed to extremes, it is a relatively healthy diet, being high in fibre and low in fat; second, though adherence to such a diet may prevent cancer, there is no reason to believe that it is valuable as a cancer treatment; third, the diet is bulky and difficult to digest and so may be inappropriate for many patients.

#### **Megadose vitamin C**

Nobel laureate Linus Pauling claimed that large doses of vitamin C could cure cancer, most effectively in patients who had not received chemotherapy. A randomised trial failed to support this idea.<sup>40</sup> The trial was criticised by Pauling, who claimed that the inclusion of patients who had previously received chemotherapy invalidated the results. A further trial, this time including only patients without previous chemotherapy, similarly found no survival benefit from vitamin C.<sup>41</sup> Nonetheless, proponents still advocate vitamin C, apparently on the basis of epidemiological evidence, animal studies, and accusations of bias in the cancer research community ([www.positivehealth.com/permit/Articles/Cancer/good2.htm](http://www.positivehealth.com/permit/Articles/Cancer/good2.htm); [www.vitaminfoundation.org/](http://www.vitaminfoundation.org/)).

#### **Metabolic therapy**

These therapies are based on the belief that cancer and other illnesses result from an accumulation of toxins in the colon, which leads to liver failure and death. Treatment aims to counteract liver damage with a practitioner-specific low-salt,



Figure 4. *Mahonia aquifolium* – a source of berberine.

high-potassium diet, high doses of vitamins, minerals, and enzymes, several litres of fruit and vegetable juice daily, and 'detoxification' by means of high colonic irrigation with herbs, coffee, or enzymes. Research purportedly showing a survival benefit of 'Gerson' metabolic therapy was grossly flawed by non-randomised comparisons and subgroup analysis.<sup>42</sup> A more recent case-series of 11 patients who received another variation of metabolic therapy reported encouraging findings<sup>43</sup> and serves as the basis for an ongoing controlled trial.

#### **Pau d'arco tea**

Pau d'arco tea is said to be an old Inca remedy for many illnesses, including cancer. It is made from the bark of an indigenous South American evergreen tree, and its active ingredient, lapachol, has been isolated. Although lapachol showed antitumour activity in animal studies, it does not appear to affect human cancers.<sup>44</sup> The tea can induce nausea and vomiting.

#### **Shark cartilage**

The clinical basis for the use of shark cartilage in cancer seems to be the erroneous belief that, in the words of a popular book, "sharks don't get cancer". Advocates base their therapy on its putative antiangiogenic properties, but a recent phase I/II trial of shark cartilage found no clinical benefit.<sup>45</sup> A study sponsored by the National Center for Complementary and Alternative Medicine is underway.

#### **714-X**

A liquid medicine made from camphor, 714-X contains nitrogen, ammonium salts, sodium chloride, and ethanol. It is generally given by injection. The treatment is based on an unusual set of theories about the biology of cancer, such as the importance of 'somatids', particles essential to life, which can be seen only with a special microscope, and a substance called 'cocancerogenic K factor', which is said to

protect cancer cells from immune attack. There does not seem to have been any systematic human research on 714-X.

#### **Botanicals and related problems**

Many cancer patients use medicine derived from plants ('botanical' or 'herbal' medicine).<sup>3-6</sup> Some, such as 'MGN-3', a mushroom and rice bran extract, are taken to kill cancer cells; others, such as St John's wort, are taken to cope with symptoms associated with cancer, such as depression. In the USA, such medicines are considered neither foods nor drugs and are exempted from review by the Food and Drug Administration. Instead, they are classified as 'nutritional supplements', which are available without prescription and require no data on safety, purity, or efficacy. This issue is of particular concern, because botanicals have been found to be toxic or contaminated and to interact negatively with pharmaceuticals. The very popular and useful St John's wort, for

example, induces cytochrome P450 and therefore, in theory, lowers blood concentrations of protease inhibitors (used to treat HIV infection), cyclosporin and other immunosuppressive drugs, cholesterol medications, coumadin, and chemotherapeutic agents.<sup>46</sup> Pretreatment of cancer cells with berberine (Figure 4), found in high concentration in several putative antitumour botanicals, reduces their sensitivity to paclitaxel.<sup>47</sup> We recommend that patients about to receive cancer treatments should be asked to stop botanicals and any other non-prescription products for the duration of therapy.

#### **Integrative medicine**

Some complementary therapies, such as acupuncture, traditionally have been available only outside of mainstream hospitals or cancer centres. Others, such as psychological support, humour therapy, and spiritual care, have been available for decades as 'supportive' care in oncology and other mainstream settings. In this sense, complementary medicine may be seen as an extension and an expansion of supportive care. In recent years, however, substantially greater integration of complementary and conventional medicine has occurred, often with both provided at the same site, and many additional therapies have been introduced.

At Memorial Sloan-Kettering Cancer Center, practitioners of massage, music therapy, mind-body relaxation therapies, and acupuncture work with inpatients after self-referral or referral by an oncologist or other health professional. These therapies and others are also available at our outpatient sites, along with nutritional counselling and classes in yoga, tai chi, art therapy, and various exercise programmes. Similar units have been established at other cancer centres in the USA and elsewhere.

The availability of complementary therapies within mainstream cancer centres affords the added benefit of integration at the academic and scientific level. Academic medical facilities provide an infrastructure previously absent

**Search strategy and selection criteria**

To identify papers on specific alternative remedies, we searched MEDLINE, using the name and synonyms of the therapy. Publications on complementary medicine were identified by searching the Cochrane Library. The terms used were 'compmed' to retrieve papers added to the Cochrane Controlled Trial Register by the complementary medicine field, with 'neoplasms' or 'cancer'. Additional papers were identified from the personal collections of the authors. Only papers published in English were reviewed.

from research into complementary and alternative medicine. This benefit has led, for example, to high-quality basic and clinical research in botanical cancer remedies for the first time. A small number of botanicals show promise as anticancer agents. Few of these have been promoted as cancer cures by alternative practitioners. Instead, they were developed through laboratory and epidemiological research carried out by conventionally-trained scientists. These considerations suggest that complementary and alternative medicine is best researched as well as used clinically as an integrated component of oncology care.

**Conclusion**

Both the helpful and the problematic components of complementary and alternative medicine are likely to persist in cancer medicine. Published evidence indicates that popular alternative therapies – cures promoted for use instead of mainstream treatment – do not improve survival and may, indeed, adversely affect it when patients do not receive needed care at the appropriate time. Conversely, most complementary therapies used by cancer patients have demonstrable, important benefits, including decreased symptoms and better quality of life. The challenge for the physician and for the patient is to promote and utilise beneficial complementary therapies and discard disproved or implausible alternatives.

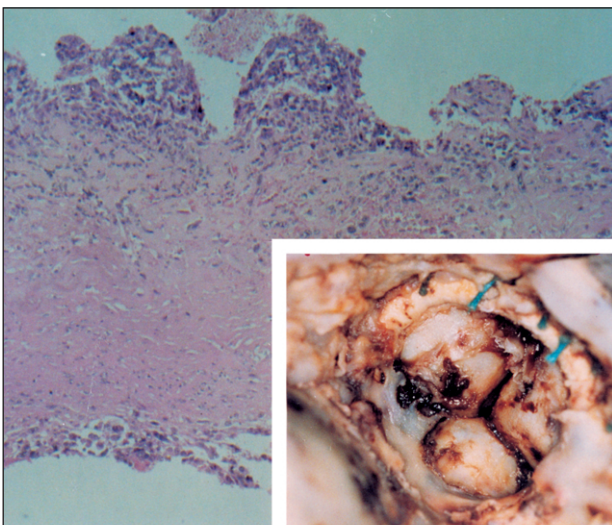
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## Clinical picture

### Metastatic neoplasia involving a mitral bioprosthesis



A 59-year-old woman with oesophageal cancer and a bovine pericardium mitral bioprosthesis was admitted to our hospital after syncope due to atrioventricular block. She died 10 days later due to cardiogenic shock. The echocardiogram taken 6 months before was unrevealing,

but by the time of admission to hospital, the patient had large masses in both atria. Computed tomography showed a tumour involving the oesophagus, lungs and both atria.

At necropsy, the oesophagus, mediastinum, and heart, as well as the mitral bioprosthesis, were infiltrated by neoplasia, which formed humps at the upper and lower borders of the prosthesis (figure; inset shows the macroscopic picture). The neoplasia was composed of large, polyhedral cells; a storiform pattern was also present. Due to massive tumour necrosis and poor fixation, the type of neoplasia was not assessed, but the most likely possibilities are melanoma or undifferentiated carcinoma.

Although bioprosthetic cardiac valves are treated to make the tissue inert, they may interact with biological agents, such as microorganisms and become infected. We report here that bovine pericardium bioprosthesis may also be seeded by neoplasia.

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