

# ACUPUNCTURE FOR PALLIATIVE CARE

## About palliative care

**Palliative care is the active holistic care of patients with advanced progressive illness, such as those with advanced cancer, end-stage renal disease, AIDs, and chronic obstructive pulmonary disorder (COPD).(WHO 2002) Management includes treatments for pain and other symptoms (e.g. fatigue, nausea and vomiting, breathlessness, anxiety, depression, vasomotor symptoms, xerostomia), as well as the provision of psychological, social and up to 457,000 people need good palliative care services every year but around 92,000 people are not being reached.(Hughes-Hallett 2011)**

The goal of palliative care is to achieve the best quality of life for patients and their families, and to provide a support system to help patients live as actively as possible until death.(WHO 2002) Ideally, palliative care is applied early in the course of illness in conjunction with other therapies intended to prolong life (such as chemotherapy or radiation therapy); investigations to better understand; and management of distressing clinical complications.(NCHSPSCS 2002; DH 2000). Conventional treatments used in palliative care include drugs such as opioids, NSAIDs, antiemetics, corticosteroids, tranquillisers and laxatives; radiotherapy; and surgery.(GP Notebook) People may be cared for in their own homes, hospices, care homes or hospitals. (Hughes-Hallett 2011)

## References

- Department of Health. The NHS Cancer Plan: a plan for investment, a plan for reform. London: DoH. September 2000.
- Hughes-Hallett T et al. Palliative care funding review. The right care and support for everyone. July 2011 [online]. Available: <http://palliativecarefunding.org.uk/wp-content/uploads/2011/06/PCFRFinal%20Report.pdf>
- Palliative care. GP Notebook [online]. Available: <http://www.gpnotebook.co.uk/simplepage.cfm?ID=1060438084>
- National Council for Hospice and Specialist Palliative Care Services. Definitions of Supportive and Palliative Care. Briefing paper 11. London: NCHSPSCS. September 2002.
- NICE 2004. Guidance on Cancer Services Improving Supportive and Palliative Care for Adults with Cancer <http://www.nice.org.uk/nicemedia/live/10893/28816/28816.pdf>
- World Health Organization. National Cancer Control Programmes: policies and guidelines. Geneva: WHO. 2002.

## How acupuncture can help

One systematic review provided limited evidence that acupuncture may provide long-term pain relief in patients with cancer (Paley 2011), and another that it is more than a placebo for commonly occurring chronic pain conditions (Hopton 2010). Another systematic review found possible benefits with acupuncture radiotherapy-induced xerostomia (O'Sullivan 2010), although not all the inter-group differences were significant. Three systematic reviews found that moxibustion or acupuncture can help relieve nausea and vomiting (Lee 2010; Chao 2009; Ezzo 2006), especially in acute situations. One systematic review found low strength evidence that acupuncture/acupressure is helpful for breathlessness, with most of the evidence coming from patients with COPD (Bausewein 2008). In a short-term pilot randomised

controlled trial, patients with advanced incurable cancer appeared to benefit from acupuncture, and it was well tolerated (Lim 2011). In another randomised controlled trial, acupuncture provided an alternative method for managing fatigue in patients with end-stage renal disease (Tsay 2004). Observational studies have suggested that acupuncture can help for symptoms in haemodialysis patients, and in people with terminal cancer (Kim 2011; Dean-Clower 2010; Takahashi 2009; Johnstone 2002). There is more about the effects of acupuncture on symptoms associated with terminal illnesses in the Anxiety, Cancer Care, Chronic Pain, COPD, Depression, and Nausea and Vomiting factsheets.

In general, acupuncture is believed to stimulate the nervous system and cause the release of neurochemical messenger molecules. The resulting biochemical changes influence the body's homeostatic mechanisms, thus promoting physical and emotional well-being.

Research has shown that acupuncture treatment may specifically benefit symptoms associated with palliative by:

- Acting on areas of the brain known to reduce sensitivity to pain and stress, as well as promoting relaxation and deactivating the 'analytical' brain, which is responsible for anxiety and worry (Hui 2010; Hui 2009);
- Regulating neurotransmitters (or their modulators) and hormones such as serotonin, noradrenaline, dopamine, GABA, neuropeptide Y and ACTH; hence altering the brains' mood chemistry to help to combat negative affective states (Lee 2009; Cheng 2009; Zhou 2008);
- Increasing the release of adenosine, which has antinociceptive properties (Goldman 2010);
- Improving muscle stiffness and joint mobility by increasing local microcirculation (Komori 2009), which aids dispersal of swelling;
- Stimulating production of endogenous opioids that affect the autonomic nervous system (Arranz 2007). Stress activates the sympathetic nervous system, while acupuncture can activate the opposing parasympathetic nervous system, which initiates the relaxation response;
- Reversing pathological changes in levels of inflammatory cytokines (Arranz 2007);
- Reducing inflammation, by promoting release of vascular and immunomodulatory factors (Kavoussi 2007, Zijlstra 2003);
- Reversing stress-induced changes in behaviour and biochemistry (Kim 2009);
- Increasing levels of T lymphocyte subsets such as CD(3) , CD(4), and CD(8) , as well as Natural Killer cells (Zhao 2010);
- Relieving nausea and vomiting by regulating gastric myo-electrical activity (Streitberger 2006) , modulating the actions of the vagal nerve and autonomic nervous system (Huang 2005), and regulating vestibular activities in the cerebellum (Streitberger 2006);
- Reducing vasopressin-induced nausea and vomiting and suppressing retrograde peristaltic contractions (Tatewaki 2005).

**N.B.** Acupuncture may be used for some of the symptoms of cancer, and the side-effects of conventional cancer treatments, but it is not used to address the cancer itself. Acupuncture needling is contraindicated in any area of actual or potential spinal instability due to cancer, as it potentially increases the risk of cord compression or transection; directly over a tumour itself or nodules or related sites, such as ascites; when there is severely disordered clotting function; into a lymphoedematous limb; directly above a prosthesis; or over any intracranial deficits following neurosurgery. Indwelling needles should not be used in patients at risk of bacteraemia, for instance in valvular heart disease and immunocompromised patients with neutropenia. (Filshie 2003) It should be noted that acupuncture can mask both cancer and disease progression.

Filshie, J. National Guidelines for the Use of Complementary Therapies in Supportive and Palliative Care. Acupuncture. The Prince of Wales's Foundation for Integrated Health; National Council for Hospice and Specialist Palliative Care Services. May 2003.

## About traditional acupuncture

Acupuncture is a tried and tested system of traditional medicine, which has been used in China and other eastern cultures for thousands of years to restore, promote and maintain good health. Its benefits are now widely acknowledged all over the world and in the past decade traditional acupuncture has begun to feature more prominently in mainstream healthcare in the UK. In conjunction with needling, the practitioner may use techniques such as moxibustion, cupping, massage or electro-acupuncture. They may also suggest dietary or lifestyle changes.

Traditional acupuncture takes a holistic approach to health and regards illness as a sign that the body is out of balance. The exact pattern and degree of imbalance is unique to each individual. The traditional acupuncturist's skill lies in identifying the precise nature of the underlying disharmony and selecting the most effective treatment. The choice of acupuncture points will be specific to each patient's needs. Traditional acupuncture can also be used as a preventive measure to strengthen the constitution and promote general well-being.

An increasing weight of evidence from Western scientific research (see overleaf) is demonstrating the effectiveness of acupuncture for treating a wide variety of conditions. From a biomedical viewpoint, acupuncture is believed to stimulate the nervous system, influencing the production of the body's communication substances - hormones and neurotransmitters. The resulting biochemical changes activate the body's self-regulating homeostatic systems, stimulating its natural healing abilities and promoting physical and emotional well-being.

## About the British Acupuncture Council

With over 3000 members, the British Acupuncture Council (BAcC) is the UK's largest professional body for traditional acupuncturists. Membership of the BAcC guarantees excellence in training, safe practice and professional conduct. To find a qualified traditional acupuncturist, contact the BAcC on 020 8735 0400 or visit

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# ACUPUNCTURE AND PALLIATIVE CARE

## The evidence

Research	Conclusion
<b>Systematic reviews</b>	
Paley CA et al. Acupuncture for cancer pain in adults. Cochrane Database Syst Rev. 2011 Jan 19;(1):CD007753.	A systematic review that evaluated the efficacy of acupuncture for the relief of cancer-related pain in adults. It included three randomised controlled trials (involving a total of 204 patients) that evaluated any type of invasive acupuncture for pain directly related to cancer in adults of 18 years or over. One high quality study investigated the effect of auricular acupuncture compared with auricular acupuncture at 'placebo' points and with non-invasive ear seeds attached at 'placebo' points. Participants in the two acupuncture groups were blinded, but blinding was not possible in the ear seeds group because seeds were attached using tape. This may have biased results in favour of acupuncture groups. Participants in the real acupuncture group had lower pain scores at 2 month's follow-up than either the placebo or ear seeds group. There was high risk of bias in the other two studies because of low methodological quality. One study that compared acupuncture with medication concluded that both methods were effective in controlling pain, although acupuncture was the most effective. The second study compared acupuncture, point-injection and medication in participants with stomach cancer. Long-term pain relief was reported for both acupuncture and point-injection compared with medication during the last 10 days of treatment. The reviewers concluded that there was insufficient evidence to judge whether acupuncture is effective in treating cancer pain in adults.
Hopton A, MacPherson H. Acupuncture for chronic pain: is acupuncture more than an effective placebo? A systematic review of pooled data from meta-analyses. Pain Pract 2010; 10: 94-102.	A synthesis of evidence from systematic reviews on the pooled data of high-quality randomized controlled trials comparing acupuncture to sham acupuncture for chronic pain. For short-term outcomes, acupuncture showed significant superiority over sham for back pain, knee pain, and headache. For longer-term outcomes (6 to 12 months), acupuncture was significantly more effective for knee pain and tension-type headache but inconsistent for back pain (one positive and one inconclusive). The reviewers concluded that the accumulating evidence from recent reviews suggests acupuncture is more than a placebo for commonly occurring chronic pain conditions.
O'Sullivan EM, Higginson IJ. Clinical effectiveness and safety of acupuncture in the treatment of irradiation-induced xerostomia in patients with head and neck cancer: a systematic review. Acupunct Med 2010; 28: 191-9.	A systematic review that looked at the evidence on clinical effectiveness and safety of acupuncture in irradiation-induced xerostomia in patients with head and neck cancer. In all, three randomised controlled trials were included. Two trials compared acupuncture with sham acupuncture, and the other had a control arm of 'usual care'. Outcome measurements included salivary flow rates (SFRs) in two trials and subjective questionnaires in three. All three trials reported a significant reduction in xerostomia versus

	<p>baseline SFR (<math>p &lt; 0.05</math>); one reported greater effect in the intervention group for stimulated SFR (<math>p &lt; 0.01</math>). Subjective assessment reported significant differences between real acupuncture and control in two trials (<math>p &lt; 0.02-0.05</math>). The reviewers concluded that there is limited evidence to suggest that acupuncture is beneficial for irradiation-induced xerostomia.</p>
<p>Lee MS et al. Moxibustion for cancer care: a systematic review and meta-analysis. <i>BMC Cancer</i> 2010; 10: 130.</p>	<p>A systematic review that assessed the effectiveness of moxibustion for supportive cancer care. It included five randomized controlled trials comparing the effects of moxibustion with conventional therapy. Four trials failed to show favourable effects of moxibustion for response rate compared with chemotherapy (<math>p = 0.43</math>). Two trials assessed the occurrence of side effects of chemotherapy and showed favourable effects of moxibustion. A meta-analysis showed significantly reduced nausea and vomiting from chemotherapy for with moxibustion (<math>p = 0.0005</math>). The reviewers concluded that there is limited evidence to suggest moxibustion is an effective supportive cancer care in nausea and vomiting.</p>
<p>Chao LF et al. The efficacy of acupoint stimulation for the management of therapy-related adverse events in patients with breast cancer: a systematic review. <i>Breast Cancer Res Treat</i> 2009; 118: 255-67.</p>	<p>A systematic review that assessed the evidence on the use of acupoint stimulation for managing therapy-related adverse events in patients with breast cancer. A total of 26 clinical trials, 18 in English and eight in Chinese, were included. They assessed the application of acupoint stimulation on six disparate conditions related to anticancer therapies, including vasomotor syndrome, chemotherapy-induced nausea and vomiting, lymphoedema, post-operation pain, aromatase inhibitors-related joint pain and leukopenia. Methods of acupoint stimulation included traditional acupuncture, acupressure, electroacupuncture, and the use of a magnetic device on acupuncture points. Overall, 23 trials (88%) reported positive outcomes on at least one of the conditions examined. However, only nine trials (35%) were of high quality. Three of these found that acupoint stimulation on P6 was beneficial to chemotherapy-induced nausea and vomiting. For other adverse events, the quality of many of the trials identified was found to be poor and no conclusive remarks could be made. The reviewers concluded that acupoint stimulation, particularly acupressure on the P6 acupoint, appears to be beneficial in the management of chemotherapy-induced nausea and vomiting, especially in the acute phase.</p>
<p>Bausewein C et al. Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases. <i>Cochrane Database of Systematic Reviews</i> 2008, Issue 2. Art. No.: CD005623. DOI: 10.1002/14651858.CD005623.pub2.</p>	<p>A systematic review that looked at the effectiveness of non-pharmacological and non-invasive interventions to relieve breathlessness in participants suffering from the five most common conditions causing breathlessness in advanced disease. It included 47 randomised controlled and controlled clinical trials involving a total of 2,532 participants described as suffering from breathlessness due to advanced stages of cancer, COPD, interstitial lung disease, chronic heart failure or motor neurone disease. Five of the trials were of acupuncture/acupressure, which provided low strength evidence that acupuncture/acupressure is helpful. Most of the studies had been conducted in patients with COPD.</p>
<p>Ezzo JM et al. Acupuncture-point</p>	<p>A systematic review that assessed the effectiveness of</p>

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stimulation for chemotherapy-induced nausea or vomiting. Cochrane Database of Systematic Reviews.(2):CD002285, 2006.

acupuncture-point stimulation on acute and delayed chemotherapy-induced nausea and vomiting in cancer patients. Eleven randomised trials (involving a total of 1,247 patients) were pooled. Overall, acupuncture-point stimulation given by any method reduced the incidence of acute vomiting (RR  $p=0.04$ ), but not acute or delayed nausea severity compared to control. By modality, stimulation with needles reduced the proportion of acute vomiting (RR  $p=0.01$ ), but not acute nausea severity. Electroacupuncture reduced the proportion of acute vomiting ( $p=0.02$ ), but manual acupuncture did not; delayed symptoms for acupuncture were not reported. Acupressure reduced mean acute nausea severity ( $p=0.04$ ), but not acute vomiting or delayed symptoms. Non-invasive electrostimulation showed no benefit for any outcome. All trials used concomitant pharmacologic antiemetics, and all, except electroacupuncture trials, used state-of-the-art antiemetics. The reviewers concluded that this data complements that on post-operative nausea and vomiting, suggesting a biologic effect of acupuncture-point stimulation. They also concluded that electroacupuncture has demonstrated benefits for chemotherapy-induced acute vomiting, and that self-administered acupressure appears to have a protective effect for acute nausea and can readily be taught to patients.

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### Randomised controlled trials

Lim JT et al. Is there a role for acupuncture in the symptom management of patients receiving palliative care for cancer? A pilot study of 20 patients comparing acupuncture with nurse-led supportive care. *Acupunct Med* 2011; 29: 173-9.

A 4-week pilot randomised controlled study that documented changes in symptoms after acupuncture or nurse-led supportive care in 20 patients with incurable cancer and an estimated survival of at least 3 months. Edmonton Symptom Assessment System (ESAS) scores were obtained before and after each treatment, and weekly for 6 weeks after treatment by telephone. Total symptom scores were reduced by an average of 22% after each acupuncture visit and by 14% after each supportive care visit. Compared with baseline, ESAS scores at the end of the follow-up period were reduced by 19% for the acupuncture arm and 26% for nurse-led supportive care. The researchers concluded that patients appeared to benefit from incorporating acupuncture into the treatment of advanced incurable cancer, and that it was well tolerated with no significant or unexpected side effects. Acupuncture had an immediate effect on all symptoms, whereas nurse-led supportive care had a larger impact 6 weeks after the final session.

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Tsay SL. Acupressure and fatigue in patients with end-stage renal disease- a randomized controlled trial. *Int J Nurs Stud* 2004; 41: 99-106.

A randomised controlled trial that investigated the effectiveness of acupressure on fatigue in patients with end-stage renal-disease (ESRD). A total of 106 patients were randomly assigned into acupressure group, sham group or control group. Patients in the acupressure group had reduced fatigue ( $p=0.003$ ). Comparisons indicated that there were significant differences between the acupressure group and the control group ( $p=0.01$ ) and between the sham group and control group ( $p=0.003$ ). The reviewers concluded that acupuncture provided an alternative method for healthcare providers in the management of ESRD patients with fatigue.

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## Observational studies

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Kim KH et al. Acupuncture for symptom management in hemodialysis patients: a prospective, observational pilot study. *J Altern Complement Med* 2011; 17: 741-8.

A prospective, observational pilot study that looked at the feasibility, safety, and possible benefits of acupuncture for symptom management in patients undergoing haemodialysis in 24 patients undergoing haemodialysis. Acupuncture treatments were provided twice a week for 6 consecutive weeks on a nondialysis day or on the day of haemodialysis prior to initiating treatment. Patients experienced a significant improvement of symptoms considered the most bothersome ( $p < 0.0001$ ). No serious adverse events related to acupuncture occurred. The researchers concluded that acupuncture seems feasible and safe for symptom management in patients undergoing haemodialysis.

Dean-Clower E et al. Acupuncture as palliative therapy for physical symptoms and quality of life for advanced cancer patients. *Integr Cancer Ther* 2010; 9: 158-67.

An 8-week single-armed prospective pilot study that looked at the feasibility of administering acupuncture as palliative therapy in 40 patients with advanced ovarian or breast cancer and to assess the effect on symptoms and quality of life (QOL). Among patients experiencing baseline symptoms, there was improvement in anxiety ( $p = 0.001$ ), fatigue ( $p = 0.0002$ ), pain ( $p = 0.0002$ ), and depression ( $p = 0.003$ ). QOL measures of pain severity and interference, physical and psychological distress, life satisfaction, and mood states showed improved scores during treatment, with sustained benefit at 12 weeks. The researchers concluded that their pilot study demonstrated that an 8-week outpatient acupuncture course is feasible for advanced cancer patients and produces a measurable benefit that should be evaluated in controlled trials.

Takahashi H. Effects of acupuncture on terminal cancer patients in the home care setting. *Med Acupunct* 2009; 21: 123-9.

A study that evaluated the efficacy of acupuncture on various symptoms in 12 terminal cancer patients receiving home care who had been evaluated as having less than 1 month to live at the time of discharge from hospital. The patients presented with a variety of symptoms, including pain, nausea, vomiting, constipation, dyspnoea, and general fatigue. All patients survived at least 1 month after the initiation of the acupuncture treatment at home (mean length of stay at home, 133 days). There was a moderate to significant reduction in the severity of constipation, dyspnoea, and general fatigue; the effects on pain and nausea were variable. No patient required hospitalisation for palliation of symptoms, nor did any patients experience anxiety or other psychological problems that needed further medical attention. All patients were able to remain home until death. The researchers concluded that acupuncture appeared to significantly contribute to the palliation of symptoms experienced by terminal cancer patients.

Meidell L et al. Acupuncture as an optional treatment for hospice patients with xerostomia: an intervention study. *Int J Palliat Nurs* 2009; 15: 12-20.

A 5-week study that investigated whether treatment with acupuncture is a viable option for 14 hospice patients with xerostomia. Only eight patients completed the study. The effect of acupuncture was assessed using a visual analogue scale, and by measuring the saliva production before and after treatment. All the patients experienced alleviation of dryness of the mouth and the associated symptoms. However, conducting a 5-week acupuncture intervention study was not feasible due to the patients being too

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close to death.

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Johnstone PA et al. Integration of acupuncture into the oncology clinic. Palliat Med 2002; 16: 235-9.

A paper describing the physical integration of acupuncture into an oncology clinic, and patient perspectives on its availability and efficacy. A practice outcome analysis was performed on 89 patients receiving therapy between 1 January 2000 and 30 April 2000. Major reasons for referral to the clinic included pain (53%), xerostomia (32%), hot flashes (6%) and nausea/loss of appetite (6%). Patients had a mean of five acupuncture visits (range 1-9). Most patients (60%) showed at least 30% improvement in their symptoms. About one-third of patients had no change in severity of symptoms. There were no untoward effects reported related to the acupuncture. When analysed by diagnosis, these values persist. Irrespective of response to therapy, 86% of respondents considered provision of the acupuncture service to be 'very important'. The researchers concluded that acupuncture may contribute to control of symptoms for cancer patients.

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### Possible mechanisms of acupuncture

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Goldman N et al. Adenosine A1 receptors mediate local anti-nociceptive effects of acupuncture. Nat Neurosci 2010; May 30.

A study showing that the neuromodulator adenosine, which has anti-nociceptive properties, was released during acupuncture in mice, and that its anti-nociceptive actions required adenosine A1 receptor expression. Direct injection of an adenosine A1 receptor agonist replicated the analgesic effect of acupuncture. Inhibition of enzymes involved in adenosine degradation potentiated the acupuncture-elicited increase in adenosine, as well as its anti-nociceptive effect. The researchers concluded that their observations indicate that adenosine mediates the effects of acupuncture and that interfering with adenosine metabolism may prolong the clinical benefit of acupuncture.

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Hui KK et al. Acupuncture, the limbic system, and the anticorrelated networks of the brain. Auton Neurosci 2010; 157: 81-90.

Studies have shown that acupuncture stimulation, when associated with sensations comprising deqi, evokes deactivation of a limbic-paralimbic-neocortical network, as well as activation of somatosensory brain regions. These networks closely match the default mode network and the anti-correlated task-positive network. The effect of acupuncture on the brain is integrated at multiple levels, down to the brainstem and cerebellum and appears to go beyond either simple placebo or somatosensory needling effects. Needling needs to be done carefully, as very strong or painful sensations can attenuate or even reverse the desired effects. Their results suggest that acupuncture mobilizes the functionally anti-correlated networks of the brain to mediate its actions, and that the effect is dependent on the psychophysical response. They discuss potential clinical application to disease states including chronic pain, major depression, schizophrenia, autism, and Alzheimer's disease.

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Hui K.K.-S. The salient characteristics of the central effects of acupuncture needling: limbic-paralimbic-neocortical network modulation. Human Brain Mapping 2009; 30:

This study assessed the results of fMRI on 10 healthy adults during manual acupuncture at 3 acupuncture points and a sham point on the dorsum of the foot. Although certain differences were seen between real and sham points, the hemodynamic and psychophysical responses were generally similar for all 4 points.

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1196-206.	Acupuncture produced extensive deactivation of the limbic-paralimbic-neocortical system. Clusters of deactivated regions were seen in the medial prefrontal cortex, the temporal lobe and the posterior medial cortex. The sensorimotor cortices, thalamus and occasional paralimbic structures such as the insula and anterior middle cingulate cortex showed activation. The researchers concluded that their results provided additional evidence that acupuncture modulates the limbic-paralimbic-neocortical network. They hypothesised that acupuncture may mediate its analgesic, anti-anxiety, and other therapeutic effects via this intrinsic neural circuit that plays a central role in the affective and cognitive dimensions of pain.
Zhao CL et al. Effect of acupuncture on the activity of the peripheral blood T lymphocyte subsets and NK cells in patients with colorectal cancer liver metastasis. <i>Zhongguo Zhen Jiu</i> 2010; 30: 10-2.	A study that looked at the effect of acupuncture on the immune function of 60 patients with colorectal cancer liver metastasis. The value of T lymphocyte subsets such as CD(3) , CD(4), and CD(8) , as well as Natural Killer cells were obviously increased after treatment, and there were significant differences between them before and after treatment.
Cheng CH et al. Endogenous Opiates in the Nucleus Tractus Solitarius Mediate Electroacupuncture-induced Sleep Activities in Rats. <i>Evid Based Complement Alternat Med</i> 2009; Sep 3.	An animal study that investigated the involvement of the nucleus tractus solitarius opioidergic system in electroacupuncture-induced alterations in sleep, the findings of which suggested that mechanisms of sleep enhancement may be mediated, in part, by cholinergic activation, stimulation of the opioidergic neurons to increase the concentrations of beta-endorphin and the involvement of the $\mu$ -opioid receptors.
Kim H et al. The effects of acupuncture stimulation at PC6 (Neiguan) on chronic mild stress-induced biochemical and behavioral responses. <i>Neuroscience Letters</i> . 2009; 460: 56-60.	The effects of acupuncture on the behavioural responses induced by chronic mild stress (CMS) were evaluated in rats by using a maze and a sucrose intake test. C-fos expression in the brain was examined by immunohistochemistry. Acupuncture stimulation at point P6 (3 min) (but not at point SJ5) reversed stress-induced behavioural changes and significantly attenuated c-fos expression in the hypothalamus, suggesting that acupuncture has a therapeutic effect on chronic stress-related diseases such as depression and anxiety.
Lee B et al. Effects of acupuncture on chronic corticosterone-induced depression-like behavior and expression of neuropeptide Y in the rats. <i>Neuroscience Letters</i> 2009; 453: 151-6.	In animal studies, acupuncture has been found to significantly reduce anxiety-like behaviour, and increase brain levels of neuropeptide Y, which appears to correlate with reported anxiety.
Komori M et al. Microcirculatory responses to acupuncture stimulation and phototherapy. <i>Anesth Analg</i> 2009; 108: 635-40.	Experimental study on rabbits in which acupuncture stimulation was directly observed to increase diameter and blood flow velocity of peripheral arterioles, enhancing local microcirculation.
Zhou Q et al. The effect of electro-acupuncture on the imbalance between monoamine neurotransmitters and GABA in the CNS of rats with chronic emotional	A study of the regulatory effect of electro-acupuncture on the imbalance between monoamine neurotransmitters and GABA in the central nervous system of rats with chronic emotional stress-induced anxiety. The levels of serotonin, noradrenaline and dopamine fell significantly, while GABA levels were significantly

<p>stress-induced anxiety. <i>Int J Clin Acupunct</i> 2008; 17: 79-84.</p>	<p>higher in the rats given acupuncture (<math>P &lt; 0.05</math>, or <math>P &lt; 0.0</math>). The researchers concluded that the anti-anxiety effect of electro-acupuncture may relate to its regulation of the imbalance of neurotransmitters.</p>
<p>Arranz L et al. Effect of acupuncture treatment on the immune function impairment found in anxious women. <i>American Journal of Chinese Medicine</i>. 2007;35(1):35-51</p>	<p>A study in which 34 women with anxiety received 10 acupuncture treatments over a year, until complete remission. Twenty healthy, non-anxious women formed the controls. Impaired immune functions in anxious women (chemotaxis, phagocytosis, lymphoproliferation and NK activity) were significantly improved by acupuncture, coming to the values of the healthy controls. The effects peaked 72 hours after a session and lasted up to a month after the course finished.</p> <p>In an earlier paper (Arranz et al, 2007) the authors had reported that acupuncture reversed the lowering of IL-2 levels and elevating of TNF-alpha and cortisol seen in anxious women. Therefore, these may be some of the parameters by which acupuncture could exert its therapeutic action on anxiety.</p>
<p>Kavoussi B, Ross BE. The neuroimmune basis of anti-inflammatory acupuncture. <i>Integr Cancer Ther</i> 2007; 6: 251-7.</p>	<p>Review article that suggests the anti-inflammatory actions of traditional and electro-acupuncture are mediated by efferent vagus nerve activation and inflammatory macrophage deactivation.</p>
<p>Streitberger K et al. Acupuncture for nausea and vomiting: an update of clinical and experimental studies. <i>Auton Neurosci</i> 2006; 129: 107-17.</p>	<p>An overview of clinical and experimental studies. The clinical results have already been presented above. Experimental studies showed effects of P6-stimulation on gastric myo-electrical activity, vagal modulation and cerebella vestibular activities in functional magnetic resonance imaging. There is good clinical evidence from more than 40 randomised controlled trials that acupuncture has some effect in preventing or attenuating nausea and vomiting. A growing number of experimental studies suggest mechanisms of action.</p>
<p>Huang ST et al. Increase in the vagal modulation by acupuncture at Neiguan point in the healthy subjects. <i>American Journal of Chinese Medicine</i> 2005; 33: 157-64.</p>	<p>A study that investigated whether acupuncture at the P6 point could improve vagal modulation by using heart rate variability analysis. In all, 39 subjects received acupuncture at the P6 point, 38 subjects received sham acupuncture, and 34 subjects received no treatment. The normalised high-frequency power was used as the index of vagal modulation, and the low-/high-frequency power ratio was used as the index of sympathovagal balance. The normalised high-frequency power after acupuncture increased significantly from the P6 acupuncture group, but not in the sham acupuncture or no-treatment group. In both the P6 and sham acupuncture groups, the mean RR interval (the intervals between consecutive R waves in the electrocardiogram) increased significantly after acupuncture. In the no-treatment group, there was no statistical difference in all heart rate variability measures in the initial and later sessions. The researchers concluded that acupuncture at the P6 point can increase vagal modulation of the subjects. This result may be helpful in the understanding of the mechanism underlying the effect of acupuncture or acupressure at P6 on the lessening of nausea and vomiting in clinic.</p>

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Tatewaki M et al. Effects of acupuncture on vasopressin-induced emesis in conscious dogs. *American Journal of Physiology - Regulatory Integrative and Comparative Physiology* 2005. 288: 57-2.

Vasopressin, a posterior pituitary hormone, is involved in nausea and vomiting in humans and dogs. To investigate the antiemetic effects of acupuncture on vasopressin-induced emesis, gastroduodenal motor activity and the frequency of retching and vomiting were simultaneously recorded in conscious dogs. Gastroduodenal motility was continuously monitored throughout the experiment. Electroacupuncture (EA) was performed before, during, and after the vasopressin infusion. To investigate whether the opioid pathway is involved in EA-induced antiemetic effects, naloxone (a central and peripheral opioid receptor antagonist) or naloxone methiodide (a peripheral opioid receptor antagonist) was administered before, during, and after EA and vasopressin infusion. EA at P6 significantly reduced the number of episodes of retching and vomiting induced by vasopressin. EA at P6 also suppressed retrograde peristaltic contractions. In contrast, EA at two other acupoints had no antiemetic effects. The antiemetic effect of EA was abolished by pretreatment with naloxone but not naloxone methiodide, suggesting that the antiemetic effect of acupuncture is mediated via the central opioid pathway.

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Zijlstra FJ et al. Anti-inflammatory actions of acupuncture. *Mediators Inflamm* 2003; 12: 59-69.

An article that suggests a hypothesis for anti-inflammatory action of acupuncture: Insertion of acupuncture needles initially stimulates production of beta-endorphins, CGRP and substance P, leading to further stimulation of cytokines and NO. While high levels of CGRP have been shown to be pro-inflammatory, CGRP in low concentrations exerts potent anti-inflammatory actions. Therefore, a frequently applied 'low-dose' treatment of acupuncture could provoke a sustained release of CGRP with anti-inflammatory activity, without stimulation of pro-inflammatory cells.