British Acupuncture Council

ACUPUNCTURE AND CANCER CARE

About cancer care

Cancer and the treatments for cancer are associated with various symptoms. Fatigue is the most common symptom reported by survivors of cancer (Johnston 2007). Forty percent of people with early or intermediate stage cancer, and 90% with advanced cancer, have moderate to severe pain; up to 70% of those with cancer pain do not receive adequate pain relief (Paley 2011). Hot flushes are common in women with a history of breast cancer but, while hormonal therapies are known to reduce these symptoms, they are not recommended for these women due to their potential unwanted effects (Rada 2010).

More than 70% of seriously ill patients with cancer suffer from xerostomia and the associated problems of swallowing, chewing and speaking (Meidell 2009). Leukopenia and neutropenia are common side effects during cancer treatment (Lu 2007). Many patients undergoing chemotherapy experience nausea and vomiting (Gralla 1999; Hesketh 1998). The symptoms can be severe, impairing a patient's quality of life (Osoba 1997), causing emotional distress (Love 1989), and aggravating cancer-related symptoms such as cachexia, lethargy and weakness (Griffin 1996; Roscoe 2000).

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How acupuncture can help

Pain. One systematic review provided limited evidence that acupuncture may provide long-term pain relief in patients with cancer (Paley 2011). The review found there was a shortage of good quality trials, though more recent examples have strengthened the evidence. For example, one found it more effective than usual care for pain and dysfunction after neck dissection (Pfister 2010); in another it was more effective than cobamamide for peripheral neuropathy due to chemotherapy (Xu 2010); and a third found it to be better than sham acupuncture for joint symptoms caused by aromatase inhibitors (Crew 2010).

Fatigue. Two small randomised controlled trials showed that acupuncture may be more effective than sham acupuncture (Balk 2010; Molassiotis 2007), but further data is needed to make a convincing case.

Xerostomia (radiotherapy-induced). A systematic review found possible benefits with acupuncture (O'Sullivan 2010), though not all the inter-group differences were significant.

Leukopaenia. A systematic review concluded acupuncture may possibly be effective for chemotherapy-induced leukopaenia (Lu 2007), though the studies were of poor quality. More recent randomised controlled trials found it to increase granulocyte colony-stimulating factor and improve leukopaenia (Han 2010), and to increase white blood cell values (Lu 2009).

Vasomotor symptoms. One systematic review of three trials in women with breast cancer (Lee 2009a), plus a further four more recent trials (Frisk 2011; Liljegren 2010; Walker 2010; Hervik 2009), provide mixed results from which it is hard to draw definite conclusions. Acupuncture has been found superior to sham in two out of three; better than venlafaxine in one out of two; similar to relaxation; and less effective than hormone therapy (but without the serious side effects). There is also a systematic review in respect of men with prostate cancer: the results were promising but very much preliminary (Lee 2009b).

Nausea and vomiting. Three systematic reviews found that moxibustion or acupuncture can help relieve nausea and vomiting (Lee 2010; Chao 2009; Ezzo 2006), especially in acute situations. There is more about the effects of acupuncture on these symptoms in the Nausea and Vomiting factsheet.

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 cancer and its treatment 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's 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.

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 www.acupuncture.org.uk

ACUPUNCTURE AND CANCER CARE

The evidence

Research	Conclusion
Systematic reviews	
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.
Lee MS et al. Moxibustion for cancer care: a systematic review and meta-analysis. BMC Cancer 2010; 10: 130.	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 (p=0.43). 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 (p=0.0005). The reviewers concluded that there is limited evidence to suggest moxibustion is an effective supportive cancer care in nausea and vomiting.
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 baseline SFR (p<0.05); one reported greater

	effect in the intervention group for stimulated SFR (p<0.01). Subjective assessment reported significant differences between real acupuncture and control in two trials (p<0.02-0.05). The reviewers concluded that there is limited evidence to suggest that acupuncture is beneficial for irradiation-induced xerostomia.
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. Breast Cancer Res Treat 2009; 118: 255-67.	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.
Lee MS et al. Acupuncture for treating hot flashes in breast cancer patients: a systematic review. Breast Cancer Res Treat 2009a; 115:497-503.	A systematic review that assessed the effectiveness of acupuncture as a treatment option for hot flushes in patients with breast cancer. Three randomised clinical trials comparing real with sham acupuncture were included. One trial showed favourable effects of acupuncture in reducing hot flushes frequency, while the other two failed to do so. The meta-analysis showed significant effects of acupuncture compared with sham acupuncture (p=0.05). One trial compared the effects of electroacupuncture (EA) with hormone replacement therapy. Hormone therapy was more effective than EA. Another trial compared acupuncture with venlafaxine and reported no significant intergroup difference. A further trial compared acupuncture with applied relaxation and failed to show a significant intergroup difference. The reviewers concluded that the evidence to suggest acupuncture is an effective treatment of hot flushes in patients with breast cancer was not convincing.
Lee MS et al. Acupuncture for treating hot flushes in men with prostate cancer: a systematic review. Support Care Cancer 2009b; 17: 763-70.	A systematic review that assessed the effects of acupuncture as a treatment for hot flushes in patients with prostate cancer. Six studies were included. One randomised clinical trial compared the effects of manual acupuncture with acupuncture plus electro-acupuncture. The other five studies were uncontrolled observational studies and therefore had limitations. The reviewers concluded that the evidence to suggest an effect with acupuncture on hot flushes in patients with prostate cancer was not convincing.
Lu W et al. Acupuncture for chemotherapy-induced leukopenia:	A meta-analysis of 11 randomised controlled trials that assessed the effects of acupuncture on chemotherapy-induced leukopenia

exploratory meta-analysis of randomized controlled trials. Journal of the Society For Integrative Oncology 2007; 5: 1-10.	and neutropenia. It included a total of 682 patients who were undergoing or had just completed chemotherapy or chemoradiotherapy, and who were allocated to either acupuncture therapy or usual care. The methodological quality of the trials was considered poor. In the seven trials in which white blood cell (WBC) counts were available, acupuncture use was associated with an increase in leukocytes in patients during chemotherapy or chemoradiotherapy, ($p < .0001$). The reviewers concluded that the inferior quality and publication bias present in the studies included may have led to a false-positive estimation and that the positive results should be treated in an exploratory nature only.
Ezzo JM et al. Acupuncture-point stimulation for chemotherapy-induced nausea or vomiting. Cochrane Database of Systematic Reviews.(2):CD002285, 2006.	A systematic review that assessed the effectiveness of 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.
Randomised controlled trials	
Fatigue	
Balk J et al. Pilot, randomized, modified, double-blind, placebo-controlled trial of acupuncture for cancer-related fatigue. J Soc Integr Oncol 2009; 7: 4-11. .	A randomised controlled trial that assessed the effects of acupuncture in the treatment of cancer-related fatigue. A total of 27 patients were allocated to 'true' or sham acupuncture during a 6-week course of radiation therapy. Both true and sham acupuncture groups had improved fatigue, fatigue distress, quality of life, and depression from baseline to 10 weeks, but the differences between the groups were not statistically significant. The true acupuncture group improved more than the sham on the Functional Assessment of Chronic Illness Therapy-Fatigue Subscale (5.50 v. 3.73 points), but again this difference was not statistically significant. However, the study was underpowered to find a statistically significant difference, so the researchers were able to conclude that patients with cancer-related fatigue may benefit more from true than sham acupuncture.

Molassiotis A et al. The management of cancer-related fatigue after chemotherapy with acupuncture and acupressure: a randomised controlled trial. Complementary Therapies in Medicine 2007; 15: 228-37.	A randomised controlled trial that looked at the effects of acupuncture and acupressure in managing cancer-related fatigue. Forty-seven patients with cancer who experienced moderate to severe fatigue were randomised either to an acupuncture group, an acupressure group or a sham acupressure group. Significant improvements were found with regards to General fatigue ($p<0.001$), Physical fatigue ($p=0.016$), Activity ($p=0.004$) and Motivation ($p=0.024$). At the end of the intervention, there was a 36% improvement in fatigue levels in the acupuncture group, while the acupressure group improved by 19% and the sham acupressure by 0.6%. Improvements were observed even 2 weeks after treatments, although they were lower (22%, 15%, 7%, respectively). Acupuncture was a more effective method than acupressure or sham acupressure. The researchers concluded that acupuncture shows great potential in the management of cancer-related fatigue.
Pain	
Pfister DG et al. Acupuncture for pain and dysfunction after neck dissection: results of a randomized controlled trial. J Clin Oncol 2010; 28: 2565-70.	A randomised controlled trial that assessed whether acupuncture reduces pain and dysfunction in patients with cancer with a history of neck dissection. A secondary objective was to determine whether acupuncture relieves dry mouth in this population. In all, 58 patients with chronic pain or dysfunction attributed to neck dissection were randomly assigned to weekly acupuncture or usual care (e.g. physical therapy, analgesia, and/or NSAIDs) for 4 weeks. Constant-Murley scores (a composite measure of pain, function, and activities of daily living, and the primary outcome measure) improved more in the acupuncture group ($p=0.008$). It also produced greater improvement in reported xerostomia ($p=0.02$). The researchers concluded that, in patients with cancer and post neck dissection, acupuncture results in significant reductions in pain, dysfunction, and xerostomia compared to usual care.
Xu WR et al. Clinical randomized controlled study on acupuncture for treatment of peripheral neuropathy induced by chemotherapeutic drugs. Zhongguo Zhen Jiu. 2010; 30: 457-60.	A randomised controlled trial that assessed whether acupuncture is an effective treatment for peripheral neuropathy induced by chemotherapeutic drugs. Sixty-four patients with neuropathy induced by paclitaxel or oxaliplatin were allocated to acupuncture or intramuscular injections of cobamamide. Peripheral neuropathy within the two groups was compared using a questionnaire administered before and after treatment. The total effective rate for sensory nerve disorder in the acupuncture group was 66.7%, significantly greater than that of 40.0% in the medication group ($p<0.05$). The researchers concluded that acupuncture is more effective than cobamamide for treatment of peripheral neuropathy induced by chemotherapeutic drugs, and particularly for moderate and severe sensory nerve disorder induced by paclitaxel.
Crew KD et al. Randomized, blinded, sham-controlled trial of acupuncture for the management of aromatase inhibitor-associated joint symptoms in women with early-stage breast cancer. J Clin Oncol 2010; 28: 1154-60.	A randomised controlled trial that investigated the effects of acupuncture in 43 postmenopausal women with early-stage breast cancer being treated with aromatase inhibitors and experiencing arthralgias. ‘True’ acupuncture (TA) was compared with sham acupuncture (SA) for 6 weeks. Outcome measures included the Brief Pain Inventory-Short Form (BPI-SF; the primary outcome measure), Western Ontario and McMaster

	Universities Osteoarthritis Index (WOMAC), and Modified Score for the Assessment of Chronic Rheumatoid Affections of the Hands (M-SACRAH) obtained at baseline and at 3 and 6 weeks. The mean BPI-SF worst pain scores at 6 weeks, were lower for TA compared with SA (3.0 vs. 5.5; p<0.001). There were also differences between TA and SA in pain severity (2.6 vs. 4.5; p=0.003) and pain-related interference (2.5 vs. 4.5; p=0.002) at 6 weeks. Similar findings were seen for the WOMAC and M-SACRAH scores. The acupuncture intervention was well-tolerated. The researchers concluded that women with aromatase inhibitor-induced arthralgias treated with 'true' acupuncture had significant improvement of joint pain and stiffness, which was not seen with sham acupuncture, and it is an effective and well-tolerated strategy for managing this common treatment-related side effect.
Vasomotor symptoms	
Liljegren A et al. Reducing vasomotor symptoms with acupuncture in breast cancer patients treated with adjuvant tamoxifen: a randomized controlled trial. Breast Cancer Res Treat. 2010 Dec 14. [Epub ahead of print]	Eighty-four breast cancer patients suffering from hot flushes and sweating were randomized to receive either true or control (non-insertive stimulation at non-points) acupuncture twice a week for 5 weeks. Both groups reported improvement regarding severity and frequencies in hot flushes and sweating but with no statistical difference between them. The acupuncture group was superior for severity of night sweating. No significant differences in hormonal levels were found before and after treatment. It was concluded that both true and sham acupuncture reduce vasomotor symptoms in breast cancer patients treated with adjuvant tamoxifen.
Walker EM et al. Acupuncture versus venlafaxine for the management of vasomotor symptoms in patients with hormone receptor-positive breast cancer: a randomized controlled trial. J Clin Oncol 2010; 28: 634-40.	A randomised controlled trial to see if acupuncture may be effective in reducing vasomotor symptoms from anti-oestrogen hormone treatment for breast cancer. It also assessed whether acupuncture produces fewer unwanted effects than venlafaxine, a drug used commonly to treat these vasomotor symptoms. Fifty patients were assigned to receive 12 weeks of acupuncture or venlafaxine treatment. Health outcomes were measured for up to 1 year post-treatment. Both groups had similar and significant decreases in hot flushes, depressive symptoms, and other adverse quality-of-life symptoms, and had significant improvements in mental health. However, by 2 weeks post-treatment, the venlafaxine group experienced significant increases in hot flushes, whereas hot flushes in the acupuncture group remained at low levels. The venlafaxine group experienced 18 incidences of unwanted effects (e.g. nausea, dry mouth, dizziness, anxiety), whereas the acupuncture group experienced no negative unwanted effects. Acupuncture had the additional benefit of improving sex drive in some women, and most reported an improvement in their energy, clarity of thought, and sense of well-being. The researchers concluded that acupuncture appears to be similarly effective to drug therapy in terms of improving vasomotor symptoms in women on anti-oestrogen treatment for breast cancer. Furthermore, it is a safe, and results in fewer unwanted effects.
Hervik J, Mjaland O. Acupuncture for the treatment of hot flashes in breast	A randomised controlled trial that investigated the efficacy of acupuncture in 59 women following breast cancer surgery

cancer patients, a randomized, controlled trial. Breast Cancer Res Treat 2009; 116: 311-6.	suffering from hot flushes as a result of anti-oestrogen medication (tamoxifen). The women were allocated to 10 weeks of traditional Chinese acupuncture or sham acupuncture. During the treatment period, the mean number of hot flushes was significantly reduced by traditional Chinese acupuncture (by 50% during the day and almost 60% at night), and was further reduced (by 30% both day and night) during the next 12 weeks. In the sham acupuncture group, while there was a significant reduction (by 25%) in hot flushes in the day during the treatment period, this effect did not last during the following 12 weeks, and there was no reduction in hot flushes at night. The Kupperman index was reduced by 44% from baseline to the end of the treatment period in the traditional Chinese acupuncture group, and this was largely maintained 12 weeks after treatment ended. No corresponding changes were seen in the sham acupuncture group. The researchers concluded that, compared with sham acupuncture, traditional Chinese acupuncture seems to provide effective relief from hot flushes (both day and night) in women who have had surgery for breast cancer and are being treated with tamoxifen. This treatment effect seems to coincide with a general health improvement measured using the validated Kupperman index.
Frisk J et al. Long-term follow-up of acupuncture and hormone therapy on hot flushes in women with breast cancer: a prospective, randomized, controlled multicenter trial. Climacteric 2008; 11: 166-74.	A randomised controlled trial that evaluated the effects of electro-acupuncture (EA) for 12 weeks and hormone therapy (HT) for 2 years on vasomotor symptoms in 45 women with a history of breast cancer. The number of hot flushes, and distress caused by them, was recorded daily before, during and up to 24 months after the start of treatment. The median number of hot flushes per 24 hours decreased from 9.6 to 4.3 ($p<0.001$) at the end of the 12-week EA treatment period and at 12 months' follow-up 4.9 (n=14); For the 18 women on hormone therapy the number of flushes decreased from 6.6 to 0.0 at 12 weeks.
Frisk J, et al. Acupuncture improves health-related quality-of-life (HRQoL) and sleep in women with breast cancer and hot flushes. Support Care Cancer. 2011 Apr 6. [Epub ahead of print]	In a subsequent paper the authors reported changes in sleep and quality of life. The Psychological and General Well-being Index and the Women's Health Questionnaire scores, as well as various sleep parameters, improved significantly in both groups after 12 weeks and this was maintained at the EA group's 12-month follow-up. Although flushes decreased less in the EA group than in the HT group, health-related quality of life improved at least to the same extent and it was concluded that EA should be further evaluated as a treatment for women with breast cancer (especially as HT no longer can be recommended).
Nedstrand E et al. Psychological well-being improves in women with breast cancer after treatment with applied relaxation or electro-acupuncture for vasomotor symptom. J Psychosom Obstet Gynaecol 2006; 27: 193-9.	A randomised controlled trial that evaluated the effects of applied relaxation and electroacupuncture on psychological well-being in 38 women treated for breast cancer and suffering from vasomotor symptoms. The women were allocated to either treatment with electroacupuncture (EA) or applied relaxation for 12-weeks with 6 months follow-up. Vasomotor symptoms were registered daily. A visual analogue scale was used to assess climacteric symptoms; estimation of general well-being was made using the Symptom Checklist, and mood using the Mood Scale. Hot flushes were reduced by more than 50%. Climacteric symptoms significantly decreased during treatment and remained so 6 months after treatment in both groups. Psychological well-being significantly improved during therapy

	and at follow-up visits in both groups. Mood improved significantly in the electroacupuncture treated group. The researchers concluded that psychological well-being is improved in women with breast cancer with both electroacupuncture and with applied relaxation for vasomotor symptoms.
Leukopenia and neutropenia	
Han YF et al. Clinical study on acupuncture for leukopenia induced by chemotherapy. Zhongguo Zhen Jiu 2010; 30: 802-5.	A randomised controlled trial that explored the adjunctive therapeutic effects of acupuncture for leukopenia induced by chemotherapy. Eighty six patients with leukopenia after chemotherapy treatment were allocated into a granulocyte colony-stimulating factor (G-CSF) plus acupuncture group or a G-CSF alone group. After patients were treated on the 10th day, the effective rates were both 100.0% and, on the 31st day, the effective rate was 98.9% in the G-CSF plus acupuncture group, which was higher than 91.1% in the G-CSF alone group ($p<0.05$). The white blood cell counts in the G-CSF plus acupuncture group were higher than those in the G-CSF alone group on the 10th, 17th and 24th days after treatment (all $p<0.05$). The ratios of mature neutrophilic granulocyte in the G-CSF plus acupuncture group were higher than those in the G-CSF alone group at all time points (all $p<0.01$). The researchers concluded that acupuncture can increase the therapeutic effect of G-CSF, delay the decrease of white blood cells after discontinuing G-CSF, and promote the maturation of neutrophilic granulocytes.
Lu W et al. Acupuncture for chemotherapy-induced neutropenia in patients with gynaecologic malignancies: a pilot randomized, sham-controlled clinical trial. J Altern Complement Med 2009; 15: 745-53.	A randomised controlled trial that investigated the effect of acupuncture administered during myelosuppressive chemotherapy on white blood cell count and absolute neutrophil count in 21 patients with ovarian cancer. Patients received active acupuncture or sham acupuncture while undergoing chemotherapy. The outcome measures were white blood cell count, absolute neutrophil count, and plasma granulocyte colony-stimulating factor (G-CSF). The median leukocyte value in the acupuncture arm at the first day of the third cycle of chemotherapy was significantly higher than in the control arm ($p=0.046$). The incidence of grade 2-4 leukopenia was less in the acupuncture arm than in the sham arm (30% versus 90%; $p=0.02$). However, the median leukocyte nadir, neutrophil nadir, and recovering absolute neutrophil count were all higher but not statistically significantly different ($p = 0.12$-0.16). There were no statistically significant differences in plasma G-CSF between the two groups. The researchers concluded that, with active acupuncture, they had found clinically relevant trends of higher white blood cell values during one cycle of chemotherapy in patients with ovarian cancer, which suggests a potential myeloprotective effect.
Possible mechanisms of acupuncture	
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.
Hui KK et al. Acupuncture, the limbic system, and the anticorrelated networks of the brain. Auton Neurosci 201; 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.
Hui K.K.-S. The salient characteristics of the central effects of acupuncture needling: limbic-paralimbic-neocortical network modulation. Human Brain Mapping 2009; 30: 1196-206.	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. 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. Zhongguo Zhen Jiu 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. Evid Based Complement Alternat Med 2009; Sep 3.	An animal study that investigated the involvement of the nucleus tractus soliatarius 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 μ-opioid receptors.

Kim H et al. The effects of acupuncture stimulation at PC6 (Neiguan) on chronic mild stress-induced biochemical and behavioral responses. Neuroscience Letters. 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. Neuroscience Letters 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. Anesth Analg 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 stress-induced anxiety. Int J Clin Acupunct 2008 ;17: 79-84.	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 higher in the rats given acupuncture ($P<0.05$, or $P<0.0$). The researchers concluded that the anti-anxiety effect of electro-acupuncture may relate to its regulation of the imbalance of neurotransmitters.
Arranz L et al. Effect of acupuncture treatment on the immune function impairment found in anxious women. American Journal of Chinese Medicine. 2007;35(1):35-51	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. 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.
Kavoussi B, Ross BE. The neuroimmune basis of anti-inflammatory acupuncture. Integr Cancer Ther 2007; 6: 251-7.	Review article that suggests the anti-inflammatory actions of traditional and electro-acupuncture are mediated by efferent vagus nerve activation and inflammatory macrophage deactivation.
Huang ST et al. Increase in the vagal modulation by acupuncture at Neiguan point in the healthy subjects. *American Journal of Chinese Medicine* 2005; 33: 157-64.	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.
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.
Streitberger K et al. Acupuncture for nausea and vomiting: an update of clinical and experimental studies. Auton Neurosci 2006; 129: 107-17.	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.
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.

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