

ACUPUNCTURE AND GI TRACT DISORDERS

About GI tract disorders

Around 2–4 in 1,000 people in Northern Europe have ulcerative colitis or Crohn's disease (Rubin 2000). Both are chronic, relapsing, inflammatory disorders of the gastrointestinal tract with several shared clinical features, but with largely distinct risk factors, genetic, immunological, anatomical and histological features, and response to therapy (DTB 2003). Their treatment, which includes medical and surgical approaches, is usually considered in two phases: the induction of remission in an acute attack, and the long-term maintenance of remission (DTB 2003).

Gastritis is an inflammation, irritation, or erosion of the lining of the stomach, which can be acute or chronic. Causes include irritation due to excessive alcohol use, chronic vomiting, stress, or the use of certain drugs (e.g. NSAIDs), *Helicobacter pylori* infection and pernicious anaemia. Symptoms of gastritis vary among individuals, and many have no symptoms. However, the most common symptoms include nausea, vomiting (possibly with blood), abdominal pain and bloating, indigestion, loss of appetite, and blood in the stools. Treatment usually involves drug therapy.

Gastro-oesophageal reflux is a common (affecting up to 25% of adults) relapsing condition caused by repeated exposure of the lower oesophagus to refluxed gastric contents (Moayyedi 2007). It presents in various ways: some patients just have symptoms, some have endoscopic evidence of mucosal damage (oesophagitis), with or without symptoms, and an important minority have complications such as bleeding, stricture or columnar epithelial (Barrett's) transformation of the lower oesophageal mucosa which predisposes to adenocarcinoma. Conventional treatment options include drugs and surgery.

About 20% of people in the UK have functional gastrointestinal disorders such as functional dyspepsia and irritable bowel syndrome (Jones 1990; Jones 1992). The latter condition is the subject of another professional information backgrounder, and will not be discussed further here. Functional gastrointestinal disorders are characterised by persisting gastrointestinal symptoms (e.g. pain, bloating) in the absence of any identifiable underlying structural or biochemical explanation (Drossman 2000). They are conventionally treated with drugs or with psychological treatments such as cognitive behavioural therapy, brief psychotherapy and gut-directed hypnotherapy (DTB 2005).

References

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How acupuncture can help

Acupuncture has been found superior to sham acupuncture for disease activity scores in Chrohns Disease and Ulcerative Colitis (Joos 2006; Joos 2006; Schneider 2007). Other 'placebo' comparisons have tended to show no statistical effect; however, there is as yet no satisfactory placebo intervention for acupuncture so the interpretation of such data is difficult and controversial. In comparisons with Western drug treatments acupuncture has been found beneficial for a variety of gastrointestinal diseases: dyspepsia (Chen 2005), gastritis (Ren 2009; Gu 2009), ulcerative colitis (Mu 2007; Lee 2009), reflux (Journal of the National Medical Association 2008; Zhang 2010) and pancreatitis (Wang 2007). Nevertheless most systematic reviews have been reluctant to endorse acupuncture because of the generally poor quality, and hence unreliability, of the studies to date (Schneider 2007; Lee 2009). (see Table overleaf).

Acupuncture may help in the treatment of GI tract disorders, by:

- inhibiting gastric and duodenal motility by activating sympathetic nerves via spinal reflexes, and increasing motility via the vagus nerve and supraspinal reflexes (Chang 2001; Takahashi 2006; Sehn 2006; Yao 2006; Noguchi 2008);
- altering acid secretion, and visceral pain (Takahashi 2006)
- improving delayed gastric emptying (Xu 2006)
- reducing inflammation, by promoting release of vascular and immunomodulatory factors (Zijlstra 2003)
- stimulating areas in the brain that are involved in gastric perception (Zeng 2009)
- inhibiting stress-induced pro-opiomelanocortin expression in the hypothalamus (Sun 2008)
- increasing vasoactive intestinal peptide and nitric oxide in plasma, gastric mucosal and bulb tissues, and elevating expression of vasoactive intestinal peptide in antral smooth muscle (Shen 2006);
- decreasing permeability of intestinal mucosa in patients with acute pancreatitis, and reducing accumulation of endogenous inflammatory mediators and vascular active substance in intestinal mucosa (Wang 2007).

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 wellbeing.

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 wellbeing.

About the British Acupuncture Council

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The evidence

Research	Conclusion
Systematic reviews	
Lee D-H et al. Moxibustion for ulcerative colitis: A systematic review and meta-analysis. <i>BMC</i> <i>Gastroenterology</i> 2009; 10, Article Number: 36.	A systematic review and meta-analysis that assessed the clinical evidence for moxibustion as a treatment for ulcerative colitis. Five randomised controlled trials with a total of 407 patients were included (published up to February 10, 2010). All the trials were considered to be of low methodological quality. They all compared the effects of moxibustion with conventional drug therapy. Three tested moxibustion against sulfasalazine and two against sulfasalazine plus other drugs. Meta-analysis of the five trials showed favourable effects of moxibustion on response rate compared to conventional drug therapy (n = 407; risk ratio = 1.24 , 95% CI = 1.11 to 1.38 ; P < 0.0001). However, the reviewers concluded that current evidence is insufficient to show that moxibustion is an effective treatment of ulcerative colitis because most of included trials had a high risk of bias.
Mu JP et al. Meta-analysis on acupuncture and moxibustion for treatment of ulcerative colitis. [Chinese]. <i>Zhongguo Zhenjiu</i> 2007; 27: 687-90.	A meta-analysis that assessed the effectiveness and safety of acupuncture and moxibustion for the treatment of ulcerative colitis. A total of 11 randomised controlled trials or clinical controlled were included (all published within 10 years). Statistical analysis indicated the odds ratio in favour of acupuncture and moxibustion was 3.82 (95% CI 2.65 to 5.52). The therapeutic effect and the cure rate in the treatment group were significantly higher than those of the control group (p<0.01). The reviewers concluded that the therapeutic effect and safety of acupuncture and moxibustion on ulcerative colitis is superior to that of western medicine.
Schneider A et al. Acupuncture treatment in gastrointestinal diseases: A systematic review. <i>World</i> <i>Journal of Gastroenterology</i> 2007; 13: 3417-24.	A systematic review that assessed the evidence for effectiveness of acupuncture treatment in gastrointestinal diseases. A total of 18 clinical studies (published up to May 2006) were included; two for irritable bowel syndrome, one for Crohn's disease and one for ulcerative colitis were randomised controlled trials. For other gastrointestinal disorders, study quality was poor. In all trials, quality of life improved significantly, but this was independent of the kind of acupuncture used (i.e. real or sham). Real acupuncture was significantly superior to sham acupuncture with regard to disease activity scores in the Crohn's and ulcerative colitis trials. The reviewers concluded that further trials of acupuncture for inflammatory bowel disease are necessary to evaluate the efficacy of acupuncture treatment.
Clinical studies	

Functional dyspepsia:

Park Y-C et al. Evaluation of manual	A single-blind randomised controlled trial that looked at the
acupuncture at classical and	efficacy of acupuncture as a treatment in 68 patients with

nondefined points for treatment of functional dyspepsia: A randomized- controlled trial. <i>Journal of Alternative</i> <i>and Complementary Medicine</i> 2009; 15: 879-84,	functional dyspepsia. Acupuncture was given three times a week for 2 weeks. Patients were either given acupuncture at classical points or undefined points Symptoms and quality of life were scored according to the Nepean Dyspepsia Index before and after treatments. Acupuncture treatment significantly decreased dyspepsia symptoms and improved the quality of life, but there was no difference between the two acupuncture groups. <u>The</u> researchers concluded that acupuncture at both classical points and undefined points improved the symptoms of patients with functional dyspepsia, but that a placebo effect could not be ruled <u>out.</u>
Chen JY et al. Effects of acupuncture on the gastric motivity in patients with functional dyspepsia. [Chinese]. Zhongguo Zhong Xi Yi Jie He Za Zhi Zhongguo Zhongxiyi Jiehe Zazhi/Chinese Journal of Integrated Traditional & Western Medicine/Zhongguo Zhong Xi Yi Jie He Xue Hui, Zhongguo Zhong Yi Yan Jiu Yuan Zhu Ban 2005; 25: 880-2.	A randomised controlled trial that looked at the effects of the acupuncture on the gastric motivity in patients with functional dyspepsia. Ninety patients were randomly allocated to acupuncture treatment, cisapride (withdrawn in the UK because of adverse effects) or granules containing azulene sulfonate sodium and L-glutamine. Symptoms, gastro-electric frequency and rhythm, and gastric emptying time and plasma motilin improved in the acupuncture and cisapride groups, and more so than in the azulene group (p<0.05). The researchers concluded that acupuncture could significantly improve the gastric motivity of patients with functional dyspepsia.
Gastritis:	
Ren R, Zhuang LX. Effect of acupuncture and moxibustion of Shu- and Mu-acupoints on the quality of life in patients chronic superficial gastritis. <i>[Zhongguo yi xue ke xue yuan Yi xue qing bao yan jiu suo bian ji]</i> 2009; 34: 262-6.	A 4-week randomised controlled trial that compared electroacupuncture plus moxibustion with omeprazole (20 mg four times daily) on the symptoms and quality of daily life in 60 patients with chronic superficial gastritis. Overall, the effective rates were 90% with acupuncture and 67% with medication (p<0.05). Self-comparison showed a marked improvement in the quality of life including physical function, bodily pain, general health, vitality, social function, and mental health in both groups after the treatment. <u>The researchers concluded that</u> <u>electroacupuncture plus moxibustion can effectively relieve</u> clinical symptoms and improve quality of life in patients with <u>chronic superficial gastritis.</u>
Gu W. Hu QC. Clinical observation on acupuncture for treatment of chronic atrophic gastritis. [Chinese]. <i>Zhongguo Zhenjiu</i> 2009; 29: 361-4.	A randomised controlled trial to compare the therapeutic effects of acupuncture and western medicine for the treatment of chronic atrophic gastritis. Eighty patients were randomly divided into an observation group treated with acupuncture and a control group given western medicine (e.g. omeprazole, amoxicillin etc.). Evaluation was carried out before treatment and after 4 and 8 weeks of treatment. The total effective rate was 92.5% in the acupuncture group and 75% in the control group (p<0.05). For pathologic changes in the gastric mucosa assessed by gastroscopic inspection, the total effective rate was 85% in the acupuncture group and 65% in the control group (p<0.05). For histopathologic improvement, the total effective rate was 87.5% in the acupuncture group and 65% in the control group (p<0.05). The researchers concluded that acupuncture therapy can significantly improve the clinical symptoms, gastroscopic expression and histopathologic situation in patients with chronic atrophic gastritis, and its therapeutic effect is better than that of

the western medicine.

Peptic ulceration:

Niu HY et al. Multicentral randomized controlled trials of acupuncture at Zhongwan (CV 12) for treatment of peptic ulcer. [Chinese]. <i>Zhongguo</i> <i>Zhenjiu</i> 2007; 27: 89-92.	A 6-week randomised controlled trial that evaluated the efficacy and safety of acupuncture for treatment of peptic ulcers in 276 patients compared with cimetidine. The therapeutic effects were evaluated by clinical symptoms and gastroscopy. The symptoms improved significantly in both groups (p <0.01), but with no significant difference between the two groups (P > 0.05). The acupuncture group was better than the control group in terms of rapid alleviation of stomachache and improvement of appetite (p <0.05). However, there was no difference between the groups in terms of the total effective rate (91% in the acupuncture group vs. 88% in the control group, p >0.05), or in terms of the therapeutic effect of gastroscopy (p >0.05). The researchers concluded that acupuncture has a reliable therapeutic effect on peptic ulcer.
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Gastro-oesophageal reflux:

Zhang CX, Qin YM, Guo BR. Clinical study on the treatment of gastroesophageal reflux by acupuncture. Chin J Integr Med. 2010 Aug;16(4):298-303.	Sixty patients with confirmed diagnosis of gastro-oesophageal reflux (GER) were randomly assigned to an acupuncture group (once a day, for 1 week, with 2-3 days between courses) or a control group taking omeprazole (20 mg twice a day) and mosapride (20 mg thrice a day). Treatment lasted 6 weeks 24-hr intra-oesophageal pH and bile reflux, endoscopic grading score and symptom score were all decreased significantly at the end of treatment in both groups (P<0.01), with insignificant difference between them (P>0.05). Four weeks later the symptom scores had reverted to a high level in the control group (P<0.05), but this did not occur in the treatment group (P>0.05). Acupuncture can effectively inhibit the intraesophageal acid and bile reflux in GER patients to alleviate patients' symptoms with good safety and is well accepted by patients
Acupuncture may have value in treating gastroesophageal reflux. Journal of the National Medical Association 2008; 100: 350.	A randomised controlled trial that compared acupuncture plus a standard dose of omeprazole with a double dose of omeprazole in 30 adult patients with a 3-month history of symptoms related to gastro-oesophageal reflux disease despite taking a standard-

	dose of omeprazole (20 mg daily) <u>The addition of acupuncture</u> to standard-dose omeprazole therapy significantly decreased – symptoms of daytime and nighttime heartburn, acid regurgitation, dysphagia and chest pain, whereas there was no change in symptoms with double-dose omeprazole. Quality of life, assessed at the end of the study using the SF-36 general health scale, was significantly improved in the acupuncture group as compared with the increased dose group.
Ulcerative colitis:	
Joos S et al. Acupuncture and moxibustion in the treatment of ulcerative colitis: a randomized controlled study. <i>Scandinavian</i> <i>Journal of Gastroenterology</i> 2006; 41: 1056-63.	A randomised controlled trial that investigated the efficacy of acupuncture and moxibustion in the treatment of mild to moderately active ulcerative colitis in 29 patients compared with sham acupuncture. The main outcome measure was the change in the Colitis Activity Index (CAI) after treatment; secondary outcome measures were changes in quality of life, general well-being and serum markers of inflammation. In the acupuncture plus moxa group, the CAI decreased from 8.0 to 4.2 points and in the control group from 6.5 to 4.8 points (p=0.048). In both groups these changes were associated with significant improvements in general well-being (from 3.0 to 1.8 and from 3.2 to 2.2, respectively) and quality of life (from 146 to 182 and from 157 to 183, respectively). No significant differences between the groups were found regarding these secondary outcome measures. The researchers concluded that differences in efficacy between traditional acupuncture and sham acupuncture were small but significant for CAI as the main outcome measure. Both traditional and sham acupuncture seem to offer an additional therapeutic benefit in patients with mild to moderately active ulcerative colitis.
Crohn's disease:	
Joos S et al. Acupuncture and moxibustion in the treatment of active Crohn's disease: A randomized controlled study. <i>Digestion</i> 2004; 69: 131-9.	A randomised controlled trial that investigated the efficacy of traditional Chinese acupuncture in the treatment of mild to moderately active Crohn's disease in 51 patients compared with sham acupuncture. The primary outcome measure was the change in the Crohn's disease activity index (CDAI). Changes in quality of life and general well-being, and serum markers of inflammation were secondary outcome measures. In the 'real' acupuncture group the CDAI decreased from 250 to 163 points as compared with a mean decrease from 220 to 181 in the sham group (p = 0.003). In both groups these changes were associated with improvements in general well-being and quality of life. With regard to general well-being, traditional acupuncture was superior to control treatment (p = 0.045). Alpha ₁ -acid glycoprotein concentration fell significantly only in the acupuncture group (p = 0.046). The researchers concluded that traditional acupuncture offers an additional therapeutic benefit in patients with mild to moderately active Crohn's disease.
Acute Pancreitis:	
Wang XY. [Electroacupuncture for treatment of acute pancreatitis and its effect on the intestinal permeability of the	A randomised controlled trial that looked at the mechanism and effects of electroacupuncture added to medication on intestinal permeability in 68 patients with acute pancreatitis. Compared to medication only (the control group), the total effective rate was greater in the acupuncture group (86.7% vs. 76.3%, p<0.05).

patient [Article in Chinese]. <i>Zhongguo Zhen Jiu</i> 2007;27: 421-3.	After treatment, changes in endothelin, nitric oxide, tumour necrosis factor and the lactulose/mannose ratio were significantly greater in the acupuncture group than in
	the control group (p<0.05). <u>The researchers concluded that</u> <u>electroacupuncture can significantly decrease permeability of</u> <u>intestinal mucosa in patients with acute pancreatitis, and reduce</u> <u>accumulation of endogenous inflammatory mediators and</u> <u>vascular active substance in intestinal mucosa, so as to alleviate</u> <u>necrosis of intestinal epithelial cells and protect the barrier of</u> <u>gastro-intestinal mucosa</u> .

Research on mechanisms of action

Human studies

Wu Q et al. 1H NMR-based metabonomic study on the metabolic changes in the plasma of patients with functional dyspepsia and the effect of acupuncture. <i>Journal of</i> <i>Pharmaceutical and Biomedical</i> <i>Analysis</i> 2010; 51: 698-704.	A study that investigated the biological effects of function dyspepsia and the effect of acupuncture on metabolism. It used nuclear magnetic resonance-based metabonomic techniques to compare the plasma metabolic profiles of six patients with functional dyspepsia before and after acupuncture treatment and six healthy controls. The results found relatively higher levels of glucose, acetate, high-density lipoprotein, and phosphatidylcholine, and lower levels of lactate, leucine/isoleucine, N-acetyl glycoprotein, and low-density lipoprotein/very low-density lipoprotein in the patients compared with the controls. Acupuncture treatment significantly changed the levels of leucine/isoleucine, lactate and glucose, and slightly changed lipid levels towards those of the healthy controls.
Zeng F et al. Brain areas involved in acupuncture treatment on functional dyspepsia patients: A PET-CT study. <i>Neuroscience Letters</i> 2009; 456: 6- 10.	A study that aimed to investigate the influence of acupuncture stimulation on brain activities in eight patients with functional dyspepsia and eight health controls. Each control received a PET-CT scan at baseline, while each patient received scans at baseline and after acupuncture stimulation. Compared to the controls, the patients showed a lower glycometabolism in the right orbital gyrus, the left caudate tail and the cingulate gyrus, and a higher glycometabolism in the left inferior temporal gyrus (p<0.005). After acupuncture, the patients showed a decrease in glycometabolism in the postcentral gyrus and the cerebella, and an increase in the visual-related cortices (p<0.005). The results suggest that the anterior cingulate cortex, the prefrontal cortices and the caudate tail are involved in processing gastric perceptions in patients with functional dyspepsia, and that acupuncture stimulation contributes to deactivation of the primary somatosensory area and the cerebella, and activation of the visual-related cortex.
Yao X-M et al. Effect of acupuncture on proximal gastric motility in patients with functional dyspepsia. <i>World Chinese Journal of</i> <i>Digestology</i> 2006; 14: 2139-41.	A study that looked at the effect of acupuncture on the proximal gastric motility in 60 patients with functional dyspepsia induced by mechanical gastric distension. Half the patients were given acupuncture with electrical stimulation and half served as the controlled group. The initial volume and pressure, the maximal tolerable volume and pressure, and the compliance were significantly higher in the acupuncture group than the control group (p<0.05).
Xu S et al. Electroacupuncture	A study that investigated the effects of electroacupuncture on

accelerates solid gastric emptying and improves dyspeptic symptoms in patients with functional dyspepsia. <i>Digestive Diseases & Sciences</i> 2006; 51: 2154-9.	solid gastric emptying and dyspeptic symptoms in 19 patients with functional dyspepsia. Ten patients showed delayed gastric emptying of solids, and acute electroacupuncture significantly improved delayed gastric emptying (p=0.007). In the nine patients with normal gastric emptying, electroacupuncture significantly decreased symptom score (p<0.001).
Chang X et al. The affects of acupuncture at Sibai and Neiting acupoints on gastric peristalsis. <i>Journal of Traditional Chinese</i> <i>Medicine</i> 2001; 21: 286-8.	A study that found the frequency and amplitude of gastric peristaltic waves were significantly changed in 15 patients given acupuncture.

Animal studies

Sun JP et al. Effect of acupuncturing at the acupoint ST 36 on substance P and proopiomelanocortin expression in hypothalamus and adrenal in rats with cold-restraint stress-induced ulcer. <i>World Chinese</i> <i>Journal of Digestology</i> 2008; 16: 1602-6.	A study that assessed the protective effect of acupuncture against cold-restraint stress-induced ulcer, and the expression of substance P and proopiomelanocortin associated with stress in the hypothalamus and adrenals in rats. Twenty-two rats were randomised into 3 groups: the normal control group, the stress group, and the acupuncture. The ulcer index and serum cortisol levels in the acupuncture group were significantly lower than those in the stress group (p<0.01). The expression of substance P was up-regulated in the hypothalamus (p<0.05) but down- regulated in adrenals (p<0.05) in the acupuncture group compared with the stress group. Acupuncture inhibited stress- induced proopiomelanocortin expression in the hypothalamus (p<0.01).
Shen GM et al. Role of vasoactive intestinal peptide and nitric oxide in the modulation of electroacupucture on gastric motility in stressed rats. <i>World Journal of Gastroenterology</i> 2006; 12: 6156-60.	An investigation into the effects and mechanisms of vasoactive intestinal peptide and nitric oxide in the modulation of electroacupuncture on gastric motility in restrained, cold-stressed rats. Gastric myoelectric activities were recorded by electrogastroenterography, and were initially found to be disordered and irregular. Following electroacupuncture, the frequency and amplitude of gastric motility were obviously lowered (p<0.01), while the levels of vasoactive intestinal peptide and nitric oxide in plasma, gastric mucosal and bulb tissues increased strikingly (p<0.01 and p<0.05, respectively) and expression of vasoactive intestinal peptide in antral smooth muscle was elevated significantly (p<0.01) in comparison with those of model group.

Reviews of mechanisms for acupuncture in GI tract disorders

Noguchi E. Mechanism of reflex regulation of the gastroduodenal function by acupuncture. <i>Evidence-</i> <i>based Complementary and</i> <i>Alternative Medicine</i> 2008; 5: 251-6.	A review of recent experimental work on the mechanism of acupuncture for reflex regulation of gastroduodenal function. It explains that acupuncture to the abdomen of anaesthetised rats has been found to excite sympathetic nerves via spinal reflexes, causing inhibition of gut motility. It also explains that acupuncture to the limbs of anaesthetised rats has been found to excite the vagus nerve via supraspinal reflexes, causing an increase in gut motility. As well as such reflexes the underlying mechanism of acupuncture in gastro-intestinal disorders may include the limbic system, the hypothalamus and the brain stem.
Takahashi T. Acupuncture for	A review discussing how acupuncture might work in the

functional gastrointestinal disorders. <i>Journal of Gastroenterology</i> 2006; 41: 408-17.	treatment of functional gastrointestinal symptoms. It suggests that acupuncture may be effective because it has been shown to alter acid secretion, gastrointestinal motility, and visceral pain. Acupuncture on the lower limbs causes muscle contractions (i.e. stimulates motility) via the somatoparasympathetic pathway, which could be beneficial in patients with gastro-oesophageal reflux disease, functional dyspepsia and constipation associated with irritable bowel syndrome, in whom peristalsis and gastric motility are impaired. Acupuncture on the upper abdomen causes muscle relaxation via the somatosympathetic pathway (i.e. inhibits motility), which could be beneficial in patients with diarrhoea-predominant irritable bowel syndrome, in whom colonic motility is enhanced and colonic transit is accelerated.
Zijlstra FJ et al. Anti-inflammatory actions of acupuncture. <i>Mediators</i> <i>Inflamm</i> 2003;12: 59-69.	A review that suggests a hypothesis for the anti-inflammatory action of acupuncture. Insertion of acupuncture needle initially stimulates production of beta-endorphins, calcitonin gene-related peptide (CGRP) and substance P, leading to further stimulation of cytokines and nitric oxide (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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