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Acupuncture in Cardiology

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1. Introduction

Acupuncture combines the Latin *acus* (needle) and *punctum* (a prick) [1]. From the historical record of Huangdi Neijing (the Yellow Emperor's Classic), acupuncture has been used in China as a therapeutic tool for at least 2000 years [2]. In ancient China, soldiers noted, after being wounded by arrows, that their pain often eased for quite a while [3]. Therefore, a cause-and-effect relationship was assumed between the arrow wound and the unexpected diminution of pain. However, acupuncture has been little known in the Western world until 1970s after U.S. President Nixon's historic visit to China in 1972 [4]. Following the initial excitement engendered by the press reports [5], acupuncture becomes one of the most popular treatments in alternative medicine (Figure 1), and accounts for more than 10 million treatments given annually in the United States [6]. Much interest was further engendered by tales by subsequent visitors to China who witnessed surgical operations being successfully performed on conscious patients under acupunctural anesthesia [7-15]. Scientific studies using modern technology on acupuncture actually began in China in the late 1950s with further progress being made since the discovery of endogenous opioids in 1975 [2,16]. Much more advances have been made in more recent years in further understanding of the basic mechanisms underlying this millennium old medical treatment and its various clinical applications in the 21st century. This chapter reviews the current role of acupuncture in cardiology.

2. Hypercholesterolemia

Electro-acupuncture at "Fenglong" (ST 40) has some therapeutic effect on decreasing the content of total cholesterol and low-density-lipoprotein cholesterol in hyperlipidemic rats and improving the gene expression of ATP-binding cassette transporter A1, peroxisome proliferator-activated receptor alpha, liver X receptor alpha and retinoid X receptor-alpha mRNA, so

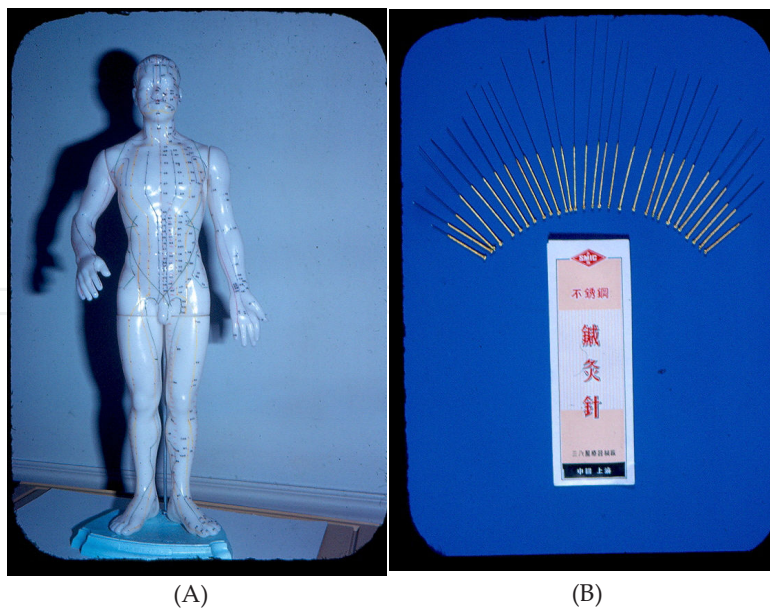


Figure 1. A) An acupuncture manikin showing the location of the various acupoints along the meridians; (B) a complete set of acupuncture needles.

as to promote reverse cholesterol transport [17]. Furthermore, real-time PCR and western blot indicate that electroacupuncture at ST 40 induces the expression of nNOS and Mt1, two genes involved in NO signal transduction [18]. Acupuncture treatment for hypercholesterolemia thus involves the modulation of several biological pathways and provides a physiological link between NO signal transduction and the cholesterol-lowering effect of acupuncture [18].

3. Coronary artery disease

The effectiveness of acupuncture in treatment of angina has been well documented [19-21]. Its antianginal effect has been shown to be secondary to an antiischemic effect, which in turn is due to a decrease in heart rate and blood pressure and reduction in left ventricular afterload [22], a reduction in myocardial oxygen consumption, and a redistribution of coronary blood flow [23], myocardial release of β -endorphin [24], coronary vasodilatation [25], and increase in coronary collateral circulation [26]. Acupoint pressing has been shown to alleviate angina faster (2.45 ± 1.67 min) than sublingual nitroglycerin (2.89 ± 2.64 min) [27]. Transmyocardial acupuncture has also been used as a novel approach to myocardial revascularization [28,29], although its rationale has been questioned [30].

Acupuncture has been successfully used to improve microcirculation and left ventricular function in acute myocardial infarction [31-33]. Animal studies demonstrated that electroacupuncture could decrease the ST-segment elevation in ECG and reduce the infarct size following coronary ligation [34], although a recent study on rats failed to show a cardioprotective effect of electroacupuncture in terms of reduction of either infarct size or ventricular

arrhythmias [35]. Acupuncture has also been successfully employed to terminate nausea and vomiting [36] and intractable hiccup [37] complicating acute myocardial infarction.

4. Cardiac arrhythmias

Acupuncture has been employed to treat both experimental [38-40] and clinical arrhythmias. The latter included ventricular extrasystoles [41,42], sinus bradycardia [43], atrial fibrillation [44,45], decreased heart rate variability [46,47,48,49,50] and sudden death [51]. In the treatment of paroxysmal atrial fibrillation and atrial flutter, acupuncture at Neiguan, Shenmen, and Danzhong is more effective than intravenous amiodarone (conversion rate: 85% vs 67%, $p < 0.01$; conversion time: 39.6 \pm 13.7 min vs 50.1 \pm 14.8 min, $p < 0.01$) [52]. Acupuncture at Neiguan, Shenmen and Xinshu also can prevent recurrences of atrial fibrillation after cardioversion in patients with persistent atrial fibrillation [53]. The advantage of acupuncture in treating atrial fibrillation is obvious, because it does not have any of the untoward effect of pharmacotherapy or ablation. Atrial fibrillation is the most common cardiac arrhythmia, and anxiety plays a significant role in either its initiation or its perpetuation [54]. Because acupuncture is very effective in treating anxiety, this therapeutic modality warrants further investigation as a promising therapeutic option.

A recently published systematic review of randomized controlled trials failed to provide conclusive evidence in support of acupuncture treatment for cardiac arrhythmias [55]. Furthermore, electro-acupuncture may interfere with demand pacemakers [56], although one recent case report from Greece indicated its safety [57]. Electro-acupuncture may also trigger inappropriate ICD discharges [58,59]. Therefore, extreme caution should be employed when electro-acupuncture is prescribed for patients with pacemakers and/or ICDs, and each patient should be considered individually with great care.

5. Congestive heart failure

In a Chinese echocardiographic study of patients with congestive heart failure due to dilated cardiomyopathy under maintenance doses of conventional drugs, including digitalis, diuretics and potassium supplements, acupuncture resulted in an increase in stroke volume [60]. Because patients with heart failure have increased sympathetic activity and acupuncture produces release of endogenous opioids in the central nervous system which would inhibit central sympathetic outflow, sympathetic activation during acute mental stress was markedly attenuated [61] or virtually eliminated [62] after acupuncture. This may explain why ear acupuncture has been used in treating chronic heart failure, because one of the acupuncture points stimulated by the needle in the ear corresponds to the closest position of the vagus nerve to the cutaneous surface (vide infra), and electrical vagus nerve stimulation has been advocated for patients with advanced heart failure [63].

Acupuncture may become an additional therapeutic strategy to improve the exercise tolerance of patients with chronic heart failure, potentially by improving skeletal muscle function [64].

The German researchers from the University Hospital of Heidelberg found a remarkable increase in 6-minute walk distance, improvement in ventilatory efficiency and post-exercise recovery, and increase in heart rate variability, despite a lack of improvement of the cardiac ejection fraction and peak oxygen uptake [64]. They recommended that further research be carried out to understand the beneficial mechanisms of acupuncture – in particular, its effects on neurohormonal balance and production of inflammatory cytokines [64].

In patients with chronic heart failure, acupuncture may reduce digitoxicity by regulating intracellular Ca^{++} , improving the function of Ca^{++} -ATPase in the sarcoplasmic reticulum, and increasing the calcium sensitivity of cardiac troponin [65]. These considerations may provide a novel clue for attenuating the toxicity of digitalis preparations given to patients with chronic heart failure.

6. Hypertension

Experimental studies have shown that acupuncture inhibits the reflex-induced hypertension by modulating the activity of cardiovascular parasympathetic neurons in the rostral ventrolateral medulla [66]. Activation of neurons in the arcuate nucleus of the hypothalamus, ventrolateral periaqueductal gray in the midbrain, and medullary nucleus raphé pallidus in the medulla by acupuncture can inhibit the activity of premotor sympathetic neurons in the rostral ventrolateral medulla. Glutamate, acetylcholine, opioids, gamma-aminobutyric acid, nociceptin, serotonin, nitric oxide and endocannabinoids in the brain all appear to participate in the antihypertensive response of acupuncture (Figure 2)[66]. Other possible mechanisms include decreases in plasma renin [67, 68], plasma neuropeptide Y [69], aldosterone [70] and angiotensin II activity [71,72]; increased excretion of sodium [73,74]; changes in plasma norepinephrine [75], serotonin [75] and endorphin levels [76,77]; and lowering of blood viscosity [75,78].

However, the Stop Hypertension with the Acupuncture Research Program (SHARP) pilot trial concluded that acupuncture provided no greater benefit than invasive sham acupuncture in controlling moderate hypertension [79]. Further research is obviously required to determine whether acupuncture can enhance clinical management of hypertension if used in combination with antihypertensive agents, over longer periods, or among specific subgroups of patients.

7. Stroke

Stroke should be considered as a coronary artery disease risk equivalent [80]. Acupuncture has useful applications in both the acute and chronic phases of a stroke. In ischemic stroke, acupuncture increases local cerebral blood flow as determined by single photon emission computed tomography [81] and near-infrared spectroscopy [82]. In rats with ischemic stroke, acupuncture has been shown to promote angiogenesis [83]. Acupuncture at Baihui and Fengchi is more effective than nimopidine in relieving cerebral vasospasm after embolization

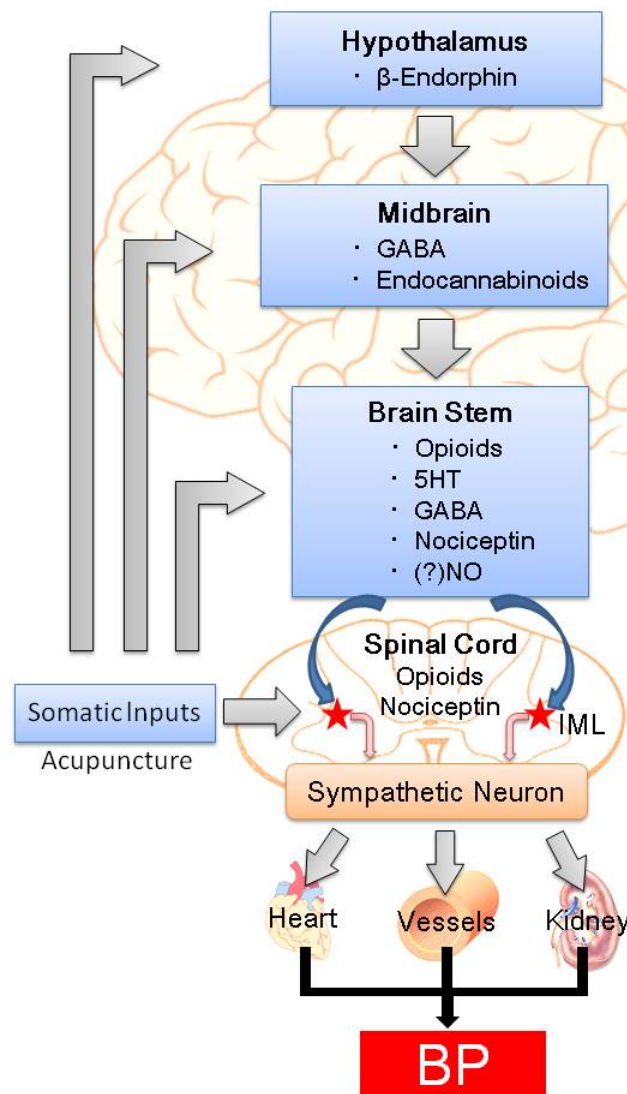


Figure 2. Neuroendocrine modulation of blood pressure by acupuncture. Abbreviations: GABA, γ -aminobutyric acid; 5HT, 5-hydroxytryptamine or serotonin; NO, nitric oxide; IML, intermediolateral column of the spinal cord. From Ref 66, courtesy W. Zhou.

of ruptured aneurysms in subarachnoid hemorrhage [84]. In a recent publication from Shanghai [85], the authors reviewed the progress of researches on the mechanism of acupuncture underlying improvement of acute cerebral hemorrhage from experimental studies and research methods. The effects of acupuncture mainly involve (1) lessening inflammatory reactions, (2) reducing impairment of free radicals and excitatory amino acids on cerebral neurons, (3) balancing release of vascular bioactive substances to increase regional cerebral blood flow, and (4) promoting repair and regeneration of the neural tissue. In regard to the research methods, many new biological techniques such as biological molecular approaches, neuro-cellular chemical methods, reverse transcription-polymerase chain reaction (RT-PCR) or quantitative real-time PCR, situ hybridization, western blotting, and electron microscopy

have been extensively applied to researches on the underlying mechanisms of acupuncture therapy for cerebral infarction. In addition, the authors also pointed out that, in spite of achieving some greater progresses in experimental studies, most of the results basically reflect static, isolated and regional changes rather than dynamic and whole body changes. For these reasons, the authors recommended more *in vivo* research techniques and noninvasive research methods in the investigation of the underlying mechanisms of acupuncture therapy for acute cerebral ischemia [85].

Acupuncture has also been used successfully for post-stroke motor rehabilitation [86], behavioral recovery [87], aphasia [88], dysphasia [89], dysphagia [90], cognition disorders [91], depression [92], and urinary incontinence and urinary tract infection [93].

8. Smoking cessation

Cigarette smoking is prevalent in China; 67% of men [94] and 40% of male physicians [95] are smokers. It is a major cause of death in China and a principal cause of coronary heart disease in China [96]. In addition, secondhand smoke exposure (52% of nonsmokers in China are exposed to tobacco smoke for at least 15 minutes daily for >1 day per week [97]) was responsible for increased mortality due to coronary heart disease, ischemic stroke, lung cancer and chronic obstructive pulmonary disease in a recently published 17-year cohort study in China [98]. Another recently completed Chinese population study, the Kailuan community study, showed smoking cessation to be one of the seven key components of an essential population-wide strategy to reduce cardiovascular disease [99]. Although a 2012-15 blueprint on chronic disease prevention and control released by the Chinese Ministry of Health on May 21, 2012 set goals of reducing the adult smoking rate to below 25% among other goals [100], I have serious doubts as to how successful the Chinese Health Ministry's effort will be [101]. Nevertheless, any effective measure in curtailing cigarette smoking should be actively and urgently pursued.

Acupuncture has been found in a recently published review of smoking cessation intervention studies in China to yield a much higher abstinence rate than pharmacotherapy or counseling [102]. This observation was confirmed by two recently published meta-analyses of randomized controlled trials [103,104]. It has been postulated that, by increasing the levels of endorphin, enkephalin, epinephrine, norepinephrine, serotonin, and dopamine in the central nervous system and plasma, acupuncture provides the smoker with a deterioration in the taste of smoking, a decrease in the desire of smoking, and the obstruction of psychological symptoms resulting from smoking cessation [105]. The latest theory is that one of the acupuncture points stimulated by the acupuncture needle in the ear corresponds to the closest position of the vagus nerve to the cutaneous surface. Therefore, by stimulating this point, the acupuncturist blocks the outflow of withdrawal symptoms coming from the parasympathetic nervous system through the vagus nerve. However, more studies are needed to determine whether acupuncture is as efficacious as, or even more so than, pharmacotherapies.

9. Diabetes

Diabetes is associated with a marked increase in the risk of coronary artery disease, so much so that patients with diabetes should be treated as if they have existing coronary artery disease [106,107,108,109]. As a matter of fact, diabetes should be considered as a coronary artery disease equivalent [95,110]. The prevalence of diabetes is rising [108]. The main reasons for the rising prevalence of diabetes are smoking and obesity, which are certainly true for China [111,112]. A recent study from the University of North Carolina School of Global Public Health, using data from the China Health and Nutrition Survey, the longest ongoing study of its kind in China, reported that Chinese teenagers have a rate of diabetes nearly four to five times greater than their counterparts in the United States (1.9% vs 0.5% for boys and 0.4% for girls) [113]. Although acupuncture has been advocated for treatment of obesity (vide infra), a recent review of the literature questioned its validity owing to small sample size and low methodology quality of the studies [114].

On the other hand, acupuncture has been found to be effective in the management of patients with diabetes, by causing the release of endogenous opioid peptides such as β -endorphin from adrenal gland and thereby enhancing insulin secretion [115]. A recent literature review showed acupuncture to be effective in lowering blood glucose in both humans and rats [115]. Ear acupuncture in 45 diabetics in Peking University of Shenzhen Hospital, Shenzhen, Guangdong Province, China resulted in significant improvement in fasting plasma glucose, blood glucose load after 2-hour 75 gm oral glucose tolerance test and glycosylated hemoglobin [116]. Two recent studies from Beijing, China on patients with impaired glucose tolerance reported similar improvement in these parameters following electro-acupuncture, thus confirming its effectiveness in the prevention and treatment of diabetes at the early stage [117,118]. Another study from Nanjing, China reported acupuncture to be effective in lowering fasting blood leptin level, which may contribute to its clinical effect in improving diabetes [119]. Electro-acupuncture has also been used successfully for the treatment of diabetic peripheral neuropathy in rats [120] as well as in patients [121], although the quality of reports about randomized controlled trials is moderate to low [122]. Finally, acupuncture has been used in treating urinary tract infection in diabetic patients [123].

10. Obesity

Obesity is another risk factor for coronary artery disease, hypertension, chronic heart failure, stroke and diabetes [124]. It is increasing in prevalence worldwide, especially in developing countries like China [95,125,126]. Two recent systematic reviews, one published in 2009 [127] and the other in 2012 [114], both suggested that acupuncture is an effective treatment for obesity, with fewer adverse effects of the various dieting plans and Western anti-obesity drugs. A recent study in obese rats showed that electro-acupuncture led to a reduction of body weight, decrease in the plasma leptin levels, and an increase in leptin receptor expression in the hypothalamus, suggesting that regulating the expression of leptin and the leptin receptor

might be one of the molecular mechanisms underlying the reduction of body weight in diet-induced obese rats by electro-acupuncture treatment [128]. Another human study reported in 2010 found that laser acupuncture exerted a therapeutic effect on simple obesity by reducing both body weight and body mass index [129]. However, the amount of evidence is not fully convincing, because of the small sample size and poor methodological quality of all the reported trials to date.

11. Acupunctural anesthesia for cardiac surgery

The most amazing application of acupuncture is acupunctural anesthesia. Skeptics who deny that acupunctural anesthesia can work have suggested that acupuncture is nothing more than an effective use of hypnosis or autosuggestion. I was also a skeptic until I witnessed with my own eyes several operative procedures performed on conscious patients under acupunctural anesthesia including those with acquired valvular and congenital heart diseases (Figures 3 and 4). Being a native-born Chinese, I was able to communicate directly with the patients, without going through any interpreters, who may either inadvertently or deliberately omit or distort any actual expressions from the patients, to find out what discomfort they might experience during the procedures. Of course, I was not the only physician who was impressed by cardiac surgery under acupunctural anesthesia. Other well-known surgeons around the world, such as DeBakey from the United States [130], Hollinger et al from Germany [131], and Caracausi from Italy [132] were too.

Acupuncture also has a cardioprotective effect as a pretreatment on patients undergoing heart valve replacement. Cardiac ischemia-reperfusion injury after cardiopulmonary bypass often contributes to postoperative morbidity and mortality in patients undergoing heart valve replacement. A randomized controlled trial, which was reported from Xi'an, China in 2010, showed that electro-acupuncture pretreatment significantly reduced overall serum troponin I release at 6 hours, 12 hours and 24 hours after aortic cross-clamping removal [133]. Meanwhile, electroacupuncture pretreatment also reduced the inotrope score at 12 hours, 24 hours, and 48 hours after the intensive care unit arrival and shortened intensive care unit stay time ($p < 0.05$) [133]. The cardioprotective effect of transcutaneous electric acupoint stimulation was further confirmed recently in the pediatric cardiac patients with congenital heart disease [134].

After its initial enthusiasm in China in the 1970s, in the subsequent years acupunctural anesthesia for open heart surgery gradually became less and less frequently used throughout China, because of its limitations and disadvantages [3,135]. Fortunately, with recent modification of the technique by combining acupuncture with conscious sedation, Zhou et al [135] were able to demonstrate its effectiveness again. This modification, which will be discussed bodes well for the future of acupunctural anesthesia for cardiac surgery, not only because of its sound physiological principles, simplicity in clinical application, significant benefit to the patient and favorable cost effectiveness, but also for its positive impact on healthcare cost.

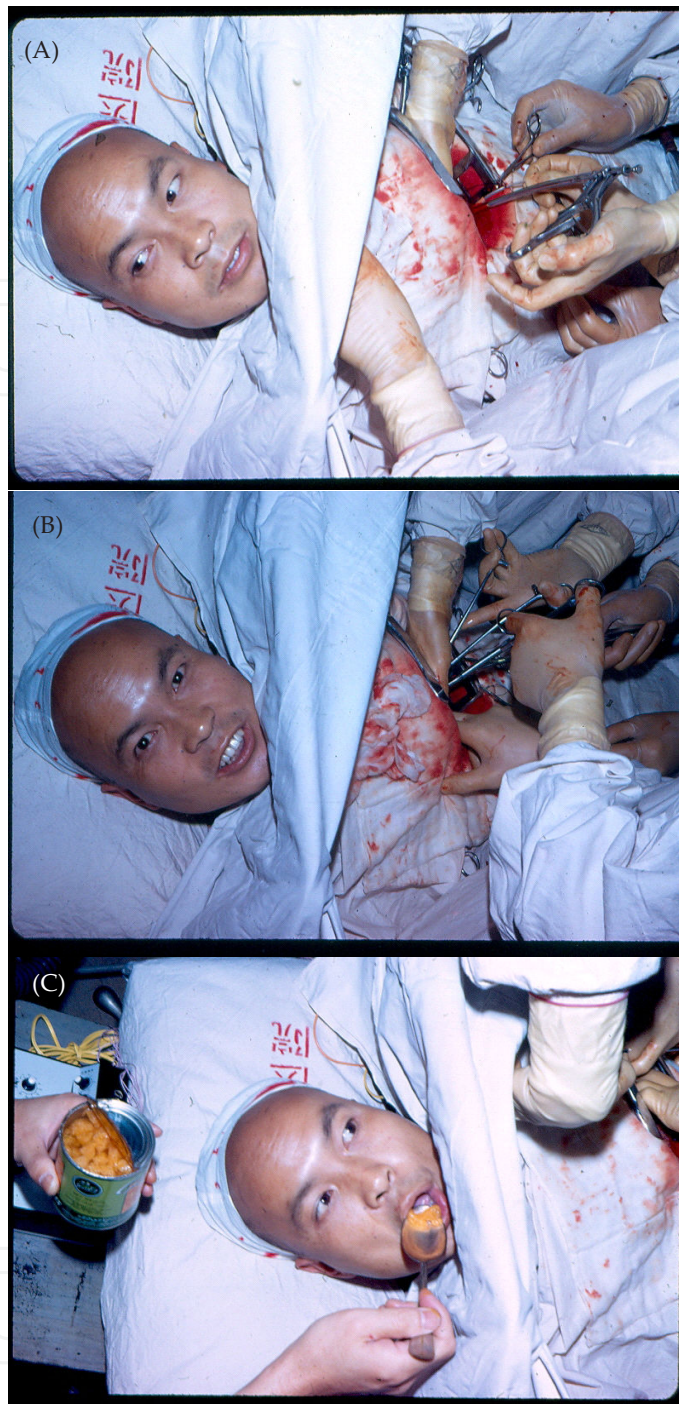


Figure 3. A man undergoing a closed transventricular mitral commissurotomy under acupuncture anesthesia in a hospital in Shanghai. (A) Patient fully awake and comfortable; (B) Patient smiling during the procedure; (C) Patient eating oranges during the operation. All photographs taken by the author during his 1972 visit to China.

12. Adverse effects and complications

Although acupuncture is extremely safe, adverse effects and sometimes serious complications have been reported. These include infective endocarditis [136,137,138], pericardial effusion

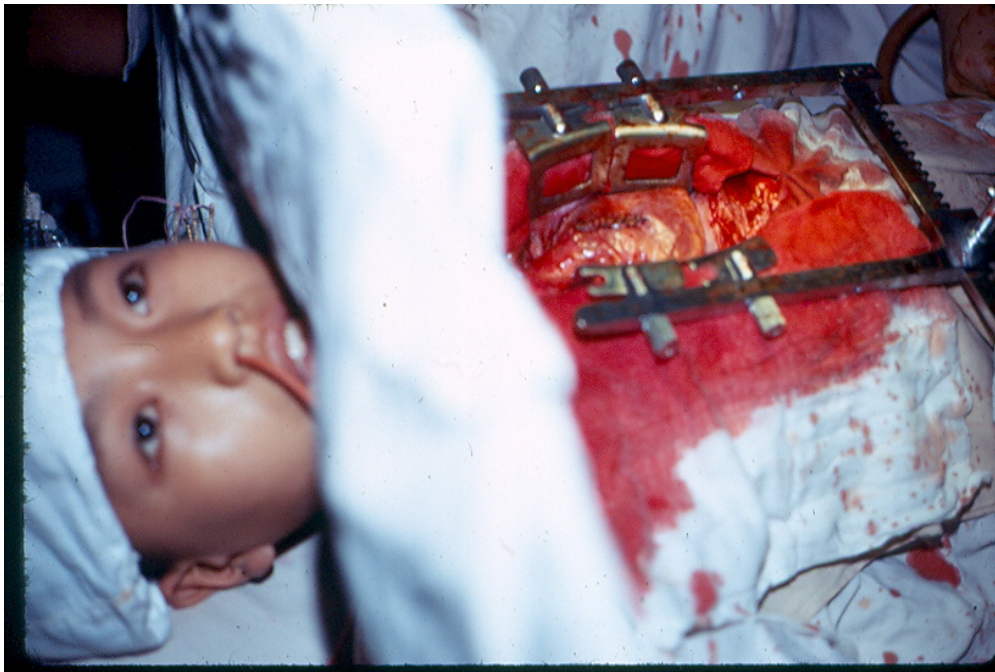


Figure 4. A child fully awake and comfortable while undergoing open heart surgical closure of a ventricular septal defect under acupunctural anesthesia. Photograph taken by the author during his 1972 visit to China.

[139], cardiac tamponade [138,140], pneumothorax [141] and AIDS [138,142]. However, infective endocarditis and AIDS are not due to acupuncture per se, but to the unsterile technique that was employed during acupuncture. Hundreds of thousands of acupuncturists worldwide perform millions of acupuncture procedures per year [143]. Considering the small number of reported complications in the literature, acupuncture is very safe indeed [143,144,145,146,147]. As a matter of fact, the recent report of the successful use of electroacupuncture for treatment of arthritis in a patient with a total artificial heart is further testimonial to its safety [148].

13. Conclusion

Acupuncture has a definite place in cardiology. When performed by trained acupuncturists, it is safe, effective, cost-effective, and widely available. As more research evidence for acupuncture efficacy, including the application of functional magnetic resonance imaging technique in recent years [149], becomes available, it will be possible to increase physician knowledge and change attitudes towards acupuncture [150,151], as it was so predicted by the NIH Consensus Development Panel on Acupuncture convened a decade and a half ago [152]. When incorporated into conventional health care as an integrated approach, the future of this ancient Chinese therapeutic modality is bright. As a matter of fact, acupuncture should prove to be an attractive alternative to Western medicine in the current era of cost containment in healthcare [153]. Although Western medicine may be preferred in the management of some acute cardiac conditions, such as acute myocardial infarction or malignant arrhythmias,

traditional Chinese medicine, of which acupuncture is an essential component, has a definite place in the management of various subacute and chronic cardiovascular disorders and risk factors. However, a recent systematic review showed that, in acute low back pain, acupuncture appears to be actually more effective than drugs for symptomatic improvement [154]. Therefore, more registered high-quality clinical trials need to be continued worldwide on this 2,000+-year-old ancient Chinese therapy [155].

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