UNIVERSITY OF Southampton

University of Southampton Research Repository
ePrints Soton

Copyright © and Moral Rights for this thesis are retained by the author and/or other copyright owners. A copy can be downloaded for personal non-commercial research or study, without prior permission or charge. This thesis cannot be reproduced or quoted extensively from without first obtaining permission in writing from the copyright holder/s. The content must not be changed in any way or sold commercially in any format or medium without the formal permission of the copyright holders.

When referring to this work, full bibliographic details including the author, title, awarding institution and date of the thesis must be given e.g.

AUTHOR (year of submission) "Full thesis title", University of Southampton, name of the University School or Department, PhD Thesis, pagination

http://eprints.soton.ac.uk

UNIVERSITY OF SOUTHAMPTON

THE CLINICAL EFFECTS OF ACUPUNCTURE: METHODS OF EVALUATION

VOLUME I

George Thomas Lewith, MA, MB, BChir, MRCP, MRCGP

A thesis submitted for the degree of

Doctor of Medicine

Primary Medical Care (1980-1983)
Aldermoor Health Centre
Southampton SO1 6ST

February 1994

THE UNIVERSITY OF SOUTHAMPTON

ABSTRACT

FACULTY OF MEDICINE

Doctor of Medicine

THE CLINICAL EFFECTS OF ACUPUNCTURE: METHODS OF EVALUATION

by George Thomas Lewith, MA, MB, BChir, MRCP, MRCGP

This thesis is divided into four sections. The first of these comprises chapters 1-4 which provide a background to acupuncture and its mechanism of action.

Section 2 concerns methodological issues including placebo effects, a review of previous studies on acupuncture, the selection of patients for such studies and the need to assess acupuncture critically.

Section 3 represents the original contributions of the author, including clinical trials of acupuncture in a variety of situations such as the management of pain, smoking cessation and the treatment of nausea. Each of these issues is tackled in separate chapters and the specific findings are discussed at the end of each chapter.

Section 4 represents an overall discussion of the findings as well as suggestions for further research.

ACKNOWLEDGEMENTS

I should like to acknowledge the help of Professor Charles George in his role as my adviser and Mrs. Jackie Burnham for her untiring efforts at typing and retyping my drafts. Last but not least I should like to thank my family for their tolerance while I completed this thesis.

CONTENTS

SECTION 2

SECTION 4

SUMMARY

Acupuncture is an ancient therapeutic art, firmly rooted in traditional Chinese medicine. It has been practised in the East for at least three thousand years, but only recently has it attracted Western medical attention. The concepts that underpin traditional Chinese medicine are outlined in Chapter 2, as well as the philosophy involved which represent a complete medical system with its own physiology, anatomy, diagnostic skills and therapeutics.

The physiologic effects of acupuncture, particularly the mechanisms that may be involved in the treatment of chronic pain, are discussed in Chapter 4 in which the endorphin hypothesis is explored. Chapter 5 is devoted to the placebo effect which is particularly relevant to acupuncture. Consequently an understanding of placebos and their underlying mechanism is essential. Evidence for the two common "control or placebo treatments" that have been used as comparators for real acupuncture is reviewed. Chapter 6 provides a literature review of the clinical trials published to-date and focuses on pain, addiction (smoking withdrawal) and the use of a specific acupuncture point (P6) in the treatment of nausea. Chapter 7 reviews the particular problems that surround the selection of patients for trials within complementary medicine, while chapter 8 introduces the research section of this thesis.

The aim of the study was to develop clinical trials methodology for evaluating the effects of acupuncture in a variety of conditions including pain, the treatment of addiction to nicotine and the control of nausea.

Chapter 9 reproduces a paper by Lewith and Machin (1983) which was the first attempt to provide a theoretical model that underpinned evaluation within complementary medicine. It concentrated on pain and suggested that

real acupuncture (acupuncture in an appropriate point) provided effective treatment in 70% of individuals, sham acupuncture or random needling (acupuncture at an inappropriate point) was effective in 50% of individuals and that a true placebo such as mock TNS provided effective treatment for only 30% of individuals.

Painful conditions

A single blind study of auricular and body acupuncture compared with placebo (mock transcutaneous nerve stimulation) was performed on 62 patients with post-herpetic neuralgia. There was no difference in the amount of pain relief recorded in the two groups during or after treatment. This suggests that acupuncture is of little value as an analgesic therapy for post-herpetic neuralgia. However, the study method and the use of mock TNS as a placebo would appear to be of value when assessing the effects of acupuncture in other painful conditions.

A second single blind study analysed the effect of acupuncture as a treatment for migrainous headaches in 48 patients. After an initial period of 4 weeks during which their headache intensity and severity were assessed, they were randomised and given either real acupuncture or mock TNS. Treatment continued for a period of 6 weeks and follow-up was continued for a further period of 24 weeks. Patients filled in daily diary cards providing information about the intensity and frequency of the headaches throughout this period. A survival curve technique was then used to analyse the results, looking at time to return of headache with respect to baseline headache levels. Acupuncture had, at best, a 20% treatment advantage over placebo (mock TNS) but this was not statistically significant, possibly due to the fact that too few patients were entered into the study.

The final study on pain was a single blind randomised controlled trial, to evaluate the effects of acupuncture on trapezio-metacarpal joint osteoarthritis (TMC joint OA). This study was more thorough in that it attempted both to assess subjective pain by both visual analogue and verbal scales) and objective measurements of joint function. Patients were entered into the study and their pain was recorded for a baseline period of one week. They were then randomised and given 6 treatments over a period of 2 weeks, before being followed up for a further 2 weeks. Throughout this time they completed a daily pain diary. Objective assessment of joint tenderness and joint function were carried out at entry into the study, after 2 weeks' treatment and again at the end of the follow-up period. The study showed a statistically significant difference between real acupuncture and mock TNS: 76% of patients in the acupuncture group showed significant pain reduction, while only 20% in the mock TNS group showed significant pain reduction.

Smoking

Chapter 11 evaluates the effect of acupuncture as a treatment for smoking withdrawal. Eighty-one volunteers were entered into a study to compare acupuncture and group therapy as methods of smoking withdrawal. Group A received acupuncture at a point said to be effective for smoking withdrawal, Group B received acupuncture at a point said to be ineffective for smoking withdrawal and Group C received group therapy. Six months after the completion of treatment, 18% of patients in Group A, 15% of patients in Group B and 11% of patients in Group C had apparently given up smoking completely. There was no significant difference between the real and sham acupuncture treatment groups. Thus while acupuncture might represent a good treatment for smoking cessation, its effects are not point

specific.

Nausea

Chapter 12 looked at the use of P6 as a treatment for nausea. Two study models were used: the first employed P6 acupressure with Sea-Bands as an anti-emetic in patients receiving cancer chemotherapy. The study model was a randomised single-blind cross-over study comparing acupressure on the correct point (P6) with an incorrect point on the ankle (sham acupressure). Patients were given either real or sham acupressure at subsequent chemotherapy cycles. Fifty-three patients were entered and 38 completed the study. The study demonstrated a highly significant difference between sham and real acupressure. Those receiving wrist acupressure had significantly less sickness (53% in the real acupressure group as compared to 29% in the sham acupressure group) and nausea (55% in the real acupressure group as compared with 26% in the sham acupressure group). The overall mood and condition was also substantially better in those treated at the correct acupressure point. These differences were particularly noticeable in those receiving chemotherapy with a high emetogenic potential. The second study involved the treatment of early morning sickness. The model employed was a "double blind" cross-over study. Patients were entered in early pregnancy and given clear instructions about the real and sham acupressure points that should be used. The investigator was unaware of which points were being used and the results were recorded using a simple daily diary. Fewer patients were entered into the study (23 were entered and 15 completed the study) but the results were highly significant. P6 acupressure was significantly more effective than sham acupressure in the relief of nausea as measured by daily visual analogue scales ($P = 0.019$). The credibility of sham

acupressure was assessed and was found to be convincing by most patients entered into the study.

The results obtained from these clinical trials have allowed us to develop an overview of how acupuncture can be evaluated. These are discussed in some detail in chapter 13 but in essence suggest that different diseases may require different evaluating techniques.

In summary, the central objective of this thesis was to attempt to develop better clinical trial methodology in order to evaluate acupuncture. Three areas have been studied, pain, addiction and the use of pericardium 6 as a treatment for nausea. In all these areas, the research presented in this thesis has provided a further, more detailed insight into the development of specific clinical trial methodology. Furthermore, it has allowed for the development of an overall strategy for the evaluation of the clinical effects of acupuncture. The hypothesis suggested in the discussion section creates a unified approach which takes into account the assumptions made in traditional Chinese medicine, our knowledge of the neurophysiology of acupuncture in both pain and addiction and the information gleaned from the clinical trials discussed in this thesis and those published elsewhere.

SECTION 1

ACUPUNCTURE: HISTORY AND POTENTIAL MECHANISMS OF ACTION

CHAPTERS 1 - 4

CHAPTER 1

HISTORICAL AND GENERAL INTRODUCTION

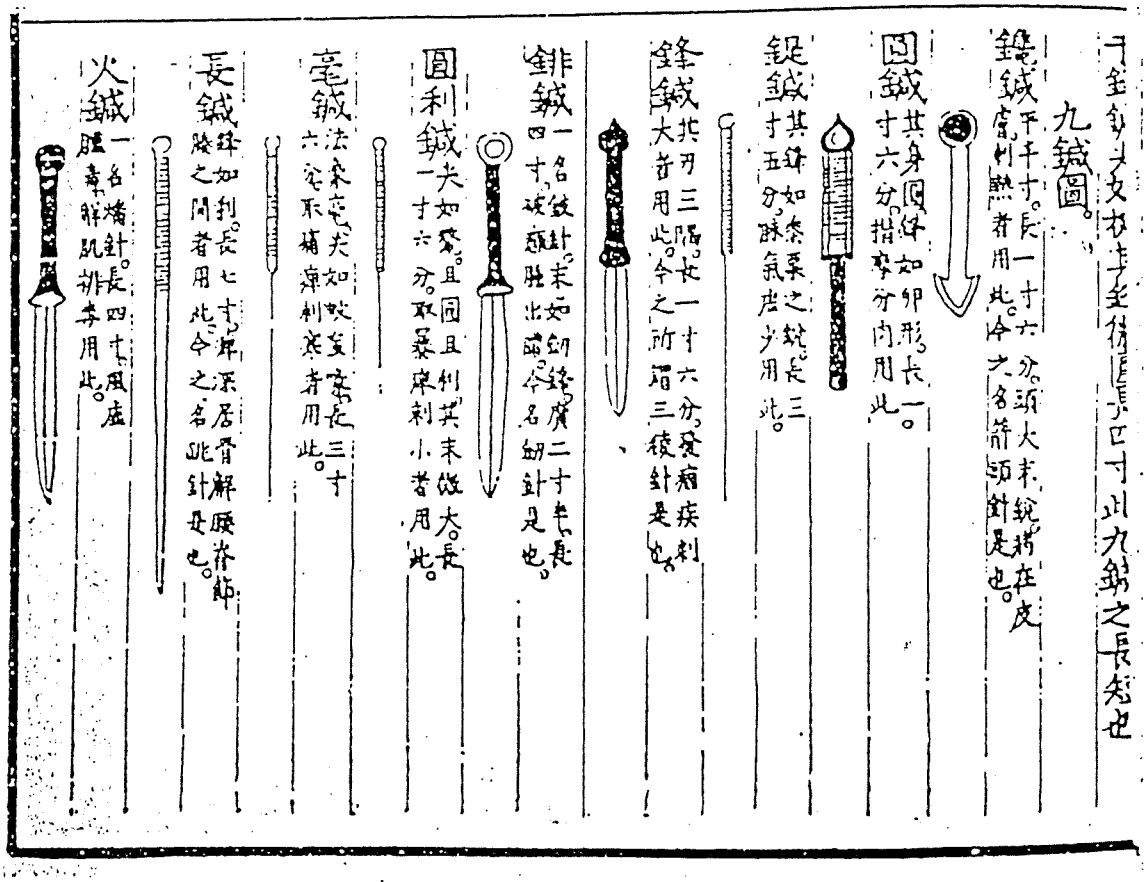
One of the first books ever published, the Huang Ti Nei Ching Su Wen (the Yellow Emperor's Classic of Internal Medicine) is a treatise on traditional Chinese medicine. It involves a discussion between Huang Ti (the Yellow Emperor) and his chief minister Chi Po. It was probably written just at the beginning of the warring states period (approximately 500 BC), although some authorities suggest that much of the information therein may date from 500 years earlier than that, placing some of the text at 1000 BC. A modern translation of the "Huang Ti Nei Ching Su Wen" by Veith (1972) is available in English along with an appropriate commentary.

The Nei Ching Su Wen lays the philosophical, pysiological and practical ground rules for the whole system of traditional Chinese medicine. Acupuncture represents just one of the treatments within this system; equal emphasis is given to massage and traditional Chinese herbal remedies. Some of the observations made within this text are fascinating; the Chinese quite clearly demonstrate they had a good knowledge of the double circulation of blood some 2000 years before William Harvey. Presumably the fact that William Harvey's Mandarin was limited may have had something to do with the Western belief that he discovered and described this phenomena.

Not only did the ancient Chinese appear to have an understanding of modern physiology, but also they had begun to use some simple surgical techniques probably a thousand years before Christ. It has been suggested by a number of authorities including Needham (Needham and Lu, 1980) that "Bian

stones" for puncturing or draining abscesses were the forerunners of modern acupuncture needles. By 500 BC these had developed into a fairly sophisticated and standardised Chinese surgical kit; the classical 9 needles have been found in a number of sites throughout China constructed of many metals including gold, silver and bronze. These were used for simple surgical procedures and one of the classical nine, the filliform needle, has become the standard acupuncture needle (Figure 1.1).

Figure 1.1 **The classic nine acupuncture needles taken from the Compendium of Acupuncture and Moxibustion compiled in 1601.**



The third from the right is the modern filliform acupuncture needle.

The ancient Chinese developed a system of anatomy and physiology. While this appears to predate a number of the observations subsequently made by Western science, they also emphasised one very important area which was significantly different from Western medicine and which they considered to be central to their form of medicine. This was the concept of Qi or energy. Most traditional forms of medicine have some vitalistic element which is used to explain the difference between living and dead matter. Perhaps a Western equivalent to this vitalistic approach might have been the Alchemist's search for the philosopher's stone. The Chinese system of medicine depends on manipulating Qi in order to correct the body's imbalance and thereby return it to health. Their system of physiology, while again making many similar observations to those which we have in Western medicine, also looked at the organs from an energetic point of view with the channels and the acupuncture points on them, reflecting the organs energetic status in both health and disease.

Jesuit missionaries visited the Ming Court during the late sixteenth and early seventeenth centuries. Information then began to flow much more coherently between the scientists and philosophers in the East and the West. The West benefited by learning about traditional Chinese herbal remedies and acupuncture, and we begin to see reports of acupuncture in Western medical literature by the middle seventeenth century (Needham and Lu, 1980).

It is interesting to note that interest in acupuncture, in the United Kingdom, is over 150 years old. John Elliottson, a physician at St. Thomas's Hospital, reported on a case of chronic rheumatism cured by acupuncture in an edition of The Lancet published in 1827 (Elliottson, 1827). Enthusiasm for acupuncture was particularly apparent in The

Lancet publications between 1820 and 1840; in all 20 papers concerning acupuncture appeared during this period. Subsequently, there was a singular lack of interest in acupuncture with the odd publication occurring towards the end of the nineteenth century and nothing of note in the mainstream medical journals until 1970. Between 1970 and 1990 over 60 papers concerning acupuncture have been published in the British Medical Journal and over 50 in The Lancet (Saks, 1991).

Acupuncture is not therefore a new phenomenon within British academic medicine but perhaps the rise of conventional medical science during the first 60 or 70 years of this century swamped such apparently bizarre treatments.

Nixon's visit to China in 1972 together with an understanding of the neurophysiology of pain have had major effects to increase the popularity of techniques such as acupuncture. Acupuncture is no longer solely a mystical procedure in which a needle is inserted and somehow, by magic, causes analgesia. We understand a great deal about the physiology of acupuncture and, therefore, can begin to feel confident in using this technique more widely. This confidence underpins the widespread use of acupuncture in pain clinics and physiotherapy departments throughout the United Kingdom and is reflected in the increase in publications about acupuncture over the last 20 years.

Acupuncture, along with many other different complementary medical techniques, is growing in popularity. It is interesting to speculate why these "traditional" approaches to medicine are becoming more popular when our knowledge of conventional medicine has increased exponentially. In the mid '70s when I began to practice acupuncture, such techniques were considered to be very much in the "alternative" field. Within the United

Kingdom, the term complementary is used more commonly to describe these areas of medicine. Complementary in effect means that these approaches should ideally be used in conjunction with conventional medicine. A patient seeking treatment should be able to decide which approach offers them the best and most acceptable therapy and that this decision should be made based on a combination of preference and good, hard clinical evidence. Such decisions are not easy to make even within conventional medicine, as all too frequently we do not have enough evidence to justify absolutely the clinical decision we make when confronted with a patient's individual and particular problems.

What is complementary medicine?

Complementary medicine is difficult to define, as the Prince of Wales suggested while president of the British Medical Association, "Today's alternatives are tomorrow's orthodoxy". Over the last 20 years acupuncture has moved from being largely unacceptable to the majority of the conventional medical profession to something that is available in many National Health Service Hospitals. Manipulative techniques such as osteopathy and chiropractic have achieved a similar status. In the 1930s doctors could be "struck off" the medical register for even talking to an osteopath, whereas now many osteopathic techniques are used regularly by physiotherapists and medically qualified individuals in general practice and in hospital rheumatology medicine departments. The division between conventional and complementary (or alternative) is perpetually changing. There is often no clear division and one cannot easily argue that one therapy is now acceptably conventional whereas another is purely complementary or alternative. Taking these arguments into account it is probably acceptable to view techniques such as acupuncture, homoeopathy,

osteopathy, chiropractic, aromatherapy and reflexology as being largely within the complementary field. However, this list could be extended further and others would argue that osteopathy and the practise of acupuncture by physiotherapists is more conventional than alternative.

Acupuncture: can it be defined?

Acupuncture as a specific therapy has by virtue of its name quite a straightforward definition. That is to puncture the skin at strategic points called acupuncture points in order to "rebalance" the body and thereby treat disease. However, acupuncture has come to mean many different things. In some instances, acupuncture involves stimulating acupuncture points with a laser or with equipment designed to provide heat over an acupuncture point. In addition there are many different acupuncture techniques including ear acupuncture, hand acupuncture, scalp acupuncture and foot acupuncture to name but a few. Therefore, the relatively simple traditional Chinese concept of acupuncture points connected by channels is not necessarily a comprehensive basis upon which to select points requiring treatment. There are some schools that inject acupuncture points with a variety of different conventional and homoeopathic remedies. The one consistent observation that can be made about acupuncture is that it involves stimulating or treating specific points on the body. By and large these points are treated by needle insertion in the first instance, although frequently other stimulatory techniques are applied to the acupuncture point. We must accept this somewhat woolly definition if we are to consider all the techniques which have come to be considered under the general heading of acupuncture. However, the specific research that will be discussed in this thesis will involve clear definitions of both the disease being treated, and the

acupuncture techniques applied.

My interest

My personal interest in acupuncture began in 1977 after some discussions with lay acupuncturists in the United Kingdom. I then decided to try and visit China in order to learn more and was accepted on a three month course in the College of Traditional Chinese Medicine in Nanjing. This course ran for three months in early 1978 and allowed me to develop a theoretical and practical understanding of traditional Chinese medicine and acupuncture. I subsequently travelled to Australia and began to use acupuncture in the context of Australian general practice; much to my surprise it worked on the Australians as well as the Chinese! On my return to the United Kingdom I became fascinated by the whole subject of traditional Chinese medicine and quite specifically acupuncture. I was then appointed as lecturer in primary medical care at the University of Southampton and began to develop my research interests within this area. The majority of the work that will be presented in this thesis is a product of the research development that began while in post as a lecturer in primary medical care.

When I began this work there was almost no research culture within acupuncture or indeed any of the complementary therapies. The first serious methodological paper written about any of the complementary therapies was that produced by Lewith and Machin in 1983 and concerned the study models used to evaluate acupuncture. At the present time, 25% of the controlled trials comparing acupuncture with placebo have been published by Lewith (Vincent 1993).

The introduction to this thesis sets the background and asks why we should assess complementary medicine; what do we understand about acupuncture, how

does acupuncture work and what clinical evidence is there to sustain its use in practice? Initially, I was involved in a data collection exercise which will be presented briefly in Chapter 9. The following chapters will review a number of different clinical trials designed to assess acupuncture and acupressure in a range of conditions. The object of this thesis is to find better methods for evaluating the clinical effect of acupuncture rather than necessarily to prove that it is effective.

CHAPTER 2

THE CONCEPTUAL BASIS OF TRADITIONAL CHINESE MEDICINE

Introduction

Needham and Lu have reviewed the history rationale and development of acupuncture (1980). The following summary of the major concepts within traditional Chinese medicine is presented in order to place acupuncture in its historical context and to demonstrate how the technique of acupuncture evolved from a totally different and discrete system of medicine. While the main thrust of this thesis focuses on the clinical evaluation of acupuncture, this therapy cannot be divorced from its antecedents, for to do so would mean that when researchers came to evaluate acupuncture they may ultimately test what they feel acupuncture ought to be rather than what it actually is. All these concepts are discussed in detail in Lewith and Lewith (1980).

One of the major assumptions inherent in traditional Chinese medicine is that disease is due to an internal imbalance of Yin and Yang; therefore disease can be treated by correcting the Yin Yang imbalance, thereby returning the body to a healthy state. This concept was applied to both individuals and society at large. In individual terms the ancient Chinese physicians preached moderation in all things, such as alcoholic intake and gastronomic excess. They also stated that daily activities should include mental as well as physical tasks. The wealthier Chinese visited their doctor when they were well, paying a retainer to the doctor to keep them healthy. If they became ill the doctor lost his fee.

Such a highly sophisticated and personal system of health care is impracticable within the current limitations of Western society, but the

concept behind such ideas represents a radically different approach to health and disease. The Chinese culture was also one of the first to grasp the potential within the broader field of preventative medicine. Many of these ideas were effected in the public health measures, which first began to be introduced during the Warring States period.

The body is a delicate balance of Yin and Yang. Yin represents water, quiet, substance and night, whilst Yang represents fire, noise, function and day. The two are polar opposites and because of this one must be present to allow the other to exist; for instance, how can you experience joy if you do not understand misery? The state of the body is determined by the balance of Yin and Yang within it. Each of the organs of the body has an element of Yin and Yang, although one organ may be more Yang in its nature, whilst the other is more Yin. One organ may be more important in its substantive form (Yin) whilst another is more important because of its functional abilities (Yang). When the healthy body is examined as a complete functioning system the Yin and Yang properties within it are in a fluctuating balance.

The balance of Yin and Yang is not always exact. Sometimes a person's mood may be more fiery, or Yang, whilst at other times he may be quieter and therefore more Yin. Normally the balance changes from hour to hour and day to day, but if the balance is permanently disordered, for instance if Yin consistently outweighs Yang, then the body is unhealthy and disease results.

The Therapeutic Application of Yin and Yang

When there is imbalance external agents can invade the body and cause disease, these external agents being called pathogens. The essential principle of Chinese traditional medicine is to decide on the exact nature

of the imbalance between Yin and Yang, and the pathogen causing the trouble, and then to correct these pathological processes. As the natural forces of the body return to a normal balance the disease is then cured.

The art of traditional Chinese medicine is to particularize the imbalance accurately so that it can be corrected quite specifically. The patient is then treated by using specific acupuncture points on the body in order to re-balance the body. This broad system of traditional medicine applies to all aspects of therapy used by the ancient Chinese, particularly acupuncture and herbal medicine.

The diagnostic and therapeutic principles of Yin and Yang and the pathogens are based on a system of anatomy and physiology peculiar to traditional medicine. The anatomy of traditional medicine is represented by the acupuncture points and the channels that connect them. The physiology is represented by the organ functions that are outlined in the "Nei Ching Su Wen" (Veith 1972).

The Anatomy of Traditional Chinese Medicine

The channels are a system of conduits that carry and distribute Qi, or vital energy, throughout the body. Each of the organs of the body is represented by a channel, and diseases of a particular organ can be treated by using acupuncture points on the channel representing that organ.

Disease is said to be present when the flow of vital energy through the channels is disrupted. This may occur when the integrity of the channels themselves is damaged by a sprain or strain. The Chinese describe this as a disease of 'Bi', or pain, caused by a localized disruption to the flow of Qi. The flow of Qi through the channels may also reflect the result of internal disease; for instance, if there is a disease of the liver then the flow of Qi through the liver channel will be abnormal.

The concept of channels exists exclusively in traditional Chinese medicine, but what evidence do we have for them within our conventional paradigm? A considerable amount of work has been carried out particularly in China on the possible anatomical basis of meridians and acupuncture points. Propagated channel sensation (PCS) has been investigated extensively by many Chinese authors. PCS refers to the sensations experienced by a small proportion of individuals when acupuncture points are needled; these sensations tend to run along the acupuncture meridians though it is not clear whether the subjects, who are presumably all Chinese, know in advance where the meridian pathways are supposed to be (Bensoussan 1991). Changes in skin resistance and temperature have also been suggested as providing evidence for the existence of meridians (Zhaowei et al, 1985). Reviewing this work Macdonald (1989) acknowledges that sensations may follow meridian lines, but suggests that such phenomena can be explained without postulating the existence of a meridian system. Meridians or channels have also been detected by the injection of radio tracers into acupuncture points, but more recent work suggests that the pattern of spread of radio tracer corresponds to the vascular drainage of the tracer (Lazorthes et al, 1990). In China research on the meridian phenomena continues, but most Western researchers would probably dismiss the idea of a meridian system. At the very least, we must conclude that on current evidence the existence of the meridians remains unproven.

Research on acupuncture points, however, has been more fruitful. There are definite links between the observations made by acupuncturists and phenomena observed by other clinicians and scientists. The existence and location of acupuncture points is crucial for a proper evaluation of clinical studies. Macdonald (1989) makes a number of comments. Firstly

it is difficult to be precise about the location of acupuncture points. Their position is usually assessed according to the size and shape of the patient and while there is reasonable agreement about the locations of many fundamental points (Vincent and Richardson, 1986) the number of points continues to grow. Secondly there is evidence that they become tender when a patient is sick and there is considerable overlap with the independently developed concept of trigger points noted by Melzack et al (1977). Thirdly, it is possible that acupuncture point locations have some kind of neurophysiological basis, perhaps corresponding to the termination of peripheral nerve endings. For our purpose it is important to realise that while acupuncture point locations may provide useful therapeutic guidelines, it is unlikely that they have a precise and constant location. The effect of acupuncture may be stronger at some points than others, but again this is unlikely to be an all or nothing phenomenon. Further discussion of acupuncture points and in particular their electrical properties, is to be found in the section on neurophysiological explanations for acupuncture.

According to traditional Chinese medicine, however, acupuncture points are quite specific areas on the channels. They represent points of maximum influence on the flow of vital energy, or Qi, through the channels. This can be demonstrated clinically by thinking about the disease process that occurs when someone tears a muscle. The traditional Chinese explanation for this disorder is that the channel running through the damaged muscle has been physically disrupted, resulting in local pain, a disease of Bi. In order to treat the pain, the integrity of the channel and the flow of vital energy through the channel, must be restored. This can be achieved by the selective use of acupuncture points on the damaged channel, which

restores the flow of Qi and relieves the pain.

If the internal balance of Yin and Yang is seriously disrupted (so that disease results), then there will be an abnormal flow of Qi, or vital energy, through the channel representing the diseased organ. The diseased organ must be diagnosed and then acupuncture points can be selected from the relevant channel. The use of these specific acupuncture points corrects the flow of Qi in the channel and this, in turn, has an effect on the diseased internal organ. The overall result of this therapy is to correct the imbalance within the body, and thus heal the disease; an internal disease can therefore be treated by external means.

The Physiology of Traditional Chinese Medicine

The physiology of traditional Chinese medicine has many similarities to that of Western medicine. Most of the specific organ functions defined in the "Nei Ching Su Wen" are astonishingly accurate in the light of modern scientific discoveries.

The heart is said to dominate the circulation of the blood. The "Nei Ching Su Wen" says, 'The heart fills the pulse with blood ..... and the force of the pulse flows into the arteries and the force of the arteries ascends into the lungs'. This seems to be a clear description of the circulation of the blood through the body, via the lungs. The idea that blood circulated in this way was peculiar to Chinese medicine until it was 'rediscovered' by William Harvey in the early seventeenth century. The publication of Harvey's work "Du Motu Cordis" has subsequently been hailed as one of the great landmarks of Western medicine, although at the time Harvey was thought to be mad, 'inflaming the medical profession by the suggestion of such a preposterous idea'.

The"Nie Ching Su Wen" also makes some surprising observations about the

kidneys. It states that the kidneys dominate bone, that they play an integral part in the process of growth and reproduction (in fact the Chinese character for kidney and testicle is sometimes indistinguishable) and that the kidneys control body fluid in concert with the lungs. These observations, made originally some 2,500 years ago, are astonishing in view of our current understanding of bone metabolism and embryology.

The Five Zang Organs

Although many organs have the same functions as in Western medicine there are also radical differences between the Western and Chinese systems. In traditional Chinese medicine the major functions of the body are built around the five main organs which are the heart, the lungs, the kidneys, the liver and the spleen. In Western medicine these organs are important, but not to the same extent as in traditional Chinese medicine. The Chinese call them the five Zang or five solid organs, and the system of the five Zang organs controls the main Yin Yang balance of the body.

Each of the Zang, or solid, organs is linked to a hollow or Fu organ. For instance, the kidney is linked both structurally and functionally to the urinary bladder. In Eastern and Western medicine both organs control the production and passage of urine. The channels representing the kidney and urinary bladder are also 'paired' as Qi is said to flow from one channel to the other. The liver and gall bladder are linked in a similar manner; they are also 'paired' channels.

For these specific 'paired' organs the linked functions are exactly the same as in Western medicine. The 'pairing' of the channels is particularly important when deciding on which acupuncture points should be used. Diseases of any organ can be treated by using the 'paired' channels; for example, diseases of the liver can be treated by using

acupuncture points on the gall bladder channel. Traditional Chinese medicine considers migraine headaches to be a disease of the liver and they can be effectively treated (with acupuncture) by using points on the gall bladder channel.

The emotions too are governed by individual organs. They do not consider the brain, or subconscious, as discrete entities, therefore the body and the mind are a real part of the same functional system. Each organ is given a particular emotion; for instance, the liver is said to be the organ affected by anger.

Vital Energy (Qi) and Blood

The force behind the biological functions occurring in any living tissue is Qi. Qi represents the vital energy of the body but it also has a material form. It is both substance and function; the substantive or material form of Qi is oxygen (clean Qi) or food, the non-substantive form of Qi is the real but evasive concept of 'vital force'. The idea of a 'vital force' is common to many early medical systems, but it has been highly developed within the concept of traditional Chinese medicine.

If a substance has no Qi then it is dead. The Qi of the liver is the functional ability of the liver, and the Qi of the body is the total vital force of a human being. Qi is disseminated throughout the body by the channels. It is also divided into various sub-groups such as original Qi, or the Qi with which you are born, and nourishing Qi, or the Qi that you gain from the food you eat. Defensive Qi is the Qi that protects the body from invasion by disease, circulating just below the skin and fending off invasion by viruses and bacteria (pathogens).

Qi is a very wide concept, difficult to understand in detail, but it is an essential part of the traditional Chinese picture of the body. Blood also

exists in the system of traditional Chinese medicine, and blood production is said to be dependent on the liver, the kidney and the bone marrow.

The Qi that flows through a particular channel or meridian is said to represent the functional well-being of that organ. Consequently, if an organ is diseased or out of balance, selecting an appropriate point from that meridian should, according to traditional Chinese medical theory, balance the flow of energy which in turn will reflect back on the functional integrity of the organ represented by the meridian. This effect should ultimately rebalance the organ, thereby returning it to health.

Pathogens

Disease results when the Qi of the body is weakened and unable to resist the onslaught of pathogens (disease-causing factors). In Chinese medicine the agents that cause disease are given the name of meteorological conditions; an infection (often associated with a fever) is called a disease of heat, and a chronically painful joint is usually a disease of cold. These pathogens allow diseases to be grouped according to their broad symptoms. The pathogen wind is an interesting idea. Wind means a changeable symptom, so the type of muscular ache often occurring with 'flu, would be classed as invasion by wind. The idea that disease is due to physical conditions is an intuitive explanation for many common aches and pains. People often complain that 'they caught a chill when they got wet', or that their 'neck is stiff after having slept in a draught'. The Chinese pathogens represent a formalization of this approach.

A particular pathogen usually presents itself with a defined symptom complex. By using the information gained from the history of the disease, and the physical examination of the patient, it is often possible to make a

clear diagnosis of the pathogen causing the disease. If the patient has a fever then heat is one of the pathogens involved in the disease process. Once the diagnosis has been made, then specific acupuncture points can be used to disperse the pathogen; when heat is the invading pathogen, then specific points are used to reduce the fever. Acupuncture points are therefore used to correct the Yin Yang balance of the body and to disperse pathogens.

If the pathogen cold is responsible for a particular disease process, then heat must be used to treat it. Moxa is the Chinese version of the heat lamp and, as will be discussed in a later chapter, the Chinese burn the dried leaves of Artemisia vulgaris over the areas that require heat. Heat, or more specifically smouldering moxa, provides local heat for a variety of chronic muscular aches. It is interesting to note that the types of diseases due to cold are commonly the muscular and rheumatic aches, which are often temporarily alleviated by heat.

More than one pathogen can invade at the same time; if a patient is suffering from 'flu, then there will be a fever and also muscular aches that wander all over the body. This is defined as invasion by the pathogens wind and heat.

The Chinese also have a complex system describing mental pathogens. For instance, anger affects the liver and grief the spleen. This has a direct clinical implication, in that specific emotions can, according to traditional Chinese medical theory, be treated by needling specific acupuncture points on particular channels.

The Pulse and Traditional Chinese Diagnosis

For the acupuncturist, one of the most difficult aspects of traditional Chinese medicine is the diagnosis of the specific organ affected by any

particular disease. In ancient China this was achieved by using a refined form of pulse diagnosis.

The palpation of the pulse enables the acupuncturist to assess which organ is diseased, whether the organ is over- or under- active, and the pathogen causing the damage. This is achieved by feeling the pulse at three positions at each wrist, and by feeling the pulse at the superficial and deep positions at each end of three positions on the wrist. There are six pulses at each wrist, three superficial and three deep. There are twelve main organs in the Chinese medical system (heart, kidney, liver, spleen, lung, pericardium, triplewarmer, large intestine, small intestine, stomach, gall bladder and urinary bladder) and each of these is represented by one of the pulses at one of the wrist positions. It is unclear how this system of pulse diagnosis came into existence but it was both refined and very important by the time the "Nei Ching Su Wen" was written. This method of diagnosis allows the whole body to be assessed, and it also defines the relative balance between each of the organs. In addition, pulse diagnosis is said to give a clear idea of the type of disease process, whether it is acute or chronic, and to give a prognosis for that disease in that individual patient. This allowed the Chinese physician to give an indication of how the disease would affect the individual.

The observation that each of these pulses represents a different organ is difficult to accept and understand. It is astonishing to think that different organs are represented by the pulse in the left and right hands, and that these pulses are separated only by a centimetre or so. There are also several different types of pulse that can be felt in any given position, for instance the pulse in the spleen position cna be described as a 'Fu' pulse in one disease, or a 'Ch'en' pulse in another disease. These

pulses were given rather poetic descriptions. A 'Fu' pulse is described as a superficial pulse, it is light and flowing like a piece of wood floating on water, whilst a 'Ch'en' pulse is a deep pulse, like a stone thrown into water.

Several attempts have been made to measure and record the pulse using conventional technology. These efforts have been successful, and it appears that within the paradigms of traditional Chinese medicine, different pulse characteristics do emerge and seem to obey the laws within traditional Chinese medicine (Kenyon 1983). In general, however, there have been few objective attempts to evaluate the pulse. Kohl (1975) carried out a series of small studies examining the reliability and validity of pulse diagnosis. She concluded that pulse diagnosis, "is not apparently a means of objective analysis, but offers a subjective meaning to the practitioner and is a vehicle for meaningful and helpful interaction with the patient". Clearly further studies on the process of pulse diagnosis and its relationship to treatment and traditional Chinese medicine in general, would be extremely valuable.

Pulse Diagnosis

Pulse diagnosis is not used in isolation, but as part of a system that involves taking the history of the disease and examining the patient. The facial complexion, smell and posture of the patient are also used diagnostically. Assessing the history of the complaint is the basis of all good medical practice, whether Western or Eastern, and can be summed up by an old Chinese quotation called the ten askings: 'One, ask chill and fever; two, perspiration; three, ask head and trunk; four, stool and urine; five, food intake and six, chest. Deafness and thirst are seven and eight; nine, past history and ten, causes. Besides this, you should

ask about the drugs taken and for women you should ask the menstrual and obstetric history. Finally, for infants ask about normal childhood diseases'. This ancient Chinese system of history-taking is almost exactly the same as that employed in the West today. Pulse diagnosis was therefore included as an important part of a sophisticated system for diagnosing disease.

Modern Chinese Diagnosis

Modern Chinese acupuncture differs from the old traditional system. The old traditional system of diagnosis by the 'twelve pulses' takes many years to learn to a standard of competence which allows the acupuncturist to make a clear diagnosis. Although there are some people in both China and the West who are able to diagnose by the twelve pulses, they are few in number, and a modified system of pulse diagnosis has therefore been developed by the Chinese. This allows a simple but relatively accurate system of traditional diagnosis to be taught and practised, quite quickly and proficiently, the mainstays of this 'shorter method' being the use of a pulse generalization and the tongue.

Modern Chinese acupuncture is outlined in some detail by Lewith and Lewith (1980). This acupuncture textbook represents a summary of current Chinese approaches to acupuncture in which conventional diagnoses are made and then the common traditional Chinese symptom pictures or syndromes for each Western diagnosis are outlined. This means that a particular practitioner may make a diagnosis of asthma or duodenal ulcer, and then look up the common symptom pictures which may present with this Western diagnosis. This allows the conventional doctor a simple way in to traditional Chinese medicine as the point from which they start is a clear diagnosis within conventional Western medicine.

The Selection of Acupuncture Points

The diagnosis of a particular problem does not tell the acupuncturist where to place the acupuncture needle. A set of therapeutic rules must be applied to solve that problem. To a large degree all medical systems are based on clinical experience and acupuncture is no exception to this; the rules that govern point selection are therefore based on a combination of philosophical concepts and empirical clinical experience.

There are special points that can be used to disperse the invasion of specific pathogens, such as cold or heat, and judging by some recent Chinese research work it would seem that the points used to disperse heat do lower fever. These pathogen-dispersing points are based largely on practical experience, and they form part of the basic grammar of acupuncture.

The other rules of point selection are many and varied; for example, points can be selected on the basis of the law of the five elements. This law assumes that each of the organs represents one of the five elements in traditional Chinese thought (earth, fire, water, metal and wood). They have a creating and destroying cycle.

On each of the channels there are points representing one of these elements and by applying a complex set of rules the diseased organ can be sedated, (if it is overactive) or tonified, (if it is underactive). There are also points on the back and front of the body that represent specific organs, and these too can be used to treat the represented organs when they are diseased. There are a plethora of such rules, each of which is applied in specific conditions and at specific times. The problem for the acupuncturist is to define the few points that will be best in any particular condition. The skill of point selection is based largely on

clinical experience; the rules of point selection give guidelines, although they are not the complete answer.

Why does traditional Chinese acupuncture need such specific diagnostic and treatment methods? Why not use all the acupuncture points at the same time? It would seem logical that if one acupuncture point helps, then two will help even more, and if all the points are used then the patient is bound to get better!

Traditional Chinese medicine along with many other complementary therapies implies that a small stimulus is probably more effective than a large one. Biological systems do seem to respond to small stimuli; for instance, a small change in the ecology of a 'food chain' can be amplified to cause major damage to another animal species in that environment. The emphasis in acupuncture therapy is therefore to select a minimal number of acupuncture points in order to give the body a small but specific stimulus.

Needling sensation

Needling sensation or de qi literally means obtaining qi. The sensation elicited is quite specific, it's a dull, deep, numb or sometimes burning sensation. PSC will not be found in any patient unless they first experience needling sensation. Needling sensation as far as the ancient Chinese were concerned, is essential for acupuncture to be successful. Another ancient text, the Ling Xu states, "when the qi arrives the treatment is effective. This is the essential of needling".

The Chinese have studied needling sensation quite intensely, and found that needling sensation does not occur in patients with syringomyelia, consequently they have suggested that it is mediated through the spinothalamic tracts (Bensouson 1991). However, one of the earliest and most clear-cut papers on needling sensation was published by Chaing (1973).

In this paper he showed that in order to produce analgesia it was essential to elicit de qi. Subcutaneous injection of local anaesthetic did not block de qi, but intramuscular procaine did (Chaing 1973). Moreover when de qi was blocked so was acupuncture analgesia, but this was not in itself target specific. Acupuncture points in the arm appeared to produce the same amount of analgesia in all parts of the body (Anderson 1979).

This has led Pomeranz to suggest that acupuncture maps are essential for locating the sites where de qi can be best achieved. He suggests that this is as near as possible to type II and type III muscle afferents (Pomeranz 1991). Probably the best experiments supporting the importance of de qi have been done in humans with direct microelectrode recording from single fibres in the median nerve while acupuncture was performed distally (Wang et al, 1985). When the patient experienced de qi, type II muscle afferents produced a numbness, type III gave sensations of heaviness, distension and aching and the type IV unmyelinated fibres gave a feeling of soreness. Soreness is an uncommon aspect of de qi, the sensations most commonly experienced are those which we know are related to type II and type III afferents (the small myelinated afferents from muscle). It would appear therefore the ancient Chinese observation that it is necessary to obtain de qi in order to have effective acupuncture, is at least in part supported by conventional neurophysiology.

Conclusion

Traditional Chinese medicine is completley distinct from conventional medicine in terms of its illness models. It sees illness based on its fundamentally vitalistic philosophy, and translates all disease processes into a disturbance of qi, and how this may affect the body.

A number of the assumptions within traditional Chinese medicine do appear

to have some physiological validity, but the vast majority remain unproven and untested. Nevertheless they form the foundation of acupuncture, and to attempt to evaluate acupuncture without an understanding of traditional Chinese medicine is rather like attempting to evaluate a new drug without any understanding of pharmacology or biochemistry. If one is to test acupuncture in the context of a clinical trial, then ideally, one should try and test the best acupuncture treatment for the condition being studied. As far as the majority of acupuncturists in the world are concerned, the most widely held view would be that the best acupuncture cannot be practised without some understanding of traditional Chinese medicine. Whereas a Western diagnostic system may allow for one individual's asthma being exactly the same as another, this does not hold true within traditional Chinese medicine. Therefore a traditional Chinese diagnosis must be made on the patient with asthma, and appropriate points for that individual must be selected.

CHAPTER 3

WESTERN ACUPUNCTURE

Tender regions in the muscles have been the subject of special studies from the 1920s onwards. The seminal work in this area however was carried out by Travell and Rinzler in 1952. Their paper, The Myofascial Genesis of Pain has made tender point acupuncture respectable.

The Chinese have long recognised that treating the tender point or as they term it, the Ah Shi point, is effective in musculoskeletal conditions. However, traditional Chinese medicine emphasises that the Ah Shi point should only be used in conjunction with an internal diagnosis and a proper traditional Chinese approach. Many Western doctors, using Travell and Rinzler's work, have focused on the active needling and therefore abandoned much of traditional Chinese medicine.

Finding the local tender trigger point is easy to achieve simply by examining the patient. Melzack et al (1977) have shown clearly that just over 70% of these tender points are in fact acupuncture points in muscles which become tender when local, and in particular segemental, pathology is present. Pomeranz (1991) demonstrates that treating tender points has a segmental effect both neurologically and through segmental endorphin release. Baldry (1989) has published a practical textbook that concentrates solely on using tender trigger points to treat a whole range of musculoskeletal conditions.

Most practitioners using simple tender point acupuncture such as MacDonald (1983) do not elicit needling sensation as part of their technique. In many ways, modern Western acupuncture has abandoned its roots in

traditional Chinese medicine and has focused on the act of needling itself. This approach can undoubtedly produce analgesia as MacDonald has demonstrated (MacDonald et al, 1983). At the present time it is unclear as to whether traditional Chinese or Western approaches or indeed a combination of the two are the most effective form of acupuncture. On neurophysiological grounds alone it would seem that obtaining de qi appears to be a valuable therapeutic asset. Furthermore, treating non-painful conditions such as asthma is a little impractical if one is solely dependent on finding a tender point.

Whatever technique is used, then this approach must be clearly stated at the outset and described accurately within the methods section of any publication.

CHAPTER 4

THE MECHANISM OF ACUPUNCTURE

Over the last 20 years there has been considerable research into the physiological mechanism of acupuncture. There have been two main and partially interlinked areas which have been investigated; the purely neurological and those which have involved a neurohumoral, mainly an endorphin and enkephalin based mechanism. A review of the mechanisms is important and relevant in relation to clinical trials, particularly because non-specific forms of needle puncture have been shown to have a clear effect on the neurological and neurohumoral mechanisms that purport to be the basis of acupuncture analgesia.

Neurological mechanisms

Chiang has suggested that acupuncture is primarily mediated through the nervous system (1973). He experimented with 21 adult volunteers and noted the local analgesic effect obtained by needling a point in the hand (large intestine 4); the extent of analgesia was measured by the patient's response to a painful electrical stimulus in the hand. Vascular occlusion of the upper arm did not alter the analgesia obtained. Endorphins and enkephalins had not yet been discovered at this time, but as these peptides are neurotransmitters their discovery does not contradict the view proposed by Chiang and supported by much of the research that will be discussed in this review. Thus it is probably correct to think of the physiological changes initiated by acupuncture as being mediated through the peripheral nervous sytem in the first instance. The first physiological theory used

to explain acupuncture was the gate control theory developed by Melzack and Wall (1965).

It has been suggested that acupuncture is only effective at certain points on the body surface. In fact comparison with anatomical atlases shows that many acupuncture points correspond with the points to which small nerve bundles penetrate the fascia; Chan (1984) cites two Chinese studies which showed that 309 acupuncture points are situated on or very close to nerves while a further 286 are on or very close to major blood vessels surrounded by their perivascular complexes of nervi vasorum. That sympathetic nerves may be involved was first demonstrated by Goulden (1921) who showed that acupuncture points along the sciatic nerve and its branches had lower impedance than surrounding skin. Yoshio (1967) showed that ryodoraku points may have low impedance/high conductance. Many acupuncture points were of course deep to the skin; Melzack et al (1977) demonstrated that they correlate closely with Travell's trigger points, while Liu et al (1977) have shown that others correspond with motor points of muscles. What type of receptor must be stimulated to produce the acupuncture effect? The fact that a needle or some other intense stimulus must be used points to a high threshold receptor (Bowsher, 1976). Wang et al (1985) showed that A delta or group 3 fibres are in fact the group concerned.

The gate control theory of pain

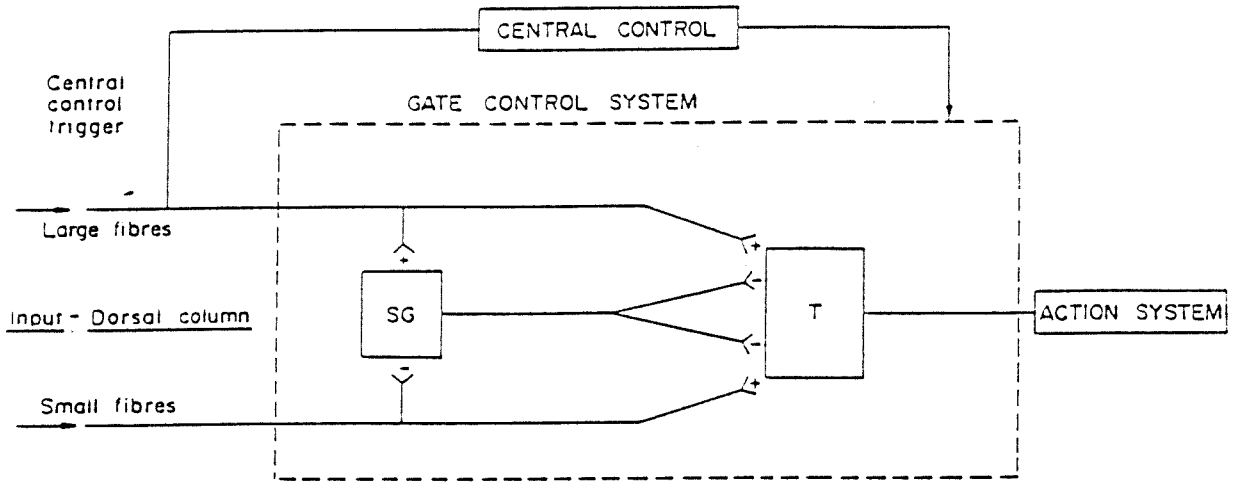
Until the publication of the gate control theory it was assumed that impulses carrying cutaneous information arrived at the spinal cord and would be transmitted along ascending relay pathways to the cerebral cortex (Bishop, 1980). Work done by Matthews in 1934 had been largely ignored. He showed that sensory input travelling along large diameter afferent

fibres depolarised the central terminals of other dorsal root fibres and called this phenomenon 'primary afferent depolarisation' or the 'dorsal reflex'. These ideas were re-examined in considerable detail by Melzack and Wall in the late 1950s and their importance was finally recognised as the basis for a theory of the neural mechanisms underlying pain. They relied on evidence available from earlier workers such as that of Zotterman (1939) who had demonstrated that dull, slow, diffuse burning pain is carried from the periphery by small unmyelinated (C) fibres, while the sensation of light touch is carried by large myelinated (A) fibres. Such early observations have been supported by more recent work such as that of Burke (1975) who isolated A Beta fibres as transmitting the sensation of light touch.

The gate control theory stated that the transmission of sensation is controlled by the balance of activity in these two types of fibres. According to this theory, low level activity in the small fibres is normally blocked at the first synapse by activity in the large diameter fibres. The 'gate' at the first synapse is opened by intense activity of the C fibres, while a predominance in A Beta fibre activity closes the gate. The gate through which pain signals pass to the transmitter (T) cells is variable. The sensation of pain is dependent on the activity of the A fibres and will result from C fibre dominance over A fibres.

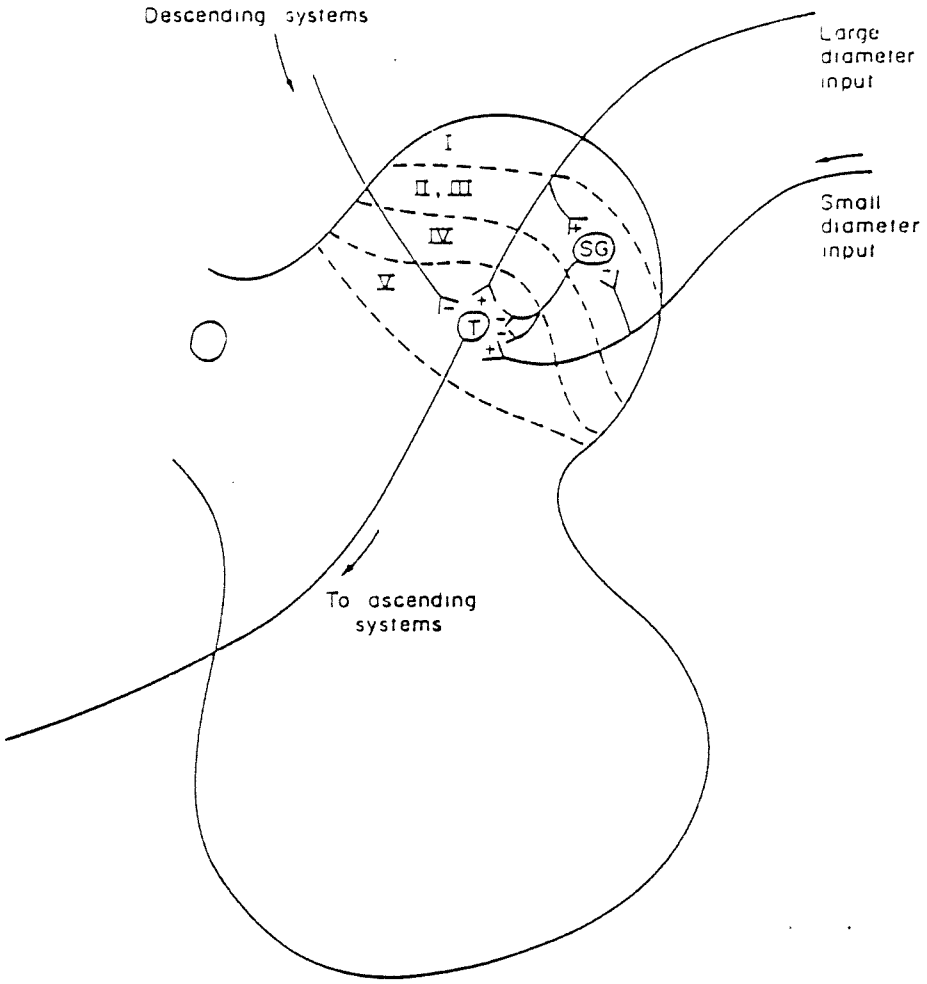
It follows from this that by forcing A fibres to carry sensations of light touch by stimulating the area, pain signals from C fibres can be blocked. The gate is said to be an intermediate structure between so-called T cells in lamina V, which must be stimulated in order that pain interpretation and response can take place, and the sensory fibres which enter lamina I via the dorsal root (see Figs 4.1 and 4.2).

Figure 4.1 **Schematic representation of gate control theory of pain mechanisms .**



SG substantia gelatinosa
T transmitter cells
\+ facilitatory synapse
\- inhibitory synapse

Figure 4.2 **Schematic representation of location of 'gate' mechanism in the posterior horn of the spinal cord**



SG substantia gelatinosa
T transmitter cells
\+ facilitatory synapse
\- inhibitory synapse

Roman numerals refer to laminae within the dorsal spinal grey matter.

Wall and Sweet applied the gate control theory of pain clinically using implanted stimulating devices with low voltage percutaneous electrical stimulation (Wall and Sweet, 1967). This led Sweet to develop further the stimulation of both peripheral nerves and the posterior part of the spinal cord in order to promote analgesia (Sweet and Wepsic, 1963, 1974).

Melzack found it difficult to explain how high intensity electrical stimulation can selectively activate small diameter nerve fibres, and suggests that stimulation would cause both A and C fibre activity (Melzack, 1975). Nathan and Rudge tested the gate control theory by artificially inducing C fibre activity and then attempting to abolish it by electrical stimulation of A fibres (Nathan, 1974). They could not abolish the pain produced by C fibre stimulation (in humans) and concluded that their experimental results were inconsistent with the gate control theory. Similar observations were made by Nathan again in 1976 and by Strassbourg et al in 1977 (Nathan, 1976, Strassbourg, 1977).

Brief, intense stimulation with either acupuncture or transcutaneous nerve stimulation (TNS) may cause prolonged pain relief (Melzack, 1975), but this reproducible clinical phenomenon cannot be explained by the gate control theory. Melzack suggests that brief, intense stimulation may cause prolonged pain relief either by activating 'a central biasing mechanism' or by breaking up a proposed 'memory-like process' through which pain may be mediated. He suggests that pain may be due to prolonged activity within self-exciting neurone chains and that brief, intense input could break up or disrupt this activity and thereby abolish pain perception for prolonged periods (Melzack, 1975).

Chien-Ping used electro-acupuncture on decerebrate cats (Chien-Ping et al, 1974). He was able to demonstrate a clear inhibitory effect in the

discharges recorded in the dorsolateral fasciculus when stimulating A fibres in the peripheral nerve. The inhibitory effect was greatest if the whole spectrum of A fibres was stimulated rather than selectively stimulating A Beta fibres. Andersson and Holmgren were unable, selectively to stimulate A Beta fibres with electro-acupuncture, but did provide circumstantial evidence for the specific stimulation of these fibres as having a pain inhibitory effect (Andersson, 1975). Janko has shown that TNS does stimulate both A Beta and A Delta fibres and suggests that this may be the mechanism through which TNS causes analgesia (Janko, 1980). An essentialy similar blockade of the sensation of pain can be obtained by various types of stimulation, some of which are thought to be similar to acupuncture. These include vibration and electrical high frequency peripheral or dorsal column stimulation (Shealy et al, 1970, Mayer et al, 1972,).

Rubbing appears to activate the large low threshold cutaneous afferents (A Beta). Since sustained pressure does not produce pain relief the effective units must be rapidly adapting and excited by transient stimuli. Therapeutically, pain relief by activation of low threshold cutaneous afferents is obtained by transcutaneous electrical nerve stimulation (TNS) (Wall and Sweet, 1967). It can also be obtained by the application of vibratory stimuli (Lundeberg, 1983) which presumably activate rapidly adapting A Beta primary afferents in the muscle.

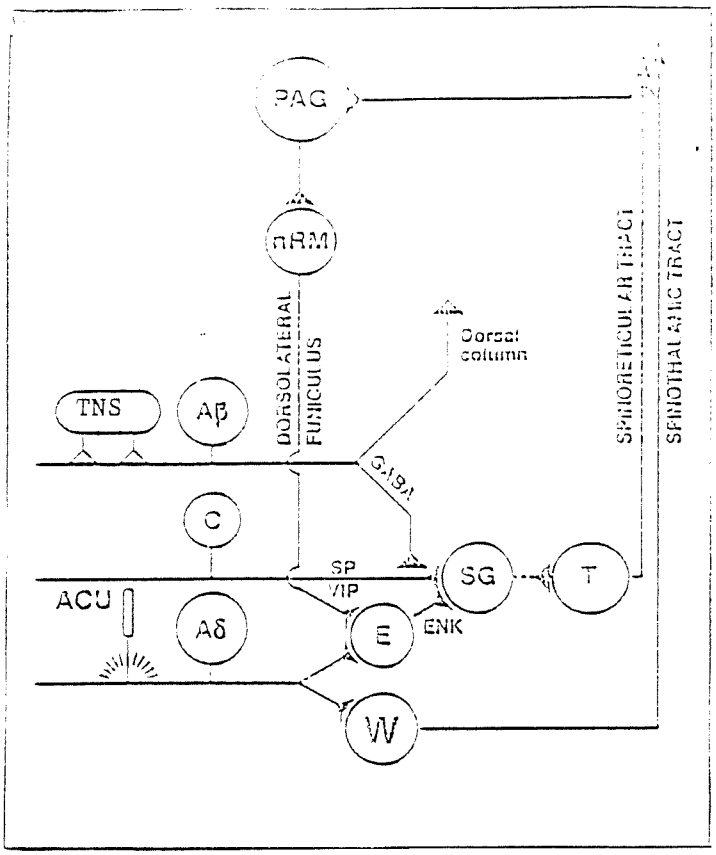
The next question to be asked is where and how do these two types of afferent (A Beta and A Delta) synapse in the spinal cord? Fortunately, recent advances in anatomy and physiology can tell us a great deal about these questions.

Primary afferent A Beta fibres enter the spinal cord in the medial part of

the dorsal root and pass rostrally without synapsing in the dorsal columns to end in the dorsal column (gracile and cuneate) nuclei. However, on entry to the spinal cord these fibres give off a segmental collateral which penetrates the grey matter of the dorsal horn. Some of this branch may make contact with a superficial part of the dorsal horn, probably through a GABA-inergic interneurone (Todd and McKenzie, 1989) with the terminals of small incoming primary afferent fibres (Brown et al, 1978). Such an anatomical arrangement would explain the GABA-inergic inhibition observed by Duggan and Foong (1985) following the dorsal column simulation, which retrogradely drives the segmental collaterals responsible for TNS. It is of course well known that these systems respond to high frequency stimulation. We therefore have a circuit capable of explaining at a segmental level the effects of TNS and vibration. This circuit does not involve any opioidergic synapses and therefore the analgesia produced is segmental and is not reversible by naloxone (Sjolund and Eriksson, 1979). Acupuncture induced analgesia, on the other hand, is naloxone reversible (Mayer et al, 1977, Sjolund and Eriksson, 1979, Cheng and Pomeranz, 1980) and we must thus look for an entirely different explanation for its effects. The A Delta primary afferents which carry the pinprick messages to the spinal cord make their principal intra spinal contact with large Waldemeyer cells in lamina I of the dorsal horn (Kumazawa and Perl, 1978). There are inhibitory enkephalinergic "stalked cells" on the borders of lamina I and II (Abdel-Maguid and Bowsher, 1984) with which collaterals of the A Delta primary afferents make synaptic contact (Gobel et al, 1980). Ruda et al (1984) have shown that these inhibitory interneurones are able to block the transmission of messages arriving along C polymodal nociceptive primary afferents to the cells of origin of the crossed

ascending anterolateral funiculus. In addition to this post synaptic effect a presynaptic inhibitory effect from enkephalinergic interneurones on the terminal of primary afferent C fibres has been demonstrated (Solodkin et al, 1984). It has been shown also that the spinal interneurones do not react to frequencies of stimulation above about 3 Hz (Harper and Lawson, 1985). These mechanisms are quite adequate to explain the segmental mechanism of acupuncture analgesia. At a segmental level both high frequency low intensity analgesic stimulation (TNS) and low frequency high intensity analgesic stimulation (acupuncture) are at least partially explained by the gate control theory of Melzack and Wall. TNS acts presynaptically to close the gate from the outside and acupuncture pushes it shut from within. Figure 4.3 explains both these mechanisms and how they may be integrated into a coherent circuit.

Figure 4.3 **Circuitry for high-intensity low-frequency (Acupuncture) and high-frequency low-intensity (TNS) stimulation.**



PAG	=	Periaqueductal grey
nRM	=	nucleus Raphe Magnus
SG	=	Substantia Gelatinosa
T	=	Transmission cell
W	=	Waldeyer cell
GABA	=	y amino butyric acid
SP	=	Substance P
VIP	=	Vasoactive intestinal peptide
E	=	Enkephalinergic interneurone
ENK	=	Enkephalin

1. Fine myelinated A Delta primary afferents are activated by high-intensity (pinprick) stimuli. Within the cord, they synapse directly with interneurones (E) which, using the inhibitory transmitter enkephalin (Enk) can inhibit transmission from substantia gelatinosa (SG) neurones which receive nociceptive input via unmyelinated (C) primary afferents using Substance P (SP) or vasoactive intentinal peptide (VIP) as a transmitter (Segmental acupuncture).

A Delta primary afferents also end on lamina 1 cells (W) which transmit pinprick information directly to consciousness via the spinothalamic tract; this gives off collaterals to the periaqueductal grey matter (PAG), which activates a descending system relaying in the nucleus Raphe Magnus (nRM) of the medulla oblongata to excite inhibitory enkephalinergic interneurones (E) through the dorsolateral spinal funiculus (heterotopic acupuncture).

2. Large low-threshold primary afferents (AB) pass directly up the dorsal columns on entering the cord; but they also give off a segmental collateral which excites an inhibitory GABA-ergic interneurone (not shown) which presynaptically inhibits transmission from primary afferent nociceptive (C) terminals (TNS).

Ascending pathways

Low threshold mechanoreceptive primary afferents carrying the kind of information induced by TNS pass up the dorsal columns to end in the gracile and cuneate nuclei. From the dorsal column nuclei axons emerge at the medial lemniscus and after decussating in the medulla oblongata pass rostrally to end chiefly in the ventrobasal thalamus. However, the medial lemniscus gives off a number of collateral branches on the way, most notably in the mid-brain. The connection in which we are most interested in the present context is to the anterior pretectal nucleus (Bjorkeland and Boivie, 1984, Rees and Roberts, 1989a). This nucleus projects to the periaqueductal grey matter (PAG) (Rees and Roberts, 1989b) and thence activates the descending inhibitory system.

High threshold information passes up the antero-lateral funiculus on the side opposite to that on which it enters the cord (Kuru, 1949). The medial brain stem reticular formation receives the majority of the ascending axons (Bowsher, 1957). It is now known that these fibres originate from the deep spinal laminae (VII, VIII) (Kevetter et al, 1982), having been activated through the substantia gelatinosa by primary afferent unmyelinated polymodal nociceptors. These terminate principally in the substantia gelatinosa (Sugiura and Lee, 1986), though some spinoreticular fibres also arise from lamina V in the neck of the dorsal horn. A smaller component of the ascending anterolateral funiculus reaches the ventrobasal thalamus (Bowsher, 1957). This component arises principally from laminae I and V (Willis et al, 1979) and gives off collaterals to the PAG of the mid brain. Mantyh (1982) showed that this projection comes from lamina I of the spinal grey matter. Pechura and Liu (1986) suggested that some of the spino-PAG neurones also reside in lamina V. It is in lamina I and

lamina V that fine myelinated (A Delta) primary afferent fibres terminate (Heimer and Wall, 1986). Thus, there exist pathways whereby pinprick information is conveyed to the PAG.

Descending inhibitory influences and the thalamus

Further work by Melzack into relief of chronic pain by repeated electrical stimulation has brought forward speculation that a central biasing mechanism exists within the brain stem (Melzack, 1975). He believes that chronic pain may be partially due to 'a neural reverberating circuit', involving the periaqueductal grey areas. He suggests that both TNS and acupuncture could activate a central biasing mechanism, thereby inhibiting the transmission of painful stimuli through the neuraxis. The second possible explanation is that prolonged pathological pain may result in permanent or semi-permanent changes in central neural activity (Melzack, 1973). Fox and Melzack suggest that these changes may take the form of self-exciting circuits that result in memory-like processes which could be disrupted by brief intense input from either acupuncture or TNS; such disruption could long outlast the duration of stimulation (Fox and Melzack, 1976). If central activities were to restart they might involve fewer neurones and invoke less pain, therefore gradually diminishing the perception of pain. These concepts have yet to be verified.

Man and Chen postulated a second gate within the reticular activating system, with a main gate at the thalamus (Man and Chen, 1975). The main evidence cited for the thalamic gate is that stimulation of areas supplied only by the cranial nerves would cause impulses to go directly to the main gate, the thalamus. They also rely on studies from the Shanghai College of Acupuncture Group (Shanghai Acupuncture Group, 1973) which demonstrate that the response of mid-brain reticular formation to painful stimuli is

largely abolished by electro-acupuncture. But, on closer analysis the evidence quoted does not really support Man and Chen's hypothesis of the second (thalamic) gate. Nevertheless, the reticular activating system may well be important in mediating analgesic effects of acupuncture. Chen-Yu et al (Chen-Yu, 1975) and Ke-Fei et al (1977), in the Shanghai Institute of Physiology, studied the effects of noxious stimulation modulated by electro-acupuncture on rabbits and have shown that stimulating the reticular formation has a marked inhibitory effect on pain. Chen-Yu observed that section of the dorsal column alone did not produce any detectable change in either the pain threshold or the effect of electro-acupuncture on pain threshold. Neither did superficial cordotomy significantly modify the analgesic effect of acupuncture (Chen-Yu, 1975). Ke Fei et al noted that electro-stimulation of the medial medullary reticular formation had a marked inhibitory effect on pain perception and neuronal discharges in the region of the thalamus (Ke-Fei et al, 1977). Reynolds demonstrated that electro-stimulation of the periaqueductal grey (PAG) and a region close by, (the nucleus raphe magnus (NRM)) resulted in analgesia in rats (Reynolds, 1969). This observation has been subsequently verified by a number of studies in both humans and animals (Mayer and Leibeskind, 1974, Melzack and Melinkoff, 1974, Oliveras et al, 1974). Studies by Akil et al (Akil et al, 1976, Akil, 1976) demonstrated that such focal brain stimulation released endorphins. These studies imply that a 'descending inhibitory control system' for pain may exist. Such a system is also probably endorphin mediated. Micro injection of opioids into the PAG elicits analgesia (Mayer and Price, 1976) and opioid antagonists can abolish the analgesia elicited by brain stimulation (Akil et al, 1976). Neurones from the PAG and NRM are closely linked (Gebart,

1982) and excitation of the PAG enhances the activity of NRM neurones (Behbehani, 1979). Furthermore, neurones originating in the NRM are found in laminae I, II and V of the dorsal horn and direct stimulation of the latter elicits inhibition of nociceptive neurones in the dorsal horn. The neurones originating in the NRM pass into the dorsal horn via the dorsolateral funiculus (Fields and Basbaum, 1978) which demonstrates the existence of a descending inhibitory control system that can be activated either centrally, by direct stimulation of the periaqueductal grey, or peripherally by acupuncture.

The pathway descending from the PAG relays in the nucleus raphe magnus (NRM) of the medulla oblongata, probably by neurotensinergic fibres (Beitz, 1982), at least in the rat. From the NRM mainly serotoninergic fibres descend in the dorsolateral funiculus to the spinal cord to terminate directly on enkephalinergic interneurones at the boundaries between laminae I and II of the spinal dorsal horn (Glazer and Basbaum, 1984) in the cat. There are also serotoninergic nerve terminals ending non-synaptically in the superficial dorsal horn (Maxwell et al, 1983, Leranth et al, 1984 and Hammond et al, 1985).

Chang suggests that the thalamus performs an important integrative function in the process of acupuncture analgesia (1973). He implicates the nucleus parafascicularis and the nucleus centralis lateralis, and has demonstrated that discharges, from both these thalamic nuclei, can be inhibited by electro-acupuncture. The nucleus parafascicularis and the nucleus centralis lateralis gave rise to characteristic unit discharges in response to painful stimuli. These discharges were abolished by electro-acupuncture, but if the stimulus applied was too powerful then the response to pain seemed to be exaggerated. Pain discharges from the thalamic

neurones persisted after section of the dorsal column and could not be produced by electrical stimulation of the severed dorsal column above the lesion. This implies that the main pathway of pain, as mediated through the thalamus, is not within the dorsal column. Chang goes on to suggest that the thalamus probably has an integrative function in pain perception and it is this that can be modified by acupuncture to produce an analgesic effect (1973). Most of the cortically projecting thalamic nuclei also receive afferents from the ascending reticular neurones (Bowsher, 1977). Bowsher suggests that, "If as seems likely, most reticulo-thalamic axons collateralise widely, then it is probable the endings in the cortically projecting nuclei may be collateral to those which terminate in the intralaminar nuclei". It is possible therefore that a series of excitatory and inhibitory feedback loops are present. These start in the cord and subsequently travel up the nervous system via the thalamus to where pain is finally perceived within the cortex. Acupuncture can modulate the transmission of noxious stimuli at many levels in the central nervous system, and it would be wrong to think of any one theory providing a complete or unified explanation for this complex series of interactions.

Viscero-somatic reflexes

Mann has stated that cutaneo-visceral and intersegmental reflexes are particularly important in mediating the effects of acupuncture (Mann, 1977). The clinical evidence for this hypothesis is that insertion of needles into points far distant from the site of pain can frequently result in a swift and dramatic analgesic effect (Miles et al, 1973). Studies mentioned previously imply that acupuncture produces the greatest possible A fibre activity (thereby implying it should have the greatest analgesic effect) when the stimulus is applied to the same dermatome as the pain.

However, some attempt must be made to explain the bizarre intersegmental effects that are observed in clinical practice.

Sherrington described the scratch reflex in the spinal dog in which stimulation anywhere in a saddle shaped area extending from the pectoral to the pelvic girdle caused rapid scratching movements in the ipsilateral hind leg and rigidity in the contra-lateral limb (Sherrington, 1906). If the stimulus was moved to the opposite side of the back, the hind legs reversed their roles. Ipsilateral hemisection of the spinal cord abolished the reflex whereas contralateral hemisection left it unaffected. Dowman studied cats who had spinal transection performed at the level of their first thoracic vertebrae. He demonstrated that splanchnic nerve stimulation spread up the cord by two pathways, one a fast extraspinal route in the sympathetic chain on the same side and the other a slower intraspinal route (Dowman, 1955).

Miller and Ward stimulated the viscera and obtained muscle contractions in the expected appropriate dermatome (Miller and Ward, 1925). They also found that distension of the stomach by air, traction on the stomach, mustard oil on the gastric mucosa and squeezing the small intestine all elicited the same reflex. Brown-Sequard (1860) was probably the first to describe viscero-somatic reflexes. He relates an experiment on a dog which had a tube tied into its ureter. When the internal abdominal wall was pricked within the sensory distribution of the first lumbar nerve, the secretion of urine was considerably diminished. Mann suggested that these bizarre, and largely unexplained, reflexes may explain how acupuncture at a distant site may alleviate pain (Mann, 1977).

More recently, Travell and Rinzler have observed that trigger areas occur on the front of the chest in true cardiac pain: furthermore that

stimulation of these areas with needles had an analgesic effect (Travell and Rinzler, 1946, Travell and Rinzler, 1952). Shen-Eh et al looked at the possibility of relaxing abdominal muscles during abdominal surgery under acupuncture anaesthesia (Shen-Eh et al, 1975). He studied the cat and demonstrated that acupuncture could cause muscle relaxation but that high spinal cord transection abolished this reflex. Further work by Huan-Ji and Yan-Shang, again studying cats, has shown that such viscero-somatic reflex can be largely abolished by lesioning the medulla (including the nucleus raphe magnus) and completely abolished by transection of both the lower medulla and cervical cord (Huan-Ji and Yan-Shang, 1976). At present we have an incomplete picture of the relevance of these reflexes and how they can be integrated into a unified system which might be affected by peripheral stimuli such as acupuncture. However, we can observe that viscero-somatic reflexes exist and in some instances are affected by acupuncture.

Diffuse noxious inhibitory control (DNIC)

Le Bars et al have suggested that noxious stimuli when applied to any part of the body can produce analgesic effects at distant sites (Le Bars et al, 1979). They recorded input from 68 convergent dorsal horn neurones in anaesthetised rats and noticed that both A and C fibre afferents could be activated by both low and high frequency peripheral electrostimulation. Furthermore, the stimulation of these neurones was inhibited by any noxious stimulus applied to the body. They therefore called this response diffuse noxious inhibitory control (DNIC). The most effective areas for eliciting this response were the tail and the muzzle of the rat. The stimulation of the tail or muzzle both electrically (TNS) and by noxious radiant heat significantly modified the C fibre response and long lasting effects could

be observed which were related directly to the duration of the conditioning painful stimulus.

Since 1979 many more detailed studies have been published implicating DNIC as a possible mechanism for acupuncture. An excellent review of DNIC is published elsewhere (Le Bars et al, 1991) and its principal conclusions are of great importance when considering clinical trials involving acupuncture, in particular sham acupuncture.

DNIC is not observed in anaesthetised or decerebrate animals (Cadden 1983, Morton, 1987). Therefore, supraspinal structures must be involved. However, let us first consider the peripheral mechanisms. The relationship of the intensity of stimulus and the strength of DNIC was explored using the rat and applying various temperature stimuli to its tail, hind paw and face. The threshold for producing DNIC was between 40-44^{o}C, the higher the temperature the greater the DNIC. This reinforces the idea that DNIC is triggered by a peripheral nocioceptors and carried by A delta and C fibres (Dubner and Beitel 1976, Torebjork et al 1984, Villanueva and Le Bars 1985). Further experiments have suggested that stimulation of A delta fibres forms the most important initial trigger for DNIC (Le Bars et al, 1991).

DNIC is not observed in decerebrate animals so a complex loop involving supraspinal structures must be involved. Electrical stimulation of the nucleus raphe magnus (NRM) produces inhibition of spinal convergent neurones which are a potent aspect of DNIC. DNIC is also reduced following lesion of the nucleus raphe magnus and amplified by the administration of 5-hydroxytyramine (Villaneuva and Le Bars 1986, Le Bars, 1988). Furthermore both DNIC and stimulation of the NRM are naloxone reversible (Le Bars et al, 1981b). This demonstrates that both mechanisms

are similar and mediated through the endogenous opioid system. Furthermore, DNIC seems to be mediated through exactly the same pathways and mechanisms as acupuncture.

Analagous results have been reported in man (Willer et al, 1984, 1989). The model used for this was electrical stimulation of the sural nerve. The stronger the stimuli applied the greater the depression of pre-existing pain and its associated nocioceptive reflex. By repeating the experiments on tetraplegics Roby-Brami et al (1987) were able to demonstrate a supraspinal involvement in man which appears to be working in the same way as that observed in the rat. Willer et al also demonstrated (1990) that these inhibitory phenomena in man are naloxone reversible.

Based on these observations, Le Bars (1991) goes on to develop a number of hypotheses concerning the mechanism of action of acupuncture, needling sensation (Deqi) and DNIC. It is clear that there is a well substantiated neurological and neurohumoral loop through which sham and real acupuncture can operate using the same mechanisms. These mechanisms attenuate experimental pain in both man and animals, and most important of all they are NOT point specific.

Other neurological mechanisms suggested as explanations for the effect of acupuncture

Becker et al suggest that acupuncture's effects are mediated through a primitive nervous system (1976). He and his co-workers hypothesise that (as in many control systems involving a high energetic process), a control system involving signals of low energy content may be present. He uses as support for this argument various experiments on bone healing, leg regeneration in the salamander and some detailed studies on the electro-physiological correlates of acupuncture points. Whether the proposed

transmission and control system for the nervous system is present, or can be modified by acupuncture, remains unproved.

Arguments that acupuncture can modify the activity of the autonomic nervous system can be supported by studies already mentioned on the effect of acupuncture on viscero-somatic reflexes. A number of observations have been made on experimental animal models that lend support to the idea that acupuncture is at least partially mediated through the autonomic nervous system. Acupuncture has been shown to reduce the mortality from shock in experimentally exsanguinated cats and dogs (Anon, 1974; Lee et al, 1974). It can also be shown to have a significant effect on gastro-intestinal function in both man and animals (O'Connor, 1975). Specific effects can be shown on the gastro-intestinal circulation, gastric motility, gastric secretion and absorption of fluid from the peritoneal cavity in rabbits (Anon, 1975). Consequently, it is probable that acupuncture is having a very widespread effect throughout both the somatic and autonomic nervous system.

Neurohumoral Mechanisms

Endorphins

It has been recognised for many years that morphine and other opioids are excellent analgesics, but the mechanism through which they produce analgesia has only recently been elucidated (Bishop, 1980). In 1975 Hughes et al discovered two pentapeptides in porcine brain, leu- and met-enkephalin (Hughes et al, 1975). Met-enkephalin is also found in human brain, in extracts of the pituitary and other neural tissues, and is part of a larger molecule (30 amino acids) beta endorphin (Bradbury et al, 1976). Both beta endorphin and dynorphin (the extended form of leu-

enkephalin) seem to have greater analgesic potency than their pentapeptides. In addition there are a number of related opiate peptides (a and y endorphin and a and beta neo-endorphin). Endorphin seems to be mainly found in the basal hypothalamic nuclei and in ascending collaterals to many nuclei throughout the brain (Uhl, Childers and Snyder, 1979). The enkephalins are mainly found in the short interneurones within the limbic system, hypothalamus, basal ganglia, periaqueductal grey area, medulla oblongata and spinal cord (Dupont et al, 1980).

Naloxone reversibility of acupuncture was initially reported by two groups (Pomeranz and Chiu 1976, Mayer et al, 1977). Pomeranz has published an excellent review of the case for the acupuncture endorphin hypothesis (Pomeranz, 1991) and argues conclusively that acupuncture analgesia for acute pain, in both man and animals, is naloxone reversible.

The early experiments, Mayer et al in 1977 studied acute laboratory-induced tooth pain in human volunteers. Analgesia was produced by manual needle stimulation of site Large Intestine 4 (LI4) and then in a double blind design one group of subjects was given intravenous naloxone while the other received intravenous saline. The saline group achieved analgesia, with a 30 minute onset and a duration of one hour. The naloxone group showed no sign of analgesia. Unfortunately, there were no controls who received naloxone alone, but naloxone rarely produces analgesia on its own (Goldstein, 1979). In this study Mayer also gave a control group placebo injections. The controls were told to expect strong analgesia but none was observed. The other early study by Pomeranz and Chiu (1976) was carried out using mice as a model. They used the mouse squeak latency paradigm and gave electroacupuncture at Large Intestine 4. Numerous control groups were used in an attempt to pick out the possible artefacts.

One group received acupuncture alone, another electroacupuncture plus saline, a third electroacupuncture and intravenous naloxone. A fourth received sham acupuncture, a fifth naloxone alone and a sixth saline alone and finally no treatment at all. The results were unequivocal, naloxone completely blocked acupuncture analgesia and in this experiment sham acupuncture produced no effect. Naloxone alone produced only a very small amount of analgesia, far less than that produced by electroacupuncture. This suggests that acupuncture has purely a psychological effect which could be blocked by naloxone. A later study by Cheng (1979) demonstrated a dose response curve for naloxone and found that increasing the dose of naloxone produced an increasing block of acupuncture analgesia. A further study by Pomeranz and Cheng involved recording from lamina V cells in the spinal cord and showed that the neurological effects of electroacupuncture could be completely blocked with intravenous naloxone (Pomeranz and Cheng, 1979). Since these early papers there have been numerous studies in which systemically administered endorphin antagonists have been used to test the endorphin acupuncture hypotheses. These are reviewed by Pomeranz (Pomeranz, 1991) and the majority demonstrate the same phenomena. Seven studies did not find any effect from naloxone. Three of these 7 "failures" were obtained with high frequency low intensity stimulation, which probably does not produce endorphin release (Wolf et al, 1978, Abrams et al 1981 and Walker and Katz 1981). In one of the failures low intensity stimulation was used and no needling sensation or Deqi was elicited (Chapman et al, 1980). In spite of this somewhat inadequate acupuncture, 4 of the 7 subjects in the study did show naloxone reversible. In the other 3 papers the negative results obtained have no clear explanation (Chapman et al 1980, Pertovaara et al 1982 and Tay et al 1982).

The antagonists appear to work best before treatment and thus may fail to reverse already established acupuncture analgesia (Watkins and Mayer, 1982; Pomeranz and Bibic 1988). However, taken together the overwhelming weight of evidence shows that naloxone antagonises acupuncture analgesia and the few negative results may possibly reflect poor timing of the naloxone administration.

Cheng and Pomeranz (1979) again using the mouse squeak model, observed that small doses of cyclazocine, diprenorphine or naltrexone all blocked acupuncture analgesia in the same manner as naloxone. Type 1 opioid receptors are naloxone reversible and, therefore, it seems likely that type 1 opioid receptors are involved in the acupuncture analgesia studied in these experiments. Furthermore, injection of dextro-naloxone (an inactive stereo-isomer) had no effect on reversing acupuncture analgesia (Cheng and Pomeranz, 1979). These observations add further support to the argument that stereospecific opioid receptors mediate acupuncture analgesia, as for the involvement of endorphins.

Using a strain of mice (CX BK) who have congenital deficiency of opioid receptors, Peets and Pomeranz (1973) showed that these mice demonstrated a significantly lower response to acupuncture analgesia, thereby implying that endorphin receptors are necessary if acupuncture is to have an analgesic effect. They speculated that some people may have a deficiency within their endorphin system similar to that observed in the CX BK mice strain. This might explain why 30% of humans do not experience either morphine or acupuncture analgesia. Takeshige et al (1978) studied acupuncture analgesia in rats. Forty per cent of the rats failed to demonstrate acupuncture analgesia and when these animals were sacrificed they were found to be deficient in opioid receptors, suggesting that both

endorphins and opioid receptors are essential for effective acupuncture analgesia. Sjolund et al (1977) have provided some evidence for the segmental release of endorphins. They treated backache by inserting acupuncture needles into the lumbar region and observed the doubling of endorphin levels in the lumbar CSF. However when they treated facial pain by using acupuncture points in the hand, no increased endorphin levels in the CSF of the lumbar region were noted. In both instances, the acupuncture seems to be equally clinically effective, thereby implying endorphins may be released in a regional manner in response to acupuncture. In 1975 a Chinese neurosurgeon in Hong Kong, Dr Wen, reported symptoms of heroin withdrawal could be alleviated by electro-acupuncture. This resulted in a collaborative study with Professor Besser's unit at St. Bartholomew's Hospital (London) in which it was shown that electro-acupuncture caused a significant rise of met-enkephalin in the CSF of such addicts (Clement-Jones et al, 1979). Electroacupuncture in patients with chronic pain showed an increase in CSF beta endorphin, but met-enkephalin levels were unchanged in these patients (Clement-Jones et al, 1980). These results suggest that the mechanism implicated in heroin withdrawal and pain relief may be different.

Having established that endorphin release can be stimulated by acupuncture it is necessary to demonstrate that these physiological changes do correlate with clinical pain relief. Electrical stimulation of the periventricular brain in man causes profound analgesia accompanied by a massive increase in beta endorphin levels (Akil, 1978) and intrathecal administration of Beta endorphin produces a long-lasting analgesic effect in cancer patients (Oyama et al, 1980). It has also been noted that patients with chronic pain seem to have a low CSF Beta endorphin level, but

that these levels do not seem to correlate with the severity of duration of pain (Akil, 1978). Such observations in humans are further supported by animal work from Shanghai Academy (Gang et al, 1979). A similar case has been made for the mechanism of TNS, in that it has been also shown that this form of stimulation therapy causes a rise in Beta endorphin levels within the CSF.

There is now a huge amount of convergent evidence that supports the acupuncture endorphin hypothesis and suggests that this is far more than simply a placebo effect.

Psychological Mechanisms

Although the majority of mechanisms suggested for acupuncture have concentrated on physiological theories, some more psychologically orientated explanations are available.

It is important to understand that patients in pain are physiologically disturbed (Pilowsky and Spence, 1975). For instance, they are more likely to be depressed (Skevington, 1983). Timmermans and Sternback analysed the personality and pain reaction variables in 119 patients with chronic pain (1974). They demonstrated that these patients were likely to have qualities such as 'inter-personal alienation and manipulativeness'. Whether these attributes were present prior to the complaint of pain, or produced by the presence of a chronic intractable pain state is unclear. In some instances pain complaints are part of a 'pain game', played by the patient on both the patient's immediate family and the physician (Sternbach, 1974). It has been recognised for some years that the experience of chronic pain can be alleviated by the use of anti-depressant medication (Menges, 1983). Perhaps this somatic complaint represents a legitimate avenue through which the depressed patient can seek medical help

(Merskey and Spear, 1967). Such background information must necessarily preface any purely psychological theory that might be used to explain the mechanism of acupuncture.

Do particular types of patients respond to acupuncture?

Toomey et al analysed the psycho-social factors affecting response to acupuncture (1977). Patients who responded to acupuncture were found to be less depressed, less passive and have shorter duration of pain than those that failed to respond to this therapy. However, there was little difference in the way responders and non-responders described their pain. Also, the 'noxiousness' of the stimulus causing pain did not correlate with the response to therapy. The non-responders were more prone to stress; for instance, the presence of non-pain related co-existent physical illness was more likely to be associated with a failure to respond to acupuncture. Mendelson et al studied 77 patients with low back pain using a double-blind cross over study comparing acupuncture and placebo acupuncture (1983). They measured anxiety, depression and pain duration, and subsequently correlated these measures with response to treatment. None of these psychological variables predicted which patients would respond to acupuncture and/or placebo. Levine et al (1976) suggested that acupuncture works best on depressed, anxious patients while other studies imply the reverse (Hossenlopp, 1976). Our knowledge of pain and depression would suggest that a less depressed patient is more likely to respond to any therapy for chronic pain. However, from the limited information available it is not possible to predict whether certain specific patients will respond to acupuncture.

Hypnosis

Hypnotic suggestion has been implicated as one of the possible mechanisms

involved in acupuncture. Kroger has suggested that acupuncture analgesia works by 'suggesting in slow motion hypnosis' (1975). Wall has stated that, "acupuncture is an effective use of hypnosis. This in no way diminishes that value of acupuncture, but it does place it in a class of phenomena with which we are familiar" (1972). Kroger, reviewing the common denominators in acupuncture and hypno-anaesthesia, suggested there are many similarities; for instance neither can be used to best effect on tense or apprehensive patients (1975). He implied that the high rate of success of acupuncture analgesia in China stem from the regimented environment of Chinese society, and the consequent limitations on complaint behaviour of Chinese citizens! Therefore acupuncture could be closely related to the operant conditioning techniques for shaping and altering desired behavioural responses. However, little hard evidence is provided to support these suppositions.

Finer has suggested that hypnotic analgesia may be acting via Melzack and Wall's gate control theory (1980). Hagbarth has shown that dorsal column activity in the cat can be inhibited by stimulation of the reticular formation, an area of the nervous system that is affected by hypnotherapy. Furthermore, in man the abdominal spinal reflex can be affected by suggestion thus implying that hypnosis may affect viscero-somatic reflexes (Hagbarth and Kugelberg, 1976). The evidence available to support these mechanisms for hypnotic analgesia is limited, but nevertheless the suggested mechanisms are similar to some of the physiological ones proposed for acupuncture.

Studies by Pomeranz and Chiu (1976) show that naloxone reversed acupuncture analgesia but had no effect on hypnotic analgesia. This has been confirmed by Sjolund and Eriksson (1976) and Hilgard and Hilgard (1975).

Therefore, it would seem that hypnosis is not mediated through the same kind of endorphin mechanisms that have been proposed for acupuncture.

A number of clinical studies have attempted to correlate hypnotic suggestibility with response to acupuncture. Goldberger and Turskey (1976) investigated the relationship between these two phenomena in a group of healthy volunteers. They created analgesia in the forearm by using surface electrodes located over acupuncture points, stimulated electrically. One group of patients were given the explicit suggestion that acupuncture would fail to produce analgesia. But subsequent noxious stimulus demonstrated that analgesia was present and that the hypnotic suggestion that the arm was particularly sensitive could not overcome the analgesic effects of acupuncture. A control group was included who received stimulation over random loci and given explicit suggestions that analgesia would be present in the arm. No alteration in the perception of pain intensity was demonstrable in the control group at any time during the experiment. However, subsequent stimulation of the "correct" acupuncture points in the control group produced significant analgesia and overcame the counter suggestion of sensitisation. Moore and Burke (1976) studied the effects of acupuncture and suggestibility on chronic shoulder pain. Patients were placed in one of two environments. One was positive and supportive, suggesting the therapy would work and the other was negative, suggesting the therapy would be ineffective. Neither of these settings affected treatement outcome. Those patients rated as highly susceptible to hypnosis tended to fail to achieve the highest levels of pain relief, but hypnotic suggestibility could not be significantly correlated with treatment outcome in the context of this study. Liao and Wan also reached a similar conclusion that highly suggestible patients did not necessarily

do well with acupuncture (1976).

Only one study to date has noted a correlation between suggestibilty and response to acupuncture, that of Katz et al (1974). They noted a close correlation between hypnotizability and pain relief, and suggested that acupuncture and hypnosis may be working through parallel mechanisms.

The exact mechanism of hypnosis remains unclear, but there is some evidence to suggest that acupuncture and hypnosis may be affecting the same neurological pathways. However, hypnosis does not seem to be endorphin mediated (naloxone reversible) whereas acupuncture almost certainly is. The evidence available suggests that acupuncture and hypnosis are probably unrelated in that suggestibility is not an essential factor in the success or failure of acupuncture therapy for pain.

Race

Early reports of acupuncture in China have implied that acupuncture was a useful therapy for the Chinese but would never work in the West. Perhaps because of the inscrutable face of the Orient the Chinese were thought to be almost resistant to pain. Studies by Chapman et al (1982) and Knox et al (1977) show that Orientals are at least as susceptible to experimental pain as Occidental races. In fact, Knox's work shows that Orientals have a significantly lower pain tolerance than Caucasians. It therefore seems unlikely that race has any significant effect on the outcome from this form of therapy.

In the United Kingdom, acupuncture is used mainly as a therapy for chronic pain. Patients in chronic pain are likely to be depressed, but it is unclear as to whether any specific psychological variables affect the outcome of acupuncture therapy. Acupuncture and hypnosis are almost certainly different phenomena and acupuncture cannot be thought of as a

complex form of hypnotic suggestibility. All therapies have a placebo effect, and acupuncture is no exception to this general rule. Complementary medicines are becoming more popular throughout Europe, and it may be that patients who seek such therapy are more likely to respond to it, particularly within the context of private practice where the patient may be given the facility for a more relaxed consultation.

CONCLUSION

There is clearly a large amount of evidence which looks at how acupuncture may affect the nervous system. While initially the gate control theory was thought to explain the basis of acupuncture analgesia, the picture soon broadened to include work on natural opioid systems. It is now clear that there are both neurological and neurohumoral mechanisms through which acupuncture is mediated. However, most of the neurophysiological and neurohumoral information relating to these areas, has been obtained from animal experiments involving acute pain. It is still questionable how much of this relates to the chronic human pain in which acupuncture is frequently used.

The most interesting, important and relevant information from the neurophysiology with respect to the clinical trials is that of DNIC. It is clear that DNIC operates in both animals and man, and it is therefore reasonable to suppose any noxious stimulus including acupuncture at the wrong point will elicit an analgesic effect. Consequently, one has to be particularly careful when designing placebos in the field of acupuncture. Furthermore it is reasonable to argue that inappropriate random or sham acupuncture (that is acupuncture placed in an inappropriate point for the condition being treated) is most unlikely to be a pure placebo.

SECTION 2

METHODOLOGICAL ISSUES, PLACEBO EFFECTS, PREVIOUS ACUPUNCTURE STUDIES AND THE SELECTION OF FOUR ACUPUNCTURE STUDIES

CHAPTERS 5 - 8

CHAPTER 5

PLACEBOS: ARE THEY POSSIBLE AND CREDIBLE?

Introduction

The medical scientist seems to view the placebo response as a problem that must be rigorously controlled in the context of scientific clinical trials, so that the objective value of specific treatment can be assessed. While this may be overstating the view of clinicians, such an approach has some validity. We must have criteria for evaluating the effects of treatment. Defining the term placebo presents us with problems. Laurence implies that the placebo response is, 'a subjective improvement in the patient's condition that is not directly attributable to the pharmacological or physiological effects of treatment' (1980) while Wolf suggests that the placebo effect is 'any effect attributable to a pill, potion or procedure, but not to its pharmacodynamic or specific properties' (1959).

These definitions allow us to analyse the effect of placebos in the context of clinical trials evaluating pharmacological preparations. However, they tell us nothing about the possible placebo effect of the quality and quantity of personal contact between the doctor and the patient. Furthermore, because our current concept of the placebo tends to be reductionist and materialistic, the definitions available are formulated in order to explain the observed placebo response encountered during controlled clinical trials. The argument is tautological; patients get better naturally even when suffering from severe chronic complaints; therefore we must invoke some explanation for this phenomenon. The model used does not adequately analyse the possible reasons for improvement, but simply uses a jargon word (placebo) to reinforce, and consequently make

respectable, our empiricism.

The Placebo Response

Placebos have undoubtedly been a vital part of the physician's toolkit since time immemorial, but before the 1950s very little had been written about them. Beecher was one of the first to look at the placebo response in the context of both medication and surgical procedures (1955, 1961). His conclusions are based on a variety of studies which include conditions such as post-operative pain, angina, headache, cough, anxiety and even the common cold. These studies provide conclusive evidence that the placebo is effective in a wide range of conditions. Furthermore the placebo response is consistent (35.2% ± 2.2%). The main method of defining this response had been based on the patient's subjective evaluation of response to treatment. It is impossible to measure many symptoms, such as pain, objectively and so most clinical studies, however carefully constructed, are necessarily subjective when it comes to measuring important end points such as treatment efficacy ((Huskisson 1974). Surgery is also a powerful placebo, and undoubtedly the surgeon's enthusiasm has a significant effect on outcome. This observation is supported by detailed investigation into two surgical procedures: ligation of the internal mammary arteries for angina and the treatment of duodenal ulcer by gastroenterostomy.

Enthusiasts supporting the operation of internal mammary ligation for the treatment of intractable angina began to report excellent results during the late 1950s. Complete or significant pain relief associated with subjective reports of good improvement in function occurred very shortly after the operation, in a large number of patients. An early study by Kitchell et al (1956) suggested that 68% showed significant subjective clinical improvement, but only 42% showed an objective improvement on

investigations such as ECG and exercise tolerance. Sceptics such as Cobb, using exactly the same procedure, reported only a 6% success rate (1959). In a sense the debate about arterial ligation was answered in a paper by Dimond et al, they carried out a double-blind study of internal mammary ligation in 18 patients. Skin incisions were made in all 18, but only 13 had ligation. The cardiologist assessing the patient's response to the operation was unaware as to which procedure they had undergone. A marked improvement in clinical state and anginal pain occurred in 10 of the 13 ligated patients. All 5 who had the sham operation also described a marked clinical improvement (Dimond et al, 1958 and Dimond et al, 1960).

A similarly dramatic difference in clinical response can be elicited when evaluating the effect of gastroenterostomy as a long-term treatment for duodenal ulcers. Enthusiasts like Douglas claimed an 82% five-year cure with almost no unpleasant or adverse reactions, whereas sceptics such as Lewishon claimed only a 47% five-year cure rate with a much higher proportion of adverse reactions (Beecher 1961). Surgery therefore is a powerful placebo, and illustrates dramatically how the enthusiasm of the operator can have a major effect on treatment outcome over a prolonged follow-up period.

Patients respond to placebos in a variable manner; Lasagna et al report a double-blind placebo-controlled study on post-operative pain, which suggests that 14% of patients were consistent placebo responders and 21% were non-consistent placebo responders. The remaining 65% varied in their degree of placebo response in no obvious or predictable manner (Lasagna 1961). Placebos have their own pharmacology; the dose response curve to placebo treatment is similar to that of many real medications. Patients experience adverse reactions to placebos and on occasion can become quite

ill in response to placebo medication. Cumulative or 'carry-over' effects can also occur if the placebo medication is given repeatedly; patients may complain of feeling over-medicated or even addicted to the drug (Lasagna 1958).

We have, therefore, made an attempt to quantify the placebo response. We must be aware that a placebo effect will occur in response to almost any procedure, in approximately 35% of patients. Usually, the effect is variable although there is a small group of consistent placebo responders. Furthermore, placebos have a discrete pharmacology which includes both a dose response curve and the potential for adverse reactions.

The Psychology of the Placebo Response

What are the psychological parameters governing the placebo response? Beecher has shown that the more anxious the patient, or the more anxiety provoking the procedure - for instance heart surgery - the more likely is it that a placebo response will be elicited (Beecher 1956). Therefore, procedures such as open-heart surgery which are dangerous and life-threatening, and which also involve prolonged periods of recuperation in stressful, high-technology environments must be successful at invoking a significant placebo response.

Sex, educational background, attitudes towards drugs, doctors, nurses, hospitals and church membership are not important predictors of the placebo response (Lasagna 1955). However, it does appear that placebo reactors have a tendency to be more emotional, gushing and neurotic. They are more grateful for, and impressed by, hospital care and ask less frequently for medication. In one study the nursing staff noted that placebo responders tended to be more co-operative and talkative than non-responders. Furthermore, the placebo responders more commonly gave a history of

psychosomatic symptoms and had a higher chance than a control population of being addicted to purgatives or analgesics. Female placebo responders tended to be more prone to dysmenorrhoea, psychological testing suggested that placebo responders were more inward looking and preoccupied with their own internal body processes (Hankoff 1965). This psychological picture does not provide enough information to predict which patients will (or will not) respond to a given placebo. It does, however, suggest that placebo responders may have a tendency to be more sensitive and neurotic.

The doctor/patient relationship is often an essential factor in eliciting the placebo response. Wolf reports the case of a patient with achlorhydria in whom a gastric cancer was suspected. She was saved from laparotomy when the surgeon who had enquired into her background asked: "Why did you not take your husband back when he returned from overseas?" She promptly produced gastric acid without a histamine stimulus (Wolf 1959). Further support for the importance of the therapeutic relationship as one of the possible initiators for the placebo response can be found from Hankoff et al. They treated schizophrenic patients first with a placebo and then with an active medication. Of the patients who failed to respond to a placebo, 87% also failed to respond to the active medication. The common factor in deciding upon patient response seems to be the relationship between the patient and the doctor. Hankoff et al regard the placebo response as a non-verbal communication between patient and doctor (Hankoff 1960).

Gliedman et al have suggested that the placebo response is in some ways similar to a conditioned relfex (1953). It is quite clear that patients' responses can be conditioned to a certain extent by the expectation of the doctor or therapist dealing with them. Such conditioning is enhanced by

central excitatory states, such as those frequently seen in doctor/patient consultations. Therefore the expectation of help when the patient consults a doctor may be part of a 'conditioned placebo response' of a nature that we have come to expect from almost any therapy.

The mechanism of the placebo response

Levine et al have suggested that the placebo response is endorphin mediated, as it can, in some instances, be reversed by naloxone (Levine et al, 1978). This implies that an unknown trigger may be stimulating a response within the central nervous system that is at least partially mediated through known neurotransmitters. It is possible that the trigger stimulating endorphin release may be variable; a stressful situation may stimulate the same neurohumoral pathway as the warmth and sympathy of a good doctor/patient relationship or the effect of a trained healer. Perhaps the healer's art may be to maximise the placebo response by stimulating the body's own natural powers of homeostasis and recuperation through such neurohumoral mechanisms.

The emerging field of psychoneuroimmunology was predicted by Wolf in 1959. He suggested that 'strong experimental evidence indicates that many of the component changes in disease process, including fever, leucocytosis, headache and nausea, are capable of being set in motion by impulses arising in the cerebral cortex'. By suggesting this he did not mean that all illnesses are psychosomatic or neurotic, but rather that the psyche has a significant influence on the progress and outcome of somatic disease (Wolf 1959).

Solomon's more recent review provides some 14 hypotheses through which psychological events may affect the immune system of both man and experimental animals (1985). For instance, the hypothesis that 'severe

emotional disturbance should be accompanied by immunological abnormalities', is supported by data demonstrating that clinical depression causes immune suppression (Kronfoe et al, 1982) and that schizophrenics display abnormal lymphocytes both functionally and morphologically (Fessel and Hirata-Hibi, 1963). The detailed information presented by Solomon is overwhelming; how we feel obviously affects how we deal with illness at a physical as well as a psychological level.

We now know that certain stressful environments, if they are controlled by the individual or animal under stress, can be used in a positive and constructive manner and appear to potentiate our immune response. By contrast feeling out of control or overwhelmed by any stress causes a significant depression of the immune response. Psychoneuroimmunology has vindicated Wolf's original suggestion 25 years ago; the mind does affect how we deal with illness. How we feel must to some extent be affected by our relationships with others and, therefore, our relationships with others must in turn affect how we deal with illness. This must, necessarily, include the doctor/patient relationship as well as all the other personal interactions we experience on a day-to-day basis.

All too often treatments are promoted because the researcher has failed to understand that an illness may improve spontaneously. For instance, post-herpetic neuralgia shows a 50% spontaneous resolution rate in the first three months after the last evidence of acute shingles has disappeared (Hope-Simpson 1975). Studies evaluating potential treatments must either be an improvement on the expected natural history, or be instituted after the pain has been established for three months (when the rate of spontaneous improvement diminishes significantly). The fact that many chronic illnesses tend to improve eventually, or at least show relapses and

remissions, must not be confused with the concept of the placebo response. The placebo response implies a natural healing process that is triggered by events as yet unclearly defined.

Is placebo acupuncture possible?

We have established that acupuncture may be working partially through DNIC. Therefore any noxious stimulus whether it be through needling or indeed any other comparable technique, cannot be thought of as being purely a placebo. There is some argument that just bringing a needle to the skin may affect the magnetic fields around the body and this in turn may trigger an acupuncture-like effect without the needle penetrating the skin (Kenyon et al, 1992). As a consequence, there have been many arguments about placebo acupuncture.

A large volume of work has been published using sham acupuncture. While at first sham acupuncture may appear to be a logical and coherent way to test the effects of acupuncture, several arguments can be put forward which imply that sham acupuncture is not a true placebo. The first and most obvious is that sham acupuncture must be causing an effect through DNIC. Therefore the noxious stimulus involved in inserting an acupuncture needle through the skin may, in itself, activate the analgesic mechanisms through which acupuncture operates. Many acupuncturists would also argue that while a fixed set of points or fixed point prescription may be the best way to approach a particular problem, many other acupuncture points can also be useful in that condition. There are, therefore, good arguments within traditional Chinese medicine for using a whole range of acupuncture points. It is quite possible that an attempt at sham acupuncture may in effect be using what some acupuncturists consider to be appropriate points for the condition being treated.

Lewith and Machin reviewed trial methodology within acupuncture in 1983; this was a seminal paper as it was the first attempt to develop a coherent model for assessing any of the complementary therapies. These issues will be discussed in a subsequent chapter, but it is apparent from the very simple statistical approach reviewed (Lewith and Machin 1983) that sham acupuncture appears to have a greater effect than that expected from placebo treatment. Consequently, the arguments pertaining to DNIC and appropriate versus inappropriate acupuncture points for the condition being treated, seem to be supported by the available clinical trials. While some papers using sham acupuncture have shown a clear treatment effect over real acupuncture, the majority have not and as a consequence acupuncture itself may have been inappropriately evaluated. (Real acupuncture is acupuncture given appropriately at points that should treat the presenting condition. Sham acupuncture is acupuncture given inappropriately, at points that are either not acupuncture points or should not in theory be appropriate for treating the presenting condition). If one is attempting to use a treatment which really amounts to less effective acupuncture (sham acupuncture) then treatment advantages between sham acupuncture and real acupuncture are bound to be smaller than treatment advantages between a true placebo and real acupuncture.

Campbell (1991) compares the quest for a true acupuncture placebo with, "hunting the snark". His conclusion is that, "the quest for the perfect placebo form of acupuncture is really an attempt to find some treatment that does not involve effective needling, but has the same psychological impact as inserting a needle. This is the hunt for the snark; no such treatment can exist. Either you needle the patient, in which case you have performed acupuncture, or you don't; if you don't it's not an exactly

equivalent form of treatment to acupuncture." Campbell's arguments are logical and coherent, it is very probable that the perfect placebo is an unattainable goal within the context of acupuncture trials. However, as clinicians we are morally, ethically and scientifically bound at least to make some attempt to evaluate acupuncture by controlled trials, and we have to develop some form of placebo treatment with which to compare acupuncture. Two placebo models have been suggested: mock transcutaneous nerve stimulation and minimal needling.

Mock TNS

Lewith and Machin (1983) argued that the only placebo currently available placebo was that of mock TNS. Mock TNS itself involves a transcutaneous nerve stimulator which has visual and/or auditory output and, therefore, the actual small stimulator is in itself functioning. However, the output lead is disconnected so no current can travel from the stimulator to the patient. The disconnection can occur either at the output socket or within the jack plug which is placed into the socket. The first people to attempt to evaluate the use of mock TNS were Thorsteinsson et al who analysed the effect of real TNS treatment versus placebo (1978). They used a very complex form of trial methodology in which real TNS and placebo TNS were allocated at random to patients in pain, and neither the patient nor the operator was aware of which were real and which were placebo machines. They were able to demonstrate that placebo treatment provided the expected 30% placebo response in chronic pain and used this as a justification for the fact that placebo or mock TNS was a viable method with which to compare real TNS. A similar defunctioned machine was used by Macdonald et al (1983). They used a very early obstetric monitor, a huge machine with many visual and auditory signals which was

disconnected at its output and used as a placebo against which to compare acupuncture in the treatment of myofascial pain. There was a significant difference between real treatment and placebo, but the placebo produced a 30% response in the treatment of myofascial pain syndromes. Macdonald noted, however, that placebo treatment is not without its side effects. Some patients noted a worsening while others were very reluctant to give up the treatment at the end of the clinical trial. These arguments substantiate the credibility of mock TNS as a placebo, but do not completely refute Campbell's arguments that the perfect placebo is an unattainable goal.

Petrie and Hazleman (1985) decided that such relatively superficial arguments were inadequate to justify the use of mock TNS as a placebo, and wished to look at the credibility of mock TNS as compared to acupuncture in patients with chronic pain. Petrie and Langley's initial study in 1983 reported a good result with acupuncture as compared with mock TNS in the treatment of cervical spondylosis, but felt this study had significant problems. Although mock TNS was delivered in a very positive way with verbal suggestion, they felt that acupuncture may have offered a "better treatment" because of its, " associated public perception and consequent intrinsic suggestibility". They, therefore, used a scale first suggested by Borkovec and Nau to compare the perceived effectiveness of treatments, by trying to analyse the expectations of people receiving acupuncture and mock TNS as treatments for chronic pain (Borkovec and Nau, 1972). They presented mock TNS to the patients as a subliminal pulse therapy. A standard statement was read out to each of the 39 patients receiving mock TNS. This stated that, "electrical stimulation has been used for many years to treat pain as it is known that all nerves carry messages by small

electric currents and that some nerves can actually block the pain messages of other nerves. Until recently electrical stimulation was given by machines that stimulated a lot of nerves and this could be felt as vibration. Subliminal pulsed therapy machines electrically stimulate only those nerves which will stop pain messages being transmitted and no sensation of vibration is felt. This form of machine is therefore an effective therapy for rheumatic and arthritic pain." Eighty-four patients were entered into this study, 45 of them received classical acupuncture. The two groups were similar in terms of diagnostic categories, age, sex and duration of illness. The pain scores in both groups were also very similar. However, the aim of this study was not to assess whether acupuncture produced analgesia, but rather to assess whether mock TNS was a credible treatment.

Each patient in the Petrie and Hazleman study was asked a number of questions directly taken from Borkovec and Nau's work (1972). The questions were:

1. How logical does this treatment seem to you? (Not at all logical/very logical)
2. How confident would you be that this treatment could be successful in reducing your pain? (Not at all confident/absolutely confident)
3. How confident would you be in recommending this treatment to a friend who has rheumatic or arthritic pain? (Not at all confident/absolutely confident)
4. If you were offered this treatment for rheumatic or arthritic pain, would you be willing to have it? (Not at all willing/very willing)
5. How successful do you feel this treatment would be in reducing different sorts of pain, for instance migraine headaches? (Not at

all successful/very successful)

A single questionnaire was given to the patient at the end of treatment and they were asked to note their preferences on a 10 cm visual analogue scale in response to each of the questions. A credibility rating or suggestibility score was then devised by adding up all the responses to these five questions and then comparing the two groups (mock TNS and acupuncture). The outcome suggested that mock TNS appeared to be more credible than acupuncture, substantiating the argument that while mock TNS is not a perfect placebo, it is certainly a reasonable, acceptable and above all a believable placebo.

Minimal acupuncture

The vast majority of acupuncturists now accept that sham acupuncture is not an ideal placebo, and so minimal acupuncture has been employed. Vincent has written extensively about acupuncture trial methodology and has suggested that minimal acupuncture appears to be the most acceptable and logical placebo (Vincent and Richardson 1986). Minimal acupuncture in effect involves just touching the skin with a needle or placing it just a millimetre into the skin. There are arguments against this in that even minimal needle puncture is to some extent a noxious stimulus. Furthermore, if acupuncture points have some external electrical or electromagnetic field associated with them, then even minimal acupuncture may possibly have some physiological effect (Kenyon et al, 1992). The first reported use of minimal acupuncture was by Hansen and Hansen in the treatment of facial pain (1981). They demonstrated that minimal acupuncture was far less effective than real acupuncture in the management of chronic facial pain and appeared to be able to construct a study model which seemed acceptable to patients. Needles were inserted just one

millimetre into the skin far away from points that would be deemed as useful in the management of facial pain. Vincent's study on migraine (Vincent 1989 and Vincent 1990) used a similar procedure to that of Hansen in that needles did penetrate but only minimally. Both clinical trials demonstrated a significant therapeutic advantage for acupuncture over minimal acupuncture but indicated also that minimal acupuncture was producing the expected placebo response of around 30%. A parallel study, again using the criteria suggested by Borkovec and Nau in 1972, was carried out by Vincent concurrently with his migraine trial. This involved two assessments, one at the beginning of treatment and one some 4-6 weeks after treatment had started. Four questions were asked:

1. How confident do you feel that this treatment can alleviate your complaint?
2. How confident would you be in recommending this treatment to a friend who has suffered from similar complaints?
3. How logical does this treatment seem to you?
4. How successful do you think this treatment would be in alleviating other complaints?

The four questions posed by Vincent were then analysed under the categories of confident (question 1), friend (question 2), logical (question 3) and successful (question 4). A 6 point verbal scale was used by the patient to reply to each of these questions. Questionnaires were given to 50 people randomly allocated to either real or minimal acupuncture. Vincent's results and conclusions were very similar to Petrie and Hazleman's earlier study. However his statistics are far more sophisticated in that inter-item acupuncture appeared to be as credible as real acupuncture in all four categories. In the last category, which

looked at success of treatment, minimal acupuncture was perceived on the second occasion as being less successful than on the first, but in the other three areas the scores remained consistent throughout treatment. Consequently, Vincent has demonstrated that while minimal acupuncture may not provide the perfect placebo, it is certainly credible and would appear to be an effective control for real acupuncture.

Who provides the treatment?

The evidence presented suggests that a single doctor should provide both real and placebo treatments. If the doctor is able to elicit an appropriate "healing response" (which appears to be part of the placebo response) then that influence should remain consistent among all treatment groups. While this was possible in many of the simple, relatively small clinical trials that have been completed within the field of acupuncture, it would obviously be impratical if one were to consider a much larger clinical study or indeed a multicentre trial.

It would appear from studies both by Petrie and Hazleman and by Vincent that even though the studies on mock TNS and minimal acupuncture were single blind they were convincing to the patients. Therefore, the fact that the therapist was aware that he or she was providing a placebo treatment did not appear to undermine the patient's belief in the therapeutic effectiveness of that treatment. In spite of this observation, the evidence presented by Beecher (vide supra) would suggest that a lack of belief on the part of the therapist could have a significant effect on outcome. Consequently, it would be wise to develop a clear and coherent protocol along with a standard form of words which would be used both for real and placebo treatment groups. Ideally, both treatment groups should receive exactly the same time allocation. It may also be

sensible to develop a system which would allow consultations to be recorded on video and subsequently scored. The scoring system would be designed to assess non-verbal communication and consultation technique in general. This would allow an investigator to be certain that any therapeutic effects triggered by consultation technique, empathy or perhaps other non-verbal skills would be elicited in an equal way, in both treatment groups. Thomas (1987) has shown that positive consultation techniques elicit different treatment outcomes to negative consultation techniques in general practice. Consequently, the aim of evaluating the general approach used during a consultation would be to make sure that the technique used was similar for all treatment groups and, therefore, could not have a biased effect on outcome.

Conclusion

Placebos are a particularly complex area, but one that it is essential to address prior to constructing a proper controlled trial. All those who have worked within the field of acupuncture accept that the perfect placebo is probably unobtainable. However, both mock TNS and minimal acupuncture (in spite of their inherent difficulties) have been shown to be credible placebos. In the vast majority of instances the clinical trials that form the basis of this thesis do not address the problem of placebo credibility in enough depth (mock TNS, acupressure and in one instance sham acupuncture). Only in one of the studies on acupressure versus sham acupressure has some attempt been made to assess the credibility of the placebo. However there would appear to be sufficient evidence at present to substantiate the use of mock TNS as a placebo, but it would certainly be advisable in future studies to improve and extend this literature so that future researchers can feel more confident about using mock TNS as a

placebo control group.

CHAPTER 6

THE CLINICAL EFFECTIVENESS OF ACUPUNCTURE IN PAIN AND AS A TREATMENT FOR ADDICTION AND NAUSEA

Introduction

The research within this thesis was initiated during the late 70s and early 80s. At that time there were very few acupuncture studies published in the literature, and almost no coherent rationale for the development of research strategy within this area. While this thesis should not become bogged down in an endless literature review, it is important to establish the antecedents of the research discussed.

Therefore, the initial part of this literature review will be based on a review paper which summarises the situation, with respect to the use of acupuncture in chronic pain, in the early 80s (Lewith 1984). Further developments will then be discussed, particularly in relation to other reviews and the more recent use of meta-analysis as applied to studies within the field of acupuncture. A section on the use of acupuncture as a treatment for smoking withdrawal and as an antiemetic will also be included. Clinical trials looking at these two areas will be presented and, therefore, it is essential to place these studies in context with an appropriate, allbeit brief, literature review.

An extensive search of the literature during 1981 and 1982 revealed approximately 20 controlled trials that had attempted to evaluate acupuncture as a treatment for painful, mainly musculoskeletal conditions. These studies can be divided into three broad categories; acupuncture compared with conventional therapy, acupuncture compared with sham

acupuncture (the random insertion of acupuncture needles) and acupuncture compared with a physical placebo.

Acupuncture compared with conventional therapy

Six studies will be reviewed in which acupuncture was compared with conventional therapy (see Table 6.1).

Junilla's study evaluated the use of acupuncture versus piroxicam (Feldene) therapy for osteoarthritis of the hip, knee and shoulder joint in 32 patients (16 in each group) (Junilla 1982). He concluded that acupuncture was significantly more effective in reducing pain than piroxicam and demonstrated that the patients receiving acupuncture noted far fewer side-effects than with drug therapy. At follow-up after four months, the effects of acupuncture still seemed to be superior to that of piroxicam.

Fernandes and colleagues studied patients with rotator cuff injuries of the shoulder (Fernandes, Berry, Clark et al, 1980). They compared five treatment groups: acupuncture; local steroid injection, physiotherapy; local steroid injection combined with nonsteroidal anti-inflammatory agents; and placebo drug administration combined with placebo ultrasound. Each treatment group contained 12 patients; no real treatment differences could be shown between the outcome of any of these five groups. Although the number of patients in each treatment group in the two studies was small, both trials were well constructed with clear definitions for the success or failure of treatment.

Milligan and colleagues studied 100 patients with osteoarthritis of the knee, randomly selected for acupuncture treatment (50 patients) or conventional physiotherapy (50 patients) (Milligan, Glennie Smith, Dowson et al, 1981). Patients were given a standard treatment regime for both acupuncture and conventional physiotherapy, and pain relief was measured on

a visual analogue scale. The authors concluded that, overall, acupuncture and physiotherapy were equally effective in the management of this condition.

Gunn and colleagues reported a study in which acupuncture was added to a conventional treatment regime for chronic low back pain (Gunn, Milbrandt, Little et al, 1980). All the 56 patients who entered the study had failed to benefit from eight weeks of conventional therapy; 27 patients continued with conventional therapy and 29 received acupuncture plus conventional therapy. The pain relief in the acupuncture group was significantly greater than in the group continuing with conventional therapy. The study, however, was poorly constructed; a group of patients receiving a failed treatment regime cannot realistically be thought of as a control group to be compared with patients being offered a 'new' treatment such as acupuncture.

Man and Baragar studied 20 patients with seropositive rheumatoid arthritis causing bilaterally painful knees (Man and Baragar, 1974). In one group (10 patients) acupuncture was used on one knee and local corticosteroid injections on the other. The second group (10 patients) received steroid injections in one knee and random needling as a treatment for the other. Nine patients in the acupuncture group noted a 50 per cent reduction in pain, which lasted for between one and three months. One patient in the group receiving random needling noted a similar level of improvement for a period of one day. The effects of the intra-articular corticosteroid injection were not reported. This study also had its faults: only 20 patients were entered and, therefore, the surprisingly low response to random needling and the unusually high response to acupuncture must be interpreted with caution.

Brattenberg studied 60 patients with tennis elbow (Brattenberg 1983), 34 patients received acupuncture and 26 received a local corticosteroid injection in the elbow. At three-months follow-up, 62 per cent of patients in the acupuncture group were completely pain-free whereas only 30 per cent of those who received steroid injections were free of pain at follow-up, a surprisingly low response rate for injection therapy.

Four of these six studies suggested that acupuncture is more effective than conventional treatments for the management of chronic musculoskeletal pain. The other two studies showed no significant difference between the two types of treatment. No side-effects of acupuncture were reported in any of these clinical trials; Junilla emphasized this point and suggested that, in the hands of a competent practitioner, acupuncture is a safe form of therapy ((Junilla 1982).

Acupuncture compared with sham acupuncture

Nine studies which have used the model of sham acupuncture verus acupuncture will be reviewed.

As discussed previously, these authors have assumed that any therapeutic benefit obtained from sham acupuncture is purely that of a placebo. As discussed previously (vida supra) this assumption is almost certainly incorrect. Therefore studies using random needling are perhaps best thought of as an evaluation of acupuncture versus a less effective form of needle puncture.

Gaw and colleagues studied the effects of acupuncture versus random needling on osteoarthritic pain in 40 patients (20 in each treatment group) (1975). They concluded that both groups achieved pain relief, but that there was no significant difference between the effects of these two therapies. A similar conclusion was reached by Godfrey and Morgan, who

studied 193 patients with musculoskeletal pain (1978). Unfortunately, their study involved a wide spectrum of diseases with different natural histories. Their two treatment groups were not stratified or balanced for specific diagnoses, and the published results did not state clearly the exact diagnostic spectrum of musculoskeletal disease in each treatment group. Furthermore, as discussed by Lewith and Machin (1983) the statistical power of Gaw et al's study is only 30%, because so few patients were entered. This criticism can be levelled at almost all the acupuncture studies reviewed.

Matsumoto and colleagues studied shoulder pain (1974), 24 patients were entered into the study and divided into treatment groups (eight patients in each group). Two groups received slightly different forms of acupuncture treatment and one received random needling. The authors stated that acupuncture was effective in alleviating pain in approximately 80 per cent of patients in the study, but that no real difference could be shown between the three forms of treatment (Matsumoto, Levy and Ambruso, 1974). However, the definition of success or failure of treatment was unclear and the number of patients entered into this study was small, which probably explains why no clear difference emerged between the treatment groups.

Moore and Berk investigated shoulder pain in 42 patients (21 in each treatment group), assessing the relative effects of acupuncture versus random needling and also the influence of suggestibility on the effect of treatment (1976). They demonstrated that suggestibility did not affect the outcome in their study. A higher proportion of patients experienced significant pain relief in the random needling group than in the acupuncture group, but again no statistically significant difference could be demonstrated in the pain relief experienced between the two treatment

groups.

Co and colleagues evaluated the effect of acupuncture as a treatment for the pain experienced during sickling crises (1979). They showed acupuncture to be an effective analgesic, but again found no statistically significant difference in effect between random needling and properly performed acupuncture.

Mendelson and colleagues performed a complex cross-over study in which acupuncture was compared with lignocaine injection followed by needle insertion into the analgesic area (1983); 77 patients with low back pain were studied and visual analogue scales were used to measure pain. Overall, pain reduction was 36 per cent for the acupuncture group and 22 per cent for those who received lignocaine injection and random needling.

Edelist and colleagues studied pain resulting from prolapsed intervertebral discs (1976); 30 patients were entered into the study, 15 in each treatment group. They reported that 46 per cent of their patients obtained significant pain relief in the acupuncture group and 40 per cent in the group receiving random needling.

Lee studied 261 patients with chronic pain (Lee, Andersen, Modell et al, 1975). The diagnoses for the patients' complaints ranged from trigeminal neuralgia to generalized osteoarthritis. One group of 128 patients received four consecutive treatments: acupuncture; random needling; acupuncture; random needling. Another group of 131 patients received only acupuncture. Both groups responded in much the same manner but, overall, acupuncture accounted for 50 per cent pain reduction in 70 per cent of patients at the end of treatment. The proportion of patients noting this level of pain reduction at four weeks follow-up had decreased to 35 per cent. This study was poorly designed in that it was difficult to assess

the differential effects of acupuncture versus random needling when every patient was given each treatment at weekly intervals. It would therefore be best to interpret the results obtained by Lee as a descriptive study rather than one which realistically compares acupuncture with random needle insertion.

There are two studies which demonstrated a statistically significant difference between the effects of acupuncture and random needling. Weintraub and colleagues, studying musculoskeletal pain, attempted to use a double blind model in which the acupuncturist was unaware of the exact diagnosis, but was simply instructed to insert needles into points on the body designated for each individual patient (Weintraub, Petursson, Schwartz et al, 1975). They were able to demonstrate a more pronounced analgesic effect from acupuncture compared with random needling one week after the first treatment.

It is not surprising that the majority of these studies did not produce a statistically significant result as only small numbers of patients were entered into each individual clinical trial; for instance, the study reported by Gaw had only a one in three chance of detecting a significant difference between acupuncture and random needling if we assume that the predicted 70 per cent and 50 per cent response rate is correct (Gaw, Lenning and Shaw, 1975).

Acupuncture compared with placebo

Three studies in which acupuncture was compared with minimal needle have been identified (Jensen, Melson and Jensen, 1979; Junilla, 1982) (Table 6.3).

Junilla studied 44 patients with pain and randomly allocated them into two treatment groups (22 patients in each group) (1982). The patients entered

were those who could be treated by random insertion of acupuncture needles in the back so that they would be lying face down while receiving therapy. The acupuncture group had needles inserted into their tender trigger points on the back. The placebo group were treated by the 'minimal peripheral stimulus' of pinching their backs with a finger-nail a few centimetres away from the tender trigger point that would have been the site of needle insertion. A clear treatment difference was demonstrated between these two groups of patients; 72 per cent (16 patients) in the acupuncture group and 22 per cent (5 patients) in the placebo group noted complete absence of pain one month after the completion of therapy. Two problems can be identified: first, a noxious stimulus, however minimal, may attentuate pain perception elsewhere (Le Bars et al, 1991), and second, the primary diagnosis or cause of pain was not stratified or balanced between the treatment groups.

A study of facial pain by Hansen and Hansen involved 16 patients in a double-blind controlled cross-over model (1981). Each patient received four weeks of therapy with a two-week treatment-free period between the courses of treatment. Acupuncture was shown to be significantly better than minimal needling with respect to visual analogue pain scales recorded throughout the study period of 16 weeks.

Jensen and colleagues, investigating headache, used a partial cross-over method in which 19 patients received acupuncture and 10 received placebo treatment (1979). The 10 patients who were receiving placebo were crossed over to acupuncture with a treatment-free period of 120 days between treatments. Symptoms relating to headache were recorded using a daily diary. The authors noted that 50 per cent of patients in the placebo group improved whereas 68 per cent of those receiving acupuncture improved.

The placebo treatment involved superficially pricking the skin with a needle over the normal acupuncture point. This again represents a minimal noxious stimulus and cannot therefore be thought of as purely a placebo.

Other workers have compared a different physical placebo with acupuncture (Macdonald, MacRae, Master et al, 1983; Lewith, Field and Machin, 1984). Macdonald and colleagues studied 17 patients with low back pain, and compared the effects of acupuncture with placebo using a large defunctioned eight-channel obstetric monitor (1983). When switched on, the machine produced both audio and visual signals (flashing lights). Patients were connected to this equipment via surface electrodes on their back. No known stimulus of any description was transferred from the machine to the patients. Real acupuncture produced a response of 75 per cent and the placebo produced a 25 per cent response.

Lewith et al's group studied 62 patients with post-herpetic neuralgia, randomly allocated to placebo and acupuncture treatment groups (1984). A defunctioned transcutaneous nerve stimulator was used to provide the placebo. This machine produced a visual signal and patients were connected to it by surface electrodes around the painful area. Acupuncture resulted in improvement in 24 per cent of patients and the placebo in a 21 per cent response. It has been shown previously that a defunctioned transcutaneous nerve stimulator - a physical placebo - will produce a placebo response of the order of 30 per cent (Thorsteinsson, Stonnington, Stilwell et al, 1978; Lewith and Machin, 1981; Smith, Lewith and Machin, 1983). All the above clinical trials noted a placebo response of this magnitude, similar to that expected from placebo medication. The response to acupuncture was similar to that noted in the studies comparing acupuncture with random needling.

The situation in 1983

Having ignored the morass of descriptive data, largely published by acupuncturists and almost invariably claiming that acupuncture could effectively treat everything, these studies allow a clearer picture to emerge. In the first group of studies (acupuncture compared with other physical therapies), an average response to acupuncture of 68% was noted, in the second group 61% and in the third group 63%. Therefore a consistent picture emerged of acupuncture being effective in between 60-70% of the conditions studied. Random needling appeared to be more effective than placebo, and the placebo studies reported the expected response of around 30%. These data encouraged Lewith and Machin (1983) to develop some theoretical models for acupuncture studies.

Lewith and Machin observed that many of the studies published within this field were statistically weak and methodologically flawed, an observation that has not escaped the critical eye of other authors (Ter Reit et al, 1990). However it does appear, even from the limited evidence available in 1983, that acupuncture is consistently reported as having a greater effect than that expected from placebo. Furthermore, placebo treatments were having the expected 30% effect, and that appeared to be less of an effect than could be obtained from sham acupuncture.

Further developments over the last 10 years

Several reviews have been published since 1984, all looking at different aspects of acupuncture and pain. Probably the most comprehensive review is that by Richardson and Vincent (1986). Their conclusions are similar to those reported by Lewith in 1984; acupuncture seems to be effective in between 60-70% of those individuals suffering from chronic pain. However, Richardson and Vincent are very critical of some of these studies,

particularly in relation to headache. Many of the studies have poor methodology; the randomisation procedure is described unclearly, treatment groups are far too small to draw the conclusions suggested by the authors. The statistical analyses are limited and often inaccurate, and the use of a control or placebo group is sometimes ignored and all too often addressed inadequately. Lewith and Machin (1983) make the same points when discussing the study methodology and statistical interpretation of many of the papers published on acupuncture. Some of these inadequate studies were published in high quality peer review journals. Richardson and Vincent's data add a further 9 controlled or comparative studies published between the years 1983 and 1986.

In 1989 the first meta analysis of acupuncture became available. Patel et al analysed 14 clinical trials using much the same data as that available to Lewith (1984) and Richardson and Vincent (1986). The aim of meta analysis is to set methodological criteria for each of the studies, and then attempt to pool the information from these studies. The studies are then evaluated as a group in order to ascertain whether the methodology is adequate and, based on the pooled results, whether more information can be gained about the efficacy or otherwise of any given treatment. Three sub-groups of illnesses were analysed, all involving pain: low back pain, head and neck pain including headache and other illnesses such as osteoarthritis of the shoulder. Two sub-groups were also used to analyse the type of trial, type of treatment, type of control, blindness of participating agents, trial size and type of journal in which the results were published. Patel shows clearly that while few individual trials had statistically significant results, pooled results were significant. Overall pooled results were significantly in favour of acupuncture, particularly so for

headache and neck pain, and for low back pain but to a lesser extent. Results from the three other studies looking at other sites of pain suggested that the control group obtained better results than the acupuncture group. Acupuncture compared to conventional treatment was more favourable to acupuncture than trials where acupuncture was compared against a placebo. Interestingly, Patel et al noted that patients receiving classical acupuncture at sites that varied from treatment to treatment did better than patients receiving a formula or fixed prescription type of acupuncture. This argues strongly in favour of maximum adaptability and the use of traditional Chinese medicine within trials to assess acupuncture, the same points made by Wiegant et al (1991) and Bensoussan (1991). The methodology for meta analysis suggested by Patel (1989) and Hunter et al (1982) was followed rigorously. Patel et al make the point that many of these studies are inadequately controlled and would benefit from clearer methodology. However, overall the results indicate that acupuncture is a useful therapy in the management of chronic pain.

A second meta analysis carried out by Ter Reit et al (1990) looking at much the same data but using slightly different criteria, came to completely different conclusions. Fifty-one controlled trials were analysed, all looking at the effectiveness of acupuncture in chronic pain. These studies again followed the standard criteria for meta analysis; 18 pre-determined methodological criteria were analysed for each study and a maximum of 100 point for study design could be earned in 4 major categories: comparability of prognosis, adequate intervention, adequate effect measurement and data presentation. Ter Reit et al found that the quality of even the better studies proved to be mediocre. No study earned

more than 62% of the maximum score and the results from the better studies, those earning greater than 50%, are highly contradictory and indicate that little clinical effect can be obtained. Ter Reit et al conclude that no studies of high quality exist within the acupuncture field, and therefore it is impossible to reach a clear conclusion about the efficacy of acupuncture in the management of chronic pain. No new data is presented and the meta analysis and its subsequent conclusions are based on data previously analysed by Patel (1989), Hunter (1982) and Richardson and Vincent (1986). They point out the problems originally identified by Lewith and Machin (1983) concerning the physiological effect of sham acupuncture. They recognise that the methodology needed for acupuncture studies is different to that required for studies on pharmacological preparations and identify the problems of placebo, double or single-blindness, the difficulties of conducting a cross-over study and the flexibility of point selection. They conclude that using mock TNS is a "fatal mistake" but fail to research the literature on whether mock TNS is an acceptable placebo. Ter Reit et al point out many of the problems that exist within acupuncture studies, but unfortunately fail to give any coherent answers or solutions to the outstanding methodological problem. The National Council Against Health Fraud (1991) again have selectively quoted from the clinical trials and meta analyses available, suggesting that no evidence exists for the use of acupuncture in the management of chronic pain.

Pomeranz (1991) argues that acupuncture is effective in chronic pain and is one of the few authors to cite in his review the evidence from animal studies. It is difficult to believe arguments about suggestibility and placebo when one can quote such straightforward and dramatic responses in

the context of animal work, particularly that performed under carefully controlled laboratory conditions (Pomeranz 1991).

A recent review by Vincent (Vincent 1993) looks at the controlled trials of acupuncture as a method of pain relief, which have involved either minimal acupuncture or mock TNS.

These 12 studies are the only realistic attempts to analyse acupuncture in a properly controlled manner, with randomisation and some attempt at an adequate placebo. It is interesting to note that 5 of the studies involved minimal acupuncture as placebo and 7 involved mock TNS. Twenty five per cent of these studies will be reported in the ensuing research discussion within this thesis.

Overall, the data from these 12 studies would suggest that acupuncture has a significantly greater effect than placebo, but there are obvious problems in reaching a clear conclusion. Some studies support the validity of the placebo while others are less clear, largely because of the limited number of patients included. Many of the studies are too small and not enough of them, including the studies published by Lewith et al, have enough validation of the placebo procedure. Only Petrie and Hazleman (1986) and Vincent (1989) have made any real attempt to evaluate the placebo procedure adequately.

Conclusion - Pain

The evidence for acupuncture's clinical effectiveness in pain is certainly open to debate. There are only a limited number of adequately designed controlled trials and they have major problems associated with them. It is indeed surprising when one considers that acupuncture has been used for over two and a half thousand years, that so little clear evidence exists to justify its continued use in chronic pain. From the standpoint of this

thesis, however, it is equally important to recognise that the first methodological paper along with 25% of the published placebo controlled trials in which acupuncture has been evaluated for chronic pain, have been produced by the author.

Introduction to the treatment of addiction and nausea

Much of the initial work for this thesis was based on using acupuncture as a mechanism for treating pain. Pain is a complex phenomenon, both within traditional Chinese medicine and conventional medicine, so consequently many different acupuncture points may be used in the treatment of any given painful condition. Furthermore, pain is difficult to assess. Evaluating acupuncture in chronic painful conditions is therefore complex; it is difficult to agree on the right treatment and even when a clear treatment approach is possible, it is even more difficult to agree on whether the treatment has been effective.

The use of acupuncture as a method for smoking withdrawal is much simpler. The end points are clear, patients either cease to smoke or continue. Furthermore, although there are a number of different methods of promoting smoking withdrawal with acupuncture, there is a common consensus about the basis principles involved. In this condition, acupuncture is largely being used to promote endorphin release and hence ease nicotine withdrawal.

The final group of studies presented for this thesis is the evaluation of acupressure as a treatment for nausea. In this condition only one point is used for treatment. There is no debate about the use of this point between the more traditional acupuncturists and those who espouse a western approach to acupuncture. Vomiting is an objective phenomenon, nausea a far more subjective one. Even so, the requirement for anti-emetic therapy and the use of simple patient diaries for nausea and vomiting would appear to be far more likely to give clear end points of success or failure than the rather more subjective and debatable methods that have been used to evaluate chronic pain.

A review of the literature on both smoking and the use of acupuncture as an

anti-emetic are therefore discussed in order to provide background information for the clinical trial on smoking and the two clinical trials on acupressure as a treatment for nausea.

Acupuncture as a treatment for smoking addiction

The technique employed to aid withdrawal from smoking is different from the usual methods of acupuncture. The basic technique is the insertion of a stud in a particular acupuncture point in the ear. The stud is left in place and the patient is instructed to press it when a desire to smoke overtakes him or her. The actual point involved varies from study to study. Other studies have used electrical stimulation of needles in the ear but with nothing being left in place (Fuller 1982).

A number of authors have claimed impressive reductions in smoking after acupuncture treatment. Sacks (1975), for example, claimed that 61% of a sample of 642 smokers were abstinent after six months, but his paper contained almost no details of how he arrived at this conclusion. Systematic controlled studies have been less encouraging. Lamontagne and colleagues (1980) compared self-monitoring with two types of acupuncture, one aimed specifically at smoking withdrawal and the other at enhancing relaxation. Subjects in the self-monitoring group had two weekly 20-minute sessions with a therapist to report on their own efforts to reduce smoking with the aid of a wrist counter (Lamontagne, Gagnon and Gaudelle, 1978). Both types of acupuncture were significantly more effective than self-monitoring in the two weeks post-treatment but these differences disappeared at one, three and six months of follow-up. Clavel and Benhamou (1985) compared acupuncture, nicotine gum and a minimal intervention control in a study involving 651 smokers. Acupuncture was as effective as nicotine gum and both were significantly more effective than

the control at one and 13 months follow-up. As usual there was a high rate of relapse; at one month 19% and 22% of smokers were abstinent in the acupuncture and nicotine gum groups respectively and at 13 months 8% and 12%.

Cottraux and colleagues (1983) found acupuncture to be superior to behaviour therapy after nine and 12 months but equal to placebo medication. They concluded that 'as in most smoking cessation studies the overall effect was small and non-specific'. This is similar to the findings of Gillams and Lewith (1984) who concluded that 'the claims made for acupuncture are somewhat over-enthusiastic, however acupuncture does seem to be as effective as other methods of smoking withdrawal'. Gillams and Lewith also considered the question of the siting of the ear stud, but found no difference between the recommended 'lung' point and a nearby 'incorrect' site.

Results from Fuller's technique of incorporating electrical stimulation combined with a discussion of the medical risks look more encouraging (Fuller, 1982); 95% of his subjects stopped smoking after three acupuncture treatments given over four days. After one month, however, only 71% of subjects were abstinent and at two years this figure had fallen to 30%. Various aspects of the design, in particular the manner of subject selection and the exclusion of subjects not replying to follow-up questionnaires, makes it likely that these figures are an overestimate.

It is clearly important to distinguish between an intervention that assists people in the initial withdrawal period and one designed to discourage them from resuming smoking. There seems to be no reason to suppose that acupuncture or any other physical intervention will be of direct help in preventing relapse several months after it is given. On the other hand it

does seem to be as useful as other methods in the initial stages of withdrawal. Fuller's combination of electroacupuncture and discussion seems a potent initial influence on smoking, and perhaps we should not hope for more. It is unfortunate that the design of the study does not permit any examination of the specific role of electroacupuncture. Indeed it is not yet clear from any of the studies what the actual stimulation contributes to the overall effect of acupuncture treatment.

A meta analysis by Ter Reit et al (1990) specifically looked at the effects of acupuncture on addiction. Ter Reit and colleagues analysed the same data as that of a previous review by Vincent and Richardson (1987). His analysis demonstrates yet again that many of the studies involving acupuncture are poorly constructed and he concludes that because of this the evidence for acupuncture as a treatment for smoking addiction is limited. Ter Reit et al state that, "although we have found more controlled clinical trials into the effect of acupuncture on addiction to tobacco than have authors of earlier and more informal reviews (Vincent and Richardson, 1987) our conclusions are very similar. Basically there is no evidence that acupuncture is efficacious in the treatment of addiction to smoking".

This fundamentally represents Vincent and Richardson who suggest that while acupuncture is not the magical cure claimed by some, it is certainly as good a treatment as any currently available in aiding smoking withdrawal and sustaining that result over a prolonged period. Ter Reit et al note somewhat grudgingly that other interventions do not seem to be particularly efficacious (Lam et al, 1987). Even acupuncture enthusiasts such as Gillams and Lewith (1984) conclude that acupuncture is only as good as the other "best" methods of smoking cessation. Consequently Ter Reit et

al present a nihilistic view when they suggest that nothing works particularly well. Almost every doctor would agree with that statement, but would also note that of the treatments available acupuncture is as efficacious as the other "best treatments" available." However, Ter Reit et al mention (1990) there is little doubt of the need for more comprehensive and better constructed studies.

Acupuncture as a treatment for nausea and vomiting

The Chinese have claimed for many thousands of years that pericardium 6 can alleviate nausea. This point is about two inches above the wrist on the ventral surface of the arm. For some reason this very simple observation attracted Professor John Dundee at Queen's University, Belfast. The first paper by Dundee et al in 1986 looked at the reduction in emetic effects of opioid pre-anaesthetic medication by acupuncture. Acupuncture needles were inserted into patients for 5 minutes and stimulated with a low electrical frequency (10-15 hertz) immediately after the administration of opioid pre-anaesthesia. In a series of studies with different opioids patients were randomly allocated to receive acupuncture or no anti emetic treatment and were then evaluated pre-operatively and post-operatively for the occurrence of nausea and/or vomiting. The results showed a very significant reduction after acupuncture in the nausea and vomiting produced by Pethidine, Nalbuphine and the more recently introduced opioid drug Meptazinol (Dundee et al, 1986). Dundee and his colleagues were aware of the criticism that the acupuncture procedure itself might have led to a placebo effect and, therefore, carried out a study involving sham acupuncture. In this the acupuncture at pericardium 6 was compared with needling a point on the lateral elbow crease. Nausea and vomiting following pre-medication with nalbuphine was significantly less in the

patients receiving acupuncture than in those who received sham acupuncture (Dundee et al, 1986). There was no significant difference in the prevalence of emetic sequelae in the patients having sham acupuncture as compared with those having no acupuncture at all.

Nausea in association with cancer chemotherapy is another area which Dundee et al studied exhaustively. About two thirds of patients receiving cancer chemotherapy experienced some degree of nausea and vomiting. There is a marked anticipatory element in this emetic experience. Dundee et al (1987) noted that out of 165 patients 140 expected nausea or vomiting after chemotherapy. In a series of studies, Dundee et al demonstrated that acupuncture at P6, but not sham acupuncture, produced good results with large numbers of drugs used in cancer chemotherapy (Dundee et al, 1989). Overall, figures suggested that 63% of patients had complete absence of sickness for at least 8 hours and only 5% showed no benefit at all. The least satisfying results occurred in those patients receiving the highly emetogenic drug, cisplatin. But, even in this group, there was significantly less sickness when true acupuncture was used as compared with sham acupuncture (Dundee et al, 1987). A further study to compare acupuncture at pericardium 6 with the effects of conventional anti-emetic therapy (metoclopramide) indicated that acupuncture and metoclopramide were probably equally effective (Dundee et al, 1988).

Acupressure was also investigated by Dundee but used in an uncontrolled way. He noted that simple acupressure helped reduce post-anaesthetic nausea and vomiting (Bill and Dundee, 1988). Furthermore, acupressure used after acupuncture increased and prolonged the anti-emetic effects of acupuncture itself (Dundee et al, 1990a, Dundee et al, 1990b). Two studies involving pericardium 6 are reported in this thesis; both use

acupressure and are carefully controlled studies. They add to the literature presented by Dundee by evaluating acupressure versus sham acupressure and evaluating the quality and acceptability of sham acupressure as a placebo.

Dundee et al (1991) also went on to evaluate the effects of TNS over pericardium 6 as a mechanism for relieving nausea. They found that TNS was as effective as acupressure but both were of a shorter duration than acupuncture. Dundee was also able to demonstrate that either TNS or acupressure, used after acupuncture, prolonged the effects of acupuncture.

The investigations triggered by Professor John Dundee in relation to pericardium 6 were certainly the most watertight of all the clinical trials involving acupuncture techniques. The results are clear and conclusive for three related forms of treatment: acupuncture, acupressure and TNS. While Dundee failed to complete properly controlled studies in the field of acupressure versus sham acupressure and TNS versus mock TNS, his work was thorough, clear and conclusive. There is little doubt that acupuncture has an anti-emetic effect, in all probability equal to that of powerful conventional anti emetic medication.

TABLES FOR CHAPTER 6

Table 6.1

Acupuncture compared with other physical therapies

(Success as defined by the authors of each paper at the end of treatment, expressed as a % of patients entered into each treatment group.)

		Drugs (non-steroidal anti-inflammatory drugs & steroid injections)	Acupuncture	Physio-therapy	Disease
1.	JUNILLA 1982	32	61		OA large joints
2.	FERNANDES, BERRY & CLARK 1980	50	50	50	Shoulder pain
3.	MILLIGAN & GLENNIE SMITH 1981		82	48	OA knees
4.	MAN & BARAGAR 1974	10	90		RA knees
5.	GUNN, MILBRANDT & LITTLE 1980		62	15	Low back pain
6.	BRATTENBERG 1983	30	68		Tennis elbow

The average response to drugs is 30%

The average response to acupuncture is 68%

The average response to physiotherapy is 38%

Table 6.2

(Success as defined by the authors of each paper at the end of treatment, expressed as a % of patients entered.)

		Random Needling	Acupuncture	Disease
		40%	61%	
1.	MOORE & BERK 1976	39	23	Shoulder pain
2.	CO & SCHMITZ 1979	50	81	Pain from sickling crisis
3.	MATSUMOTO & LEVY 1974	Only mean scores given		Shoulder pain
4.	GAW & LENNING 1975	36	58	OA pain
5.	GODFREY & MORGAN 1978	54	63	Musculoskeletal pain
6.	WEINTRAUB & PETURSSON 1975	Only mean scores given		Musculoskeletal pain
7.	LEE & ANDERSEN 1975	-	70	Chronic pain
8.	MENDELSON & SELWOOD 1983	22	26 (mean scores)	Back pain
9.	EDELIST & GROSS 1976	40	46	Back pain

Table 6.3

(Success as defined by the authors of each paper at the end of treatment, expressed as a % of patients entered in each treatment group.)

		Placebo	Acupuncture	Disease
1.	JUNILLA 1982	22	72	Musculoskeletal pain
2.	JENSEN & MELSON 1979	50	68	Headache
3.	MACDONALD & MACRAE 1983	25	75	Back pain
4.	LEWITH & MACHIN 1984	21	24	Post-herpetic neuralgia
5.	HANSEN & HANSEN 1983	45	75	Facial pain

TABLE 6.4

ACUPUNCTURE FOR CHRONIC PAIN: STUDIES WITH ACCEPTABLE PLACEBO CONTROLS

Authors	Population	N	Design	Control	Type of Acupuncture	Dependent Measures	Follow-up	Results
Junilla 1982	Musculo-skeletal pain	32	Group comparison	Minimal acupunc.	4 treatments	Daily pain ratings	4 weeks	22% placebo benefit 72% acupuncture
Hansen & Hansen 1983	Facial pain	16	Cross-over	Minimal acupunc.	Classical 10 daily sessions	Daily pain ratings	4 weeks	66% patients improved. True acupuncture. sig > control
Macdonald et al 1983	Low back pain	17	Group comparison	Mock TENS	Tender areas & trigger points. Some EA. Up to 10 sessions.	Various pain VASs, mood, independent clinician's assessment	None	Acupuncture sig. > placebo for pain relief, activity, physical signs in pain area
Petrie & Langley 1983	Cervical pain	13	Group comparison	Mock TENS	Classical 8 sessions, twice weekly	Self-ratings	None	84% acupuncture group reported good pain relief. Acupuncture sig. > placebo
Lewith et al 1983	Post-herpetic neuralgia	62	Group comparison	Mock TENS	Classical & auricular 6-8 sessions	Daily records sleep, moderation sleep disturbance	2 mths	Sig. improvement in only 7 patients in each group. No. sig. difference between groups.
Dowson, Lewith et al 1984	Migraine headache	48	Group comparison	Mock TENS	Classical 6 sessions	Frequency, duration, intensity, medication	24 weeks	56% acup. and 30% placebo showed 33% pain relief 44% acup. and 57% placebo less frequent headaches. No. sig. difference between groups.

TABLE 6.4 (Sheet 2)

Authors	Population	N	Design	Control	Type of Acupuncture	Dependent Measures	Follow-up	Results
Petrie & Hazleman 1985	Chronic neck pain	25	Group comparison	Mock TENS	8 sessions, twice weekly	Daily diary: pain intensity disability, medication.	1 mth	45% of acup. group & 30% of placebo group show sig. response. No sig. difference between groups.
Lehmann et al 1986	Chronic low back	53	Group comparison	Mock TENS	EA group and TENS group (all groups had additional treatment)	Physician assessment. VRS measures of pain & disability.	6 mths	EA sig. > TENS and mock TENS
Ballegaard et al 1986	Severe angina	26	Group comparison	Minimal acup.	Classical 7 sessions over 3 weeks	Exercise tests, pain diaries, medication.	3 weeks	Acup. sig. > control for cardiac work capacity only.
Vincent 1989	Migraine	30	Group comparison	Minimal acup.	Classical acup. 6 weekly sessions.	4 x daily ratings of pain and medication	I year	43% reduction in weekly pain score for acup. group, 14% for control. Acup. sig. > control for pain levels, but not for medication reduction.
Dickens & Lewith 1989	Osteo-arthritis	13	Group comparison	Mock TENS	Classical acup. 6 sessions over 2 weeks	Diames. VAS pain scores medication sleep, grip, tenderness.	3 weeks	76% reduction in pain in acup. group. 10% in control, but no sig. difference between groups.
Ballegaard et al 1990	Moderate angina	49	Group comparison	Minimal acup.	Classical. 10 sessions over 3 weeks	Exercise tests, pain diaries, medication, well-being	6 mths	Reduction of 50% in attacks & medication No. sig. difference between groups.

CHAPTER 7

THE SELECTION OF PATIENTS FOR TRIALS WITHIN COMPLEMENTARY MEDICINE

The problems

The radical differences between traditional Chinese medicine and simple tender point acupuncture highlight the problems which acupuncturists experience when attempting to launch a clinical trial. A condition such as back pain could be treated in many different ways: the traditional Chinese approach may suggest that point selection is based solely on energetic imbalances, while those using tender point acupuncture may simply examine the patient and insert the needle into trigger points.

Similar problems have exercised the minds of many classical homoeopaths. Migraine or a particular rheumatological disease, while representing a single diagnosis within conventional medicine may suggest any one of twenty homoeopathic remedies. Consequently patients may be entered with a specific and widely agreed conventional diagnosis, but the treatment they receive may be very variable. It must, however, be appropriate for the complementary therapy being tested (Fisher 1989).

For example, patients may be entered into a trial and all could be assessed for an appropriate homoeopathic medicine. Randomisation would then take place and the treatment prescribed may be any one of say twenty different remedies versus a single placebo. The trial would then be a real assessment of how homoeopathy is used to its best advantage in clinical practice, and not an assessment of a single remedy for what to the homoeopath may be a complex condition.

Similar ground rules can be applied to acupuncture. In Jobst's study on disabling breathlessness (1986), patients were entered into the trial based on clear, conventional criteria. However the treatment they received differed from one individual to another. The aim of the study was to compare acupuncture based on a traditional Chinese model with sham acupuncture. Not all of the patients having acupuncture received the same point prescriptions since in the majority of instances their traditional Chinese diagnosis was significantly different.

There has been a tendency in the past to think of acupuncture and homoeopathy as single unified therapies. Consequently some investigators have tested a standard point prescription for treatment of specific conditions such as back pain (Mendelson et al, 1983). Those involved in complementary medicine have begun to rebel against this straight-jacket and argued coherently for the need to test complementary therapies to their best advantage (Bensoussan 1991; Weigant et al, 1991). Both Weigant and Bensoussan recommend that the actual treatment protocol for the complementary therapy being tested should be adaptable, in line with current clinical practice within that therapy.

Within normal clinical practice the actual point prescription used by any acupuncturist may change from one treatment session to another. This will occur whatever type of acupuncture is used; classical traditional Chinese medicine or simple tender point acupuncture. It would be logical therefore to have a similarly adaptable placebo so that patients felt that treatment was being modified in accordance with their symptoms, much the same as the treatment group receiving real acupuncture.

All the clinical studies reported within this thesis contain this fundamental adaptability. Patients entered into the trial on post-

UNIVERSITY OF SOUTHAMPTON LIBRARY

herpetic neuralgia and headache were not treated with a pre-determined group of acupuncture points. The investigator was allowed to choose from a range of commonly used acupuncture points applicable to that condition. The points most likely to benefit the individual were then used based on the symptoms the patient presented at any individual treatment session. Equally with the placebo, the location of the mock TNS pads was changed if there was no initial response to treatment. Such individualisation and adaptability is the essence of all complementary medicine. Therefore as Weigant et al and Bensoussan have suggested, such individual adaptability must be translated into clinical trial methodology, if the therapy is to be tested to its best advantage.

Possible models

Patient selection for clinical trials involving complementary medicine can follow one of two paths. The first would be to follow the model suggested by Fisher et al in the treatment of fibromyalgia (Fisher et al, 1989). Here patients were selected on agreed conventional diagnostic criteria, and all patients entered into the study were diagnosed as having fibromyalgia. Subsequently a second selection procedure was employed: all patients initially entered into the study were then interviewed with a view to making a homoeopathic diagnosis, and only those patients in whom Rhus Tox was indicated as a treatment went on to randomisation. The study then compared the use of a single homoeopathic remedy (Rhus Tox) versus placebo. Fisher et al were able to obtain a completely coherent group of patients by using this double selection procedure; a similar approach could be applied to the treatment of asthma or low back pain with acupuncture.

The second approach involves selecting patients with a particular agreed diagnosis such as back pain and then building into the protocol adaptable

treatment regimes from the point of view of both real acupuncture and placebo treatment. In many ways the second option is far more practical. Obtaining reasonable numbers of patients in the relatively short periods of time allowed for clinical trials always represents a problem. So by employing the double selection procedure suggested by Fisher it is possible that the numbers entered into the trial may be very limited.

Conclusion

It is important to realise that complementary medicine involves different diagnostic models to those employed within conventional medicine. It is therefore not valid to translate a conventional diagnosis into a pre-determined treatment regime. Providing some form of adaptability is built into either patient selection or the subsequent treatment employed then it is likely that the complementary therapy will be assessed appropriately. Conventionally trained doctors must recognise the potential validity of these differing diagnostic and therapeutic criteria.

CHAPTER 8

COMPLEMENTARY MEDICINE: WHY SHOULD WE BOTHER TO ASSESS IT?

Although much was written about acupuncture in the early Nineteenth Century (Sacks 1991), the rise of modern scientific medicine, particularly after the Second World War, meant that many forms of complementary medicine were considered irrelevant. In general there were few practitioners of acupuncture and homoeopathy, and relatively little public demand. Therefore this area of medicine did not attract serious attention, either from the general public or from conventional doctors. Perhaps the one exception to this general trend were techniques of manual medicine such as osteopathy and chiropractic. While these were considered complete quackery during the 1930s, they have slowly become integrated into conventional medicine over the last 50 years, largely through the efforts of interested rheumatologists such as Cyriax and the efforts of the physiotherapy profession as a whole (Schoitz and Cyriax, 1975).

However over the last 15 years public demand for many of the therapies within complementary medicine has grown dramatically. In spite of the many attacks against acupuncture and related techniques (National Council Against Health Fraud 1991) it appears that an increasing number of conventional doctors are interested in learning about these areas of medicine (Wharton and Lewith 1986). This introductory chapter is directed at asking what sorts of people seek complementary medicine, why they come, and what sorts of illness they consider amenable to treatment by complementary medical practitioners. The data we have available relating to general practitioners and how they perceive this area of medicine, will

also be discusssed.

Over the last 10 years there has been a dramatic increase in interest in complementary medicine both by the general public and the medical profession. It is therefore a matter of public concern and importance that techniques such as acupuncture and homoeopathy should be assessed as objectively as possible.

The General Picture

The first survey of the use of complementary medicine in the United Kingdom was carried out by Fulder and Monro and commissioned by the Threshold Foundation in 1980. The results were subsequently published in the Lancet in 1985 (Fulder and Monro 1985). Non medical practitioners in 7 areas of the UK were located by consulting the Yellow Pages telephone directory, registers of professional bodies and by notices in local papers. On the basis of this survey the researchers calculated that the number of consultations occurring within the UK in 1980 lay between 11.7 and 15.4 million per year. This represents between 6.5% and 8.6% of the number of general practitioners' consultations per year. The average course of treatment involved 9.7 consultations and therefore they deduced that there were approximately 2 million people using complementary medicine at that time. The main therapists consulted were acupuncturists, osteopaths and chiropractors, about 2 million consultations were occurring within each of these disciplines per annum. A subsequent study carried out by Peter Davis for the Institute of Complementary Medicine in 1984 (Davis 1984) suggested a more conservative estimate of 4.6 million consultations a year involving about 1 million people. The gap between these two very different estimates may be due in part to the fact that Fulder and Munro considered non-orthodox practitioners of all kinds whereas Davies drew his

sample only from those listed in 10 professional registers covering six therapies, Fulder and Munro noted that approximately half the practitioners surveyed in their study were not members of professional bodies and were only in practice on a part-time basis.

A further study carried out for Swanhouse Special Events in 1984 looked at users of complementary medicine rather than practitioners (Research Surveys of Great Britain 1984). They found that as many as 30% of a representative sample of approximately 2,000 adults had used one or more of a range of non-orthodox therapies over a period of one year. Another survey by Market and Opinion Research Information (MORI) in 1989 took a sample of approximately 2,000 adults in various parts of Britain. They demonstrated that 27% had used non-orthodox medicine at one time or another. Unfortunately, these two surveys are not directly comparable as the Research Surveys of Great Britain looked at herbal medicine whereas that later poll carried out by MORI did not. As far as acupuncture is concerned, both surveys looked at this particular area; MORI suggested that 4% of the population were receiving acupuncture while Research Surveys of Great Britain suggested that 3% of their sample had sought acupuncture to ameliorate their condition.

The Consumer's Association published a survey of their members in 1985 (Which 1986) and found that 1 in 7 had used some form of complementary medicine. Forty-two per cent of those who had used complementary medicine had used osteopathy and 23% had used acupuncture. A similar survey carried out in 1992 (Which 1992) suggested that now 1 in 4 of those surveyed within the Consumer's Association had used complementary medicine within the previous year.

While it is impossible to give an absolutely accurate figure for those

using complementary medicine in the United Kingdom, it is probable that at least 2 million people and probably more are using a range of complementary or unorthodox therapies on a regular basis. The surveys published by MORI, Which and Research Surveys of Great Britain all suggest that osteopathy, herbal medicine and homoeopathy are the three most commonly used therapies, while acupuncture is used by approximately half the numbers using osteopathy. The Consumer's Association reports are necessarily biased as they look only at a small group within the population. However, within this group it appears that the use of complementary medicine has almost doubled over a period of 7 years. Complementary medicine in general and acupuncture in particular therefore represent a substantial and, almost certainly, growing area of medical practice within the UK. Britain is not alone in experiencing such growth. Information from throughout Western Europe would suggest that France, Germany, Finland, the Netherlands, Belgium, Switzerland, Denmark and Italy are experiencing similar patterns of growth within complementary medicine (Sharma 1992; Lewith & Aldridge, 1992).

Why do people seek help with complementary medicine?

In 1983 two fourth year medical students from Southampton University, Cathy Phipps and Judith Moore, initiated a fourth year project at The Centre for the Study of Complementary Medicine (Phipps and Moore, 1985). They specifically wished to look at the reasons behind the growing popularity of complementary medicine and constructed a questionnaire designed to assess the characteristics of patients seeking treatment, the scope of their presenting problems, the reasons why patients elected to be treated by complementary medicine and finally the patient's knowledge, attitudes and expectations of such treatment. Help was sought from Dr. Donald Marcer,

the Department of Psychology at Southampton University, in order to construct the questionnaire.

In 1983 no-one had considered asking patients why growing numbers were seeking help from a variety of complementary medical techniques. Two questionnaires were used, one at the patient's first visit to the Centre and one a postal follow-up questionnaire 8 weeks' later. A framework of questions was compiled and based on this, informal interviews were carried out with 5 patients. These tapes were then used as the basis for constructing a more specific questionnaire which was then piloted on a further 10 patients and subsequently used in the study. The second questionnaire was used on a postal follow-up basis 8 weeks after the first in order to assess whether the treatment approaches used had been beneficial to the patient. However, the initial questionnaire was by far the most important, as it gave us information about who was seeking complementary medicine and why.

The questionnaire was given 65 new patients attending the Centre over a 2-week period. Twenty minute interviews took place after the patients had seen one of the doctors working at the Centre. Eight weeks after the first interview, a follow-up questionnaire was sent and efforts were made to ensure maximum response. Fifty-six of the original 65 patients completed the follow-up questionnaire. The presenting problems are summarized in Table 8.1

The major presenting problem was pain, particularly in the back. Later the "Which" survey carried out in 1985 suggested that pain or a joint problem was the most common reason for consultation with a complementary practitioner. Seventy-one per cent of those using complementary medicine had done so for this specific problem. The report published for the

Institute of Complementary Medicine by Davies (1984) also emphasises this point, suggesting that, "In Britain, the largest single group of problems taken to non-orthodox practitioners are disorders of the musculoskeletal system especially back pain."

Those seeking complementary medicine do so only when their problems have become chronic. In our study the duration of symptoms varied from 3 months to 44 years with a mean of 9 years. Of the patients attending the Centre, 8.8% had their problem for less than 6 months, a further 8.8% for less than 1 year, 36.8% between 1 and 5 years and 23.5% between 6 and 15 years. The remaining balance of patients (22%) had had their problem for greater than 15 years. Seeing a complementary practitioner was therefore not a first port of call for many individuals, but an approach which many wished to try as a method of managing their long-term problem.

Perhaps one might think patients are seeking help from complementary medicine because they are dissatisfied with their general practitioner. Table 8.2 reproduced from our survey would suggest quite the contrary; most patients felt very happy with their own GPs and in fact only 2 of the original 65 patients interviewed in our survey by-passed their General Practitioner. The impression gained from the interviews in our survey was that while the GP was competent and the patients were in general happy with them, the GPs were not able to deal with the specific problem for which the patient required help. Our patients made it quite clear that they would be more than happy to go back to their own GP with other problems. They saw their General Practitioner as their first port of call should they wish to consult a doctor about their difficulties.

Sharma came to similar conclusions, but her study involved in depth interviews with 34 patients (Sharma 1991). The major reason for seeking

complementary medical help was to cure a condition in which orthodox medicine had been unable to offer any relief. However Sharma's in depth interviews bought to life other perceptions of orthodox and complementary medicine. A recurrent theme was that orthodox medicine treats symptoms rather than causes. She also noted that many of the patients she saw were unhappy about the over-liberal dispensation of drugs and that these drugs represented, "unnatural chemical interventions". Some of her interviewees suggested that orthodox treatments seemed to be too drastic and were therefore rejected (Sharma 1991).

The clear picture emerges that complementary medicine in general and acupuncture in particular is sought out by patients for problems that have not been resolved by conventional medical approaches. Musculoskeletal pain and low back pain in particular forming the largest single group of problems.

Who seeks help from complementary medicine?

The survey completed in our practice by Moore and Phipps in 1983/1984 demonstrated some interesting demographic data. The vast majority of patients we saw were middle class, and the largest single group were females in their middle years (see Table 8.3).

This fits well with Sharma's small survey. She suggests that 50% of those using complementary medicine were from the professional and managerial classes but the rest were equally divided among white collar, manual and working class patients. There were far more women than men but the majority of patients were between 40 and 60 years of age (Sharma 1989).

A further study carried out at the Centre in 1990 provided an interesting insight into those seeking complementary medicine. We initially decided to try and develop a questionnaire which could be used as a tool to

quantitatively measure a person's commitment to alternative medicine. In order to do this three procedures were used (Finnegan 1991a). First a brief instruction sheet was given to 20 psychology students at Oxford Polytechnic, seeking their general views about complementary medicine. The 20 produced 89 decipherable statements relating to complementary medicine and by identifying the underlying themes within these statements, it was possible to condense them to 35. Of these 35 statements, 12 were sympathetic to alternative medicine and 23 expressed antagonism towards it. Statements were then arranged in a standard Likert scale ranging from 1: strongly agree to 6: strongly disagree. There was no option for a mid-response, "neither agree nor disagree". The 35 statement scale was given to a total of 79 undergraduate students at Oxford Polytechnic. Several statistical procedures were then carried out on this questionnaire, the most important using factor analysis. This involved analysing the statements in several areas:

1. Statements suggesting that complementary medicine was advantageous, particularly in relation to conventional drugs.
2. The technicalities and practicalities of alternative medicine in relation to its availability and scope.
3. These questions were intended to enquire into the extent of bias that an individual had about alternative medicine.
4. The fourth factor related to the underlying practical use of alternative medicine.
5. Here a general theme of comparing alternative medicine to conventional medicine was explored.
6. In this group of questions, conventional medicine was attacked and the participant's attitude towards this was analysed.

Having identified these major factors and chosen themes thought to be most suitable, it was necessary to ensure that the questions would fulfil their task. Each statement was then analysed statistically so ideally it should have a mean around its mid-point with a standard deviation of at least 1 implying that the statement would produce a normal distribution in a normal population. Having completed this analysis, the questionnaire was then slimmed down to 19 statements. A second study was carried out using these 19 statements and again applying similar statistical analysis. A final questionnaire was developed which only used 14 statements.

The first phase of the study was to develop the questionnaire using standard methodology (Finnegan 1991a). The second was to use the attitude to alternative medicine scale (AAM) and a Walliston Health Locus of Control Scale on 35 patients attending for treatment at the Centre for the Study of Complementary Medicine (Finnegan 1991b). Again we were able to identify the same trends in this study as in our study carried out 6 years previously. The main reason for patients seeking complementary medicine was the failure of conventional medicine to bring about a satisfactory improvement in their condition. The ailments seen were largely long-term chronic ailments, much as previously had been identified by Moore and Phipps (1985).

It is interesting to note that in our 1984 study the major presenting problem was found to be pain with generalised non-specific illness making up only 13% of our sample. The Finnigan study offered different figures: 45% had generalised non-specific illness for which no definite diagnosis had been made and the occurrence of musculoskeletal problems in our second sample had decreased substantially. Both samples are relatively small and represent a simple "snapshot" of the practice over two short periods six

years apart. It is therefore difficult to draw definitive and directly comparable conclusions from these two studies, but it might demonstrate a trend by both patients and general practitioners to accept that complementary medicine may have a part to play in illnesses which are not immediately understood or indeed diagnosable by conventional methods. The mean duration of symptoms prior to presentation at the Centre in the Finnigan study was 9.4 years and the majority of patients (82.4%) had had their problem for over a year. This is almost exactly the same as the earlier study by Moore and Phipps.

When comparing the health locus of control scale (HLC) and the AAM scales, it became apparent that two types of patient appeared to be seeking complementary medicine. The first group were those who turned to complementary medicine as a last resort and do not appear to embrace the theory or underlying philosophy of this approach. Their HLC scales were very much what one would expect from a normal population, and their AAM scales showed no overt sympathy or understanding or indeed belief in complementary medicine.

The second type of patient showed a much greater commitment to alternative medicine in general. Their AAM scales demonstrated a high degree of fundamental belief in this area of medicine and they appeared to be more likely to choose complementary medicine due to belief in it rather than as a last resort. Their HLC scales were significantly more internal than either the general population or the first group of patients.

Finnigan's study does not correlate the type of patient attending for complementary medicine with outcome. The study published earlier by Moore and Phipps does. Two thirds of the patients in the Moore and Phipps study believed that complementary medicine would be an effective approach to

their problem, and many had very high expectations of treatment.

Expectation of success did appear in our earlier study to correlate with outcome, so it is likely that those who understand and believe in complementary medicine, will have a higher internal health locus of control and in turn will be likely to benefit more from complementary medicine.

Does this influence clinical trials?

These two studies have clear implications for clinical trials. They indicate that complementary medicine has become a matter of belief in a small but significant group within the population. This group is likely to involve primarily middle class women in their middle years although it is by no means exclusively comprised of individuals drawn from this group. It is also clear that believers, particularly those who have high expectations from treatment, are more likely to experience the improvements they seek. Increasing numbers of individuals are seeking complementary medicine and this sustains the argument that more clinical trials are needed. However, when constructing these clinical trials, should we take into account whether the person is a "believer or a non-believer"? Should this be an important factor in our consideration for randomisation to treatment or placebo? Are believers more likely to respond to placebo acupuncture because they have such a strong belief in the treatment itself (providing of course they receive convincing placebo acupuncture). If the complementary medical practice is composed largely of female middle-class believers, then their response to treatment is likely to be good. Consequently, would it be reasonable to assess a therapy that appears to work well within this social group by studying the response of male working-class non-believers? These remain open questions, but they raise issues that have yet to be addressed within the context of clinical trials

carried out within complementary medicine.

The Doctor's View

Many doctors have reacted angrily to the suggestion that complementary medicine can be effective. One of the more recent attacks has been through an American organisation called the National Council Against Health Fraud. Their publication in the controversy corner of the clinical journal of Pain (National Council Against Health Fraud 1991) suggests that it is almost malpractice to use acupuncture. They quote a number of learned scientific articles which they believe indicate acupuncture is a totally ineffective therapy. It is interesting to note GP referral rate in our 2 studies at the Centre. The first in 1986 demonstrated that 22% of patients seen were referred by their GP, whereas the second in 1990 indicated a 38% referral rate. Obviously in two such small studies this may simply be a random event, but our impression substantiates these observations and would suggest that general practitioners are increasingly referring patients for a whole variety of complementary medical techniques. Wharton and Lewith (1986) addressed this problem directly. Our aim was to find out how much general practitioners knew about complementary medicine, whether they practised it and whether they intended to develop more knowledge and/or skills within this area in the immediate future. We also wished to know whether they had referred patients for complementary medicine and whether this had been to a medically trained practitioner or a non-medically qualified individual. In order to achieve this a simple questionnaire was designed and subsequently piloted among a group of trainee GPs. A four page postal questionnaire was sent to every GP in the Avon area. While we knew trainee general practitioners had a favourable view of complementary medicine (Taylor-Reilly 1983), we did not know the

views that were likely to be expressed by established GPs. Of 193 questionnaires sent out to actively practising general practitioners, 145 were returned. Consequently we were able to get a realistic impression of what was happening in relation to complementary medicine within the Avon area. The non-responders were analysed for age, sex and location (rural or urban). There seemed to be no difference in the demography of those who responded and those who did not. In the ensuing results, figures were calculated on the basis of 145 responders and the non-responders were excluded from the survey.

Of those who responded, roughly one third had already gained training in one form or other of complementary medicine, and a further 15% wished to receive training. Table 8.4 shows those doctors who are trained or intend to train in the six main areas surveyed (acupuncture, homoeopathy, herbal medicine, manipulation, hypnosis and healing).

Judging by the current response to courses run by the British Medical Acupuncture Society and the Faculty of Homoeopathy, it is safe to assume that a similar survey carried out now would elicit a far larger number of GPs who have received training within complementary medicine and a further larger percentage who wished to receive training. The membership of the British Medical Acupuncture Society has grown from 200 in 1985 when the survey was carried out to 800 at the beginning of 1992.

Table 8.5 shows the perceived value that GPs attribute to specific therapies. 57% consider acupuncture to be useful or very useful and 89% consider spinal manipulation (osteopathy and chiropractic) to be useful or very useful. Therefore, in spite of the limited clinical trials within these two areas, their perceived value in practice would appear to be high. General Practitioners did not know very much about the details of these

therapies, as table 8.6 suggests.

In spite of the fact that 89% of respondents perceived spinal manipulation to be useful, only 44% felt they had a knowledge of this subject that was moderate or better. In acupuncture, the figures are even lower, 22% of our responders felt they had a moderate to very good knowledge of this particular discipline.

A lack of information, however, did not seem to affect referral patterns. Table 8.7 shows rates of referral to medical and non-medically qualified practitioners. Overall, in the year prior to the survey, 76% of doctors responding had referred patients to a medical colleague for complementary medicine and 72% had referred patients to a non-medical practitioner for some form of complementary medicine.

These figures are particularly surprising in relation to non-medically qualified practitioners and indicate a far greater level of acceptance for complementary medicine than one would at first suppose when reading documents such as the last BMA scientific report analysing the underlying evidence which sustains such practices (BMA 1986).

Most (93%) of the GPs who replied believed that complementary practitioners needed some form of statutory regulation, but only 3% of responding GPs felt that such non orthodox therapeutic methods should be banned or indeed taken out of the hands of non-medically qualified practitioners. The most significant factor influencing the opinions of general practitioners appeared to be the perceived benefit to patients. A high proportion of general practitioners made the comment that either they or their families had personally benefited from complementary medicine (38%) and this seemed to be an important factor in influencing their referral patterns.

Overall the impression gained from this survey was that complementary

medicine was popular and actively used by GPs in the Avon area. Could this be sustained in other areas? A similar survey was being carried out at roughly the same time by Anderson and Anderson (1987) in the Oxford region. They sent a questionnaire to 274 general practitioners, and 222 replied. Their results were similar to those from the Avon area. 31% said they had a working knowledge of at least one form of alternative medicine and 30% had actively sought and read publications about alternative medical techniques. Forty-one per cent had attended lectures or classes about some form of complementary medicine, but only 12% (as opposed to 33% in Avon) had a practical working knowledge of one of the major techniques within this area. However, 42% wished to receive some form of training in acupuncture, homoeopathy or spinal manipulation.

The majority of doctors (95%) had said that patients had discussed alternative medicine with them during the past year and 59% had referred patients to some form of complementary or alternative medicine. 41% of the Oxford doctors felt that alternative systems of medicine were valid and 54% defined alternative or complementary medicine as an additional and useful technique which could aid their patients. Sixteen per cent suggested that alternative medicine was unscientific and improperly validated.

While the figures from Oxfordshire are slightly different to those in Avon, they do demonstrate a sustained interest and commitment to complementary medicine within general practice. Further studies pertaining to GPs' attitudes within complementary medicine are not widely available, and these two studies were the first to look specifically at how British general practice viewed techniques such as acupuncture, homoeopathy and manipulation. There is little doubt that while some areas of hospital-

based academic medicine may perceive techniques such as acupuncture with a great deal of concern and disbelief, this is not reflected as a whole in the two surveys reporting the attitude of British general practitioners in the mid 80s.

Again, these surveys raise interesting questions. Why, if we are scientifically trained, are large groups of the medical profession prepared to accept, use and learn about treatments which at best have only been partially validated by adequate clinical trials? Here we see GPs responding to public demand which in turn is based on perceived benefit to individual patients. It is not only the patients who feel they are benefiting from these approaches, but according to our survey in Avon, the general practitioners themselves perceive that substantial benefit to patients may be gained from onward referral to an acupuncturist, homoeopath or spinal manipulator.

Conclusion

I have demonstrated that complementary medicine is in widespread use in the United Kingdom, and its popularity would appear to be increasing. There are certainly millions of consultations per year within complementary medicine in the United Kingdom, although exactly how many is difficult to ascertain and to a certain extent depends on how you define a complementary medical practitioner, be they medical or non-medically qualified. Specific patient groups are seeking complementary medicine and it may well be that the type of individual who seeks out this treatment and believes in it will have a significantly different response to therapy than those for whom it is just provided as one of many different therapeutic alternatives. General practitioners are clearly interested and, in many ways, surprisingly committed to complementary medicine. This change within

general practice has occurred without adequate clinical trial evidence to sustain it. It is therefore essential that we attempt to design and effect the best available clinical trials in order to evaluate techniques such as acupuncture.

TABLES FOR CHAPTER 8

Table 8.1

Presenting problems of patients

Complaint	No.of patients	Specification of complaint
Pain	30	Arthritis, back pain, abdominal pain, headaches
Allergies	10	Eczema, urticaria, asthma, rhinitis
Non-specific symptoms	9	Malaise, feeling unwell, run down
Psychological	3	Anxiety, smoking
Gynaecological	2	Dysmenorrhoea, candidiasis
Gastrointestinal	3	Coeliac disease, spastic colon, diarrhoea, inflammatory bowel disease
Hypertension	2	
Loss of balance	2	
Others	6	Loss of voice, catarrhal deafness, Raynaud's disease, acne, muscle wasting, facial rash

Table 8.2

In general how do you get on with your GP?

Percentage of Patients

Response	1st Questionnaire (n = 65)	Follow-up (n = 56)
Excellent	31 (20)	32 (18)
Good	31 (20)	36 (20)
Satisfactory	28 (18)	20 (11)
Poor	3 (2)	11 (6)
Hostile	5 (3)	2 (1)
No Answer	2 (1)	0

(brackets denote actual numbers of patients)

Table 8.3

Demographic Data

n = 65

SEX	TOTAL	AGE				
		< 25	26-50	> 51	MARRIED	SINGLE
Male	40%(26)	4.5%(3)	17% (11)	18.5%(12)	32.3%(21)	7.7%(5)
Female	60%(39)	3% (2)	38.5%(25)	18.5%(12)	47.7%(31)	12.3%(8)

Social class n = 60. 5 were unspecified

I	II	III	IV	V
12.3% (8)	64.6% (42)	13.9% (9)	1.5% (1)	0

Table 8.4

No (%) of respondents with training in, and currently practising, complementary medicine.

	Training received	Practising	Training intended	No training
Spinal manipulation	38 (26)	34 (24)	14 (10)	93 (64)
Acupuncture	4 (3)	4 (3)	9 (6)	132 (91)
Hypnosis	17 (12)	7 (5)	4 (3)	124 (85)
Herbal medicine	1 (1)	1 (1)	1 (1)	142 (98)
Homoeopathy	7 (5)	7 (5)	9 (6)	129 (89)
Spiritual healing	8 (5)	10 (7)	1 (1)	136 (94)

Table 8.5

Perceived value by doctors of complementary techniques to patients (figures are No(%) c those responding to questionnaire)

	Very Useful	Useful	No Opinion	Not Useful	Harmful
Spinal manipulation	39(27)	90(62)	9(6)	3(2)	4(2)
Acupuncture	11 (8)	85(59)	38(26)	11(8)	
Hypnosis	12 (8)	103(71)	25(17)	4(3)	1(1)
Herbal medicine	1 (1)	32(22)	70(48)	38(26)	4(3)
Homoeopathy	5 (3)	64(44)	52(36)	23(16)	1(1)
Spiritual healing	9 (6)	58(40)	45(31)	24(16)	9(6)

Table 8.6

GP assessment of their own knowledge of complementary medicine.

	Very good/ good	Moderate	Poor	Very poor
Spinal manipulation	16 (11)	49 (34)	49 (34)	31 (21)
Acupuncture	6 (4)	25 (18)	57 (39)	57 (39)
Hypnosis	12 (8)	36 (25)	58 (40)	39 (27)
Herbal medicine	3 (2)	4 (3)	57 (39)	81 (56)
Homoeopathy	1 (1)	29 (20)	52 (36)	63 (43)
Spiritual healing	12 (8)	20 (14)	45 (31)	68 (47)

Table 8.7

Referral patterns for complementary techniques (figures are No(%) of those responding to questionnaire, *except where indicated)

	Never refer	Refer to doctors	Average No. of patients referred to doctors/year	Refer to non-medical practitioners	Average No. of patients referred to non-medical practitioners of complementary medicine/year
Spinal manipulation	23 (16)	77 (51)	6	62 (43)	13
Acupuncture	57 (37)	44 (28)	3	45 (30)	4
Hypnosis	47 (33)	66 (44)	4	40 (28)	4
Herbal medicine	131 (92)	2 (2)	1	9 (6)	2
Homoeopathy	57 (40)	68 (42)	4	18 (13)	2
Faith healing	115 (80)	2 (2)	2	25 (18)	3

* Not all respondents were able to answer this question with a clear positive or negative response, and some gave more than one answer so the figures do not add up.

OBJECTIVES

The thesis should be judged against a background of a complete absence of any clinical research culture in complementary medicine in general, and in acupuncture in particular, prior to the late 1970s.

The central research objective of this thesis is to develop the design of clinical trials to evaluate the effects of acupuncture in a variety of different conditions including pain, the treatment of addiction to nicotine and the control of nausea.

The objectives were:

i) to select appropriate acupuncture methods

ii) to define and establish appropriate controls for clinical trials, including placebos

iii) to adapt current statistical techniques to clinical trials in acupuncture

iv) to evaluate the use of a variety of subjective and objective methods for assessing benefits and outcome in clinical trials of acupuncture.

Six clinical trials are presented in the following chapters. These were designed to evaluate acupuncture as a treatment for chronic pain (post-herpetic neuralgia, headache and osteoarthritis), addiction (smoking withdrawal) and nausea (chemotherapeutically induced and early morning sickness). These studies serve as models in order to facilitate the development and evolution of trial methodology within this clinical discipline.

SECTION 3

CLINICAL TRIALS ON ACUPUNCTURE IN A VARIETY OF SITUATIONS INCLUDING THE MANAGEMENT OF PAIN, SMOKING CESSATION AND THE TREATMENT OF NAUSEA

CHAPTERS 9 - 12

CHAPTER 9

THE EVALUATION OF THE CLINICAL EFFECTS OF ACUPUNCTURE

Introduction

In 1979 a research clinic was established within the Department of Primary Medical Care at the University of Southampton. The overall aim was to collect a large but uncontrolled data base of the clinical effects of acupuncture in a variety of different illnesses. It was never envisaged that such an exercise would replace the need for randomised controlled clinical trials with well-defined end points designed to answer particular questions about specific diseases. However, it was felt that this system would allow useful information to be collected that would complement such studies. Furthermore, specific questions might emerge from this exercise in data collection, which would allow for better study design.

This data collection exercise should be viewed in the context of the activities of the Department of Primary Medical Care at Southampton University, in the late 1970s. Substantial resources had been set aside to develop a system for recording consultations. At each consultation the doctor filled in "Encounter Forms" which conformed with a problem oriented notation system. These Encounter Forms were then coded and typed into the notes. The coding took the form of punched cards and the data were then stored on the medical school's main frame computer (Southampton University, 1980). When the author joined the Department in 1979, it was quite logical that, within this context, an attempt should be made to record data in this special area of interest (acupuncture) using the same disease coding.

Over 500 patients were entered into this system. Their symptoms were

recorded at entry, after the end of treatment and at three months' follow-up. The areas assessed were pain, headache, gastrointestinal symptoms and breathlessness. It was shown to be a swift and effective method for auditing the effects of acupuncture in a range of chronic conditions. The exact data collection methods employed have been published elsewhere (Lewith and Machin, 1981). The single largest group identified within this audit were those suffering from back pain and sciatica. Again, a detailed analysis of these 151 patients has been presented elsewhere (Lewith et al, 1984). As an exercise in audit it was uncontrolled and descriptive; however, it did demonstrate that acupuncture was of help to patients with many chronic conditions, in particular low back pain and sciatica. Patients with both low back pain and sciatica responded equally well to intervention with acupuncture. Over 80% gained substantial benefit from acupuncture by the end of treatment, although this response appeared to fade slightly at 3 months' follow-up. Nevertheless, acupuncture could produce long term benefit in a substantial number of individuals. It appeared that acupuncture was slightly less effective in those aged over 65 and interestingly females demonstrated a better response to acupuncture than males. The duration of symptoms prior to therapy did not influence outcome and prior local surgery such as laminectomy again had little influence on overall outcome in the group studied.

This exercise in data collection was both important and relevant in establishing the broad clinical response to acupuncture. It allowed for a better understanding of the individual responses to acupuncture, and consequently helped to improve the selection of patients and design of randomised controlled clinical trials. It was thought initially that this exercise in data collection could form the basis of an DM thesis, but

subsequent developments overtook these initial ideas and it became apparent that the development of better methodology for randomised trial would provide the best way forward to understanding and evaluating the effects of acupuncture. Therefore, while this exercise in data collection was a valuable beginning, it has been excluded from the research presented because it does not provide anything more than background information upon which better clinical trial methodology was subsequently constructed.

Study models for controlled clinical trials

It is unusual to directly reproduce an already published paper in a thesis submitted for a research degree. However, the paper by Lewith and Machin, "On the evaluation of the clinical effects of acupuncture" (1983) was the first paper published which attempted to establish proper trial methodology within the complementary therapies. Such trial methodology required cooperation between a competent clinician well versed in the therapy and a statistician who was prepared to review the standard statistical format used in controlled clinical trials and apply innovative statistical ideas to a new clinical situation. This cooperation provided the framework through which the initial controlled trial on post-herpetic neuralgia was developed. It subsequently became apparent that the study model used could act as the foundation for further clinical trials within the field of acupuncture and thus demanded detailed conceptual consideration. The paper by Lewith and Machin was published as a direct result of these considerations, and further clinical trials were built on this foundation. Over the last 10 years more detailed methodological literature has emerged, and there is now a clearly developed research culture within complementary medicine (Lewith and Aldridge, 1992). The development of this research culture has been in response to public demand for more complementary

therapies and the subsequent need to develop better methods for evaluating these specific therapies. This paper, which is now reproduced in full, should be considered in this context.

The model

It is essential that clearly controlled, randomised clinical trials become available in this area before this technique is accepted, or rejected. A simple hypothesis is suggested based on some of the studies already available in this field, which will define the statistical problems of assessing the benefits of acupuncture.

The use of mock transcutaneous electrical nerve stimulation (TNS) has been shown to be effective in about 30-35% of patients with chronic pain (Thorsteinsson, Stonnington, Stilwell and Elveback, 1978; Lewith and Machin, 1981). Mock TNS is the use of a defunctioned TNS machine which in all aspects appears to be functioning, other than the fact that no current reaches the patient. The placebo effect of mock TNS has been equated with the placebo response expected in drug trials, in similar conditions (Thorsteinsson, Stonnington, Stilwell and Elveback, 1978). Therefore, for the purposes of this paper mock TNS is considered to be a placebo treatment as it has been reported to be consistently effective in eliciting a placebo response.

Many of the clinical trials on acupuncture have used a real versus sham acupuncture model in order to evaluate the effects of acupuncture (Gaw, Chang and Shaw, 1975; Moore and Berk, 1976; Godfrey and Morgan, 1978; Co, Schmitz, Havdala, Reyes and Westerman, 1979). Real acupuncture involves the use of acupuncture needles inserted into acupuncture points supposed therapeutically effective, for the condition being treated, and can be considered to be properly performed acupuncture. Sham acupuncture

is the insertion of needles into parts of the body supposed therapeutically ineffective for the condition being treated and can be considered to be improperly performed acupuncture. There is a strong argument to suggest that sham acupuncture groups are having their chronic pain attenuated through mechanisms such as diffuse noxious inhibitory control (DNIC) (Le Bars, Dickenson and Besson, 1979; Menetrey, Chaouch and Besson, 1979). Therefore sham acupuncture cannot be considered a placebo, but rather a 'poor form of acupuncture treatment'. Although the definition of real and sham acupuncture may be open to some debate (for instance all therapy has some element of the placebo response within it) these terms are used as defined above for the purpose of this paper. Most of the clinical trials using a real versus sham acupuncture model show that sham acupuncture is effective in relieving the pain of approximately 50% of patients while real acupuncture is shown to be effective in approximnately 60-75% of patients with chronic pain (Gaw, Chang and Shaw, 1975; Godfrey and Morgan, 1978; Co, Schmitz, Havdala, Reyes and Westerman, 1979). Such a level of effectiveness with real acupuncture is supported by many of the uncontrolled studies in the literature.

Therefore one can construct the following hypothesis: (1) A placebo is effective in 30-35% of patients with chronic pain. (2) Sham acupuncture is a form of acupuncture therapy and is effective in approximately 50% of patients with chronic pain. (3) Real acupuncture is effective in 60-75% of patients with chronic pain.

As will be discussed in the review of some of the available clinical studies this hypothesis has not been adequately tested. For the purposes of this paper it will be assumed that real acupuncture is clinically effective in 70% of patients although this is possibly optimistic since in

some categories of chronic pain the beneficial effects of real acupuncture are less.

There is considerable debate about the desirable approach to acupuncture methodology, point selection and the methods of needle stimulation. These therapeutic controversies are far from resolved and many hypotheses are both unproven and untested and so the discussion in this paper has been deliberately limited to the statistical methods that can be employed to evaluate the clinical effects of acupuncture. It is assumed for the purposes of this paper that all the trials reviewed have provided the most effective form of real acupuncture available, thereby giving them the maximum amount of therapeutic credibility and statistical power.

Practical considerations

General

In designing any trial it is necessary to have firm objectives in view. Thus, it is preferable to have clearly different and well defined alternative treatments, clear patient entry criteria and unambiguous definitions of end points or outcome criteria. A clear knowledge and understanding of the natural history of the disease being studied is essential before constructing any trial. All patients entered into the trial, and randomised, should be followed up in the same manner, irrespective of whether or not the treatment continues for that individual patient. Since treatment advantages may be small, one should choose at the planning stage treatments to be as different as possible; for example one may contrast placebo with real acupuncture. The real acupuncture should be as effective as possible so that if there is some treatment benefit it will emerge. If it is usual practice to stimulate the acupuncture points for 20 min a trial comparing placebo and acupuncture

which only stimulates for 10 min would not be generally desirable.

Although some attempts have been made, it is almost impossible to construct a satisfactory double blind trial involving acupuncture. However, single blind trials are possible, the most straightforward and useful involves a blind assessor to determine whether the protocol criteria are fulfilled, to enter and randomise the patient into the trial and then to assess and evaluate the patient's progress and follow up in an independent manner, without knowledge of the particular treatment being given. In some cases it might be possible to use patient diaries or some other form of self-assessment, in order to provide the blind assessment.

It could be argued that different therapists should provide the different treatments. However, there is a real danger of comparing the enthusiasm of the therapists rather than the treatments. If the same therapist provides both treatments then one particular treatment may be sold in a less than enthusiastic manner to the patients. One of these options must be chosen, but both have obvious faults. Within the context of acupuncture trials it is difficult to conceive of a valid placebo which can be used consistently without the therapist's knowledge.

End points or outcome criteria

As indicated above, specific end points or outcome criteria for the trial must be defined at the planning stage. These measurements will determine success or failure of therapy for each individual patient entered into the trial. However, such differentiation between effective and ineffective therapy is necessarily arbitrary. Two of the main methods currently in use to assess chronic pain are the Visual Analogue Scale (Scott and Huskisson, 1976) and the McGill Pain Questionnaire (Melzack, 1975). It is beyond the scope of this paper to discuss in detail appropriate assessment

systems for chronic pain, but these subjects do warrant careful consideration. Ideally, the outcome or end point criteria for differentiating an effective treatment from an ineffective one should include information about the subjective experience of pain, analgesic intake and the patient's level of activity, before, during and after therapy. It is important to understand that no clear objective methods of assessing chronic pain are currently available.

Multiple end points should be avoided, if possible, although there are obvious difficulties in trials designed to assess pain relief. Single end points are particularly important if interim statistical analysis is to be made while patients are still being recruited to the trial. One end point may indicate, at interim analysis, a clear advantage to a particular treatment and therefore recruitment to the trial could be stopped. If at the same time a contrary advantage for a second end point emerges there is clearly some difficulty. It is advisable to choose, at the design stage, the principal end point and make interim analyses using that end point only. In addition, although multivariate methods of statistical analysis are available they have not so far played an important role in the analysis of clinical trial data since they are somewhat complex, often difficult to present clearly and not readily understood by the clinician wishing to interpret the results.

Whatever end point definitions are used they must be framed in such a way that they can be unambiguously evaluated for each patient. It is important to realise that the efficacy of a particular treatment may inhibit the calculation of an end point. For example, if a particular treatment is not working then a patient may not return for the next follow-up appointment at which the intended evaluation was to take place. Methods

of incorporating such patients into the evaluation should be included.

In many studies the preliminary assessment of pain is used against subsequent evaluation(s) of pain. A decrease in pain score may indicate the success of the treatment for that particular patient. An alternative measure might be to determine the period of time from the first treatment to the return of pain at pretreatment levels. In this instance the end point might be the number of hours or days of pain relief recorded for each patient. Comparison between alternative therapies using time as the end point variable involves 'survival' curve techniques which compare groups over the whole period in which the patient is experiencing pain relief rather than at one fixed time point after randomisation (Peto et al, 1976 & 1977).

Design

An appropriate statistical design for a particular study is as much dependent on practical considerations as statistical theory. For example, if one is unable to recruit patients, no trial can be mounted whatever its desirability. As has been indicated earlier, treatment advantages may be small but nevertheless worthwhile. If such small differences are to be demonstrated, then large numbers of patients need to be recruited and multicentre co-operation may well be needed to achieve the requisite numbers.

The objective of treatment is to achieve pain relief (pain reduction) in the context of chronic illness. It is very unlikely that the pain will ever completely and permanently disappear in such conditions. Cross-over designs, in which the therapies on trial are given sequentially in random order to each patient entered, have been suggested (Fox and Melzack, 1976; Jensen, Melsen and Jensen, 1979) when giving clinical treatment such as

acupuncture. For many physical therapies including acupuncture it is difficult to find treatments that appear the same to the patient. Furthermore, a patient may be reluctant to change treatment if what he is currently receiving is effective. Physical treatments may have a long term benefit associated with them (Fox and Melzack, 1976) and this effect may vary from a period of days to months and may differ considerably between patients. It is, therefore, impossible to clarify the exact effects of each treatment in a cross-over model unless there is a very prolonged period (some months) between therapies. Cross-over experimental designs have been discussed by Layard and Arvesen (1978) with respect to trials comparing the efficacy of drugs in reducing the frequency of acute symptoms for patients with chronic diseases. One also faces the difficulty of patients who withdraw during the course of the study and refuse or are unable to take part at the second treatment stage, and one is thus unlikely to be able to benefit from the extra sensitivity that can be achieved using Latin square or other block designs (Armitage, 1974). Cross-over designs are nevertheless possible (Fox and Melzack, 1976) if treatment efficacy is assessed at some fixed time after treatment and the difficulties indicated earlier can be overcome. Cross-over trials are not possible if one is comparing pain free periods between alternative treatments.

Peto (1978) on the other hand argues that factoral (e.g. 2 x 2) designs are appropriate for clinical trials and can greatly increase the amount of useful information derived. However, there is no known application of this technique to trials on physical therapy, but the suggestion is worthy of further thought.

Designs involving sequential allocation of successive patients are unlikely

to be of value as they require more or less instant response to the success or otherwise of the treatment. Armitage (1975) gives a review of sequential methods in medical research. Sequential analysis of results is also likely to be difficult, especially if patients are treated in several collaborating clinics.

Practical considerations usually demand that a trial should have a simple design but nevertheless be addressing fundamental and worthwhile questions. The simplest design consists of equal numbers of patients being randomised to one of two alternative treatments.

Choice of trial size

The number of patients which it is necessary to recruit to a particular trial depends on several factors. These factors are the anticipated clinical differences between the alternative treatments, the level of statistical significance the investigator considers appropriate and the chance of detecting that difference.

For purposes of illustration placebo (control) is denoted by C, sham acupuncture by S and real acupuncture by A, and consider a two arm trial comparing treatments C and A with the subsequent analysis comparing the proportions of treatment successes between the two groups.

In a typical randomised control trial the aim is to estimate the difference, δ, between the true success rate π A of the real acupuncture under study and the true success rate π C of the placebo. The acupuncture group of patients yields a treatment success rate pA, which is an estimate of π A, and the placebo gives a treatment success rate pC which is an estimate of π C. Thus d, the observed difference (i.e. pA - pC) is an estimate of the true difference δ.

Even when πA and πC are equal (i.e., real acupuncture is no more effective

than placebo) observed differences d = pA - pC other than zero will occur. The probability, P, corresponding to the observed differences, can be calculated. If under the null hypothesis that $\pi A = \pi C$ (i.e., assuming the treatments do not differ in efficacy) the difference actually observed, $\hat{d}$, has a very small probability of occurring by chance, then one would reject this null hypothesis and conclude that the two treatments do indeed differ in efficacy. One must then decide, however, at what level of probability one would regard an event as unlikely to have occurred by chance.

It is quite arbitrary what critical value one takes for the probability P, this critical value is denoted by a. If $P \leq a$ one rejects the null hypothesis, conversely if $P > a$ one does <u>not</u> reject the null hypothesis. A value of a = 0.05 or 5% is commonly used in clinical trials, thus a P value of less than 5% would be regarded as indicating statistically significant differences between treatments. There is a risk that such a conclusion is incorrect. This false positive error is called a type I error and has the probability a referred to above. The quantity a is referred to as either the test size, significance level or probability of type I error.

The clinical trial could give a difference d that would lead to P being greater than a even though the null hypothesis is really untrue (i.e., πA is indeed greater than πC). One then makes the error of not rejecting the null hypothesis when it is false. This false negative error is called a type II error and its probability is denoted by β. The probability of a type I error is calculated on the assumption that the null hypothesis is true, that is $\hat{d} = \pi A - \pi C = 0$. On the other hand the probability of a type II error is based on the assumption that the null hypothesis is not true, that is $d = \pi A - \pi C > 0$. There are clearly many such values of $\hat{d}$ in

this instance and each would give a different value for β. The power is defined as one minus the probability of a type II error. Therefore if the probability of a type II error is 0.2 (B = 0.2), then the power is 0.8 or 80%.

Figure 9.1 **Relation between sample size and power to detect as significant (one sided test: = 0.05) a difference under the assumptions of 30, 50 and 70% efficacy of placebo, sham acupuncture and real acupuncture.**

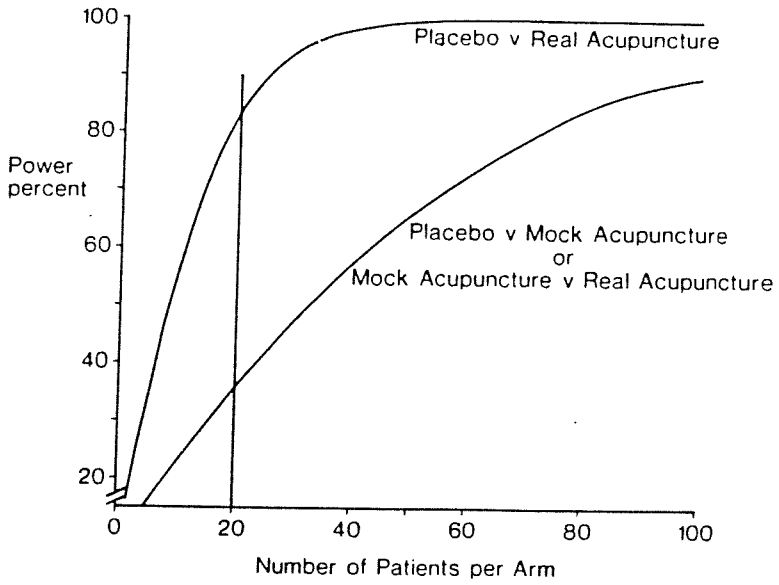


Fig. 9.1 shows the power for a given number of patients per arm for trials which assume responses of 30, 50 and 70% for placebo, sham acupuncture and real acupuncture respectively. Calculations have been based on a one sided test (Armitage, 1974) with a = 0.05 and show power curves for two trials. The first trial compares placebo with real acupuncture and the second trial could be either placebo versus sham acupuncture or sham acupuncture versus real acupuncture. If we take the trial of Gaw et al (1975) as an example they randomised 40 patients with osteoarthritic pain, 20 received sham acupuncture S and 20 real acupuncture A. Assuming a true response rate for S of 50% and for A of 70% then reading vertically upwards from 20 patients on the horizontal axis of Fig. 9.1, as far as the lower curve, indicates that the trial has a power of 36%. This is interpreted as follows:

If 20 patients are recruited to each group of a trial in which the anticipated response rates are 50 and 70% respectively, then with a one sided test size a = 0.05 (or 5%) there is only about a 1 in 3 chance or more exactly 36% chance of detecting such a difference with this trial.

To facilitate the design of trials with anticipated response rates difference to those suggested in this paper we have calculated Table 1 using the method of Aleong and Bartlett (1979) for one sided tests of size 0.05 and 0.01 and powers of 0.80, 0.90 and 0.95 respectively. To make use of the table one first fixes the size of the type I and type II errors for the study. It is then necessary to estimate the likely responses on the two alternative treatments; labelling these responses as p1 and p2 (p2 > p1) one can read off the number of patients required per group for the given error sizes chosen. Thus, if a = 0.05, power = 0.8, p1 = 0.05, p2 = 0.15, the number of patients required, n, in each group of the trial is

130. To use the table if p1 > 0.5, calculate q1 = 1 - p1 and use the column with the particular value of q1 in place of p1.

It should be noted that, if Peto's (1978) suggestion to consider factorial designs is implemented, then patient numbers should be calculated on the basis of the anticipated responses to the principal treatment comparison being made.

Sample size requirements for outcome criteria which can be regarded as having normal distributions are discussed by Cohen (1977) and more recently by Guenther (1981), the former gives a good discussion of the interrelationship between sample size, anticipated clinical differences and the a and b errors (see Tables 9.1 and 9.2).

'Survival' curve comparisons

Even if a group of patients, all being treated by real acupuncture, achieve immediate relief of their pain, unless acupuncture gives a permanent cure, the pain will return at some stage. This clinical picture is a frequently observed occurrence when using acupuncture or similar techniques. If we ask patients to record their pain free time, that is the time from receiving first treatment to recurrence of pain at the level they were experiencing before treatment, these 'pain free times' can be used to evaluate the efficacy of acupuncture. Gross and Lam (1981) give an example of this statistical technique when looking at the period of pain relief from headache.

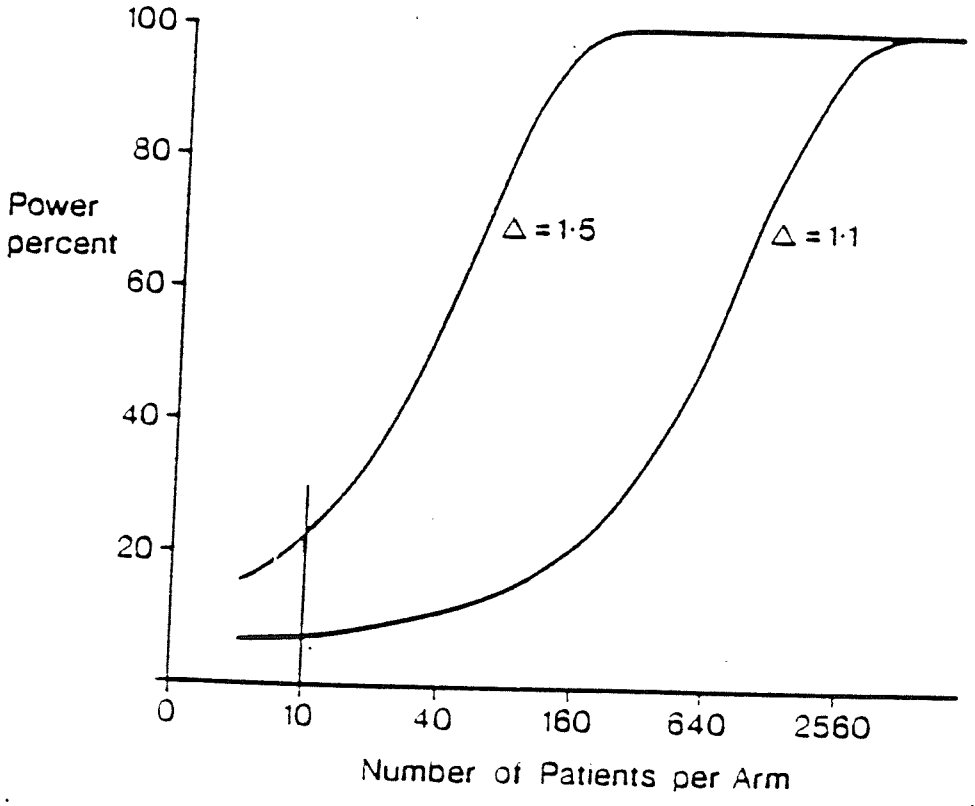
The problems associated with test size and power are similar to those discussed when comparing proportions. Prior to embarking on the trial one must estimate the likely improvement when comparing various treatments in order to calculate the appropriate number of patients who will be required for the trial (see Table 9.3). George and Desu (1974) have calculated

these numbers assuming pain free or 'survival' time to be exponentially distributed and a summary of their results is given in Table 9.2 for particular values of a, power and Δ , where Δ is the ratio of the postulated median pain free times for each treatment. Fig. 9.2 shows the power curve for a one sided test size of a = 0.05 and postulated improvements of 10 and 50% respectively in the median pain free interval of the acupuncture arm as compared with the placebo. Fig. 9.2 can be interpreted as follows: if 10 patients per arm are recruited, and the anticipated improvement in the median is 10%, then the power of such a trial would be approximately 8%. If the anticipated improvement in the median is of the order of 50% then the power will be approximately 25%. To achieve a power of 80% with a 50% improvement in the median pain free period, and a one sided test size of a = 0.05, it would be necessary to recruit about 80 patients to each treatment group. It is important to emphasise that these numbers refer to patients recruited and followed up until the appropriate end point is reached. If a significant 'drop out' rate is expected then recruitment for the trial should be increased by an estimate of the losses expected.

There are a number of potential difficulties with trials using the 'survival' curve technique specifically in relation to variable follow-up periods for each patient. These problems have been discussed in the context of cancer trials by Peto et al (1976; 1977) which provide the basic references for this technique. The 'survival' curve technique is one that has not been used to analyse the information obtained from acupuncture trials but would seem an appropriate statistical method for this form of therapy. Acupuncture is primarily used as a treatment for pain, and many authors have observed that its effect is often of variable duration. It

would therefore be useful to look at the pain free period in more detail.

Figure 9.2 **Relation between sample size and power to detect as significant (one sided test: = 0.05) a 10 and 50% improvement in median 'pain free' interval.**



Trial review

This section is not intended to be a detailed clinical review of the studies mentioned, but it does provide a basis upon which to discuss the statistical aspects of trial design. Real acupuncture has been assumed to be effective in 70% of the patients studied, and it is assumed that all the trials have provided the most effective form of acupuncture available. If either of these assumptions are incorrect, for instance if acupuncture is only effective in 60% of patients with chronic pain, the calculated power of these trials would decrease. Evaluation of these trials is made more difficult by the absence of clear outcome or end point criteria in three of the studies reviewed (Matsumoto, Levy and Ambruso, 1974; Godfrey and Morgan, 1978; Jensen, Melsen and Jensen, 1979). The trials reviewed are summarized in Table 9.4. In order to obtain the power of each of these trials we have assumed a simple two group randomised prospective trial and a type I error of 5%. For pilot or preliminary trials there are good arguments for increasing this probability as a precaution against rejecting what may turn out to be a useful treatment on more extensive study. We have ignored the fact that two of the trials reviewed have incorporated cross-over designs; in certain situations the use of cross-over would improve the power of the trial over that of the simple two arm trial we have proposed (Hills and Armitage, 1979). However, we have argued that this method may be inappropriate for evaluating acupuncture.

It is apparent that the majority of the published reports have a very low power, and consequently very few conclusions about the efficacy of acupuncture can be drawn from much of this work. Moore and Berk (1976) and Godfrey and Morgan (1978) have obtained interpretable results in that their trials have a reasonable power and suggest that real acupuncture is

no more effective than sham acupuncture. Moore and Berk (1976) find real acupuncture to be less effective than sham acupuncture; this is the only trial that we have been able to find that comes to this conclusion. Godfrey and Morgan (1978) have confused the picture somewhat by using musculoskeletal pain of multiple origin as the criterion for entry into the trial. Their analysis has not accounted for possible imbalances of primary diagnosis and site of pain between the treatment arms.

Discussion

Analysis of the available literature (Table 9.4) lends considerable support to the hypothesis which assumes real acupuncture to be effective in 60-70% of patients, sham acupuncture in 50% of patients and a placebo (control) in 30% of patients, only Moore and Berk (1976) contradict it. It is not claimed that the reports listed in Table 9.4 are an exhaustive list of prospective trials in this field. Nevertheless it is quite clear that the majority of these trials are too small to achieve their anticipatied ends and the case for or against the efficacy of real acupuncture has not yet been argued coherently. If the estimate of the true response to real acupuncture is exaggerated then the power of the various trials discussed here would be even smaller. For example, Moore and Berk's (1976) trial would only have a power of 40% if the response to real acupuncture is as low as 50%. It has been attempted to establish a model for the evaluation of acupuncture and argued that simple designs should be used. Furthermore, the detailed statistical information provided will allow future workers to test this or alternative models. What is proposed is not new statistical methodology although this is being developed (George and Desu, 1974). Indeed many writers have emphasised the need for appropriate numbers of patients to be recruited to clinical trials (Feinstein, 1977; Freiman, Chalmers, Smith and Kuebler, 1978; Altman, 1980; Gore, 1981). Altman (1980) in particular has emphasised the ethical aspects of performing trials which are of an unsatisfactory statistical design.

It is suggested that the use of survival curves as a method is well suited to evaluation of acupuncture. This statistical technique looks at the period of time during which the patient receives benefit from any particular treatment as many clinicians have observed that the effects of

acupuncture may be short lived. However, even short term pain relief may be of significant benefit to the patient. It is important that acupuncture is properly evaluated in the light of this clinical observation. This paper provides a model for the further evaluation of acupuncture in the treatment of chronic pain. Acupuncture is a safe and relatively side effect free method of treatment, and deserves careful study.

TABLES FOR CHAPTER 9

TABLE 9.1

NUMBER OF PATIENTS REQUIRED PER GROUP FOR A TWO GROUP TRIAL COMPARING PROPORTIONS

One-tailed test a = 0.05 (after Aleong and Bartlett)

$P_2 - P_1$	P_1 = smaller percentage of success									
	0.05	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.45	0.50
0.05	382	580	753	901	1025	1124	1198	1248	1273	1273
	513	787	1027	1233	1405	1541	1644	1713	1747	1747
	638	984	1287	1547	1764	1937	2067	2153	2197	2197
0.10	130	177	217	251	279	300	316	325	328	325
	172	237	292	339	378	408	429	442	447	442
	212	293	364	423	472	510	537	553	559	553
0.15	72	92	108	122	133	141	147	150	150	147
	95	121	144	163	179	190	198	202	202	198
	116	150	179	203	222	236	246	251	251	246
0.20	48	58	67	74	79	83	86	86	86	83
	63	77	88	98	106	111	114	115	114	111
	76	94	109	121	131	137	142	143	142	137
0.25	36	42	47	51	54	55	56	56	55	54
	46	54	61	66	71	73	75	75	73	71
	55	66	75	82	87	90	92	92	90	87
0.30	28	33	35	37	39	40	40	40	39	37
	35	41	45	48	51	52	53	52	51	48
	43	49	55	59	62	64	64	64	62	59
0.35	22	25	27	29	30	30	30	30	29	27
	28	32	35	37	38	39	39	38	37	35
	34	38	42	45	46	47	47	46	45	42
0.40	19	20	22	23	23	23	23	23	22	20
	23	26	28	29	30	30	30	29	28	26
	28	31	33	35	36	36	36	35	33	31
0.45	16	17	18	19	19	19	19	18	17	16
	20	21	23	23	24	24	23	23	21	20
	23	25	27	28	29	29	28	27	25	23

TABLE 9.1 (Continued)

	0.05	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.45	0.50
0.50	13	14	15	15	16	15	15	14	13	-
	17	18	19	19	19	19	19	18	17	-
	20	21	22	23	23	23	22	21	20	-
0.55	12	12	13	13	13	13	12	12	-	-
	14	15	16	16	16	16	15	14	-	-
	17	18	19	19	19	19	18	17	-	
0.60	10	11	11	11	11	11	10	-		
	12	13	13	14	13	13	12	-		
	14	15	16	16	16	15	14	-		
0.65	9	9	9	9	9	9	-			
	11	11	11	11	11	11	-			
	12	13	13	13	13	12	-			
0.70	8	8	8	8	8	-				
	9	10	10	10	9	-				
	11	11	11	11	11	-				
0.75	7	7	7	7	-					
	8	8	8	8	-					
	9	10	10	9	-					
0.80	6	6	6	-						
	7	7	7	-						
	8	8	8	-						
0.85	6	6	-							
	6	6	-							
	7	7	-							
0.90	5	-								
	5	-								
	6	-								

The 3 values for each p, and $p_2 - p_1$ correspond to powers of 80, 90 and 95% respectively, reducing down the columns.

TABLE 9.2

NUMBER OF PATIENTS REQUIRED PER GROUP FOR A TWO GROUP TRIAL COMPARING PROPORTIONS

One-tailed test a = 0.01 (after Aleong and Bartlett)

$P_2 - P_1$	P_1 = smaller percentage of success									
	0.05	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.45	0.50
0.05	595	917	1198	1439	1640	1800	1921	2001	2041	2041
	760	1177	1541	1854	2114	2322	2479	2583	2635	2635
	912	1417	1858	2237	2552	2805	2994	3120	3183	3183
0.10	199	275	340	395	440	476	501	516	521	516
	252	350	434	506	565	610	643	662	669	662
	301	419	522	608	679	735	774	798	806	798
0.15	110	141	168	190	208	221	230	235	235	230
	138	178	213	242	265	283	294	300	300	294
	164	213	255	290	318	339	353	360	360	353
0.20	73	89	103	114	123	129	133	134	133	129
	91	112	130	145	156	164	169	171	169	164
	107	133	155	173	186	196	202	204	202	196
0.25	53	63	71	77	82	85	87	87	85	82
	66	79	89	97	104	108	110	110	108	104
	78	93	106	116	123	128	131	131	128	123
0.30	41	47	52	56	59	61	61	61	59	56
	51	59	65	70	74	76	77	76	74	70
	60	69	77	83	88	90	91	90	88	83
0.35	33	37	41	43	45	46	46	45	43	41
	41	46	50	54	56	57	57	56	54	50
	48	54	59	63	66	67	67	66	63	59
0.40	27	30	32	34	35	35	35	34	32	30
	33	37	40	42	43	44	43	42	40	37
	39	43	47	49	51	51	51	49	47	43
0.45	23	25	27	28	28	28	28	27	25	23
	28	31	33	34	34	34	34	33	31	28
	32	36	38	40	40	40	40	38	36	32

TABLE 9.2 (Continued)

	0.05	0.10	0.15	0.20	0.25	0.30	0.35	0.40	0.45	0.50
0.50	20	21	22	23	23	23	22	21	20	-
	24	26	27	28	28	28	27	26	24	-
	27	30	31	32	33	32	31	30	27	-
0.55	17	15	19	19	19	19	18	17	-	
	20	22	23	23	23	23	22	20	-	
	23	25	26	27	27	26	25	25	-	
0.60	15	16	16	16	16	16	15	-		
	18	19	19	19	19	19	18	-		
	20	21	22	22	22	21	20	-		
0.65	13	14	14	14	14	13	-			
	15	16	16	16	16	15	-			
	17	18	19	19	18	17	-			
0.70	11	12	12	12	11	-				
	13	14	14	14	13	-				
	15	16	16	16	15	-				
0.75	10	10	10	10	-					
	12	12	12	12	-					
	13	13	13	13	-					
0.80	9	9	9	-						
	10	10	10	-						
	11	11	11	-						
0.85	8	8	-							
	9	9	-							
	10	10	-							
0.90	7	-								
	8	-								
	8	-								

3 values for each p_1 and $p_2 - p_1$ correspond to powers of 80, 90 and 95% respectively, reading down the columns.

TABLE 9.3

NUMBER OF PATIENTS PER GROUP, n, REQUIRED TO DETECT A SIGNIFICANT DIFFERENCE BETWEEN TWO 'PAIN RELIEF' DISTRIBUTIONS (after George and Desu)

a	Δ	n	Δ	n	Δ	n	Δ	n
0.05	1.1	1360	1.6	56	2.1	23	2.6	14
		1884		78		32		19
		2384		98		40		24
	1.2	372	1.7	44	2.2	20	2.8	12
		515		61		28		17
		652		77		35		21
	1.3	180	1.8	36	2.3	18	3.0	11
		249		50		25		15
		315		63		32		18
	1.4	110	1.9	30	2.4	17	3.5	8
		152		42		23		11
		192		53		29		14
	1.5	76	2.0	26	2.5	15	4.0	7
		105		36		21		9
		132		46		26		12
0.01	1.1	2213	1.6	91	2.1	37	2.6	22
		2870		118		48		29
		3479		144		58		35
	1.2	605	1.7	72	2.2	33	2.8	19
		785		93		42		25
		951		113		51		30
	1.3	292	1.8	59	2.3	29	3.0	17
		379		76		38		22
		460		92		46		27
	1.4	178	1.9	49	2.4	27	3.5	13
		231		64		34		17
		280		77		42		21
	1.5	123	2.0	42	2.5	24	4.0	11
		159		55		32		14
		193		66		38		17

Three values for each Δ correspond to powers of 80, 90 and 95% respectively, reading down the columns.

TABLE 9.4

POWER OF SOME RECENTLY PUBLISHED TRIALS OF ACUPUNCTURE

Study	Disease/pain	Design	No. of patients at first randomisation				Reported or estimated response (%)			Power per cent (assuming response rates of: placebo, 30%; sham, 50%; real, 70%)	Comments
			Placebo	Sham	Real	Total	Placebo	Sham	Real		
1. Matsumoto et al.	Cervical osteoarthritis	Two group single blind	-	-	12 12	24	-	-	67 67	26	Manual versus electroacupuncture. Multiple diagnoses, unclear end points.
2. Gaw et al.	Osteoarthritic pain	Two group single blind	-	20	20	40	only mean scores given			36	
3. Fox and Melzack	Low back pain	Cross-over	-	-	12 12	12	-	66	75	17	Real acupuncture compared with TNS; the effects of cross-over in such physical treatments are unclear.
4. Moore and Berk	Shoulder pain	Two group single blind	-	20	20	(42)[a]	-	39	23	87	No definition of end points only mean scores available.
5. Godfrey and Morgan	Musculo-skeletal pain	Two group double blind	-	84	84	(193)	-	54	63	85	Response to acupuncture lower than placebo. Multiple diagnoses of musculo-skeletal disease used.
6. Co et al	Sickle cell anaemia	Simultaneous treatment in both groups	-	10	10	10	-	50	81	23	Sham and real acupuncture given simultaneously therefore difficult to interpret.
7. Jensen et al.	Headache	Partial cross-over	10	-	19	(32)	50	-	68	67	

[a] Parentheses indicate some patients excluded from analysis.

CHAPTER 10

ACUPUNCTURE VERSUS MOCK TNS IN THE EVALUATION OF 3 PAINFUL CONDITIONS

INTRODUCTION

There are three studies involving a single blind randomised controlled methodology, specifically comparing acupuncture with mock TNS. Each of these studies, while following the same basic principles, involve different treatment protocols and assessment systems. The first study evaluates acupuncture compared with placebo (mock TNS) in post-herpetic pain. This study was developed during the latter half of 1979 and was carried out at the Department of Primary Care at the University of Southampton. The original proposal involved two studies, one on shingles and one on post-herpetic neuralgia. Both studies utilised similar trial methodology. The shingles study was designed to demonstrate that acupuncture would diminish the duration and severity of pain experienced during an acute attack of shingles. A second hypothesis was also suggested for the shingles study; that acupuncture would diminish the incidence of post-herpetic neuralgia. Hope-Simpson (1975) has suggested that approximately one in ten individuals with shingles go on to develop post-herpetic neuralgia. The shingles study therefore required large numbers of patients in order to demonstrate a significant difference between real and placebo treatments. It rapidly became apparent that general practitioners in the Southampton area were unprepared to refer adequate numbers of patients to the research clinics at the Aldermoor Health Centre. Therefore, the shingles study was abandoned after the first six months when only some 5 patients had been referred to the research clinics.

The study on post-herpetic neuralgia was designed to run in parallel with the shingles study. Patients were to be seen at the same research clinics within the Aldermoor Health Centre and slightly different acupuncture techniques were proposed to deal with this chronic and painful problem. This study attracted adequate numbers of patients and the research clinics ran from mid 1980 to mid 1981. The research team for the post-herpetic neuralgia study involved Dr. Lewith as the prime investigator with assessments being carried out by Dr. Field and with statistical help and advice from Dr. Machin. At that time, Dr. Field was a lecturer in the Department of Primary Medical Care and Dr. Machin a lecturer in the Department of Statistics at Southampton University. This study was supported by a grant from the Wessex Regional Health Authority.

The second study analysed the effects of acupuncture versus placebo (mock TNS) in the treatment of headache. The headaches evaluated were either classical migraine or migrainous in nature. Research clinics were established at the Department of Primary Medical Care and patients were drawn from local general practitioner referrals, the Aldermoor Health Centre itself and Ferndown Health Centre in Dorset. One of the investigators (Dr. Dowson) was at that time a principal in general practice at Ferndown. The study began in 1981 and ran for 2 years; the research clinic finally closed in 1983. The prime investigator was again Dr. Lewith but this burden was shared with Dr. Dowson who also ran the clinics. Dr. Machin again provided statistical advice and support from the Department of Statistics at the University of Southampton. This project was supported by internal funding from the Department of Primary Care. The money available for the research project had been raised by patient contributions for the acupuncture treatment they had received from Dr.

Lewith, on an open referral basis.

The third study, following exactly the same study model, looked at the effect of acupuncture versus placebo (mock TNS) in the treatment of trapezio-metacarpal osteoarthritis. This study was carried out by Mrs. Dickens as part of her course work for an MSc in rehabilitation. Here patients were drawn from two hospitals, Queen Alexandra, Portsmouth and Southampton General Hospital. Mrs. Dickens was the prime researcher supervised by Dr. Lewith. The project began in 1987 and was completed in 1988. No external funding was required for this project as the research was a necessary part of Mrs. Dickens's submission for a higher degree at the University of Southampton.

Post-herpetic neuralgia

Herpes zoster itself is a common disease; the incidence varies from 0.7 cases per 1000 per year below the age of 10 years to 10.1 cases per 1000 per year above the age of 70 years. For the purposes of this study, post-herpetic neuralgia was defined as pain over the dermatome that was affected by shingles after the last trace of the rash had disappeared. This point in time was defined as the moment when the last crust of the last scab of the herpes rash had completely healed. Scarring was not considered to be part of the active stage of shingles. The pain of post-herpetic neuralgia is typically described as a constant burning discomfort on which may be superimposed intermittent lacerating pains pains and dysaesthesia (Watson et al, 1988). In the older age group the incidence of post-herpetic neuralgia can vary from 35 to 50% of those suffering from herpes zoster (Hope-Simpson, 1975). A more recent epidemiological paper by Ragozzino et al found similarly that patients who developed post-herpetic neuralgia had a mean age of 67 as compared with 46 in those with uncomplicated herpes

zoster (Ragozzino et al, 1982).

Patients with grossly disturbed immune systems such as those receiving antineoplastic therapy are more likely to suffer from serious problems such as recurrent and generalised zoster (Anon 1979). However post-herpetic neuralgia is the most frequent and distressing complication; it may last for months or even years and presents problems in treatment. Analgesics, carbamazepine, antidepressants and a wide variety of local nerve blocks have been used to treat the pain (Anon 1979; Raftery 1979), but many patients do not benefit to any great extent from these therapies. A more recent review by Roberston and George (1990) concurs largely with the evidence that was at our disposal in the late 1970s. There appears to be no proven or uniformly acceptable conventional therapy for post-herpetic neuralgia, amitriptyline does appear to benefit some patients with established post-herpetic neuralgia, and seems to have an analgesic effect which is independent of its antidepressant action. A variety of local anaesthetic and surgical techniques may provide temporary relief, but again none has been shown to have a long-term or consistentbenefit. Transcutaneous nerve stimulation (TNS) does appear to be free from side effects and benefits some patients; Robertson and George (1990) feel that this physical treatment is certainly worthy of consideration in those suffering from intractable pain.

Nathan and Wall first suggested the use of electrical stimulation and techniques in 1974. They postulated that the effects could be explained by the gate control theory of pain, a concept that has also been used to explain acupuncture (Kenyon 1980). These ideas encouraged us to test the effect of acupuncture as a treatment for this pain.

Because stimulation of non-acupuncture points may produce a physiological

effect that can diminish pain elsewhere in the body (Le Bars, Dickenson and Besson, 1979; Lewith and Machin, 1983), it was decided to use a different type of physical therapy as a control treatment. This was mock transcutaneous nerve stimulation (TNS), which has been shown to produce a therapeutic effect similar to that expected from placebo medication (Thorsteinsson, Stonnington, Stilwell and Elveback, 1978; Lewith and Machin, 1981; Lewith and Machin, 1983). The aim of the study was to test the hypothesis that acupuncture may have a greater effect than placebo in diminishing the severity of pain in post-herpetic neuralgia.

Headache

At the time that this study was conceived there had been only one attempt to evaluate acupuncture as a treatment for headache, in a controlled manner (Jensen et al, 1979). Headache is a common problem in general practice, Hannay (1979) suggests that headache is the fourth most common symptom in general practice and is present in 15% of consultations. Morrell (1972) suggests that headache is the ninth most common symptom presenting in his study, being the most important reason for consulting in 8.5% of instances. Waters (1974) was responsible for much of the early epidemiological work on migraine. His studies suggested that classical migraine with at least 2 of the 3 major symptoms (headache, visual disturbance and vomiting or nausea) is present 1 out of every 10 headaches. Sixty-five per cent of those suffering classical migraine have headaches at least once a month or more frequently (Waters 1974). Headaches are therefore a common symptom for which analgesics are frequently prescribed (Bain and Haines, 1975).

It has been suggested that acupuncture is of value as an analgesic and prophylactic therapy for headache, but most of the studies substantiating this view are descriptive (Mann and Halfide, 1963; Mann, Bowsher, Mumford,

Lipton and Miles, 1973; Gwan 1977; Jensen, Tallgren, Troest and Jensen, 1977). Jensen et al (1979) published a single blind partial cross-over study which measured analgesic requirements in a population of young people with headaches. They concluded that acupuncture did provide symptomatic relief over a prolonged period of time, in this condition. We have chosen to evaluate the effects of acupuncture on migrainous headaches in a single blind randomised study. The hypothesis we wished to test is that acupuncture reduces the frequency and severity of migrainous headaches and that it can be used as a prophylactic as well as an analgesic treatment.

Trapezio-Metacarpal Osteoarthritis

Osteoarthritis (OA)is by far the most common arthritis, with an estimated 5 million people in the United Kingdom suffering pain and disability as a result of OA (Dieppe et al, 1975). It also accounts for 40% of the loss of the country's working time (Dick and Buchanan, 1977). Osteoarthritis is commonly age related, half the population over 60 and nearly everyone over 75 has osteoarthritic changes on x-ray (Dieppe 1984). Osteoarthritis is slightly more common in women than men (Dieppe et al, 1985) and women are more likely to present with radiographically severe OA (Dick & Buchanan, 1977).

At present OA is diagnosed primarily on the basis of presenting signs and symptoms. The distribution and pattern of joint involvement, time course and radiological evaluation all assist in the diagnositic process. Fundamentally, osteoarthritis is a clinical diagnosis supported with a combination of clinical evaluation and x-ray findings.

At this time few acupuncture trials for the treatment of osteoarthritis had been published and none had concentrated on the trapezio-metacarpal joint. The studies concerning acupuncture have already been extensively reviewed

(vide supra) and the ones specifically directed at osteoarthritis are relatively few in number. Gaw et al (1975) used an acupuncture versus sham acupuncture model on 40 patients with osteoarthritic pain, no significant difference was demonstrated between these two groups. A critique of the study methodology and statistics has already been presented. Matsumoto et al (1974) compared manual and electro-acupuncture in 24 patients with cervical osteoarthritis. They reported a significant result when comparing real and sham acupuncture although again a statistical analysis was inconclusive. Godfrey and Morgan's study (1978) involved 193 patients suffering from a variety of painful complaints including osteoarthritis. For a variety of reasons already discussed, this study was poor both methodologically and statistically. The largest study involving acupuncture and osteoarthritis was carried out by Milligan et al (1981) at Poole General Hospital. This involved 100 patients and compared acupuncture for osteoarthritis of the knee with standard physiotherapy. Unfortunately, the details of this study were never published although the abstract presented at a conference in 1981 suggests that acupuncture was beneficial to those patients who received it. A further study by Coan et al (1982) involved 30 patients with neck pain and in it acupuncture was compared with no treatment at all. Eighty per cent of the acupuncture group improved whereas only 2% of the untreated group showed any benefit. A similar study by Petrie and Langley (1983) used a similar model (acupuncture versus mock TNS) and found significant improvement in those receiving acupuncture as compared to mock TNS.

The available literature in 1987 was not convincing enough to suggest that acupuncture was a useful treatment for osteoarthritic pain.

Conventional treatment for trapezio-metacarpal (TMC) joint osteoarthritis

(OA) is aimed at relieving pain and maintaining and improving function. Drugs and physical therapy are commonly utilised and surgery is undertaken in severe cases. However both pharmacological and surgical therapies carry risks of complications. Although a wide variety of physiotherapy techniques have been used for TMC joint OA very few of these have been adequately investigated. This study was designed to investigate whether acupuncture was more effective than mock TNS in alleviating the pain and disability associated with TMC joint OA.

METHOD

Protocol Development

The initial protocol of post-herpetic neuralgia required many hours of discussion before it reached its final stage. This development involved a series of discussions in the research group which met regularly within the Department of Primary Medical Care at the University of Southampton. It was essential for the primary investigator (GL) to explain to his colleagues the problems associated with acupuncture studies. A series of discussions then ensued which involved the development of a detailed protocol structure taking into account the specific problems that would be encountered in an acupuncture study. This "model protocol" was then used as the basis for the development of the shingles protocol, the protocol on headache and the protocol on TMC join OA. It was used also to support a submission of the shingles and post-herpetic neuralgia study to the Regional Health Authority and the submission of the headache study for internal funding. Fundamentally, the protocol model involved the discussion and development of 13 main criteria. These were:

1. An introduction to the epidemiology of the disease.
2. The research proposal.
3. A definition of the illness to be studied.
4. The mechanism of referral.
5. Patient inclusions and exclusions.
6. The mechanism of ethical approval and patient consent.
7. The trial methodology.
8. The details of the assessment system applied for the specific condition under study.
9. The details of the treatment to be applied for the specific condition

under study. In all instances the treatment was to be adaptable, allowing the acupuncturist to change the details of therapy in response to the individual's treatment requirements. Similar adaptability was included for the placebo treatment.

10. A statistical assessment involving an estimate of the number of patients required for the study (based on an estimate of treatment responses), the statistical methods that would be applied to the study and the mechanism of data collection that would be required for subsequent statistical analysis.

11. Analgesia requirements. All these studies involve the treatment of painful conditions, so consequently some assessment of the quantity and quality of analgesics consumed by each patient was considered at the outset to be both important and relevant with respect to treatment outcome.

12. Patient withdrawal and how this should be dealt with in terms of the study and subsequent statistical analysis. Escape treatments were also considered under this heading so that patients did not continue in the study if their clinical condition worsened.

13. Completion. This defined the responsibility for continued patient management after the study had been completed.

This exercise is essential for all clinical research, and represents an important learning process for the researcher. Clearly, from some of the faulty designs that had been used to evaluate acupuncture in previous studies, it is fair to assume that such rigorous protocol development had not been part of the research agenda for many previous investigators. Both the post-herpetic neuralgia study and the migraine study, as they were carried out at the Department of Primary Medical Care, involved a rigorous

and prolonged process of protocol development based on the categories outlined. The final study on TCM joint OA was based on exactly the same protocol development, but on this occasion it was undertaken as part of the normal research supervision and did not involve group development.

Ethical Committee Approval and Consent

In all three instances, ethics committee approval was sought from the appropriate ethics committees responsible for area in which the research was effected. In all three studies this involved the joint ethics committee for Southampton University, Southampton and South West Hampshire District Health Authority. The final study also involved the ethics committee at Queen Alexandra Hospital, Portsmouth as a research clinic was established within the physiotherapy department at that hospital. There were no fundamental problems with ethics committee approval as acupuncture is a safe and side-effect free procedure provided needles are adequately sterilised (as was the case in the first 2 studies) or disposable needles were used (this was the case in the third study on TMC joint OA). However there were consistent problems in relation to obtaining informed patient consent. In all three studies detailed handouts were given to the patients and their GPs (Appendix 10.1, 10.2, 10.3, 10.4 and 10.5).

The standard consent form for clinical trials involving pharmacological preparations usually makes statements to the effect that patients will receive a real or placebo treatment, and that they will not be able to differentiate between the two treatments as the preparations will look exactly the same. The investigator will also be unaware of the exact nature of the treatment as the preparations will be coded and just given to the patients on a completely random basis. Consequently trials on pharmacological preparations can quite simply fulfil the criteria for a

double-blind randomised controlled trial. However, when comparing acupuncture and mock TNS this is impossible. The primary investigator is fully aware of the nature of the treatment and whether a placebo or real treatment is being given to the patient. Furthermore, if the patient knows that one of the treatments is a placebo, then it would be simple for them to deduce that mock TNS is the placebo against which real acupuncture is being compared.

The consent form for these studies therefore needed to be prepared with some care and involved detailed discussions with the relevant ethics committees. In the shingles, post-herpetic neuralgia and headache studies, the following form of words was used:

> "I..... understand that I am taking part in a research project to assess the treatment of shingles/post-herpetic neuralgia/headache. I understand that I will receive either acupuncture of another physical treatment, and the nature of these treatments has been explained to me. Acupuncture involves the insertion of needles into the skin. The other physical treatment involves the use of pads on the skin attached to a small electrical stimulator. This produces no abnormal sensation on the skin. I am aware that either of these treatments might prove to be ineffective."

The study on TMC joint OA involved a slightly different consent form:

> "I ..... understand that I am taking part in a research project, the aim of which is to assess the effects of two physical procedures (A or B) applied to the base of my thumb.
>
> A) Involves the placing of disposable acupuncture needles into and around the painful joint at the base of my thumb. These are then stimulated by the therapist who gently twists them. I will feel an

aching sensation during this procedure that will disappear on removal of the needles or soon after.

B) This procedure involves the use of small pads that are attached to an electrical stimulator and are placed over the joint at the base of my thumb. Due to the nature of the electrical current emitted by this machine it produces no abnormal sensation.

I understand that I will only receive one of these two procedures. I understand that I may temporarily feel more pain but this will not last long. I understand that neither of these procedures may have a beneficial effect."

These forms of consent allowed the investigator to explain to the patient both types of treatment without clearly suggesting which was the placebo. Furthermore, as will be discussed in the protocols for each specific study, the treatments were designed to be adaptable. Therefore, if a patient failed to gain benefit from either real acupuncture or mock TNS the position of the needles or electrode pads was changed in accordance with clearly defined guidelines so that it appeared both treatments were real. A standard form of words was used by the investigators employing both these treatments in order to make sure that there was no hidden bias between the two treatments. The relevance of mock TNS as a true placebo has already been discussed (vide supra). Every effort was made both when explaining the trial to the patient and asking them to sign the consent form, to maintain the belief that mock TNS was a real and useful treatment for the condition under investigation.

The ethics committees in both Southampton and Portsmouth required a detailed explanation of the study before they would accept the form of words used in the consent form. Eventually, the appropriate ethics

committees accepted the reasoning behind the form of words used in all four consent forms (shingles, post-herpetic neuralgia, headache and TMC joint OA).

Randomisation

The randomisation procedure in all three studies was the same. All three studies involved some form of entry assessment with appropriate exclusions and then a short period of baseline assessment. In the post-herpetic neuralgia this involved one week of pain recording prior to randomisation and treatment whereas in the migraine study headache diaries were kept for one month prior to randomisation and treatment. In all instances, randomisation was carried out by the use of a computer programme set up by the Department of Statistics and Medical Computing at the University of Southampton. An individual other than the actual investigator used the programme as the basis for making cards designating either real acupuncture or mock TNS treatment. These cards were placed in numbered sealed envelopes which were opened (sequentially) by the investigator at the beginning of the treatment period. Therefore, the first patient entering the study would have had their treatment designated within the sealed envelope numbered 1, the second patient would have had their treatment designated by the card in the sealed envelope numbered 2 and so on.

All three studies involved separate randomisation for males and females. The incidence of post-herpetic neuralgia, headache and osteoarthritis are all more common in females than males, so consequently stratification according to sex was essential in order for the groups to remain balanced. The natural history of these painful diseases did not suggest that it was necessary to stratify our patients by any other entry criterion such as age. The randomisation procedures used in these three studies were based

on standard conventional methods and did not require any specific changes or innovations in relation to the comparison of the two procedures (acupuncture and mock TNS).

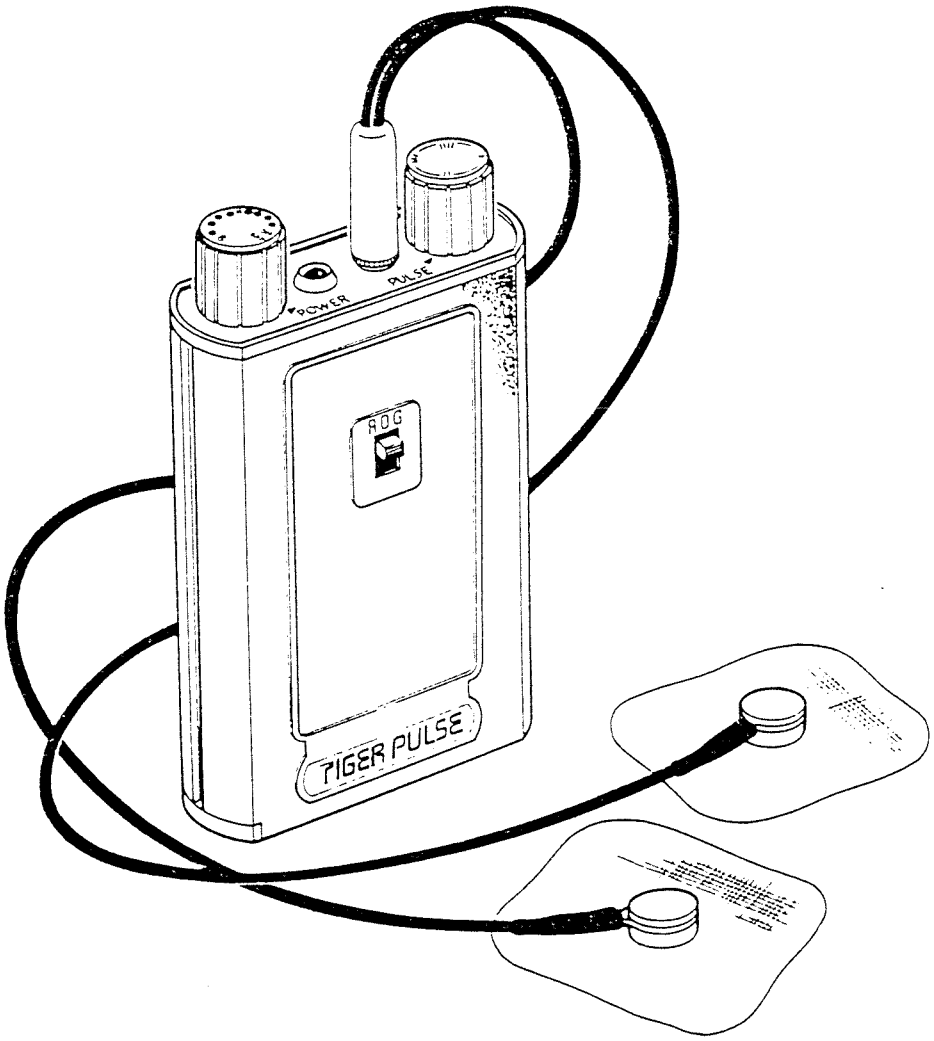
Mock TNS

The placebo used in all three studies was mock TNS. The actual mock TNS machine used was similar in all the studies. An RDG Tiger Pulse was used in the post-herpetic neuralgia and headache study and a Spembly Pulsar in the study on TMC joint osteoarthritis. The TNS machines were very simple stimulators with two controls, frequency and amplitude (Fig. 10.1). TNS produces a pulsed squarewave, both the amplitude and frequency of this squarewave can be altered. In normal TNS treatments a jack plug is connected to the output socket and the pulsed squarewave transmitted through two wires into a pair of transcutaneous electrodes. These electrodes are then placed on or around the site of pain. The machine can then be worn for many hours and will provide analgesia in a substantial proportion of patients.

The RDG Tiger Pulse also has a small flashing light between the pulse and power adjustments. This flashing light reflects the frequency of output and shows whether the machine is on or off, but it does not give any indication of output amplitude.

Figure 10.1

The RDG Tiger Pulse



For the purposes of these three studies, contact was broken at the output jack plug. Consequently, no current could travel from the machine to the patient. However, the machine could still be switched on and off and the flashing light at the top of the machine continued to suggest that the machine was on and functioning.

Patients were told that this was a very high frequency stimulation and they would not feel anything during treatment. They were also given positive encouragement that would suggest the treatment might work. For instance, in the post-herpetic neuralgia they were asked in a positive and encouraging way whether their pain felt better during and after treatment. In other words the investigators deliberately adopted an encouraging attitude in an attempt to get the patients to believe that the therapy was indeed valid and that the investigators themselves expectedmock TNS to produce a clinical result. Patients receiving mock TNS were given exactly the same treatment time as those receiving real acupuncture. As the assessments were carried out in all instances, blind to treatment, the studies could all be considered single blind.

The method of providing mock TNS in these three studies is the same as that applied by Petrie and Hazleman (1986). No specific validation techniques were used to assess the credibility of the placebo in these three studies. If placebo treatment failed to produce benefit, then the position of the pads was changed between treatment sessions. For instance, in the post-herpetic neuralgia trial, the pads may initially have been applied above and below the painful dermatome and if this failed to produce a result after one or two sessions then the pads would have been applied either on the leg, or actually over the painful dermatome or on the opposite side to the pain using "mirror image points". These methods of point selection

are similar to those that would have been used if the patients had been receiving real acupuncture.

The principles of acupuncture treatment

In all three studies the acupuncture points used were adaptable. In the study on post-herpetic neuralgia, ear acupuncture was used and points in the ear were chosen based on a standard auricular therapy protocol (Kenyon 1983). If the auricular therapy failed to produce a response in the first two or three sessions then the points were changed and body acupuncture was also used. A clear attempt was made to provide the most effective acupuncture treatment available for all the conditions being studied, so consequently the acupuncture points were changed in accordance with the therapeutic principles that an acupuncturist would apply when treating a patient in a normal clinical situation.

The main types of acupuncture used in the post-herpetic neuralgia study were auricular therapy (Kenyon 1983) followed by a traditional Chinese approach to body acupuncture. The traditional Chinese approach to body acupuncture is outlined in Lewith and Lewith (1979). Therefore patients may have had both body and ear acupuncture used simultaneously if they were in the acupuncture group and were suffering from post-herpetic neuralgia.

Those patients suffering from migraine only received body acupuncture. There are probably more than 50 acupuncture points that can be used for migraine. The choice of points depends on both the traditional Chinese diagnosis and the exact distribution of painful trigger points that an individual may experience when suffering headache. Consequently treatments were designed based on the individual's treatment requirement, and were altered during the trial based on patients changing response to treatment. The body acupuncture given utilised both a traditional Chinese

and tender point approach to the management of the condition under investigation.

In a study on TMC joint OA, points were chosen based on the tender areas around the thumb. No attempt was made to reach a traditional Chinese diagnosis, as it is normal practice to treat painful peripheral joints with local acupuncture. Some acupuncturists might consider the use of electro-acupuncture for local tender joint pain, but in this study only manual insertion of the needles was used into and around the tender joint. While the exact number of needles was not circumscribed, it was usual for patients to receive between 3 and 5 needles during their treatment. Again, the exact position of the needles was changed in accordance with the patient's response to treatment.

In all instances a clear effort was made to provide the best possible treatment for the particular condition under investigation.

Post-Herpetic Neuralgia: detailed methodology

In August 1980 all the general practitioners within a 10 mile radius of the Aldermoor Health Centre, Southampton, were contacted. The nature of the trial was explained to them and they were asked to refer suitable patients. Patients were referred with a clinical diagnosis of post-herpetic neuralgia, which we defined as pain over the dermatome where a typical shingles rash had occurred, and where the pain had continued after the last scab had disappeared. Fifty-six per cent of all patients experience spontaneous resolution during the 3 month period following an acute episode (Hope-Simpson 1975), and so patients were not entered into the study until the post-herpetic neuralgia had continued for at least 3 months. Patients were excluded if they were pregnant, had a malignancy, or a severely debilitating disease, or were taking corticosteroids or other

immunosuppressive agents. Immobile and severely ill patients were also excluded.

Patients were referred to a trial clinic at the Aldermoor Health Centre where they had a standard interview by the assessor (Dr. Jenny Field) who was also responsible for the assessment of their pain. She was unaware of the treatment the patients were receiving and throughout the study reminded patients not to provide information about their treatment. During the first examination the criteria for entry into the trial were confirmed and information was obtained about the site and duration of the pain. Patients were asked to record their pain for one week prior to subsequent randomisation and entry to treatment. An assessment of the average pain levels was recorded using a 7-point verbal pain scale ranging from 'none' to 'almost unbearable' (Appendix 10.6). The verbal pain scale employed was originally developed for use in the evaluation of migraine (Newland, Illis, Robinson, Batchelor and Waters, 1978), and has also been used for the assessment of other painful conditions (Lewith and Machin, 1981; Smith, Lewith and Machin, 1983). Sleep disturbance was measured on a 3-point scale (none, mild, severe), drug intake was recorded weekly and the patients were given a diary to record their pain daily during the period of treatment; using the 'none' to 'almost unbearable' pain scale. The four methods of assessment are shown in Fig. 10.2.

Figure 10.2

PAIN ASSESSMENT SYSTEM

Measurement	Initial week	Treatment (weeks)					Follow up (weeks)		Scale
	0	1	2	3	4	5	6	4	8	
Daily pain diary Weekly pain score		x	x	x	x	x	x	x	x	None, very mild, mild, not very severe, quite severe, very severe, almost unbearable
Sleep disturbance due to pain		x	x	x	x	x	x	x	x	None, mild, severe
Analgesic intake		x	x	x	x	x	x	x	x	Total weekly drug intake in week preceding consultation

The randomisation procedure used in all three clinical trials has already been described.

Auricular acupuncture was used in all patients, the exact site of needle insertion depending on the most tender auricular point that could be defined on the pinna (Oleson, Kroening and Bresler, 1980; Nogier 1981; Kenyon 1983). The auricular needles were inserted and left in situ for about 10 min. In view of the clinical experience of the acupuncturist (GL) it was felt that auricular acupuncture was more likely to provide effective analgesia than body acupuncture. Therefore auricular acupuncture was used first, but if no improvement occurred after 2 or 3 treatments the technique was changed to body acupuncture and continued for a series of weekly consultations to a maximum of 8. Body acupuncture poiints were selected depending on the site and distribution of the pain, in accordance with the methods described by Lewith and Lewith (1979). Needling sensation was obtained on each of the body needles (Lewith and Lewith, 1979) and no electrical stimulation was used for either auricular or body acupuncture.

The placebo treatment (mock TNS) has already been described. The protocol for its use within this study is exactly the same as that already outlined. Both treatments were provided by the investigator (GL) who asked the same questions at each consultation: 'How has your pain been over the last week? How does your pain feel now? Is your pain better now?' On each attendance the patients were interviewed by JF before treatment who recorded pain scores, sleep disturbance, analgesic intake and collected pain diaries. If after 6 treatments there was no improvement or no pain was recorded no further treatment was given and the patients were followed up twice at monthly intervals. Patients who had experienced improvement

were given 2 further treatments to a maximum of 8 before a similar follow-up period. The decision regarding further treatment was made by JF in ignorance of the specific treatment that patients were receiving. Drug treatment was continued as prescribed by the patient's doctor and patients taking analgesics were advised to take them as necessary to relieve pain. The study was designed to give an 80% chance of demonstrating (at P = 0.05) a significant difference between acupuncture and placebo of 35%.

Headache: detailed methodology

Classical migraine with all three symptoms (nausea/vomiting, unilateral headache and associated visual disturbance) is not a common disease (Newland et al, 1978). Therefore, for the purposes of the study migrainous headache was defined as a 'recurrent headache with two of the three main migrainous symptoms'. Patients were entered into the study if they suffered such headaches at least twice a week. They were excluded if they were pregnant, suffering from a serious intercurrent illness (such as cancer), had had physical therapy in the previous 3 months or were taking oral corticosteroids or ergotamine. They study population was drawn from 2 health centres, Aldermoor Health Centre, Southampton (practice population 87000) and Ferndown Health Centre, Dorset (practice population 16,000). Those referred to the study were interviewed by the investigator to assess their suitability. The age, sex, occupation, medication (for headaches and any other problem), past medical history and the presence of family history of headache was noted at this interview. Those entered were then asked to keep a daily record of their headache severity, duration, analgesic requirement and associated symptoms for a period of 4 weeks prior to treatment. After the initial 4 weeks, patients were randomly allocated to placebo or acupuncture treatment groups. Randomisation was separate

for males and females and was designated by a computer programme and effected by the use of sealed envelopes defining the treatment group. Each patient received 6 weekly treatments and was followed-up for a period of 24 weeks after the completion of therapy. Headache diaries were completed throughout the pretreatment, treatment and follow-up period (Fig. 10.3 and Appendix 10.7).

Figure 10.3

Daily assessment form

Please complete the form at the same time every day for the whole fourteen weeks of the trial. Bring completed forms with you each time you attend.

For each day mark the appropriate box for severity of pain as follows:

0 = no headache
1 = very mild headache
2 = mild headache
3 = not very severe headache
4 = quite severe headache
5 = very severe headache
6 = almost unbearable headache

Please score your AVERAGE severity of headache for that day. If this is not possible record two scores on the 6 point scale provided (one for the lowest level of pain experienced and one for the highest level of pain experienced).

Then mark the line with a cross to indicate the duration of the headache for that day (0 to 24 hours). Do not include the time that you were asleep.

Make a note of any drugs or tablets taken (the name of the tablet and the number taken that day).

Tick the appropriate box if you experience a one-sided headache, nausea and/or vomiting and associated visual disturbance.

FOR EXAMPLE: For a mild headache, in which you vomited, and lasted 5 hours, and for which you took two disprin, the form should be marked as follows:-

Severity:

0	1	2✓	3	4	5	6

Duration:

Drugs taken: Disprin 2

Vomiting and/or nausea ☑ one-sided headache ☐ associated visual disturbance

The placebo treatment used was mock TNS, the methodology for this has already been clearly outlined.

In the acupuncture group body acupuncture was used for all patients; acupuncture points were selected depending on the type and distribution of pain. The method of point selection was as described by Lewith and Lewith (1979). The relevant points were located as described in an Outline of Chinese Acupuncture (Anon 1975). The needles were inserted and left in situ for about 10 min, during this time needling sensation was obtained and no electrical stimulation was given (Lewith and Lewith, 1979). If after 2 or 3 treatment sessions no symptomatic improvement occurred the acupuncture points used were changed in accordance with the method of point selection referred to previously.

Assessment of the effects of therapy was based on the headache diary; the pain scale used had previously been validated in a large epidemiological study of headache (Newland et al, 1978). Patients were asked to record the major accompanying symptoms so that the investigators could define the presence of absence of a migrainous headache. Analgesic requirement and duration of headache were also recorded in order to assess treatment efficacy.

Statistical methods for the headache study

Pain relief has been defined as being effective by Melzack (1975) if a 33% benefit is achieved, and by Beecher (1955) if 50% benefit is achieved. For the purposes of this trial effective pain relief was defined using both these criteria. The percentage levels here quoted are relative to the patient's pretreatment scores. The trial size was determined to demonstrate with 80% power and one-sided test size of 5%, a difference between the anticipated 35% placebo, 70% acupuncture responses at the end

of treatment using Melzack's definition of benefit.

Analysis was carried out for both severity and frequency of headaches.

Formal statistical comparisons between treatment groups proceeded in 3 ways:

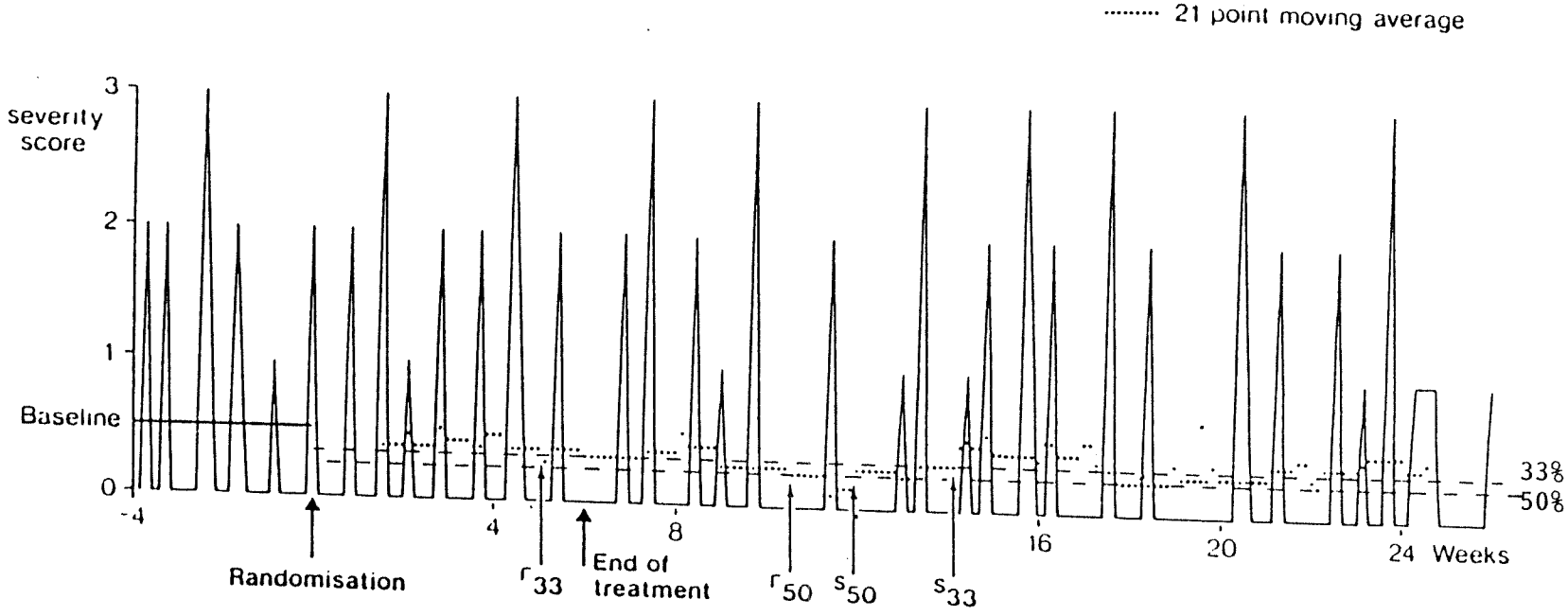
1. The number of patients experiencing 33% and 50% pain relief at the end of therapy was calculated from the average pain over the 4 weeks centred round 8 weeks post randomisation.
2. The time (days) from randomisation to achieve 33% and 50% pain relief.
3. The duration (days) of 33% and 50% pain relief.

Methods 2 and 3 used in calculating benefit are illustrated in Fig. 10.2 which describes a patient's headache diary over the whole trial period. For each patient the average score obtained from their diaries was calculated for the 4 weeks prior to treatment. This figure was regarded as the baseline from which further comparisons were made; 33% and 50% improvement in pain severity from the baseline was then calculated. It is quite clear that patient scores fluctuate daily and consequently that pain relief recorded may only be transitory. Therefore a 21-point moving average of the post-randomisation data was calculated for each patient. Successful treatment was then achieved only if the moving average crossed the lines of 33% and 50% improvement.

The times to 33% and 50% pain relief are shown as r_{33} and r_{50} in Fig. 10.4 and are read from the intersection of the moving average with the parallel lines running at 33 and 50% of the baseline. However, as in Fig. 10.4, even though the moving average has moved below the 33% line, there are shorttransitions back above that line although the patient subsequently goes on to achieve 50% relief. The number of days of such transitions is

Figure 10.4

Patient's pain severity profile over the trial period.



denoted d. The total number of days of pain relief can then be calculated. Once pain relief has been achieved the intersection of the moving average and the return to 50% and 33% relief levels are indicated by s_{50} and s_{33}. Once these figures are determined the period of at least 33% pain relief is defined as $t_{33} = s_{33} - r_{33} - d$ and for at least 50% pain relief as $t_{50} = s_{50} - r_{50}$ (in days). These were then calculated for each patient. For the patient in Fig. 12.3, $r_{33} = 36$, $r_{50} = 74$, $d = 16$, $s_{50} = 84$. $s_{33} = 99$ and $t_{50} = 10$, $t_{33} = 47$. For some patients return to defined minimal benefit levels did not occur during the follow up period, ie. they achieved and maintained a satisfactory level of relief throughout the period of the trial. In such instances censored values were recorded for the corresponding values. Survival curve analysis was used to compare times to achieve and duration of pain relief between the two treatment groups (Peto et al, 1976; Peto et al, 1977; Lewith and Machin, 1983).

At the protocol stage it appeared sensible to differentiate between headache and migraine. However different types of headache appeared to respond in the same way to the treatments used and so no attempt was made to differentiate between simple and migrainous headache in our analysis.

TMC Joint OA: detailed methodology

This study was carried out at two centre, Queen Alexandra Hospital, Portsmouth and Southampton General Hospital. Patients with a diagnosis of TMC joint OA were entered into the trial. Patients were drawn from those referred from the rheumatology to physiotherapy departments of Queen Alexandra Hospital, Portsmouth and Southampton General Hospital respectively. They were entered if there was a clinical diagnosis of TMC joint OA based upon joint tenderness, pain on movement, crepitus and pinch grip pain. There also had to be radiological confirmation of the

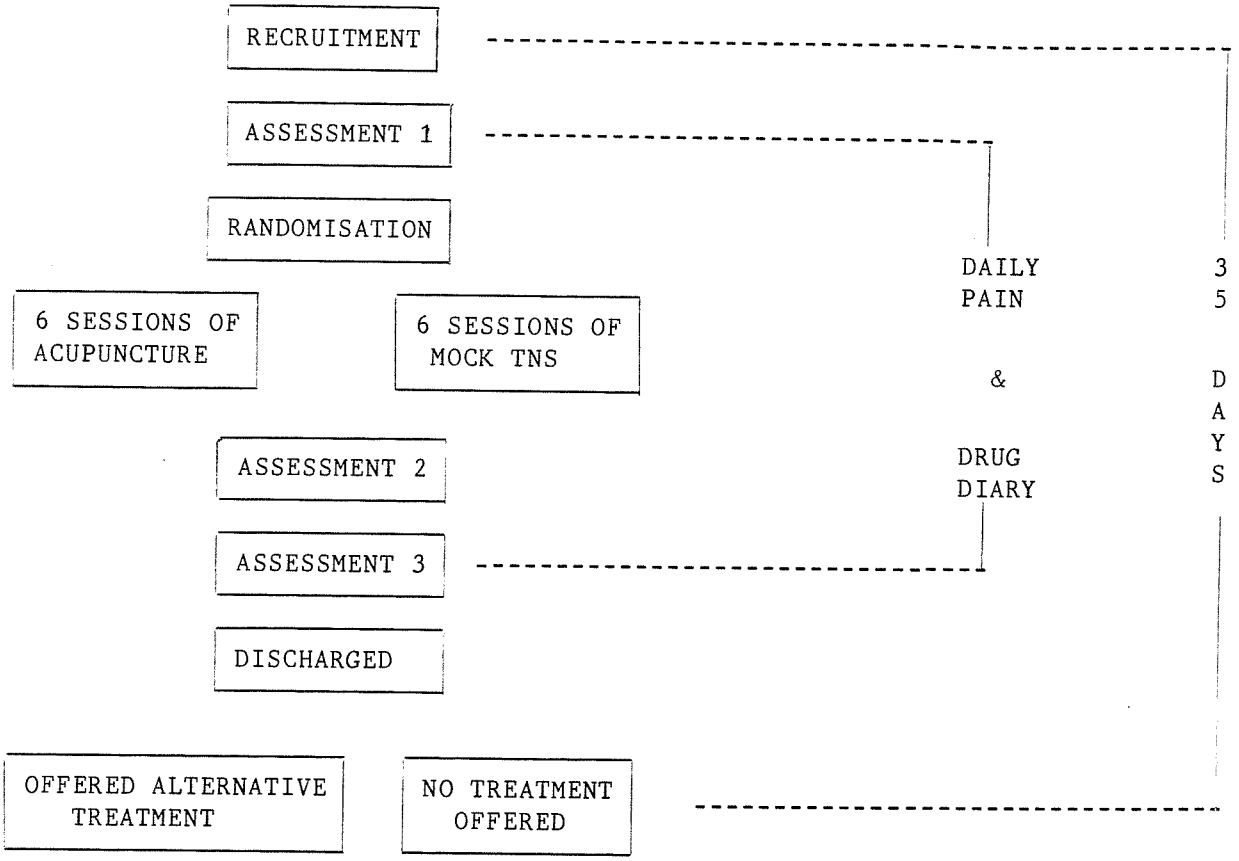
diagnosis. In order to aid assessment the TMC joint had to be the only site of chronic pain. Patients were excluded if they had previous operative intervention or previous fracture involving the thumb, they had previous TNS treatment or acupuncture, if within the last 6 months they had received corticosteroid therapy and if they were pregnant.

The treatment protocol involved the patient keeping a daily diary assessing both pain (based on a visual analogue scale and a verbal scale) and drug intake throughout the trial (Appendix 10.8, 10.9 and 10.10). The patients were entered and assessed, keeping their diaries for one week prior to the initiation of treatment. They were then randomised and given 6 treatments of either acupuncture of mock TNS over a 2 week period. They were then asssessed at the end of treatment and again at 2 weeks after treatment had been completed.

See flow chart (Fig. 10.5)

Figure 10.5

Flow chart: Summary of procedure



Randomisation was stratified by centre but not for age, sex or any other variable.

Pain is a notoriously difficult phenomenon to assess objectively (Huskisson 1974). In this study an attempt was made to reach some more objective evaluation of pain and joint movement. As well as keeping a daily pain and drug intake diary, all assessments included an objective measurement of joint tenderness and pinch grip strength. The three assessments also included a functional assessment as well as some idea of sleep disturbance, and overall verbal assessment as to whether some had improved as compared to pre-treatment levels of dysfunction and pain.

The measurement of joint tenderness occurred with a Penny and Giles myometer (model D601007, range 0-30 kgf). Although originally designed for the measurement of muscle function, a previous study had revealed that the myometer could be used for testing pain threshold as an indication of joint tenderness (Ali 1984). A standard procedure was used. This was taught by one of the physiotherapists in each department and used on the patients at each assessment. The physiotherapists carrying out this assessment were blind to the treatment procedure. The procedure involved keeping the wrist in neutral extension, midway between pronation and supernation. The myometer head was placed at the base of the first metacarpal on its radial aspect and directed towards the head of the fifth metacarpal. Pressure was then slowly applied having asked the patient to indicate immediately when the pressure became pain. At this point the pressure was released and the force (kgf) recorded by the assessor, but kept from the patient. When the assessors were being taught how to use the myometer, it rapidly became apparent that repeated measurement actually caused pain. Therefore only one myometer measurement was taken at each

assessment.

A pinch grip meter was used to measure the amount of force applied between the thumb and index finger when they were pinched together. The assessors received a standard instruction from the investigators and were able to practise the use of this pinch grip meter prior to the beginning of the trial. The patients were not able to observe the dial that provided the results from the equipment and only one measurement was taken at each assessment to avoid muscle fatigue.

A questionnaire looking at hand function was also used. This assessed the difficulty of functions such as doing up buttons, doing up shoe laces, writing, handling money or taps and unscrewing lids or using tin openers. These activities were graded as easy, difficult and impossible. The questionnaire was designed specifically for this study and piloted on a number of patients in Southampton General Physiotherapy Department prior to being used in the study.

Sleep disturbance due to thumb pain for the preceding week was reported at each assessment. This was graded as none, mild or severe. Finally, the patients were asked to provide a global evaluation of whether they felt their thumb pain had improved between each assessment; this was graded as worse, no improvement or better.

The procedures involving mock TNS and acupuncture have already been clearly described. On this occasion, a Spembly Pulsar TNS machine was used to provide the mock TNS. The machine, although slightly different in design, is fundamentally the same as a RDG Tiger Pulse. It has an amplitude and frequency button, with a flashing light, indicating the adjustment on the frequency button. It has a single output jack plug, and contact between the machine and patient was broken by disconnecting the wires at the output

jack plug.

TMC joint OA is usually treated by the use of local tender points. Therefore between 3 and 5 needles were inserted into the local tender points in and around the TMC joint until needling sensation was obtained. The needles were left in situ for 15 minutes and then withdrawn.

Both treatment procedures were carried out by the investigator (Wendy Dickens). The assessments were carried out either by the patient or by independent assessors within each of the physiotherapy departments.

The objective of the study was to demonstrate that acupuncture could provide pain relief and functional improvement for TMC joint OA as compared with placebo. In this study a combination of subjective and objective measurements were used in an attempt to produce a more valid assessment system. It was hoped that the subjective measurements of pain such as visual analogue scales would correlate closely with objective measurements such as myometric joint tenderness and pinch grip.

The study was designed so that 30 patients would be entered into each arm of the trial. It was assumed that the placebo would help 30% of those entered while real acupuncture would help 70%. If these assumptions were correct then a total trial size of 60 patients would reach 5% statistical significance with a power of 85%.

RESULTS

The results pertaining to each study are presented at the end of each section in tabular form. For the purposes of this thesis, the post-herpetic neuralgia study will be dealt with as Study A, the study on headache as Study B and the study of TMC joint OA as Study C.

Post-Herpetic Neuralgia

Sixty-two patients were entered into the study, 20 males and 42 females. Thirty received acupuncture and 32 received mock TNS. The characteristics of the two groups are shown in Table 10.1 and the distribution of the site of post-herpetic neuralgia in Table 10.2. Acupuncture patients were slightly older but other variables such as sex, dermatome affected and duration of the post-herpetic neuralgia were comparable.

Three patients were withdrawn from the trial: one because her doctor told her that she was receiving a placebo, although she had already received 5 treatments, another because the blind observer discovered which treatment the patient was receiving and a third patient dismantled the TNS stimulator and discovered that it was defunctioned. Unfortunately it was not possible to follow up all these 3 patients but where possible all those who failed to complete the protocol treatments have been included in the analysis of the results. Sixteen patients failed to complete their protocol treatment including two of those withdrawn - 13 in the acupuncture group and 3 in the mock TNS group. These patients were followed up and they are included in the results. The reasons for patients failing to complete the trial are summarised in Table 10.3.

In order to assess the effectiveness of treatment 4 indices were examined. These were the pain diaries, pain scores recorded by the blind observer at each attendance, sleep disturbance due to pain and analgesic intake.

Fifty out of a total of 60 patients were taking analgesics when entered into the study, the most frequently prescribed analgesic being paracetamol. There were many random fluctuations in analgesic intake and we were therefore unable to use this as an assessment of improvement in pain. There was good correlation between the weekly pain scores and the average daily pain score, but sleep disturbance scores were more variable than pain scores (although those noting an improvement in pain also noted a reduction in sleep disturbance due to pain).

Beecher (1955) has suggested that a 30% improvement in pain should be considered as the basis for a successful treatment in chronic painful conditions. We therefore chose a 2 point improvement in our 7 point pain scale as the basis for significant improvement in pain. Initial pre-treatment scores were compared with the score at the end of treatment and at the end of follow-up. This 2/7th or approximately 30% improvement was chosen arbitrarily to represent a significant improvement in pain. Table 10.4 shows patients with a 2 point change in pain score in the acupuncture group and mock TNS group, both at the end of treatment and at the end of follow-up. There was no significant difference between the two treatments at either assessment ($x^2 = 0.02$, df = 1, P = 0.9). A detailed study of the pain diaries and the independent assessors record suggested that it was impossible to differentiate between the two treatments at any stage during the study and, therefore, acupuncture could not be considered as an effective treatment for post-herpetic neuralgia, in the context of this study.

TABLE **10.1**

THE AGE, SEX, TREATMENT GROUP AND DURATION OF POST-HERPETIC NEURALGIA IN THE 62 PATIENTS ENTERED INTO THIS STUDY

Treatment group	Sex	Number of patients	Mean age (years)	Median duration of post-herpetic neuralgia (months on entry)	Patients with post-herpetic neuralgia for less than 1 year on entry
Acupuncture	M	10	69.8 (59-76)	19.6 (3-180)	4
Acupuncture	F	20	76.4 (72-83)	14.1 (3-153)	10
Mock TNS	M	10	62.4 (49-84)	27.0 (7-77)	3
Mock TNS	F	22	73.6 (58-87)	11.5 (4-348)	11

TABLE 10.2

DISTRIBUTION OF POST-HERPETIC NEURALGIA (IN THE TWO TREATMENT GROUPS) BY SITE

Site	Acupuncture	Mock TNS
Vth nerve	8	10
Cervical	1	5
Thoracic	18	15
Lumbo-sacral	3	2

TABLE 10.3

REASONS FOR FAILURE TO COMPLETE PROTOCOL TREATMENT (AT LEAST 5 TREATMENTS GIVEN) POST-HERPETIC NEURALGIA STUDY

Thirty patients were entered into the acupuncture group and 17 patients completed treatment. Thirty-two patients were entered into the mock TNS group and 29 patients completed treatment.

Treatment	Sex	Number of patients	Reason
Acupuncture	M	1	Intercurrent illness.
	M	2	Therapy made them worse.
	F	3	Intercurrent illness or hospital admission.
	F	3	Therapy made them worse.
	F	2	Unable to attend.
	F	1	Completely well.
	F	1	Protocol broken: withdrawn.
Mock TNS	M	1	Discovered he was receiving ineffective treatment.
	F	2	Worried that electrical stimulation had worsened the condition.

TABLE 10.4

PATIENTS OBTAINING A 2 POINT CHANGE IN PAIN SCORE
POST-HERPETIC NEURALGIA STUDY

Treatment group and number of patients entered	Better (worse) at the end of treatment	Better (worse) at the end of follow-up
Acupuncture (30)	7 (0)	5 (0)
Mock TNS (32)	7 (1)	9[a] (4)

[a] These include 4 of the 7 who were better at the end of treatment and 5 others who improved later.

Headache

Forty-eight patients were entered into this study. All patients entered completed their pain diaries during the pre-treatment period and then went on to receive their treatment. However, 4 patients in the mock TNS group and 5 patients in the acupuncture group failed to complete follow-up. The demographic information comparing the two treatment groups is shown in Table 10.5. It is apparent that both groups are broadly similar other than for the fact that the acupuncture group appears to be suffering from more frequent headaches than those receiving mock TNS.

Severity

Table 10.6 shows the number of patients achieving significant pain relief during the 4 weeks following completion of therapy. At 33% pain relief the placebo response was 30% and the acupuncture 56% (x^2 = 3.18, df = 1, P = 0.08). Comparable figures of 50% pain relief were 26 and 32% (x^2 = 0.201, df = 1, P = 0.65).

Survival curves for the attainment of 33% pain relief in severity were calculated; there appeared to be little benefit to acupuncture over mock TNS in obtaining relief (log-rank x^2 = 0.05, df = 1, P = 0.82) neither is there any difference in duration of benefit (log-rank x^2 = 0.21, df = 1, P = 0.65). Similar results hold for 50% relief and corresponding duration.

Frequency

Table 10.7 shows the number of patients achieving significant reduction in frequency of headaches during the 4 weeks following completion of therapy. At 33% required reduction the placebo response was 57% and the acupuncture was 24%. Comparable figures of 50% frequency reduction were 32 and 26%. No comparisons using life table methods achieved formal statistical analysis.

Discussion

Those patients receiving mock TNS appear to be similar in age, sex and headache severity to those receiving acupuncture. Therefore, we would have expected to establish a statistically significant result if the treatment difference between acupuncture and placebo was of the order of magnitude anticipated at the design stage. These assumptions were based on our clinical experience and the published results of a previous partial cross-over trial (Jensen et al, 1979). The placebo response in headache is high. Almost all the patients entered demonstrated a 33% improvement in their pain and the period of 33% improvement was virtually the same for both treatment groups. However the numbers entered into this study are small and we have analysed those suffering from simple headaches and migrainous headaches together. It is possible that a larger study with a separate analysis for specific types of headache might reveal that acupuncture is successful in some instances, but not in others.

The most optimistic interpretation of our study indicates that at best there is only a 20% difference between acupuncture and placebo in the treatment of headache (although 95% confidence limits for the difference are -3% -53%). Such results come from the comparison between groups measured as the average of the 4 weeks immediately following the 6 week therapy period. No such advantage appeared using survival analysis. This suggested that the method of defining treatment efficacy is of fundamental importance and one that must be addressed at the planning stage of trials. The effects we have observed in this study are clearly transitory.

Two patients in the acupuncture group were taking a maintenance therapy, one was receiving clonidine (Dixarit) and the other pizotifen (Sanomigran). Those who obtained clear benefit from treatment in both treatment groups

noted a simultaneous 70% mean decrease in analgesic consumption. The exact type or extent of analgesic requirement at entry to the study did not provide any prognostic indication about the subsequent success or failure of therapy. In this study a decrease in analgesic intake invariably went hand in hand with a decrease in pain score. It, therefore, appears that in conditions which are likely to respond effectively to simple analgesics, analgesic intake could be used as a measure of the success or failure of a physical treatment such as acupuncture. However we did not attempt to equate the relative analgesic properties of different medications.

TABLE 10.5

AGE, SEX, BASELINE SEVERITY AND MEDICATION BY TREATMENT GROUP OF THE 48 PATIENTS ENTERED IN STUDY - HEADACHE STUDY

	Acupuncture	Mock TNS
Number entered		
Male	3	5
Female	22	18
Total	25	23
Mean age (years)	39 (14-62)	42 (20-68)
Baseline severity during pretreatment period	31	22
Baseline mean number of headaches during pretreatment period	11	8
Medication		
None	4	6
Simple analgesics	21	17
Maintenance therapy	2	0
Ergotamine	1	0

TABLE 10.6

PATIENT RESPONSE IN THE 4 WEEKS POST THERAPY (SEVERITY) - HEADACHE STUDY

Treatment group	33% pain relief			50% pain relief		
	Success	Failure	Success (%)	Success	Failure	Success (%)
Acupuncture	14	11 (5)	56	8	17 (5)	32
Mock TNS	7	16 (4)	30	6	17 (4)	26

TABLE 10.7

PATIENT RESPONSE IN THE 4 WEEKS POST THERAPY (FREQUENCY) - HEADACHE STUDY

Treatment group	33% pain relief			50% pain relief		
	Success	Failure	Success (%)	Success	Failure	Success (%)
Acupuncture	11	14	44	8	17	32
Mock TNS	13	10	57	6	17	26

TMC Joint OA

Patient population was recruited from Queen Alexandra Hospital, Portsmouth and Southampton General Hospital. Thirteen patients were recruited and 12 completed the trial, 7 were female and 5 male. Table 10.8 summarizes the demography of those entered into the study.

One mock TNS patient experienced pain in his untreated hand during treatment. He was concerned despite reassurance and was therefore discharged from the study. Seven patients received acupuncture and 5 mock TNS. The two treatment groups were comparable for age, sex and duration of symptoms. Therefore differences in outcome could reasonably be assumed to be due to a treatment effect.

In assessing pain the 5 weeks of visual analogue scales were divided up into 3 sections. The week prior to treatment, the week of baseline measurement, is denoted by A. The second week of treatment is denoted by B and the second week of follow-up by C. The visual analogue scores for these 3 weeks were divided by 7 and then compared. The group results were analysed using the Wilcoxon Test for non-parametric statistics. See Tables 10.9, 10.10 and 10.11.

This revealed that the acupuncture patients experienced a significant pain reduction between periods A and B $p = 0.02$ (95% Cl - 76.14, -32.77) and A and C $p = 0.04$ (95% Cl - 90.54, -28.37). In the mock TNS group these changes were not significant $p = 0.10$ (Cl 95% - 8.01, 0.00) and $p = 0.06$ (95% Cl - 8.01, 0.00) respectively.

The percentage pain reduction between periods A and C in the acupuncture group was 76.10% and the mock TNS group 20.01%. However despite this large actual difference, with the small patient population statistical significance at the 5% level was not achieved $p = 1.0$ (Cl 95% - 69, 28).

Patients were asked to give a global impression of their improvement at assessments 2 and 3. 85.7% of the acupuncture patients and 40% of the mock TNS patients reported improvement. These data were analysed using a two by two contingency table and a Fisher's test. However, even with a small patient population this large difference between treatment groups was not statistically significant at the 5% level ($p = 0.15$, 1 d.f.).

Functional improvement occurred in all 7 acupuncture patients and 3 of the mock TNS patients. The 2 remaining mock TNS patients reported no change. An analysis of within group changes (see Table 10.12) revealed that the only significant improvement occurred in the acupuncture group between assessments 1 and 3 $p = 0.02$ (CI 95% 1, 7). However, between group differences were not statistically significant at the 5% level for any of the comparisons (Table 10.12).

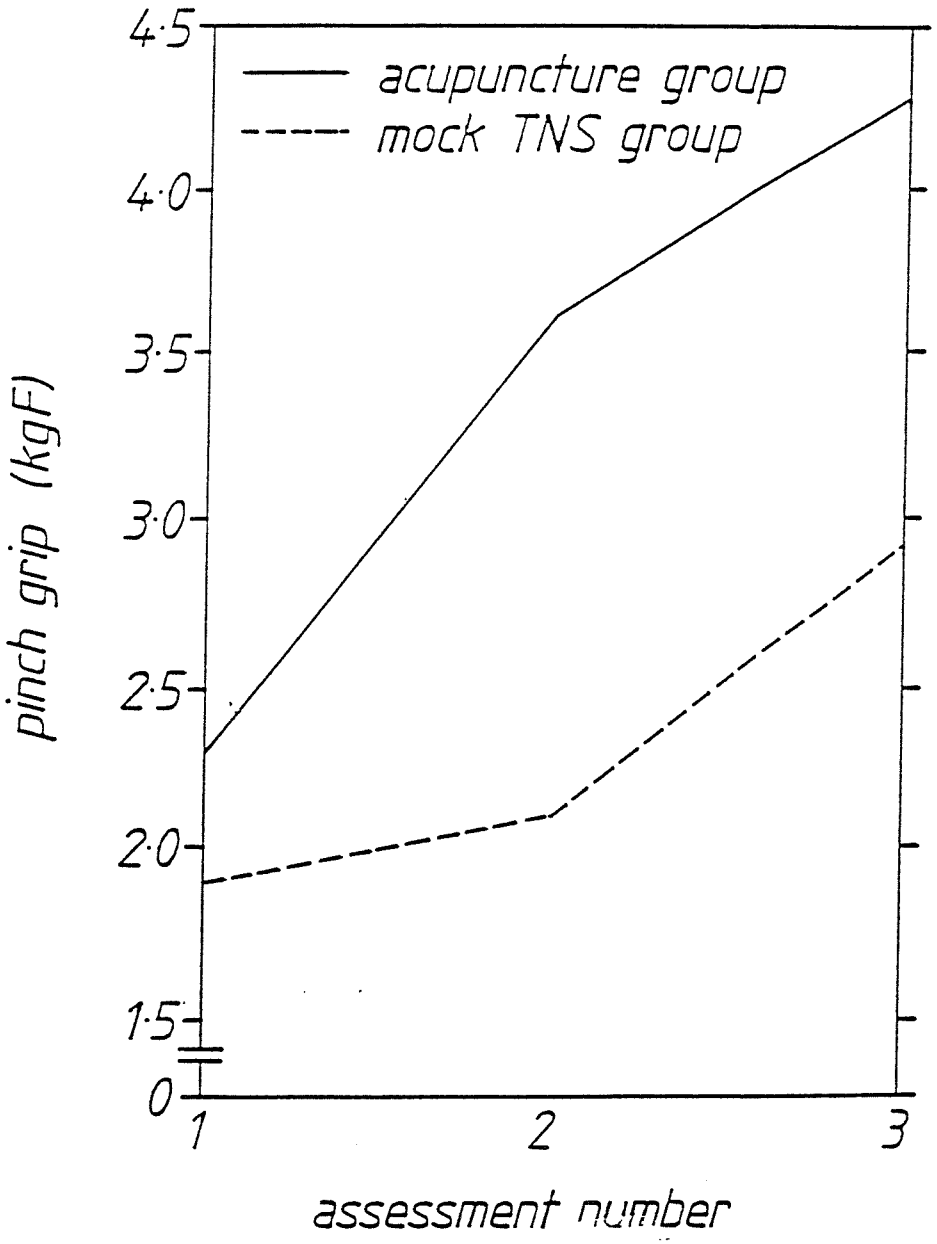
Drug intake was difficult to monitor. Only 7 patients were taking drugs prior to the trial, 3 in the acupuncture group and 4 in the mock TNS group. Of these, 1 of the acupuncture patients and 2 of the mock TNS patients were drug-free after treatment. The remaining 4 had maintained their intake. Because of the very small numbers it was difficult to draw any conclusions from this observation.

Only 2 patients reported any sleep disturbance as a result of their thumb pain. Both received acupuncture and reported no sleep disturbance at the final assessment. Again, numbers in this group are too small to drawn any valid conclusions.

This study was the only one of the three to attempt the use of objective measures to evaluate pain. Figure 10.6 shows the change in pinch grip for both the acupuncture and the mock TNS group. While the acupuncture group demonstrates a greater improvement than the mock TNS group, both show

improvement and there is no statistical difference between the groups.

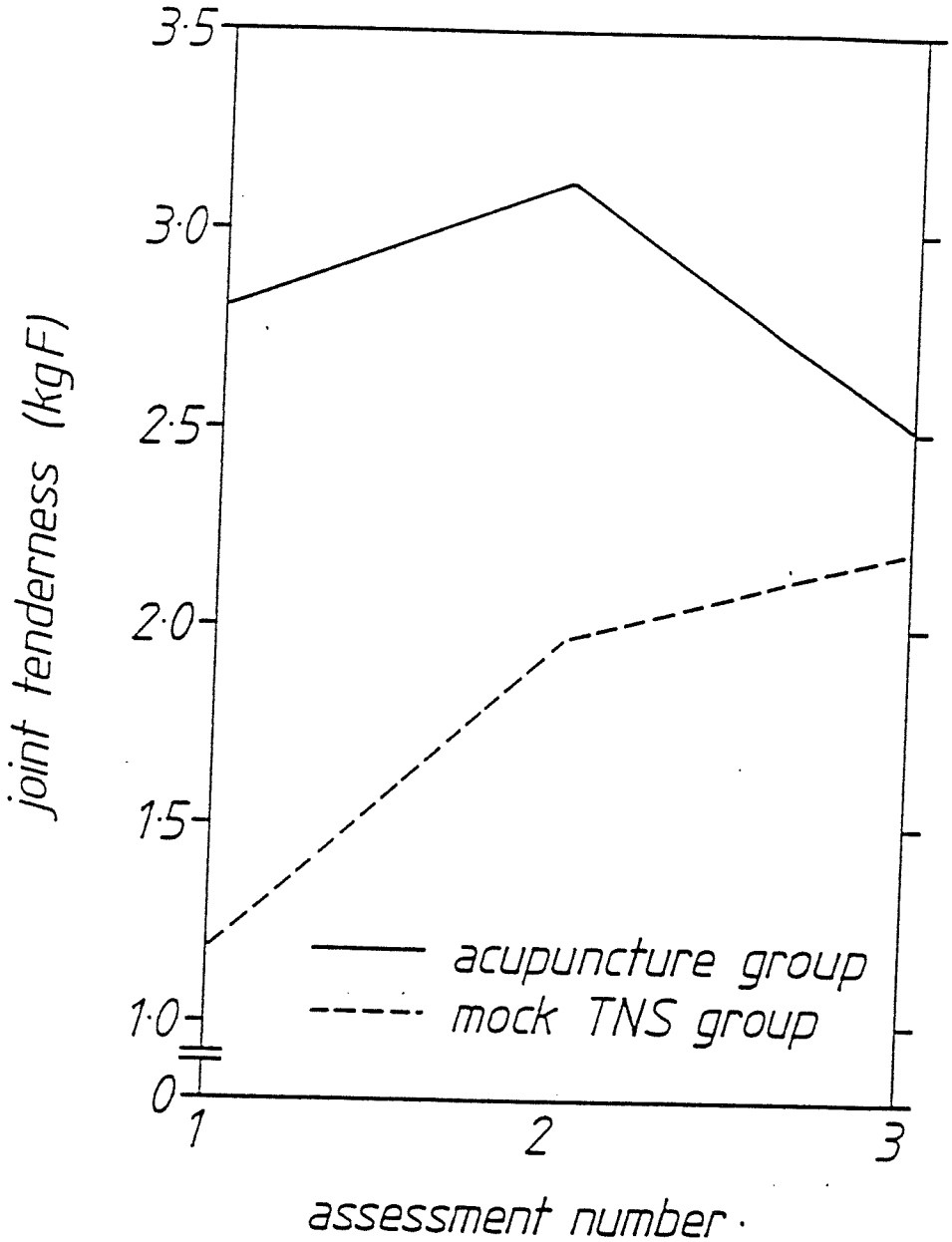
Figure 10.6 **Median pinch grip scores for each treatment group at each assessment**



Assessment 1 = baseline, 2 = end of treatment, 3 = follow up.

Figure 10.7 shows change in joint tenderness. Again both groups demonstrated an improvement in joint tenderness during treatment, but it is interesting to note that the acupuncture group had no overall improvement in joint tenderness when comparing assessments 1-3. Again no statistically significant difference existed between these two groups with respect to joint tenderness.

Figure 10.7 **Median joint tenderness scores for each treatment at each assessment**



Assessment 1 = baseline, 2 = end of treatment, 3 = follow up

TABLE 10.8

SUMMARY OF THE PATIENT POPULATION - OA STUDY

	Acupuncture	Mock TNS	Total
Women	4	3	7
Men	3	2	5
Q.A.H.	4	4	8
S.G.H.	3	1	4
Age range	44-77 years	52-69 years	48-77
Mean age	59 (SD 8.91)	59.2 (SD 6.46)	
Duration of pain	1-5 years	2-5 years	
Mean	3.2 (SD 1.68)	3.2 (SD 1.3)	

NB. Numbers in brackets are standard deviations.

TABLE 10.9

ACUPUNCTURE GROUP - OA STUDY

Periods compared	Median	Wilcoxon test results
A and B	-69.22	p=0.02 (95% CI -76.14, -32.77)*
A and C	-76.10	p=0.04 (95% CI -90.54, -28.37)*
B and C	-10.00	p=0.27 (95% CI -24.16, 12.77)

- Denotes pain reduction.

* Denotes result significant at the 5% level.

TABLE 10.10

MOCK TNS GROUP - OA STUDY

Periods compared	Median	Wilcoxon test results
A and B	-73.00	p=0.10 (95% CI - 8.01, 0.00)
A and C	-20.00	p=0.06 (95% CI -90.16, -2.39)
B and C	1.70	p=0.59 (95% CI -17.11, 60.00)

- Denotes pain reduction.

* Denotes result significant at the 5% level.

TABLE 10.11

WITHIN GROUP ANALYSIS OF CHANGES IN FUNCTIONAL SCORES - OA STUDY

Assessment comparison	Wilcoxon test results	
	Acupuncture group Median p-value 95% CI	Mock TNS grou Median p-value 95% CI
1 and 2	1 p=0.09 (0, 6)	2 p=0.10 (0, 7)
1 and 3	2 p=0.02 (1, 7)*	1 p=0.10 (0, 7)
2 and 3	1 p=0.10 (0, 2.5)	0 p=1.00 (-, 0)

- Denotes pain reduction.

* Denotes result significant at the 5% level.

TABLE 10.12

WITHIN GROUP ANALYSIS OF CHANGES IN FUNCTIONAL SCORES - OA STUDY

Assessment comparison	Wilcoxon test results					
	Acupuncture group			Mock TNS group		
	Median	p-value	95% CI	Median	p-value	95% CI
1 and 2	1	p=0.09	(0, 6)	2	p=0.10	(0, 7)
1 and 3	2	p=0.02	(1, 7)*	1	p=0.10	(0, 7)
2 and 3	1	p=0.10	(0, 2.5)	0	p=1.00	(-1, 0)

* Denotes a result significant at the 5% level.

DISCUSSION

For the purposes of the discussion the post-herpetic neuralgia study will be referred to as Study A, the headache study as Study B and the study on TMC joint OA as Study C.

Does acupuncture work?

All three studies were initially designed to have an 85% power and demonstrate a therapeutic difference of between 35-40% when comparing acupuncture with placebo. It is quite clear from the results that such therapeutic differences were not obtained in Studies A and B. Unfortunately Study C had too few patients entered, but the preliminary results suggest that a substantial analgesic effect is produced by acupuncture in OA of the TMC joint.

The only factor recognised to reduce the duration of post-herpetic neuralgia is involvement of dermatomes other than trigeminal Hope-Simpson, 1975). There is some disagreement about whether duration is related to age (De Moregas & Kierland, 1957; Hope-Simpson, 1975), and very little evidence on whether it is related to sex. However apart from the age where there was a slight difference, factors such as sex and dermatome affected were equally distributed between the two treatment groups. Patients with known malignancy or receiving immunosuppressive agents were excluded from the study. If acupuncture is an effective analgesic for post-herpetic neuralgia we should expect some differences in outcome between the treatment groups to have been demonstrated by this study. We expected a placebo response of about 30%. In fact in both groups the number of patients improved at the end of treatment was of this order, ie. a 30% (placebo) response. Consequently it is likely that acupuncture has

no clinically significant effect (within the context of this study) in alleviating the pain caused by post-herpetic neuralgia. In view of the epidemiology of post-herpetic neuralgia, this study involved a group of patients who were highly likely to be resistant to any form of treatment. Post-herpetic neuralgia resolves spontaneously with time (Hope-Simpson, 1975 and Ragozzino, 1982). Consequently, it could be argued that while the post-herpetic neuralgia study provided an effective vehicle for developing trial methodology, it may well be that the particular painful illness chosen for this study would have been one that was most unlikely to respond to any form of therapy. Indeed, the review by Robertson and George (1990) would support this view; many treatments have been tried for post-herpetic neuralgia and all have been found wanting, particularly when attempting to manage resistant long-term intractable post-herpetic pain. Thirteen out of the 30 patients in the acupuncture group and 3 out of the 32 patients in the mock TNS group failed to complete protocol therapy. This may be because auricular acupuncture is a painful and unpleasant treatment and therefore not acceptable to patients, particularly if it fails to produce swift, clear and dramatic results.

Auricular acupuncture is currently being used on a widespread basis in both Europe and the U.S.A. There has been only one attempt so far to validate its use in a scientific manner (Oleson et al, 1980), and this study did demonstrate that the presence of an homunculus on the ear is probably correct. It could be argued that the reason why acupuncture failed to provide an effective analgesia was because auricular acupuncture is an ineffective therapy. However 24 out of the 30 patients in the acupuncture group (17 who completed protocol treatment and 7 who did not) also received body acupuncture. Therefore, it is probable that it is acupuncture,

rather than a specific acupuncture technique, that is ineffective in this situation.

Although the initial expectation was that headache would show a much better response to acupuncture, the results of Study B suggest differently. The first controlled trial in this area published by Jensen et al (1977) has not only be questioned by Study B, but also by subsequent studies such as that by Vincent (1990). Headache almost certainly has a very high placebo response in relation to almost all treatments, and it is therefore likely that some of the initial enthusiasm for the use of acupuncture in headache was based on descriptive studies. Here the enthusiasm of both the therapist and the patient almost certainly has a larger part to play than in controlled trials. The evidence from controlled trials recently reviewed by Vincent (Vincent 1993) supports the argument that acupuncture is probably not particularly effective in the management of headache, migraine-like headache and classical migraine. From the controlled trial evidence available it is likely that a 20% treatment benefit over placebo is a more realistic assessment of acupuncture's efficacy in this situation. Further studies on headache should therefore be designed with this assumption in mind, rather than the 35 or 40% treatment differences which had been assumed at the outset of this study.

Study C provides some encouraging evidence to support the use of acupuncture as a method of pain relief. However, too few patients were entered into this study in order to be able to disprove the null hypothesis. Study C was carried out as part of an MSc in rehabilitation, and so consequently there was a very limited period of time in which to enter patients, treat them and follow them up. The study occurred during the summer months and therefore the two physiotherapy departments at the

Royal South Hants and Queen Alexandra, Portsmouth were not operating at full capacity. Furthermore, they were unlikely to receive large numbers of patients complaining of osteoarthritis pain during a warm, dry summer. Study C can therefore be considered as a useful indicative or pilot project, where the results do indicate acupuncture is likely to be of substantial benefit. However, it cannot be considered a conclusive study in itself, even though it offered some useful suggestions and helped to further develop the trial methodology.

Pain assessment systems

All three studies involved assessing pain. At the outset it was quite clear that no attempt would be made to blind the therapist to treatment, but it was essential that all patients were "blinded" to treatment. The assessment of outcome also had to be blind to treatment. Several types of assessment systems have been used in these three studies.

Study A involved a combination of simple self-assessment diaries as well as a second doctor to aid with "blind" assessments. Huskisson (1974) has made the point that pain is fundamentally a subjective phenomenon which cannot be evaluated objectively. There are many self-assessment systems that can be used in order to evaluate pain and the use of a blind assessor in Study A did not add in a significant way to the accuracy of pain assessment. However, the blind assessor was able to "referee the protocol" and this certainly made the study more credible. Consequently, there was no possibility that the primary investigator, clearly enthusiastic about acupuncture, could persuade patients they were better or in any way subvert the protocol. Therefore a blind assessor had some value as a referee, but did not substantially improve the quality of pain assessment.

Two types of pain measurement systems were used in these three studies.

Studies A and B involved verbal pain scale systems. In Study B this system had been well validated by its previous and much repeated use in the evaluation of migraine (Newland et al, 1978). Waters (1974) had been using this 7 point scale to assess migraine in a large number of epidemiological studies carried out over the previous 15 years. Consequently, Study B was based on a clearly validated self-assessment system that had been used repeatedly.

Study A used the same verbal assessment scale as Study B. This assessment system had been used to evaluate pain in the descriptive clinic data collection carried out at the Aldermoor Health Centre and discussed previously (vide supra). The use of simple verbal scales to measure pain was first developed by Keele (1948) and the 7 point verbal scale used in Study A could therefore be seen as a direct progression from this. Two previous studies, one looking at mock TNS versus real TNS in the treatment of osteoarthritic pain (Smith and Lewith, 1983) and another looking at the effect of infra-red stimulation of local trigger points (Lewith and Machin, 1981) had used the 7 point verbal pain scale as the basis for blind assessment. It was found to be acceptable to both patients and investigators in both these instances.

However, the other equally widely used and simple method of pain evaluation is the visual analogue scale. This was first developed and espoused by Huskisson (1974) and has now become the most popular method of pain assessment in chronic painful conditions such as osteoarthritis. Consequently an attempt was made to compare and contrast these two systems of pain measurement in a clinical trial designed to evaluate TNS versus mock TNS for the treatment of low back pain. The study by Machin and Lewith (1988) describes the appropriate statistical methodology for

assessing the repeatability and relative merits of a visual analogue scale and a verbal descriptive pain scale as methods of pain measurement for use in randomised clinical trials.

Patients entered into this study received either TNS or mock TNS for the treatment of low back pain. During the study they completed 2 patient diaries, one involving a verbal scale and the other a visual analogue scale. Statistical comparisons were then made for each measurement and for the changes in that measurement, for each patient. When comparing the two methods of pain assessment, neither was regarded as necessarily giving the true value of the actual pain experienced by the patient. But, the aim of the study was to discover whether the two give answers that are comparable. Lewith and Machin (1988) were able to demonstrate that these two scales appear to be measuring different aspects of pain. Neither scale can be considered to be objective, but it seems that the visual analogue scales gave a "linear" pain measurement. This meant that a small improvement in pain resulted in a small change in the visual analogue scale. The verbal scales, on the other hand, tended to be more "bunched". This indicated to us that the 7 point verbal scale could not necessarily be divided mathematically into 7 equal parts. Different words indicated a different quality or perceived effect from the pain and so there was a "skewed" scoring system.

It could be argued that the verbal scale provides a more realistic method of pain assessment in that pain can in most individuals be tolerated until it gets to a point where it radically interferes with activity and quality of life. The visual analogue scale, however, is mathematically easier as progression from no pain to intense pain occurs in a predictable and linear manner.

Lewith and Machin concluded that in randomised trials designed to evaluate pain, both visual analogue and verbal scales should be used together rather than concentrating on one method of estimating pain relief. It appears that both scales provide slightly different measurements for the same phenomena, and it is impossible to decide which is the best or most objective when one is assessing fundamentally subjective phenomena such as pain. It is also important to note that while pain assessment does not represent one of the central themes of this thesis, it is an important area that has been considered in some detail by the author, in the context of developing better clinical trial methodology to evaluate the effects of acupuncture in painful conditions.

Complex pain assessment systems do exist and have been described previously. Probably one of the most widely used is the McGill Pain Questionnaire developed initially by Melzack in 1975 (Melzack 1975). The McGill Pain Questionnaire assesses pain in many dimensions, but unfortunately involves a questionnaire with 170 items and takes about 45 minutes to complete. For studies that require daily assessments of pain, particularly over prolonged periods (such as Study B) a complex multidimensional pain assessment system is impractical. Therefore, simple pain assessment systems such as VAS and VDS are the only approaches which are viable over prolonged periods of time and consequently their interpretation, relevance and validity need to be considered carefully.

Sleep disturbance due to pain was a method of assessment used in both studies A and C. In Study A sleep disturbance did not appear to follow any regular pattern. Sleep disturbance did not correlate with the pain diaries, and appeared to be altered by whether the patient was depressed or agitated rather than directly due to the pain they were experiencing. In

Study C sleep disturbance did appear to correlate with pain diaries, and the 2 patients who suffered sleep disturbance prior to treatment both reported overall improvement due to acupuncture and no sleep disturbance due to pain after they had received acupuncture treatment. Sleep disturbance due to pain was not particularly relevant in Study B, and was therefore not assessed. It appears that sleep disturbance due to pain may be a good subsidiary measure of improvement, providing it correlates with the general patterns of pain improvement obtained from the pain assessment system employed. However, in studies A and C it was not central to the assessment system, and in Study A was probably misleading. It has been suggested by some acupuncturists that as acupuncture is an endorphin mediated effect, improvement in sleep pattern is one of the first effects noted by acupuncturists when dealing with chronic osteoarthritic pain. However, the information gained from the straightforward pain assessments in studies A and C was a perfectly adequate basis upon which to draw conclusions about the treatment efficacy and so measures of sleep disturbance contributed little to the overall evaluation of treatment.

Analgesic intake is also considered to be an important criterion for evaluating the efficacy of alternative analgesic treatments such as acupuncture. In one study in which electroacupuncture was used for post-operative pain (Wigram and Lewith, 1986), analgesic intake in the immediate post-operative period was used as the most important end point with which to assess the efficacy of post-operative electroacupuncture. Here electroacupuncture was used to diminish post-operative pain, so if the patients required more analgesia than an untreated control group then clearly electroacupuncture could not be seen as an effective method for post-operative pain relief. Study B also demonstrated a clear diminution

in analgesic requirement (although not a statistically significant one) in those who claimed successful treatment with acupuncture. Study C also showed some diminution in analgesic intake after treatment, although again this was in no way significant as the numbers involved were so small. In Study C the primary investigator was a physiotherapist, and patients were clearly reluctant to reduce their prescribed analgesics on the recommendation of a physiotherapist even if they did appear to have less pain. In Study A analgesic intake appeared to bear no relationship to the pain diaries and, thus, became a questionable mechanism for evaluating the analgesic effects of acupuncture in this situation. It is probable that in conditions which respond to simple analgesics such as headache, post-operative pain and osteoarthritic pain, analgesic intake could be used as a measure to evaluate the success of physical treatments such as acupuncture. However, the more chronic the condition the less likely it is to respond to simple analgesics. So consequently, using analgesic intake as an assessment method for evaluating the effects of acupuncture on post-herpetic neuralgia proved unsuccessful. It is clearly important to monitor analgesic intake when studying painful conditions. However it is also important to interpret the results with caution, particularly in chronic intractable pain.

Objective evaluation

Studies A and C concentrated primarily on pain assessment as the primary end points. In Study C an attempt was made to introduce some degree of functional assessment along with objective measures such as pinch grip and joint tenderness. This was an attempt to make the evaluation of outcome more objective. The assessment of functional disturbance showed that all 7 acupuncture patients and 3 out of the 5 mock TNS patients recorded an

improvement. This was on the basis of a simple questionnaire and certainly produced statistically significant results in the acupuncture group. It could well have been that if the study had been larger the functional assessment would have allowed a useful extra category of evaluation that did appear to correlate quite closely with the verbal and visual analogue pain scales. The measurement of pinch grip and joint tenderness was disappointing. Both groups in Study C reported increase in pinch grip between the initial assessment and the assessment at the end of follow-up. The acupuncture group recorded a more rapid and substantial rise in pinch grip and this again correlated closely with pain assessment. Joint tenderness actually increased in the acupuncture group during the study period. This is difficult to explain as one would have expected joint tenderness to correlate quite closely with the pain scores. Perhaps patients were becoming increasingly sore because of needle insertion and if follow-up had been carried out over a more prolonged period, then a greater improvement in joint tenderness would have been noted perhaps a month or two after the completion of treatment. Therefore while Study C made some attempt to introduce a degree of objectivity into the evaluation system, this was by no means a completely successful attempt and further more detailed studies are required if objective measurements are to be used in evaluating pain. Ideally joint pain should be studied and the objective measurements should be closely tailored in some way, to the functional integrity of the joint.

Time base and follow-up

The period of pain assessment varied between each of the three studies. In Study A a very simple baseline week allowed for some assessment without any treatment. This was extended very considerably in Study B. Here one

of the selection criteria for entry into the study was that patients should experience at least 2 headaches a month, and therefore during the initial assessment period of 4 weeks they should experience at least 1 headache prior to randomisation and treatment. After treatment a very prolonged period of follow-up was instituted involving 6 months of daily pain diaries. It was pleasing that so many patients were able to complete this prolonged system of pain assessment as it enabled a very clear impression to emerge as to how acupuncture may affect headache over a prolonged period. Study C was very limited by its time base. Unfortunately, as patients had to be entered, treated and followed up over a short period, the third assessment could only occur 2 weeks after treatment had been finished. Ideally this assessment period should have been extended to 3 months and this, along with a larger number of patients entered into the study, would probably have produced the most significant, best designed study of the three. The principle that underlines these three studies is, however, important. It appeared essential to have a period of measurement without treatment, against which further improvements or deterioration could be compared. Randomisation should then occur after this baseline measurement period had been completed. The baseline measurement period obviously being relevant to the condition under investigation, hence one week would be adequate in studies A and C but not in study B. A period of treatment then follows and finally a period of follow-up during which assessment should continue. Again the period of follow-up should be relevant to the condition being studied and, while it was relevant in studies A and B, it was certainly artificially truncated in study C.

The Placebo

Two previous studies had already been completed demonstrating that the

placebo, mock TNS, appeared to produce an appropriate placebo response (Lewith and Machin, 1981; Smith and Lewith, 1983). If one adds to this the volume of evidence gained from these three clinical trials as well as that presented by Petrie and Hazleman in relation to the validity of the placebo in this context (vide supra) it seems reasonable to suggest that mock TNS is a valid placebo. It produces the expected placebo response in the majority of instances and appeared to be convincing to the patients entered into these three studies. Using mock TNS is not without its pitfalls and criticisms, as has been discussed in some detail previously. However there appears to be now a considerable body of evidence which supports and validates the use of mock TNS as a placebo control. As far as studies concerning acupuncture are concerned, this certainly represents a major step forward. There have been very few serious attempts to build a body of evidence that supports and substantiates the use of any placebo with which to compare acupuncture, and while the perfect placebo may not be a practical proposition, mock TNS certainly seems a reasonable approach to resolving some of these problems.

The Study Model

These three clinical trials do not necessarily demonstrate that acupuncture is an effective treatment for pain. In fact quite the reverse, they suggest that acupuncture is almost certainly ineffective for post-herpetic neuralgia and only marginally effective in the treatment of headache. It is probably effective in TMC joint OA, but because Study C has such limited patient numbers and therefore such limited power, such conclusions are purely speculative. Overall, a study model has been developed and refined in the process of these three studies. Assessment systems for pain have also been studied closely and information from these investigations have

helped in the construction of the three studies discussed. It was felt best not to include all the clinical trials, as by including too much information one inevitably detracts from the central theme of the thesis. However, where relevant and important the findings of these other studies have been included to support the overall development of the study and assessment models.

The studies show a clear development. Study A involved a very simple assessment system while Study B a more appropriate and prolonged assessment method. Study C incorporated the findings from some previous work by the author on pain scales and so both VAS and VDS were measured for patients who entered this study were also assessed separately. Unfortunately, the study size was too small to draw any detailed comparisons between the two scales. Nevertheless the studies do show a clear progression as far as assessment systems are concerned, lessons that can be passed on to all those attempting to evaluate treatments for chronic pain.

APPENDICES TO CHAPTER 10

APPENDIX 10.1

About Postherpetic Neuralgia

Thank you for taking part in this project. We are testing out a variety of treatments for the pain that occurs after shingles, this pain is called postherpetic neuralgia.

Postherpetic neuralgia is very difficult to treat with pills, so we are testing out the possibility of treating this pain with a variety of other methods. All these methods have been claimed to work, but we do not know which of them works best. It will be of great help to all the patients who come after you, and the doctors who treat them, if we can find out what the best treatment is for this disease.

Each person who enters this trial will receive one of two treatments. One treatment will be acupuncture, which involves the insertion of very fine needles into the skin. This is not a painful process. The other treatment being tested involves the use of pads on the skin which are attached to a small stimulator. This produces no abnormal sensation on the skin. Most people who suffer from postherpetic neuralgia take drugs to relieve the pain that is caused by this disease. You will be able to continue with these tablets for as long as you need them.

The doctors who are conducting this trial are Dr. J. Field and Dr. G. Lewith. If you have any problems or questions about the treatment that you are receiving then you can ask these doctors when you see them, or you can ring them at any time on Southampton 783111.

APPENDIX 10.2

Dear

During the last few years you visited the Aldermoor Health Centre about your headaches. Dr. Dowson and Dr. Lewith are planning to undertake a research project involving the treatment of headache by a method not using drugs.

It would appear from your medical records that at some time the possibility of your suffering from migraine has been considered, and in order to find out whether this treatment might be helpful to you, I would be grateful if you could spare a few moments of your time to complete the form below and return it in the stamped addressed envelope provided.

I would add that by completing this questionnaire there is no commitment to accept any form of treatment. Only those whose headache is of the type that can be helped will be contacted, and can then make the decision as to whether they wish to take part.

Yours sincerely,

HEADACHE QUESTIONNAIRE

Question 1. Do you now have headaches twice a month or more? Yes/No

Question 2. In association with these headaches do you suffer from:
a) nausea Yes/No
b) vomiting Yes/No
c) disturbance of vision Yes/No
d) is your headache mainly one-sided Yes/No

Question 3. Are you at present taking tablets for these headaches? Yes/No
If Yes what is the name of these .....

Question 4. Have you in the last six months received any other form of treatment for your headaches apart from tablets? Yes/No
If Yes what .....

Question 5. Would you be willing to attend the Aldermoor Health Centre on Friday afternoons to take part in this reesarch project? Yes/No

APPENDIX 10.3

MIGRAINE RESEARCH TRIAL

PATIENT'S INFORMATION SHEET

Aim of the trial

It has been known for some time that acupuncture, which involves the insertion of very fine needles at specific points on the skin, can be beneficial to migraine sufferers. We will be comparing this with an alternative treatment, also claimed to be effective in migraine, which involves the use of a small electrical stimulator instead of needles. This trial will evaluate the two alternative methods, by treating half the patients with one form of therapy and half the patient with the other. The decision as to which treatment you will receive will be entirely random (this is necessary for statistical reasons). If however the treatment you receive fails to produce any result you will be offered the alternative treatment at the end of the trial. Both treatments are completely painless.

Attendances

It is planned that you would attend for an initial discussion when you will receive this sheet of information together with other forms to be completed daily, and will then reattend in four weeks time for your first treatment. Treatments will then be weekly until you have received six treatments. The first follow-up visit will be four weeks after that, the second eight weeks after treatment and the third visit twelve weeks after treatment. Thereafter it is planned that you will continue to complete the daily assessment forms until six months has elapsed from the start of treatment and you will return the completed forms then. At that time if the treatment that you have received has not shown any benefit you will be offered the alternative treatment.

Daily diary

With this sheet you will be receiving four forms to be completed by yourself in the forthcoming four weeks. It is important that these are filled in daily, and at approximately the same time each day. Full instructions regarding the completion of these forms are attached with them. We would emphasis that the entire outcome of this research trial depends on your accurate completion of these forms, as it is impossible for a subjective symptom such as pain to be measured by anyone else but yourself. Please bring the completed forms back with you each time you attend.

APPENDIX 10.4

PATIENT HANDOUT FOR TRIAL ON TRAPEZIO-METACARPAL OSTEOARTHRITIS

We would like you to read the following information relating to arthritis at the base of the thumb.

We are running a trial to compare the effect on pain, tenderness and activity of two procedures when administered to this area.

You will only receive one procedure, those under examination are:-

1. Insertion of fine disposable needles into and around the painful joint at the base of your thumb. These remain in place for up to 15 minutes during which time they may be stimulated by the therapist by gentle twisting movements, to improve the effect.

The 'aching' type of sensation felt during this procedure disappears once the needles are removed or soon after this.

2. Application of small pads to the base of the thumb, which are attached to a small battery controlled electrical stimulator. These also remain in place for 15 minutes.

The frequency of electrical pulses given out from this machine is such that no abnormal sensation is felt.

If you join the trial, and have been prescribed tablets for your thumb, we would like you to continue to take them if and when you require them.

We would also like you to keep simple records of the number of tablets you take and your pain, on forms that will be provided. These records will be kept on a daily basis over the course of the trial (ie. 5 weeks).

There is a small possibility that your pain will be temporarily increased by the procedure you receive. There is also a possibility that the procedure may have no effect.

We would like you to consider this invitation to join our trial. If you decide not to join, or wish to withdraw at a later stage you are completely free to do so. (We would be interested to know your reasons for withdrawal.)

.../...

Appendix 10.4 (Continued)

Either course of action will not in any way affect other medical treatment you may require.

This trial is being carried out by Mrs. Wendy Dickens, a Chartered Physiotherapist. If you have any problems or queries about the procedure you will receive she can be asked at your appointment.

If you are unable to keep an appointment contact her at Queen Alexandra Hospital 379451 ext 2402 or Southampton General Hospital 777222 ext 3413.

If you have any other medical problems you should contact your G.P. as normal.

APPENDIX 10.5

COPY OF LETTER TO BE SENT TO G.P.

FOR TRIAL ON TRAPEZIOMETACARPAL OSTEOARTHRITIS

DATE ../../88

Dear Dr .....

M..... whom you referred to Queen Alexandra/ Southampton General Hospital regarding their trapezio-metacarpal joint, has agreed to participate in a clinical trial which will compare the effect of treatment versus placebo for this condition.

The patient has been informed of the nature of the procedures involved and that he/she may withdraw at any point.

The trial is randomised, controlled and single-blind in design and involves two weeks of allocated treatment with assessment of pain, function and drug intake.

You will receive notification of completion of the trial period, but this correspondence will not alter that which is routinely supplied from the outpatient clinic.

If you have any queries on this matter contact Mrs. W. Dickens at the physiotherapy department of Q.A./S.G.H.

Yours sincerely,

Wendy Dickens. M.C.S.P.

APPENDIX 10.6

POSTHERPETIC NEURALGIA

PAIN CHART

NAME DATE

PLEASE SCORE YOUR PAIN ON THIS CHART

Please write down, every day, a number on the chart to show the average amount of pain you have had from your postherpetic neuralgia during that day. Each number means a different amount of pain; for instance if, on Tuesday, you had mild pain fill in 3 in the second box on the chart.

Each Monday box has a date above it to show you which week to fill in.

Please bring this chart with you the next time you come to the Aldermoor.

Date					
Mon					
Tue					
Wed					
Thurs					
Fri					
Sat					
Sun					

1. None
2. Very mild
3. Mild
4. Not very severe
5. Quite severe
6. Very severe
7. Almost unbearable

APPENDIX 10.7

ASSESSMENT FORM

NAME:

PATIENT NUMBER:
SHEET NUMBER:

DATE:

Severity: | 0 | 1 | 2 | 3 | 4 | 5 | 6 |

Duration:

0 4 8 12 16 20 24hrs

Drugs taken:

Vomiting and/or nausea [ ] one-sided headache [ ] associated visual disturbance [ ]

DATE:

Severity: | 0 | 1 | 2 | 3 | 4 | 5 | 6 |

Duration:

0 4 8 12 16 20 24hrs

Drugs taken:

Vomiting and/or nausea [ ] one-sided headache [ ] associated visual disturbance [ ]

DATE:

Severity: | 0 | 1 | 2 | 3 | 4 | 5 | 6 |

Duration:

0 4 8 12 16 20 24hrs

Drugs taken:

Vomiting and/or nausea [ ] one-sided headache [ ] associated visual disturbance [ ]

DATE:

Severity: | 0 | 1 | 2 | 3 | 4 | 5 | 6 |

Duration:

0 4 8 12 16 20 24hrs

Drugs taken:

Vomiting and/or nausea [ ] one-sided headache [ ] associated visual disturbance [ ]

DATE:

Severity: | 0 | 1 | 2 | 3 | 4 | 5 | 6 |

Duration:

0 4 8 12 16 20 24hrs

Drugs taken:

Vomiting and/or nausea [ ] one-sided headache [ ] associated visual disturbance [ ]

DATE:

Severity: | 0 | 1 | 2 | 3 | 4 | 5 | 6 |

Duration:

0 4 8 12 16 20 24hrs

Drugs taken:

Vomiting and/or nausea [ ] one-sided headache [ ] associated visual disturbance [ ]

DATE:

Severity: | 0 | 1 | 2 | 3 | 4 | 5 | 6 |

Duration:

0 4 8 12 16 20 24hrs

Drugs taken:

Vomiting and/or nausea [ ] one-sided headache [ ] associated visual disturbance [ ]

APPENDIX 10.8

EXPLANATORY NOTES FOR PAIN AND DRUG DIARY

PLEASE FILL IN SECTION A AND B FOR EACH DAY.

IF POSSIBLE, THIS SHOULD BE DONE AT THE SAME TIME THROUGHOUT THE TRIAL.

SECTION A

This is a record of the tablets you take FOR THUMB PAIN over 24 hour periods.

Simply fill in the tablet name, dosage (per tablet) and the total number you have taken from 8.00 a.m. to the following 8.00 a.m.

FOR EXAMPLE.

NAME & DOSAGE (per tablet)	NUMBER TAKEN 8.00 a.m. - 8.00 a.m.
----------	--------
----------	--------
----------	--------

****

SECTION B

This section will indicate the amount of thumb pain that you are experiencing.

The line represents the full range of pain that you could experience.
The left hand limit corresponds to no pain.
The right hand limit 'I could not have more pain', corresponds to maximum pain.
The area of line between these extremes represents the other pain levels, increasing from left to right.

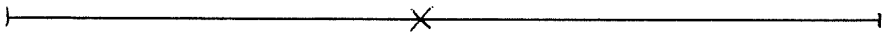
Please mark with A CROSS ON THE LINE, where you consider your thumb pain to have been during the same 24 hour period described in Section A.

FOR EXAMPLE.

If you had experienced little pain, your cross may be here:-

NO PAIN I COULD NOT HAVE MORE PAIN

Whereas if you had had moderate pain, your cross may be here:-



NO PAIN I COULD NOT HAVE MORE PAIN

APPENDIX 10.9

DAY 1

A. NAME & DOSAGE (per tablet). NUMBER TAKEN 8.00 a.m. - 8.00 a.m.

B.

NO PAIN — I COULD NOT HAVE MORE PAIN

DAY 2

A. NAME & DOSAGE (per tablet). NUMBER TAKEN 8.00 a.m. - 8.00 a.m.

B.

NO PAIN — I COULD NOT HAVE MORE PAIN

DAY 3

A. NAME & DOSAGE (per tablet). NUMBER TAKEN 8.00 a.m. - 8.00 a.m.

B.

NO PAIN — I COULD NOT HAVE MORE PAIN

DAY 4

A. NAME & DOSAGE (per tablet). NUMBER TAKEN 8.00 a.m. - 8.00 a.m.

B.

NO PAIN — I COULD NOT HAVE MORE PAIN

DAY 5

A. NAME & DOSAGE (per tablet). NUMBER TAKEN 8.00 a.m. - 8.00 a.m.

B.

NO PAIN — I COULD NOT HAVE MORE PAIN

APPENDIX 10.10

FUNCTIONAL ASSESSMENT

NAME .....

TRIAL NUMBER .....

HOW DIFFICULT ARE THE FOLLOWING ACTIVITIES?

ACTIVITY	EASY	DIFFICULT	IMPOSSIBLE	REASON	
				Pain	Other
Using buttons					
Shoelaces					
Writing					
Handling money					
Taps					
Unscrewing lids					
Using tin opener					
Using knife and fork					
Hobby					

RAW DATA RELEVANT TO CHAPTER 10

RAW DATA FOR POST-HERPETIC NEURALGIA STUDY

Patient Number	Randomised Treatment	Age	Sex	Site of Pain	Duration (Months)	Completed or Withdrawn	Baseline Initial Weekly Score	EOT	FU
1	A	73	F	V	18	W	6.3	-	-
2	A	76	M	T	180	C	7.0	5.0	5.0
3	MINS	67	M	T	10	C	4.8	5.0	7.0
4	A	76	F	C	9	W	6.8	-	-
5	MINS	58	F	T	10	C	7.0	6.2	5.0
6	MINS	67	F	V	9	W	5.0	-	-
7	MINS	74	F	T	4	C	7.0	4.5	3.0
8	A	80	F	T	4	C	6.3	6.0	5.5
9	A	76	F	T	10	C	6.0	6.0	6.0
10	MINS	63	M	T	32	C	5.0	5.0	7.0
11	A	62	M	V	22	W	5.0	-	-
12	MINS	76	F	L-S	18	C	5.8	6.0	6.5
13	A	76	F	T	23	C	6.3	3.0	4.2
14	A	75	F	V	7	W	6.2	-	-
15	MINS	72	F	T	20	C	7.0	4.5	3.0
16	A	69	M	V	18	C	5.8	3.2	5.0
17	MINS	63	M	T	41	C	6.1	6.0	5.5
18	MINS	74	F	C	11	C	6.7	4.0	3.4
19	MINS	62	M	V	23	C	6.8	6.5	6.8
20	A	76	F	T	11	W	7.0	-	-
21	MINS	77	F	T	348	C	4.5	6.5	6.8
22	A	77	F	V	16	W	6.8	-	-
23	A	76	M	L-S	22	C	6.8	6.5	6.0
24	MINS	87	F	V	5	C	6.8	5.5	6.3
25	A	76	F	T	28	C	6.3	4.0	3.0
26	MINS	58	M	T	11	W	4.5	-	-
27	A	75	F	L-S	9	C	7.0	6.5	7.0
28	A	78	F	T	8	W	7.0	-	-
29	MINS	72	F	C	9	C	5.0	5.5	6.0
30	MINS	70	F	V	7	C	4.5	6.0	5.5
31	MINS	84	M	T	30	C	6.3	6.2	6.5
32	A	76	F	T	17	C	7.0	6.0	6.5
33	A	59	M	T	18	C	7.0	7.0	7.0
34	MINS	76	F	V	30	C	4.5	4.0	5.2
35	MINS	78	F	T	19	C	6.3	4.0	3.0

RAW DATA FOR POST-HERPETIC NEURALGIA STUDY (Continued)

Patient Number	Randomised Treatment	Age	Sex	Site of Pain	Duration (Months)	Completed or Withdrawn	Baseline Initial Weekly Score	EOT	FU
36	A	77	F	V	30	W	6.8	-	-
37	MINS	61	M	C	33	C	5.8	3.5	2.0
38	MINS	72	M	T	21	C	5.8	6.0	5.8
39	A	71	M	T	10	W	6.0	-	-
40	A	76	F	T	10	C	6.2	3.0	5.0
41	MINS	78	F	C	9	W	6.3	-	-
42	MINS	65	M	T	77	C	6.4	3.0	2.0
43	A	72	M	T	11	C	6.4	3.0	2.0
44	MINS	76	F	L-S	2	C	5.0	5.0	5.0
45	A	75	F	V	18	C	5.6	5.0	5.5
46	MINS	70	F	C	16	C	5.2	3.2	2.5
47	A	74	F	T	9	W	4.5	-	-
48	MINS	53	M	V	24	C	4.5	5.0	5.5
49	MINS	72	F	V	18	C	5.0	5.5	2.5
50	A	71	M	T	6	W	6.2	-	-
51	A	76	F	T	3	C	4.0	4.0	4.0
52	A	76	F	T	23	W	6.0	-	-
53	MINS	49	M	V	7	C	4.5	5.0	4.8
54	MINS	73	F	T	19	C	7.0	5.0	4.5
55	A	77	M	T	30	C	4.2	4.5	4.0
56	A	72	M	T	36	C	6.2	6.5	6.0
57	MINS	76	F	T	8	C	4.5	5.0	4.5
58	A	72	F	V	153	W	5.5	-	-
59	MINS	73	F	T	23	C	7.0	6.5	6.0
60	MINS	73	F	V	4	C	4.0	3.0	3.5
61	A	77	F	L-S	6	C	6.2	2.0	1.0
62	MINS	76	F	V	17	C	4.5	5.0	4.0

Site of Pain: V = Vth Nerve
C = Cervical
T = Thoracic
L-S = Lumbar-sacral

RAW DATA FOR HEADACHE STUDY

No.	Rx	Sex	Age	Drug T	Base No.	Headache Base No.	Headache Base S	4/52 Post Treatment S	t_{33}	t_{50}	d_{33}	d_{50}	No.	Drug No.
1	A	F	29	S	30	12	36	12	32	77	47	10	3	5
2	A	F	38	S	26	14	37	22	50	-	30	-	10	12
3	T	F	34	S	15	10	25	18	-	-	-	-	7	11
4	A	F	43	N	X	9	25	20	-	-	-	-	8	X
5	T	M	47	S	34	12	22	10	29	32	38	12	4	8
6	T	F	43	N	X	14	30	18	52	-	30	-	6	X
7	T	F	53	5	-	6	16	Withdrawn						
8	A	F	62	S+M	-	4	24	Withdrawn						
9	T	F	20	S	20	8	26	12	43	52	44	27	3	8
10	A	F	60	S	12	5	20	8	28	35	50	36	2	4
11	T	F	58	S	36	16	34	25	-	-	-	-	10	22
12	A	M	49	S	45	20	56	25	20	60	57	5	10	15
13	A	F	39	N	X	21	40	Withdrawn						
14	T	F	39	N	X	20	37	18	24	47	46	10	12	X
15	T	F	43	S	10	6	20	15	-	-	-	-	4	5
16	A	F	53	S	-	24	48	Withdrawn						
17	T	M	52	S	32	22	50	40	-	-	-	-	17	28
18	A	F	14	S	30	14	32	18	30	-	27	-	9	21
19	A	F	50	E	12	6	26	14	42	-	36	-	5	10
20	T	F	49	N	X	4	16	Withdrawn						
21	T	F	34	S	12	8	12	10	-	-	-	-	5	13
22	T	F	39	S	14	5	22	18	-	-	-	-	5	14
23	T	F	26	S	-	6	16	Withdrawn						
24	A	M	52	S	8	4	18	16	-	-	-	-	4	8
25	A	F	47	S	24	12	30	18	22	-	45	-	8	16
26	A	F	26	N	X	16	34	10	26	35	52	14	4	X
27	A	F	29	S	10	8	32	10	22	28	37	22	3	2
28	T	F	28	N	X	6	14	10	-	-	-	-	4	X
29	A	F	32	S	12	9	26	20	-	-	-	-	7	10
30	T	F	34	S	28	7	17	8	28	37	40	15	2	3
31	A	M	43	S	20	13	30	25	-	-	-	-	13	22
32	T	F	30	S	10	4	18	15	-	-	-	-	3	8
33	T	M	44	S	10	6	11	8	-	-	-	-	3	8
34	A	F	34	S	16	9	32	2	26	32	40	31	1	0
35	A	F	36	S	12	10	24	20	-	-	-	-	9	13
36	T	F	68	S	-	5	16	Withdrawn						
37	A	F	43	S+M	24 28	16	32	20	22	-	37	-	9	12 28

RAW DATA FOR HEADACHE STUDY (Continued)

No.	Rx	Sex	Age	Drug T	Base No.	Headache No.	Base S	4/52 Post Treatment S	t_{33}	t_{50}	d_{33}	d_{50}	No.	Drug No.
38	T	M	53	N	X	4	20	22	-	-	-	-	4	X
39	T	F	42	S	18	7	24	10	23	37	48	8	2	2
40	A	F	50	S	-	20	47	Withdrawn						
41	A	F	28	S	-	6	24	Withdrawn						
42	T	F	35	N	X	4	20	24	-	-	-	-	5	X
43	T	F	50	S	12	3	12	4	24	36	52	27	1	0
44	A	F	27	N	X	4	20	12	28	-	42	-	4	X
45	A	F	32	S	14	8	26	6	15	20	48	40	2	4
46	T	M	43	S	18	8	24	20	-	-	-	-	5	10
47	A	F	25	S	23	12	32	30	-	-	-	-	10	20
48	A	F	34	S	34	17	40	18	30	30	37	32	2	4

Drugs

N = No. tablets taken
S = Simple analgesics such as paracetamol or Aspirin
M = Maintenance therapy (Clonidine)
E = Ergotamine
No = Number of tablets of simple analgesics
Rx = Treatment - A = Acupuncture
T = Mock TNS

Headaches

No = Number of headaches in given period
S = Severity of headaches in given period
t_{33} = Time to 33% relief (days)
t_{50} = Time to 50% relief (days)
d_{33} = Time of 33% relief (days)
d_{50} = Time of 50% relief (days)

TABLE A - Raw data for TMC Joint OA study

AGE, SEX AND DURATION OF PAIN AND SITE OF PAIN

PATIENT NUMBER	SEX	AGE (Years)	THUMB PAIN (Years)	DOMINANT HAND	HAND IN TRIAL	TREATMENT
1 ( )	MALE	55	2	RIGHT	RIGHT	ACUPUNCTURE
2 ( )	MALE	58	4	RIGHT	RIGHT	ACUPUNCTURE
3 ( )	FEMALE	58	5	RIGHT	LEFT	ACUPUNCTURE
4 ( )	FEMALE	61	1.5	RIGHT	LEFT	ACUPUNCTURE
5 ( )	FEMALE	48	5	RIGHT	RIGHT	ACUPUNCTURE
6 ( )	FEMALE	77	4	RIGHT	RIGHT	ACUPUNCTURE
7 ( )	MALE	56	1	RIGHT	LEFT	ACUPUNCTURE
8 ( )	FEMALE	60	3	RIGHT	RIGHT	MOCK TNS
9 ( )	FEMALE	69	5	RIGHT	RIGHT	MOCK TNS
10 ( )	FEMALE	52	4	LEFT	LEFT	MOCK TNS
11 ( )	MALE	55	2	RIGHT	LEFT	MOCK TNS
12 ( )	MALE	60	2	RIGHT	LEFT	MOCK TNS

TABLE B - Raw data for TMC Joint OA study

INDIVIDUAL AND GROUP V.A.S. SCORES

PATIENT NUMBER	WEEK 1 MEAN	WEEK 1 ST.DEV.	WEEK 2 MEAN	WEEK 2 ST.DEV.	WEEK 3 MEAN	WEEK 3 ST.DEV.
1	28.17	6.59	8.67	3.39	8.00	1.67
2	34.17	9.97	10.33	5.92	8.17	6.49
3	39.17	15.21	21.50	7.31	9.67	1.75
4	40.50	12.60	11.17	6.97	3.83	1.17
5	6.67	2.80	1.17	1.47	0.50	1.22
6	37.67	20.91	32.67	11.96	44.67	10.95
7	25.83	7.63	12.33	5.01	6.17	2.48
MEDIANS	34.17		11.17		8	
8	40.00	15.10	10.80	1.57	21.80	5.86
9	32.17	13.76	8.67	4.50	3.17	0.75
10	56.67	18.52	11.33	7.20	43.33	12.29
11	7.00	0.89	7.00	0.63	6.83	2.14
12	68.68	4.63	64.67	9.33	65.83	17.23
MEDIANS	40.00		10.80		21.80	

TABLE C - Raw data for TMC Joint OA study

FUNCTIONAL SCORES AND FUNCTIONAL SCORE CHANGES

PATIENT NUMBER	FUNCTIONAL SCORES			SCORE CHANGES		
	ASSESST 1	ASSESST 2	ASSESST 3	1-2	1-3	2-3
1	11	5	4	6	7	1
2	8	2	0	6	8	2
3	7	8	5	-1**	2	3
4	3	3	1	0	2	2
5	3	0	0	3	3	0
6	6	5	5	1	1	0
7	3	2	2	1	1	0
MEDIAN	6	3	2	1	2	1
8	12	10	10	2	2	0
9	11	4	4	7	7	0
10	5	3	4	2	1	-1**
11	6	5	5	1	1	0
12	16	16	16	0	0	0
MEDIAN	11	5	5	2	1	0

- Denotes decrease in function (**).

TABLE D - Raw data for TMC Joint OA study

JOINT TENDERNESS

PATIENT NUMBER	MYOMETER READINGS (kgf) ASSESST 1	ASSESST 2	ASSESST 3	CHANGES BETWEEN 1-2	1-3	2-3
1	3.5	3.5	3.2	0.0	0.3	0.3
2	3.3	3.1	5.1	0.2	-1.8	-2.0
3	2.5	1.0	2.3	1.5	0.2	-1.3
4	0.3	1.7	2.0	-1.4	-1.7	-0.3
5	3.5	4.2	3.5	-0.7	0.0	0.7
6	2.6	1.0	1.0	1.6	1.6	0.0
7	2.8	4.9	2.5	-2.1	0.3	2.4
MEDIAN	2.8	3.1	2.5	0.0	0.2	0.0
8	0.6	1.4	1.5	-0.8	-0.9	-0.1
9	1.0	2.0	2.2	-1.0	-1.2	-0.2
10	3.9	4.7	4.1	-0.8	-0.2	0.6
11	1.8	3.1	2.7	-1.3	-0.9	0.4
12	1.2	1.0	0.9	0.2	0.3	0.1
MEDIAN	1.2	2.0	2.2	-0.8	-0.9	0.1

- Denotes decreased joint tenderness.

TABLE E - Raw data for TMC Joint OA study

PINCH GRIP AND PINCH GRIP SCORE CHANGES

PATIENT NUMBER	PINCH PRESSURE SCORES (kgf)			SCORE CHANGES		
	ASSESST 1	ASSESST 2	ASSESST 3	2-1	3-1	3-2
1	2.5	4.4	4.5	1.9	2.0	0.1
2	2.3	3.6	4.3	1.3	2.0	0.7
3	2.1	1.9	3.0	-0.2	0.9	1.1
4	0.9	3.0	3.2	2.1	2.3	0.2
5	4.1	5.1	4.5	1.0	0.4	-0.6
6	2.0	1.3	1.0	-0.7	-1.0	-0.3
7	5.3	5.6	5.4	0.3	0.1	-0.2
MEDIAN	2.3	3.6	4.3	1.0	0.9	0.1
8	1.7	1.5	2.9	-0.2	1.2	1.4
9	1.0	2.0	2.2	1.0	1.2	0.2
10	3.9	4.7	4.1	0.8	0.2	-0.6
11	4.0	2.9	5.4	-1.1	1.4	-2,5
12	1.9	2.1	1.8	0.2	-0.1	-0.3
MEDIAN	1.9	2.1	2.9	0.2	1.2	0.2

- Denotes decrease in pinch grip.

TABLE F - Raw data for TMC Joint OA study

DRUG INTAKE

PATIENT NUMBER	DRUG TYPE	TOTAL INTAKE PERIOD A	PERIOD B	PERIOD C
1	NONE	/	/	/
2	NONE	/	/	/
3	NSAIDS	6	6	6
4	ANALGESICS	18	2	0
5	NONE	/	/	/
6	ANALGESICS	14	13	15
7	NONE	/	/	/
8	ANALGESICS	25	24	26
9	ANALGESICS	1	0	0
10	ANALGESICS	1	0	0
11	NONE	/	/	/
12	ANALGESICS	21	23	20