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Recent Advances in the Understanding of Acupuncture[1]

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The controversy about acupuncture is familiar to us since its recent reintroduction into this country. Much of its philosophical concepts were taken at their face values as the bases for condemnation. Since I last reviewed these antiquated concepts in the light of modern medicine, much has developed. It seems that if the effects of acupuncture were transmitted along the peripheral nerves to the central nervous system, it would be more effective if applied segmentally to the site of noxious stimulation. Disruption of extralamniscal pathways would abolish its analgesic effect. The distant and nonsegmentally located acupuncture points exert their influences through the integrative efforts of the reticular formation and the thalamus. The demonstration of transmissibility of acupuncture analgesia through blood and cerebrospinal fluid in animals implicates the involvement of humoral factors. Since such an effect can be suppressed by naloxone or by hypophysectomy, endorphins are thought to be involved. Such laboratory evidences indeed begin to shed some light on a possible neurohumoral mechanism of acupuncture. The differences between acupuncture and hypnosis are discussed. Acupuncture points were compared with referred pain, trigger points and motor points of the skeletal muscles. Its possible uses for other than pain, such as drug addiction, alcoholism, etc. are also reviewed.

When acupuncture was reintroduced into America in about 1971, there was zealous search for new values of life with flourishing of Oriental religious occults in this land of science and technology. Its mystique-colored concepts caused much excitement and controversy. When acupuncture anesthesia (more appropriately analgesia or hypalgesia) was first reported by Dimond, White, Rosen and Sidel in 1971 [1] it was beyond the imagination of American medicine. It was bitterly denounced mainly on the grounds that no scientific explanation was considered possible. The Federal Food and Drug Administration ruled it experimental in 1973 [2]. The American public, not understanding why such a "field-tested" effective therapeutic modality would be rejected by organized medicine, was utterly confused. The controversy about acupuncture, now familiar to us, was made worse at that time both by exaggerated claims of its usefulness in popular media and by its commercialization we may call "quacupuncture." In 1973, I reviewed its status and reported my personal opinions [3]. Now, four more years have gone by and much has happened with regard to acupuncture during this time. I indeed welcome this opportunity to review some of the significant scientific reports and try to bring acupuncture up to date for the final session of the "Alternate Forms of Healing

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It has been repeatedly demonstrated that local infiltration of acupuncture points with procaine abolished the analgesic effects of acupuncture [4, 5, 6]. This suggested the implication of afferent fibers of peripheral nerves in the transmission of impulses initiated by acupuncture.

Neurologically, a segmental relationship of the analgesic effect of acupuncture seems to exist. Chang Hsiang-Tung of Shanghai [7] stimulated the Neck-Futu (LI 18) point at the midpoint of Sternocleidomastoid muscle and produced analgesia for thyroidectomy in humans. The Neck-Futu point is supplied by the Cervical Cutaneous Nerve from the C 3 spinal nerve root while the capsule of the thyroid gland is also supplied by nerves from the C 3 segment of the spinal cord. In animal experimentation, electric discharges were recorded by a microelectrode placed in the brain when noxious stimuli were applied to the tail of a rabbit. Such evoked potentials from noxious stimulation to the tail could be eliminated by acupuncture to the hind leg but not to the fore leg [7]. Since the tail and the hind legs share the same segments of the spinal cord in nerve supply while the tail and the fore legs do not, acupuncture can only be operative through some kind of segmentally related mechanism. It was also found that acupuncture analgesia effects were bilaterally distributed and also segmental in nature [4]. In hemiplegic patients, acupuncture at the Hegu (Ho Ku, LI 4) point or the Zusanli (Tsu San Li, St 36)[2] point on the paralyzed limbs did not raise the pain threshold while the same maneuver on the normal limbs did. In paraplegic patients, acupuncture at the Zusanli (St 36) point on the legs did not raise pain threshold but that at the Hegu (LI 4) point on the hands did [5].

It was demonstrated that pathways concerned with acupuncture analgesia were located in the ventral two-thirds of the lateral funiculus [6, 8]. These ascending tracts were essentially the extralamniscal system, consisting of spinoreticular, spinomesencephalic and paleo-spinothalamic tracts, projecting to the reticular formation, central gray matter and medial thalamic nuclei. It was suggested that these supraspinal structures might be involved in the mechanism of acupuncture analgesia. These experiments did not distinguish the types of nerve fibers involved in the mediation of the afferent acupuncture impulses. Wall and Dubner [9] indicated that group I afferent activities were transmitted in the dorsal and ventral spinocerebellar tracts but that group II and III afferent activities were mainly via spinoreticular paths. Chang [11] found that pain responses of certain neurons in the Nucleus Parafascicularis and the Nucleus Centralis Lateralis of the thalamus could be inhibited by electric needling of certain acupuncture points, by squeezing Achilles tendon or by weak electric stimulation of a sensory nerve. He suggested that the thalamus exerted an integrative action in acupuncture analgesia. Though the Caudate Nucleus is not located in the pathways of pain sensation, its destruction was found to reduce pain-suppression by acupuncture [6]. Spinal anesthesia eliminated *de qi* responses (the sensations generated during needling) and evoked myoelectric potentials at acupuncture points [6].

Electric stimulation of the Cervical Cutaneous Nerve of animals (to simulate human thyroidectomy) evoked observable potentials on their sensory cortex,

[2]In this presentation, when the name of an acupuncture point is spelled, I shall use the new Chinese official romanization system, *Hanyu pinyin*, in the "Index of Acupuncture Points" [10]. It shall be followed with its former English spelling, if indicated, and its Meridian number in parenthesis.

which could be suppressed by acupuncture at the Hegu (LI 4) point and Neiguan (Nei Kuan, P 6) point. Similar cortical potentials could be evoked by electric stimulation of tooth pulp and suppressed by acupuncture at the Hegu (LI 4) point [5]. Dr. Arthur Battista and I applied measured amounts of electric current to the forearm of a monkey and recorded the evoked cortical potentials with a Computer of Averaging Transients. When electroacupuncture was applied to the Quchi (LI 11) and the Shaohai (H 3) points on the lateral and medial aspects of the ipsilateral elbow, the evoked cortical potentials were completely abolished. Such cortical potentials, though suppressible by acupuncture, need not necessarily be interpreted as pain sensations *per se*.

In order to generate adequate analgesic effect by acupuncture, an induction time of 15 to 30 minutes is usually required [5]. Recently, Pomeranz [12, 13] reported that it took 20 to 40 minutes to induce acupuncture analgesia in anesthetized or awake animals and the pain response was suppressed for an hour or more after the cessation of the procedure and then gradually returned. Chinese researchers found that the maximal inhibitory effect of electric acupuncture stimulation on firing in thalamic cells occurred 2 to 5 minutes after onset of stimulation [14]. Melzack and Melinkoff [15] raised the pain threshold by electric stimulation of the cat's midbrain reticular formation. The analgesic effect developed gradually over a period of 5 minutes or so. Since this period of delayed onset was quite similar to the induction time of acupuncture analgesia in man, they stated that "this parallel lends support to the suggestion that acupuncture analgesia is mediated by these pain-inhibitory reticular areas. These areas receive inputs from wide spread parts of the body and project to virtually all synaptic levels of the somatic projection systems, so that it is possible that intense sensory inputs, such as electric stimulation through acupuncture needles, activate discrete reticular sites which in turn exert an inhibitory influence on somatic transmission from selective body regions. In this way, conceivably, acupuncture stimulation of a region such as the wrist may produce analgesia in a distant area such as the neck." In Bowsher's recent review [16] of the reticular formation to noxious stimulation, he commented on the inability of RF neurons to respond to peripheral stimulation at a frequency above 3 Hz and the gigantocellular RF's preferential activation by peripheral A δ stimulation. Since these are also crucial parameters of acupuncture he speculated that acupuncture might indeed excite descending inhibitory reticulospinal neurons.

Vierck et al. [17] used the escape behavior of monkeys to painful electric stimuli to assess the analgesic effect of electroacupuncture at loci corresponding to human acupuncture points. The response to acupuncture was delayed in onset and persisted for up to 70 hours after cessation of acupuncture treatments, with several peaks of pain attenuation, separated by nearly normal reactivity. These findings pointed to the importance of testing for the pain reactivity frequently over a prolonged period following the termination of the treatment in order to obtain a true assessment. Their results also revealed the need for precise localization of the acupuncture points.

Chinese researchers demonstrated that acupuncture analgesia could be transmitted by humoral factors [7]. They connected two rabbits (A and B) with cross-circulation of carotid arteries and jugular veins. Acupuncture was applied only to one rabbit (A) and not to the other (B). It not only raised the pain threshold of rabbit (A) but also that of (B). They reported also that the analgesic effect could be transmitted by transfusion of cerebrospinal fluid of acupuncture-treated animals to

non-treated ones [18]. They compared its analgesic effect with morphine analgesia. Monoamines in the brain (norepinephrine, dopamine and 5-hydroxytryptamine) are indispensable for morphine analgesia. The prevention of their action by reserpine completely abolished the effects of morphine. On the contrary, reserpine enhanced the analgesic effect of acupuncture. Intraventricular replacement of these monoamines into the brain of reserpinized animals indeed eliminated the augmenting effect of reserpine on acupuncture. When the muscarinic effect of acetylcholine (another important neurotransmitter) in the brain was blocked by atropine, the analgesic effect of acupuncture was very much weakened while that of morphine was not affected at all.

Pomeranz and his associates [12, 13], using anesthetized as well as awake animals, Mayer and his colleagues [19], Chapman [20] and Sjölund and Eriksson [21], using human subjects, demonstrated that the analgesic effect of acupuncture could be blocked by naloxone which is both a morphine and endorphin antagonist. Chapman also found [20] that naloxone only partially abolished the acupuncture analgesic effect on the tooth pulp when the needles were applied to the cheek. Since the pituitary gland contains large quantities of endorphins, Pomeranz [13] applied acupuncture to hypophysectomized mice as well as normal ones and found that acupuncture did not produce analgesia in animals without the pituitary but did in those with the gland intact. Thus, acupuncture analgesia was postulated to be due to a release of endorphins for the brain and/or the pituitary. These findings seemed rather contradictory to those obtained from the above-cited reserpine experiments. At the present time, the studies on endorphins and pain are still controversial [22] and much is yet to be learned. Some of the above-mentioned differences could possibly be due to differences of the molecular sizes of the neural chemicals, the extremely rapid degradation of endorphins [23], their affinity and specificity of different host's receptor sites [24], etc. A clarification of the differences will have to wait for further research, such as of the relationship between monoamines, endorphins and acupuncture, the effect of naloxone on acupuncture in reserpinized animals, etc. As stated by B. Berthold Wolff [25], one of the foremost researchers on pain, "acupuncture sparked the nation's interest and renewed its hope that a treatment might exist for chronic pain." The study of endorphins and pain is rapidly expanding in the last few years. So far, little research has been done on the possible relationship of acupuncture to the release of these neuropeptides in patients with chronic pain and their combined effects on pain-suppression.

Stimulation of peripheral afferents of cutaneous and muscle nerves produces a direct and immediate effect on sympathetic nerve activities. Accordingly, Looney [26] asserted that acupuncture, being a form of stimulation of the somatic sensory afferents, may operate through the autonomic nervous system, since conditions involving the autonomic nervous system (such as familial dysautonomia, sympathetic dystrophy, causalgia and sympathectomy for circulatory problems) may exhibit either decreased pain perception or excessive pain.

In 1893, Henry Head [27] reported the cutaneously referred pain of visceral diseases. Application of counter-irritation to the maximal areas of tenderness of the referred pain could alleviate visceral disturbances. The referred pain followed the segmental distribution of the spinal cord but not that of spinal nerve roots. There was bilateral distribution of tenderness and referred pain especially in chronic illness. He speculated that referred pain involved sympathetic sensory nerves.

Chinese medical researchers reported [28] that points of low electric resistance

appeared mostly in an area of the rabbit's ear innervated by auricular branches of vagus nerve and in lesser number near the plexus formed by vagus and sympathetic nerve fibers.

From the above observations, it seems reasonable to speculate that referred pain and the effects of acupuncture share the same pathways with the internal organs at one end and the skin and its underlying tissues at the other. Visceral disturbances set up referred pain with maximal tender areas of skin and its underlying tissues while acupuncture at such maximal tender areas (i.e., acupuncture points) in a counter-current fashion attenuates the referred pain and, thus, visceral disturbances.

In 1973, I reported [29] that acupuncture points coincided with many trigger points which are the maximal tender areas of Henry Head. My limited investigation showed that acupuncture points also possess many of the characteristics of the trigger zones as described by Travell [30].

1. Acupuncture points are, by definition, tender on palpation and so are the trigger zones.
2. Spontaneous myoelectric discharges have been observed both in the trigger zones and in acupuncture points.
3. Travell inserted a syringe-needle into trigger zones but did not inject any medication into the tissues and to her surprise found that this maneuver abolished the referred pain. This indeed is the same as doing acupuncture.
4. Both trigger zones and acupuncture points are located segmentally, bilaterally and at a considerable distance from the affected organs.

Recently, Melzack, Stillwell and Fox [31] also found "a remarkable high-degree (71%) of correspondance" between trigger points and acupuncture points. "This close correlation suggests that trigger points and acupuncture points for pain, though discovered independently and labelled differently, represent the same phenomenon and can be explained in terms of the underlying neural mechanisms."

In addition to what I described earlier [3] I further noticed the following characteristics:

1. Acupuncture points coincided with many of the motor points of skeletal muscles [32, 33].
2. Previously I reported that the skin became erythematous on insertion of a needle at an acupuncture point but did not offer an explanation. Now, it seems that histamine, serotonin or some other humoral factors are released upon needling. The appearance of erythema also tends to indicate a better therapeutic result. It may also explain why some patients experience warmth in the acupuncture-treated areas. Ancient Chinese referred this warm sensation as part of the *de qi* response of acupuncture [34]. Whether such chemical factors are transmitted through the blood or cerebrospinal fluid or the erythema can be extinguished by endorphin-antagonists needs further exploration.

We made some very limited observations on thermography and acupuncture with an apparatus kindly provided by the AGA Company. We examined two patients with frozen shoulders. After the needles were inserted at the Tiaokou (St 38) points on the legs, an increase of temperature of the affected shoulders was observed in both patients. This was accompanied by a reduction of pain and an improvement of the mobility of the affected joints. A third patient had an abscess of a lower molar

tooth. After acupuncture needles were inserted at the Hegu (LI 4) points of both hands, there followed an increase of temperature of the cheek of the affected side. The patient also experienced a diminution of the toothache. However, when the needles were inserted on the cheek of the affected side, there was a slight reduction of temperature of the cheek. When electric stimulation was subsequently applied to the needles already on the cheek, it did not further increase or decrease the temperature of the cheek, though the patient experienced further alleviation of the pain. As a control, we had the patient smoke cigarettes after all the needles were removed. A marked decrease of the skin temperature of his fingers was observed soon after he started to do so. A fourth patient had chronic low back pain syndrome. After placing the needles on his back, there was a reduction of the skin temperature. In this instance, the low back pain was not abated during the experiment nor did he experience any change of the pain from previous or subsequent treatments. A local cooling effect was also seen in a fifth patient who had right-sided hemiparesis, possibly from embolic phenomena secondary to taking contraceptive medications. When the needles were inserted in her affected thigh, there was, as just mentioned, a local cooling effect. In this case, the patient had no pain and analgesia was not produced in the affected limb with acupuncture. Clark [35] reported that met-endorphin had a hyperthermic effect in cats. Bloom et al. [36] found that β -endorphins produced hypothermia and γ -endorphins produced hyperthermia in rats. One is tempted to speculate on a correlation between the thermic effects of acupuncture and a release of endorphins or some other chemicals in the body. I hope our cursory observations may stimulate some serious interest in thermography as a research tool in the elucidation of the mechanism of acupuncture in relation to endorphins.

Previously I commented that acupuncture was not hypnosis [3]. Last year, I reported on a group of 235 patients with various chronic pain syndromes and analyzed their hypnotizability and the results of acupuncture treatments. No significant statistical correlation was demonstrated [37]. Very recently, I reviewed this subject again in a group of 200 patients with head-pain [38] and another group of 200 patients with chronic low back pain syndrome [39]. No statistically significant correlation was found between the patients' hypnotizability and their responses to acupuncture in the alleviation of these two different types of pains. Mayer [40] found in human subjects that hypnosis increased the pain threshold more than acupuncture but that pain threshold raised in this manner could not be lowered by naloxone, the endorphin antagonist, and that hypnotic analgesia was terminated immediately by a hypnotist; yet acupuncture analgesia persisted for several hours after the removal of the needles. Goldstein and Hilgard [41] also noted that naloxone could not block analgesia induced by hypnosis. Another obvious dissimilarity between hypnosis and acupuncture is that hypnosis requires prolonged contact between the hypnotist and the patient, especially for its analgesic effect. The patient is told positively that hypnosis will work and patient must be receptive entirely to suggestions. Otherwise, it is doomed to fail. Acupuncture does not require such previous contact between the practitioner and the patient. There seems to be a tendency that the more difficult the patient is to hypnotize, the better is the result to be achieved by acupuncture [38, 39]. Our American culture is such that the public is very fearful of "needles" because of its repeated previous traumatic experience of severe pain as inflicted by syringe-needles (of much greater calibers than acupuncture needles) during adminstration of medication. The word "needle" in association with medicine and dentistry automatically inspires thoughts of un-

bearable pain in most Americans. The fear of pain is no doubt exaggerated in the minds of highly suggestible or highly hypnotizable individuals. I attempted acupuncture analgesia for tooth extraction in two highly hypnotizable individuals both of whom had the experience of successful hypnosis. After the usual induction time of 20 to 30 minutes, suppression of pain was not achieved at all in either of them. Subsequently, procaine infiltration was administered in the usual manner and complete anesthesia was obtained locally but both patients complained bitterly of pain upon tooth extraction. Because hypnotic anesthesia is accomplished in a trance state, the individual is separated from reality and the fear of pain is removed. Under acupuncture analgesia, the patient is fully awake, the reality of surgical trauma is constantly anticipated, the fear of pain would be very much heightened in the highly suggestible individuals through autohypnosis during the long waiting period of induction of analgesia. The dependence on the state of the mind indeed separates hypnotic anesthesia from acupuncture analgesia. I treated a limited number of patients who had failed to respond to hypnosis and was successful in alleviating their pain by acupuncture. Success of hypnosis depends on concentration and intelligence of the individual, thus, children, the mentally ill and animals are not suitable subjects for hypnosis and only about 10% of the population is said to be amenable to hypnotic anesthesia. Acupuncture has been used in China for centuries to treat children's and animal diseases quite successfully. I treated one horse and one dog for their arthritic pains and alleviated their symptoms completely. I translated some recent publications of veterinary acupuncture of horse and cattle [42, 43, 44]. Many of the animal acupuncture points correspond to human points.

When I wrote my appraisal of acupuncture in 1973, some researchers tried to prove the existence of Meridians without realizing that this was a taxonomic concept, while some others tried to discredit acupuncture without realizing the many pitfalls peculiar to it in dealing with proper design of controlled experiments. It is not generally appreciated that there is a regional difference in the responses to acupuncture analgesia. For example, it is easier to render head and neck analgesic than the limbs [45]. Acupuncture done to generate analgesia for the tooth pulp would very likely yield different results from that for the limbs. To produce analgesia, we may use either local points in the region of intended surgery—e.g., the Neck Futu (LI 18) point for thyroidectomy—or distant points elsewhere—e.g., the Hegu (LI 4) points on the hands for the same surgical procedure. It should be also noted that needling the local points tends to produce greater analgesia than the distant points. This clinical observation seems compatible with those findings that naloxone only partially abolished the acupuncture analgesia on the tooth pulp when the needles were applied to the cheek but did so more effectively when needles were applied to the hands. It may mean that acupuncture at local points released greater amounts of endorphins than at distant points. Pain due to certain pathologies is more amenable to acupuncture than that due to other conditions—thus, pain from degenerative arthritis is more readily attenuated than that from rheumatoid arthritis. It is further complicated by the impossibility of choosing placebo points. In this country, researchers used sites other than the classic points located along the Meridians (i.e., the "meridian points") and thought them placebo points. They did not seem to realize that there are about 1,500 points outside the meridian system and Chinese call them "extra-meridian odd points" and "new points" [46, 47]. These points have been frequently used for centuries in China and many of them are actually more therapeutically effective than the "meridian points." Thus, the

so-called placebo points as chosen by American researchers may well be some of the "extra-meridian odd points" or the "new points" [48, 49, 50, 51, 52, 53]. It is also not commonly appreciated that superficial insertion of needles may have a similar therapeutic effect as the deep insertion at the same acupuncture point.

The current concept of acupuncture in this country has centered largely around its use as an analgesic. There seems to be rather little awareness that this is only a recent development since the late 1950's and early 60's, having come about as an extension of its use as a pain-suppressor. The Chinese have used it for a multitude of other purposes, but have never claimed it as a panacea. Its uses include, among others, psychosomatic conditions (such as impotence, depression, anxiety, insomnia, tension and nervousness), chronic sinusitis and certain skin conditions. Research on endorphins and enkephalins indicates that their activity involves the release of growth hormones and prolactin [54, 55, 56, 57, 58] as well as producing profound sedation and catalepsy in animals [36, 59, 60, 61, 62, 63]. It, thus, led some to speculate on the importance of neuropeptides in behavior and mental illness. As a matter of fact, enkephalin pentapeptides were discovered because of their ability to inhibit the electrically evoked contractions of the mouse vas deferens and the guinea pig ileum by a naloxone mechanism. This was before their analgesic property was explored [22]. Since acupuncture may possibly release endorphins it seems conceivable to give credibility to the claims of its wide range of therapeutic effects.

Another recent discovery is its use in drug addiction. In 1973, Hsiang-Lai Wen, an American-trained neurosurgeon in Hong Kong, was experimenting with acupuncture analgesia on volunteers. Most of these volunteers happened to be drug addicts. In addition to the expected analgesia, they also reported a sense of well-being and suppression of withdrawal symptoms in a two-week period of treatment [64]. Lorenz Ng at the National Institute of Drug Abuse [65] used addicted rats as the animal model and relieved their withdrawal symptoms with acupuncture. He obtained similarly favorable results with human volunteers [66].

Since alcoholism may be considered an addiction to ethanol, obesity to food and smoking to cigarettes, we are using acupuncture to treat such cases when other conventional measures have failed and find that it has tranquilizing effects on these patients and satisfactory inhibitory effects on their obsessions. Further experience is desperately needed in this area of application.

Little did I anticipate that we would so soon be at the threshold to a better understanding of the mechanism of acupuncture and also the pharmacodynamics of pain. I have presented sufficient evidences to indicate that acupuncture apparently involves both the nervous system and certain humoral factors—i.e., a dual system of neurohumoral nature. Further investigations are urgently needed, particularly into its relationship to endorphins and enkephalins and the specificity of acupuncture points in such a relationship. It may also aid us to a better understanding of chronic pain as against the experimentally produced pain.

There is no need to prove or disprove the antiquated philosophical concepts of acupuncture since they were developed to suit their own times and are only of historical interest in this space-age. Let us not forget that the evolution of science from magic and of medicine from sorcery occurred in ancient times. Many lessons can be learned from this history. As I indicated in 1973, the basic concept of Chinese traditional medicine—to maintain a balance between opposing forces in our internal environment—is the same principle that we are employing in our daily practice of

medicine. The future of acupuncture and of modern medicine is in the synthesis of the best of Chinese traditional medicine and that of Western scientific medicine to form the contemporary medicine. We physicians fully realize the limitations of our scientific medicine since many common diseases are not readily amenable to what we consider real science in spite of the monumental strides made in the recent years through tremendous advances of technology. Thus, I would like to urge all physicians and dentists to learn acupuncture as an additional therapeutic modality. Otherwise, the medical and dental professions would do a disservice to the public as health consumers and would be directly or indirectly encouraging quacks to take over a meritorious medical procedure. It is, therefore, the obligation of physicians and dentists to explore acupuncture scientifically with an open mind. A lack of understanding of its mechanism is no excuse to ignore it or condemn it. Actually, we do not fully comprehend the mode of action of many of the commonly used pharmaceuticals and yet do not hesitate to prescribe them.

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