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Letter from Editor in Chief Jennifer A. M. Stone, MSOM, LAc

JASA welcomes letters to the editor from our readership. Please send them to meridiansjaom@gmail.com and be sure to include your full name and any licenses and/or titles, your phone number, and email address.

Dear Colleagues,

This past January, Centers for Medicare and Medicaid Services (CMS) announced that Medicare is now covering acupuncture for chronic low back pain. Please see this announcement and a response from our profession's leadership on p. 42.

Many unanswered questions about this coverage still remain because the specific rules that accompany this new announcement haven't yet been written by the CMS. As soon as this becomes available, the ASA and the NCCAOM will disseminate this information on how the new rule will affect all acupuncturists practicing in the U.S.

Our profession is unique—the majority of acupuncturists practicing in the U.S. do so in private clinics outside of mainstream medicine or academia. This new Medicare rule will likely require more LAcs to team up with mainstream medical clinics due to a "Catch-22"…even tho we will be able to treat a Medicare patient, we are not official Medicare providers so we cannot (yet) bill Medicare directly!

Mainstream practice is not for all LAcs, although it has been very rewarding and a lot of fun for me. I've maintained a private practice for 30 years and I've also consulted on and worked at 10 different hospital-based and academic integrative medicine centers throughout Indiana. In the 90s, mainstream CAM centers didn't last very long. When hospital administration discovered our medicine didn't make them money and just weren't sustainable, they closed them. I was fortunate I could rely on my ongoing private practice until another mainstream opportunity presented itself.

Today it's a totally different world. There are over 80 mainstream medical schools that have integrative medicine centers for education, research, and to provide clinical care. To see a list of these schools visit The Academic Consortium for Integrative Medicine and Health member listing page: https://imconsortium.org/members/member-listing/ Almost all of these centers employ LAcs.

A recent survey sent to current and past members of the Society of Integrative Oncology received 219 responses (approx. 10% response rate). Over 40% were from Chinese medicine practitioners and 70% of them worked in mainstream oncology clinics.

So how are these integrative medicine clinics now able to stay in business? Almost all of them are funded by philanthropic dollars and federal research funding. Research is profitable. In calendar year 2018, the Indiana University School of Medicine brought in a total of more than $350 million in research funding from many sources. https://medicine.iu.edu/news/2019/02/iu-school-of-medicine-researchers-set-new-nih-funding-record-in-2018/

Please know, these grants aren't all for laboratory and clinical research. They can also be used to fund new classes, additional programs and offices, and to pay for support staff, faculty salaries, and travel. Some older well-known integrative medicine cancer centers such as Memorial Sloan

Kettering Cancer Center and New York-Presbyterian/Columbia University Medical Center even enjoy a surplus of funding and are able to provide integrative therapies to cancer patients free of charge.

Grants and philanthropic funding are not only geared to universities; a majority of medical professional organizations are also funded by philanthropic grants and federal grants. Grants are available for projects, planning, conferences, meetings, writing clinical practice guidelines and high-impact papers, and more. The Society for Acupuncture Research has received conference grants from the NIH as well as meeting and planning grants from PCORI. In 2018, the Society of Integrative Oncology received a $500,000 philanthropic award to write clinical practice guidelines.

In 2019, the leaders of the ASA and JASA began to investigate options regarding philanthropic funding specifically geared towards our goals. One goal is to seek funding for a profession-wide planning project that will provide information to be used for strategic planning for the ASA and the profession. We hope this effort will generate the first of many grants and awards for the ASA and the acupuncture profession.

I want to say a sincere "thank you" to all the authors, reviewers, sponsors and advertisers, editorial board members and staff who have supported JASA. As ASA's professional journal, it remains a valuable resource providing evidence for our medicine—evidence that's needed to practice in the mainstream.

Respectfully,

Jennifer A. M. Stone, MSOM, LAc
Editor in Chief, JASA

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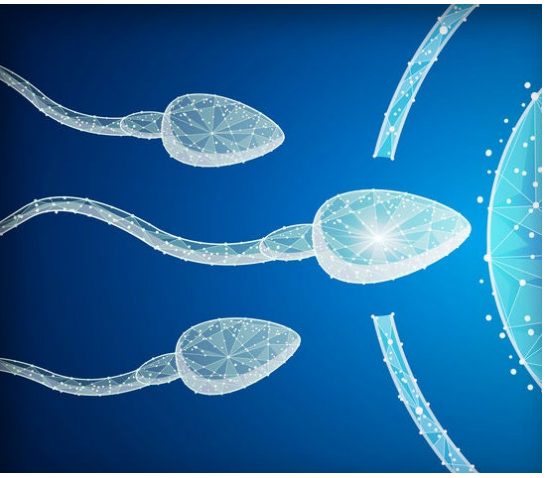


Viable Acupuncture Treatment Options for Idiopathic Male Infertility: A Literature Review Part Two

By Janel Gehrke, DAOM, LAc, Dipl OM (NCCAOM), FABORM

Dr. Gehrke completed her Master's degree in traditional Oriental medicine graduating *summa cum laude* from one of the highest ranked schools in the United States, Emperor's College of Traditional Oriental Medicine, followed by the completion of a Doctorate in acupuncture and Oriental medicine (DAOM). Her Doctoral capstone project consisted of research on the use of acupuncture as a treatment for idiopathic male infertility. In addition to her Doctoral fellowship, Dr. Gerhke has also completed a fellowship with the American Board of Oriental Reproductive Medicine (ABORM). She maintains an acupuncture practice in West Los Angeles, California, and is the Associate Dean of Clinical Education at Emperor's College of Traditional Chinese Medicine.

Abstract

Part One of this two part series discussed background information regarding male fecundity from both a current biomedical approach, including the diagnostic process and possible treatment options, as well as a traditional Chinese medical approach. Typical treatment options for men with suboptimal sperm numbers are limited and often costly; however, research shows that acupuncture can have a positive effect on sperm quality and quantity. Part Two examines the current available literature to determine if acupuncture is a viable treatment option for patients with idiopathic male infertility.

Key words: Oligospermia, acupuncture, male fertility, male infertility, idiopathic male infertility

Background

As discussed in Part One, millions of men are affected by fertility issues. The approximated numbers are reflective only of those who have reported and been diagnosed with infertility. It is possible that millions more are clinically infertile but haven't had access to medical care or have chosen not to reproduce and therefore not address fertility issues.

For men who have received a diagnosis of infertility and are trying to start a family, some research shows a link between decreased DNA quality in males of advanced paternal age. This can have adverse effects on fetal development as well as increased likelihood of miscarriage/fetal loss, single gene disorders, and congenital abnormalities.[1] Research is also showing infertility among males as being linked to other health concerns such as cancer.[2] The goal of this literature review is to ascertain if acupuncture can be a viable treatment option for those specifically diagnosed with idiopathic male infertility.

Methodology

Research for this review consisted of publications produced between 2005 and 2018. The search engines used to access the publications were PubMed and Ebscohost. Key

words used to define the search were: oligospermia, acupuncture, male fertility, male infertility, and idiopathic male infertility. The inclusion criteria allowed for studies using strictly acupuncture, any gauge disposable acupuncture needle, inserted to any depth within standard TCM guidelines, and retained for any amount of time, on male patients diagnosed with idiopathic infertility.

The studies could have been performed in any country so long as an English translation of the study was available for review. Only full text publications were eligible. There was no minimum number of participants required per study. Each study needed a minimum score of five on the modified JADAD scale. All semen samples must have been analyzed based on WHO standards.

Any publication using anecdotal case study or case report was excluded. In addition, studies involving patients with known endocrine dysfunction, systemic or infectious disease, and/or immunological conditions were also excluded. No studies that noted female infertility factors were included. Any study using TCM adjunctive techniques including electro acupuncture, moxibustion, and/or Chinese herbal preparations were excluded. Studies using pharmacological intervention and/or hormonal therapy were also excluded. Animal studies were not included.

The initial search using the key words resulted in 138 publications. Eighty-one duplications were removed, resulting in an assessment of 57 eligible publications. After applying all inclusion/exclusion criteria, 55 of the 57 eligible publications were eliminated. The two publications that met the above defined criteria were a prospective controlled trial from 2005 and a prospective randomized placebo-controlled study from 2009.

An additional 597 publications were identified using the references of 17 relevant publications from the initial search. All 597 were eliminated upon review due to lack of relevance and/or duplication. Figure 1 summarizes the research work flow.

"The inclusion criteria allowed for studies using strictly acupuncture, any gauge disposable acupuncture needle, inserted to any depth within standard TCM guidelines, and retained for any amount of time, on male patients diagnosed with idiopathic infertility."

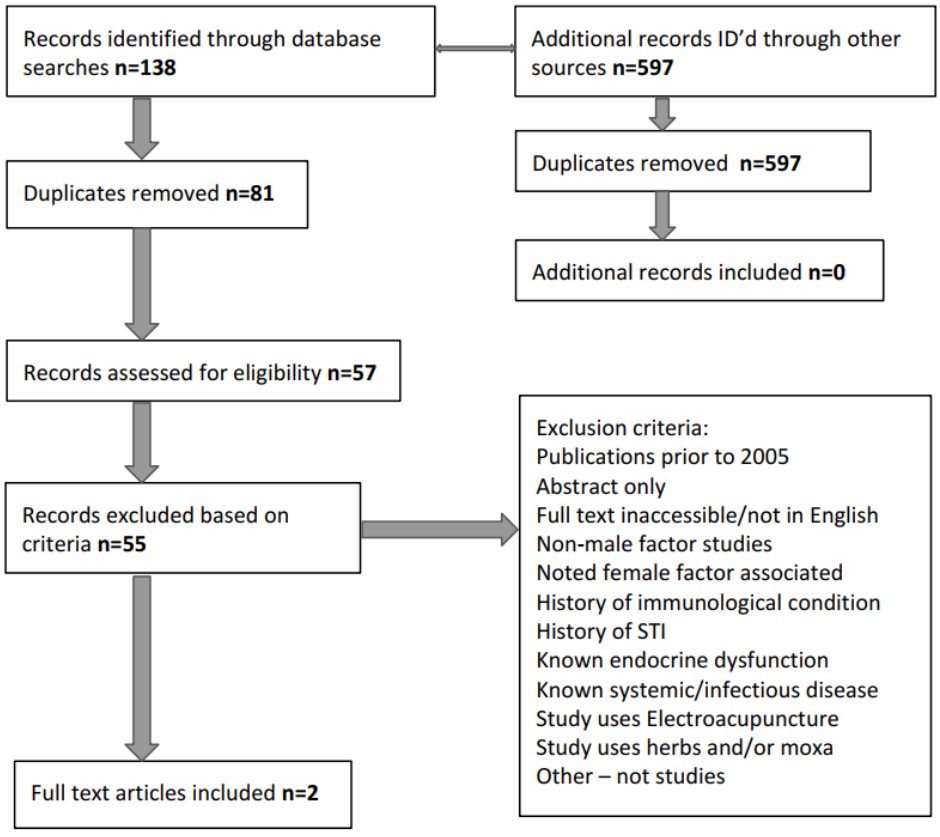
Literature Review

In 2005, Pei et al. published a prospective controlled trial that examines the effect of acupuncture on spermatozoa ultrastructure, or fine organelles involved in fertilization, in patients with IMI using transmission electron microscopy (TEM).[3] The study was approved by the ethics committee of the University of Ulm, and the participants of the study were existing patients of the Christian Lauritzen Institute in Ulm, Germany.

Recruitment was open to couples who had been trying to conceive for a minimum of two years without success. Female partners must have had at least two failed IUI cycles and had undergone rigorous infertility examinations to eliminate them as a contributing factor. The male partners also went through extensive andrological, endocrine, and laboratory examinations before being diagnosed with idiopathic infertility. They had to have a minimum of two pathological spermiograms at six week intervals according to the WHO criteria.

Any patient with thyroid dysfunction, adrenal disorders, hyperprolactinemia, pathological hormone levels, azoospermia, infectious, systemic, or immunologic-associated disease, abnormal stressors, or a detectable cause of infertility were excluded from the study. All participants gave written consent before treatment.

Figure 1. Research Flow Chart



A total of 40 participants with a mean age of 33 (range 25 years to 46 years) were selected for the trial; 28 received acupuncture twice weekly for a period of five weeks, while the control group consisted of 12 IMI patients who received no treatment but gave semen samples at the same intervals as the treatment group. An independent researcher using computer software randomized the samples taken from the untreated control group and the treatment group. Neither group received additional intervention.

All participants of the treatment group received acupuncture using Viva brand 0.25 x 25 mm or 0.25 x 40 mm sterile single-use disposable stainless steel needles inserted to a depth of 15-25 mm. The size of needles and depth of insertion was determined based on the anatomical location of the acupoint.

All acupoints were manually stimulated until the point of *deqi* [i] sensation, after which the needles were retained for 10 minutes, then re-stimulated with a total retention time of 25 minutes. The acupoints used in the study were as follows: CV-4 guanyuan, BL-23 shenshu (bilateral), BL-32 ciliao (bilateral), LIV-3 taichong (bilateral), KI-3 taixi (bilateral). The following acupoints were listed as secondary points with no further explanation: ST-36 zusanli (bilateral), SP-10 xuehai (bilateral), SP-6 sanyinjiao (bilateral), ST-29 guilai (bilateral), GV-20 bai hui. All locations were based on the WHO standards.[4]

Two semen samples were collected from each participant in the treatment group. The first one on the day before acupuncture after a three day period of abstinence, and the second after acupuncture treatment. All samples from the control group and the treatment group were assessed based on WHO laboratory manual criteria and randomized before examination by two experts who were blinded to the groups.

Evaluation of the samples was completed using TEM, performed in Siena, Italy, in the Biology Section of the University of Siena. Results of the analysis were made available to each of the participants. Following evaluation of the samples, statistical analysis of the data was performed at Augsburg University at the Institute of Mathematics.

Upon initial examination of the samples, the acupuncture group showed 0.06% healthy spermatozoa within the ejaculate; the control showed 0.16%. The expected minimum number of healthy spermatozoa per ejaculate based off the formula of Baccetti et al.[5] was 2 x 10.[6] The control group showed 0.14 x 106, and 0.04 x 106 in the acupuncture group. After the five week treatment protocol, the median percentage of healthy sperm increased to 0.26% and the median number of healthy sperm increased to 2 x 10,[6] a statistically significant change.

TEM analysis showed no significant change in median sperm number per milliliter nor in the volume of ejaculate. There was a statistically significant difference between the two groups in regard to median percentage of total motility, which increased in the control group from 32% to 37% in the control group and from 44.5% to 50% in the acupuncture group.

Table 1 summarizes the detailed results of TEM analysis on sperm ultrastructure and organelles. Pei et al. concluded that "acupuncture treatment is a simple, non-invasive method that can improve sperm quality."[3]

Table 1. Results of TEM analysis on Control and Acupuncture groups

	Control Group		Acupuncture Group		
Ultra Morphologic Features	Before	After	Before	After	*P* =
Median number of sperm/mL					0.657
Median volume of ejaculate					0.731
Median percentage of total motility in ejaculate	32%	37%	44.5%	50%	0.017
% of healthy sperm in ejaculate	0.16%		0.06%	0.26%	0.012
Median number of healthy spermatozoa in ejaculate	$0.14x10^6$		0.04×10^6	0.2×10^6	0.002
Acrosome in normal position	65%	71.5%	69.5%	77.5%	0.013
Acrosome of normal shape	26%		22.5%	38.5%	<.001
Normal nuclear shape	29%		30%	42.5%	<.001
Condensed chromatin	36%-39%		36%-39%		0.506
Normal axeome pattern	52%	38.18%	46.06%	52.19%	0.005
Normal axeome shape	67.44%	55.85%	63.64%	67.71%	0.022
Normal accessory fibers	48.68%	34.06%	34.06%	48.53%	0.005
Normal fibrous sheath	44.41%		33.33%	40.59%	*
Apoptosis	8.18%	6.43%	7.80%	7.15%	0.863
Immaturity	68.23%		71.29%		0.146
Necrosis	37.28%	44.03%	36.7%	34.3%	0.072**

[3]

*Acupuncture group showed a tendency to an increase after 5 weeks treatment

**Acupuncture group showed a trend toward a decrease after 5 weeks treatment

Following the work done by Pei et al., Dieterle et al. published a prospective randomized placebo controlled study that took place between 2006 and 2008 examining the effect of acupuncture in patients with severe oligoasthenozoospermia[ii].[6] The study took place at the University of Witten/Herdecke, Germany, and was approved by an Institutional Review Board (IRB).

Informed consent was obtained from each patient, in addition to following the guidelines of both Consolidated Standards of Reporting Trials (CONSORT) and Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA). The study population was selected from existing patients in the Reproductive Endocrinology Infertility Division with semen samples showing <1 million sperm/mL. The selected patients were not diagnosed with hypogonadotropic hypogonadism, did not have obstructive azoospermia, and had not received chemotherapy or radiation therapy within the past year.

A total of 59 participants were divided by a computer generated random allocation sequence into an acupuncture group and a placebo acupuncture group. Both groups received treatment twice weekly for six weeks with no additional interventions. The treatment of both groups was performed by two experienced acupuncture specialists from Tongji Hospital in Wuhan, China, with University level TCM training.

Needles used were 0.30 x 3.0 mm Asia-Med and insertion depth ranged from 15-30 mm, depending on the region of the body needled. Manual stimulation to the point of *deqi* sensation was performed, then manual stimulation was repeated after ten minutes. The placebo group received treatment using non-penetrating 0.30 x 3.0 mm Asia-Med placebo acupuncture needles. Both groups retained needles for a total of 45 minutes with no explanation to the patients.

The acupoint selection for both groups was based on the previous study by Pei et al.[3] The following acupoints were used on all patients: ST-36 zusanli (bilateral), SP-6 sanyinjiao (bilateral), KI-3 taixi (bilateral), LIV-3 taichong (bilateral), BL-23 shenshu (bilateral), BL-32 ciliao (bilateral), ST-29 guilai (bilateral), SP-10 xuehai (bilateral), and CV-4 guanyuan. The acupoint GV-20 bai Hui was used in the study by Pei et al.; however, it was removed from this study due to fixation concerns with placebo needles.

The acupuncture specialists were unaware of the laboratory data, and both patients and study personnel were blinded to group assignment. The study reported no adverse events or side effects in either group. The study outcomes consisted of motility, concentration, and volume. Morphology was not evaluated due to the possibility of subjective assessment in low sample volumes.

Participants of the study were selected to be of similar age, body mass, duration of infertility and abstinence. All semen analyses were done according to WHO standards. Four semen samples were taken for all patients. The first sample was collected five months before treatment protocols began. The second sample was taken less than three months before the treatment. The third sample was taken less than two months after the treatment and the fourth sample was taken less than or equal to three months after the treatment. Timing of samples is summarized in Table 2.

Table 2. Semen Sample Timeline

Sample 1	≤ 5 months before treatment
Sample 2	< 3 months before treatment
Sample 3	< 2 months after treatment
Sample 4	≤ 3 months after treatment

Sperm motility before and after acupuncture was considered the primary outcome measure of this study, while sperm concentration and semen volume were considered secondary outcome measures. All outcome measures are summarized in Table 3.

Table 3. Outcomes Before and After Acupuncture

Variable	Acupuncture group	Placebo
Motility A before intervention (%)	11.5 ± 12.5	16.0 ± 13.4
Motility A after intervention (%)	12.1 ± 8.6	13.1 ± 13.3
P value	NS	NS
Motility B before intervention (%)	8.1 ± 10.2	8.0 ± 8.0
Motility B after intervention (%)	10.5 ± 11.8	8.8 ± 7.5
P value	NS	NS
Motility C before intervention (%)	4.6 ± 6.9	8.2 ± 8.4
Motility C after intervention (%)	11.2 ± 13.7	7.8 ± 7.8
P value	NS	NS
Motility A–C before intervention (%)	24.2 ± 17.0	32.2 ± 18.1
Motility A–C after intervention (%)	33.8 ± 18.2	29.7 ± 17.6
P value	.035	NS
Motility D before intervention (%)	75.8 ± 17.0	67.8 ± 18.1
Motility D after intervention (%)	66.2 ± 18.2	70.3 ± 17.6
P value	.035	NS
Concentration before intervention (million/mL)	0.039 ± 0.128	0.016 ± 0.085
Concentration after intervention (million/mL)	0.465 ± 1.206	0.468 ± 1.712
P value	NS	.0180
Volume before intervention (mL)	4.2 ± 1.8	4.0 ± 1.8
Volume after intervention (mL)	3.7 ± 1.4	3.8 ± 1.6
P value	.041	NS

Note: Data are presented as mean ± SD. A–D = World Health Organization motility categories: rapid linear progressive, slow or nonlinear progressive, nonprogressive, and immotile, respectively; NS = non significant.

continued on page 10

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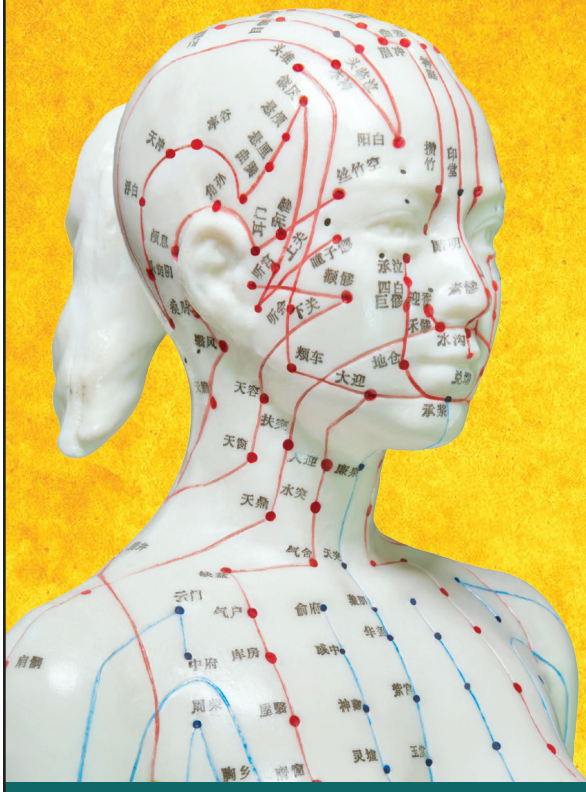

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The results of this study showed acupuncture as having a significant effect on total motility. There was a noted decrease in semen volume after acupuncture which deems further investigation. The study also found a significant increase in sperm concentration after placebo acupuncture; however, it is noted that the number of patients included in the study may not have been adequate to show a statistically significant difference in concentration. Results including *P* values are summarized in Table 4.

Table 4. Summary of Results Dieterle et al.

Outcome	After Acupuncture	Placebo	*P* value
Total Motility	Significant Increase		*P* = .035
Category A	No Significant Change		
Category B	No Significant Change		
Category C	No Significant Change		
Semen Volume	Decreased		*P* = .041
Sperm Concentration		Significant Increase	*P* = .018

Discussion

The 2005 study by Pei et al. offers a detailed examination of the positive effects of acupuncture on not only total sperm numbers, but also spermatozoa ultrastructure. Improvements were shown in both the median percentage and number of healthy sperm in the total ejaculate. The TEM analysis allowed the researchers to examine specific changes in the ultrastructure before and after acupuncture treatment. Statistically significant improvement was seen in both acrosome characteristics and nuclear shape, in addition to positive effects noted on the axoneme and accessory fibers contributing to an increase in motility from 44.5% before treatment to 50% after.[3]

Although approved by the ethics committee of the University of Ulm, neither CONSORT nor STRICTA guidelines were mentioned in the Pei et al. study design. The calculations used to determine sample size were not included in the publication.

Information regarding the training and/or experience of the individuals administering the acupuncture treatments was also not mentioned. The points chosen were listed in detail; however, the reasoning behind the selection was not given. There was no information given regarding the justification and/or use of the primary vs. secondary points. No information is given on the timing of the post-treatment semen samples with the exception of stating the sample was taken "after acupuncture treatment."[3]

"Due to the complicated and individualized process of TCM diagnostics and lack of TCM diagnosis in both studies, it can be assumed that no specific diagnosis was given to each participant."

The age of the participants was noted and the inclusion criteria of the study specifies a minimum duration of infertility. There was no mention of drop-outs, patients lost to follow up, or reported adverse events during treatment.

Dieterle et al. noted use of an IRB in addition to abiding to the guidelines of CONSORT and STRICTA. The points chosen were sourced from a previous study with no justification for point selection. Also, one of the points from the protocol was removed to accommodate placebo acupuncture, which could have affected outcomes. There was also no mention of primary or secondary points which were mentioned in the study that sourced the acupoint selection.

Timing of the semen samples was noted; however, a period of abstinence before collection and method of collection was not. The study notes that the sample size calculations may have had an effect on the secondary outcome of semen volume and that further investigation is required. The WHO was cited in the text of this publication as the standard for semen sample evaluation; however, there was no reference to the WHO within the bibliography to confirm the use of the newest edition and therefore, updated parameters.

Due to the complicated and individualized process of TCM diagnostics and lack of TCM diagnosis in both studies, it can be assumed that no specific diagnosis was given to each participant. One could argue the treatment may have been significantly more effective if acupoint selection was customized to each patient's specific TCM diagnosis. In fact, Dieterle et al. point out that the fixed acupoint protocols applied for the purposes of a randomized control trial may negatively affect the outcomes.[6]

Conclusion

Using the latest technological advances to harvest sperm from either the vas deferens, epididymis, or the testes may solve the short term problem of reproduction; however, it does not address the long term concerns potentially facing the resulting offspring and/or the long term health of the male partner. The investigation

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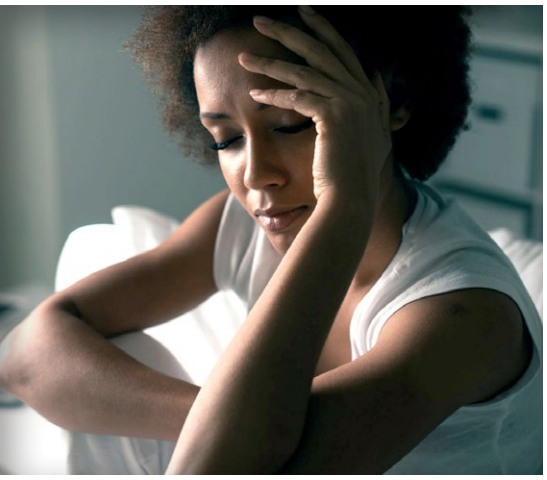

Comparing Hypertension with Liver *Qi* Stagnation to Psychosomatic Theory and Correlated Mechanisms: A Review of Chinese Literature

By Kimberly Coleman,[1] MTCM, RN, LAc, Dipl OM (NCCAOM)
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Please see bios at end of the article.

Abstract

Due to the increased pressure of modern life, mental anxiety and depression are becoming more prevalent. Stress and negative emotions can lead to elevation in blood pressure. This review aims to clarify the correlation and mechanism between two common states seen in hypertension: Liver *qi* stagnation in Chinese medicine along with anxiety and depression in psychosomatic medicine. The Chinese research database CNKI was searched using key words in Chinese and relevant articles were selected. Theoretical, experimental, and clinical research studies were reviewed to explore the mechanism of "course Liver and rectify *qi*" and to further analyze common factors and points of regulation in psychosomatic medicine's mechanism. Experimental research indexes included in Chinese medicine's clinical syndrome differentiation system were analyzed, providing the basis for this research. Integrating Chinese medicine's differential diagnoses with biomedicine's pathological mechanisms, correlations were identified in order to properly incorporate the concepts and methods for the clinical diagnosis and treatment of hypertension. Limitations include non-comprehensive database searching as well as potential bias in article selection. Based on this review of current literature, the role of "Liver governs dredging" theory in the pathogenesis and prevention of hypertension and its consistency with the correlated factors and mechanisms of psychosomatic medicine can be considered as a new hypothesis.

Key Words: hypertension; anxiety; depression; Chinese medicine; Liver *qi*

1. Introduction

According to Chinese medicine (CM) theory, the etiologies of many diseases are related to negative emotions and overthinking.[1,2] This influences Liver's ability to dredge and smooth, causing a Liver *qi* knotted pattern. Prolonged stagnation can lead to Fire, which injures *yin* and may create a pattern of Liver stagnation Fire flaring.[2]

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Although they may have CM differential diagnoses, including Liver *yang* rising, Phlegm-Damp obstructing the middle, *yin* deficiency *yang* rising, or many other pathogenic differences,[3] patients with hypertension (due to stasis of the *qi* mechanism, especially early stage hypertension or middle-aged and young patients) cannot be separated from Liver *qi* knotted.[4] The disease onsets of Liver *qi*, Liver *yang*, and Liver Fire all have their origins in Liver stagnation. This suggests that Liver stagnation is one of the most important disease pathogensis in the theory of emotional causes of disease.[2]

According to the Medical Subject Headings (MeSH) scope note, psychosomatic medicine is defined as "a system of medicine which aims at discovering the exact nature of the relationship between the emotions and bodily function, affirming the principle that the mind and body are one."[5] Fava et al. further state: "Psychosomatic medicine is a wide interdisciplinary field that is concerned with the interaction of biological, psychological, and social factors in regulating the balance between health and disease."[6]

This view strongly correlates with CM's holistic conception of the interrelation of body and mind as well as the organism with its environment. This review aims to clarify the correlation and mechanism between two common states seen in hypertension; that of Liver stagnation in Chinese medicine, along with anxiety and depression in psychosomatic medicine.

2. Methodology

Theoretical, experimental, and clinical research studies were reviewed to explore the mechanism of "course Liver and rectify *qi*" and to further analyze common factors and points of regulation in psychosomatic medicine's mechanism. To accomplish this, the Chinese-based research database CNKI was searched based on these key words (in Chinese): hypertension, anxiety, depression, Chinese medicine, Liver *qi*. See Table 1 for key word translations.

Table 1.

Key Word	Chinese Translation
Hypertension	高血压
Anxiety	焦虑
Depression	抑郁
Chinese medicine	中医
Liver *qi*	肝气

Research published since the year 2000 was searched. Relevant articles were selected and reviewed. Secondary references from selected articles were also considered. After analyzing current research on the role and influence of Liver stagnation and anxiety-depression states in the pathogenesis and pathological evolution of hypertension, the common factors related to the two states, including clinical manifestations and experimental indicators, were identified. The correlated studies on the mechanisms behind the effects of CM were then explored.

3. Analysis of the Related Current Research and Development in China

Epidemiological studies[7] show that 62% of patients with hypertension had significant symptoms of anxiety, and 82% of patients with hypertension had varying degrees of depressive symptoms. Psychological factors also have an important effect on the occurrence and development of cardiovascular disease as well as on its prognosis.[8]

The simultaneous existence of depression, anxiety, and hypertension complicates the disease and forms a vicious cycle, interacting as both cause and effect aggravating one another and possibly worsening the disease.[9] More and more scholars are calling attention to the mental-emotional problems associated with cardiovascular disease.[10,11]

Chinese cardiovascular scholar Hu Dayi was the first in China to put forward the concept of *shuang xin yi xue,* literally translated as "double heart medicine" and known as "psychocardiology" in the West. Psychocardiology is a specialty field within psychosomatic medicine and takes into account both the physiological heart organ as well as the metaphysical heart's mental-emotional aspects. Hu then founded a corresponding psychocardiology clinical practice in which cardiovascular doctors and psychiatrists (or psychologists) worked together to treat patients with coronary heart disease; their aim was to avoid misdiagnosis, improve efficacy, and arouse positive social attention.[12]

3.1 Mechanism of action between mental-emotional factors and blood pressure

Due to the establishment of this new medical treatment model of hypertension (psychocardiology)[10,12] and the gradual development of "neuro-endocrine-immune" network research,[13] greater attention is being given to researching the physiological and psychological association of diseases. The presence of mental symptoms may cause the cerebral cortex to have sustained overstimulation, leading to elevated blood pressure, which could result in the individual worrying about their illness and prognosis, which in turn may aggravate their mental symptoms.

The presence of long-term mental factors can cause disregulation in the renin-aldosterone-angiotensin system, resulting in blood pressure elevation. Research studies have shown that depression and anxiety are independent risk factors for hypertension or

"Chinese medicine theory that emotions cause disease harks back to ancient times; it focuses special attention to the close relationship between Liver Wood and emotional disease. CM holds that hypertension is often accompanied by a state of anxiety and depression, and the hypertension with Liver stagnation pattern can reveal one of its pathological roots."

elevated blood pressure, and the incidence is significantly higher than in the normal population.[14,15]

Among the psychological factors accompanying cardiovascular disease in patients, anxiety and depression are the primary manifesting symptoms. Patients with hypertension are more likely to develop clinical depression and anxiety disorders, and hypertension can lead to or aggravate depression due to the patients' lack of knowledge about their disease or their inability to self-regulate following their diagnosis.[14,15]

When a diagnosis of hypertension is regarded as a type of stress, this alone can often cause a variety of psychological reactions, such as being prone to panic, anxiety and other negative emotions. If the patient has an insufficient understanding of their condition, a relatively poor ability to adapt and regulate after the diagnosis, or excessive tension and anxiety concerning the disease, this can then give rise to different degrees of depressive manifestations.[16]

Yang Bo and fellow researchers revealed that depression leading to hypertension may be associated with hypothalamic dysfunction. On one hand, depression gives rise to adverse effects on brain function resulting in impeding function, hypothalamic blood vessel contraction, and central sympathetic nerve excitation. By passing down through the body's nervous and endocrine systems, it can arouse systemic sympathetic nerve excitation, which can then cause an increase in adrenal medullar secretion, cardiac output, and blood pressure. On the other hand, due to increased activity of the HPA axis, there is increased steroid hormone secretion and water retention, causing blood pressure to rise.[17]

It can be seen that mental emotional factors do participate in the process of elevated blood pressure, and by resolving the psychological factors of patients with hypertension, this can improve treatment efficacy.

3.2 Psychosomatic treatment of hypertension with psychological factors

Little has been reported on systematic assessment and diagnosis of patients from biological, psychological, social, and other perspectives. Pharmaceutical drugs can indeed lower blood pressure relatively rapidly and thus improve the state of mental anxiety and depression with reliable effects. For example, it is common for patients to take beta-blockers as needed for performance anxiety. However, their corresponding side effects cannot be avoided, which can result in poor patient compliance. And unfortunately, hypertensive patients' long-term terminal events are still not effectively reduced.[18] Therefore, the prevention and treatment of hypertension is no longer as simple as lowering blood pressure; rather, prevention and reversal of end-organ damage along with improvement of patients' quality of life and other psychological factors are particularly needed.

At present, the clinical treatment of hypertension has attached great importance to psychological intervention. Clinical research shows antihypertensive treatment combined with anti-anxiety and anti-depression treatment, when compared with antihypertensive treatment alone, not only can improve depressive symptoms but the antihypertensive effect is also more significant.[19,20]

3.3 Chinese Medicine research regarding hypertension with Liver stagnation

Chinese medicine theory that emotions cause disease harks back to ancient times; it focuses special attention to the close relationship between Liver Wood and emotional disease. CM holds that hypertension is often accompanied by a state of anxiety and depression, and the hypertension with Liver stagnation pattern can reveal one of its pathological roots. A number of CM experts have carried out research on this. For example, Yan Jiansheng, through analysis of changes in the concentration of free Ca2+ in red blood cells of patients exhibiting hypertension with Liver Fire blazing pattern, found that this CM pattern was related to patients' increased central sympathetic nerve excitability.[21]

Yu Jinsong and others conducted a controlled study of five CM differential diagnosis population groups: Liver *qi* knotted pattern, Liver Fire ascending pattern, Liver *qi* deficiency pattern, Liver *yang* rising pattern, and the healthy control group. They found that the Beck anxiety and depression scale measurement scores were significantly higher in those with the four types of Liver pattern differential diagnoses than in the healthy population. On the Beck anxiety scale, those with Liver Fire ascending pattern had a higher state of anxiety than Liver *qi* knotted pattern or Liver *qi* deficiency pattern.[22]

The frequency of serotonin-transporter-linked polymorphic region (5-HTTLPR) SS genetic type in those with Liver Fire ascending pattern was significantly higher than in the healthy population.

Also, the frequency of S allele in those with Liver Fire ascending pattern was significantly higher than the healthy group. It is therefore believed that 5-HTTLPR polymorphic SS type individuals may be susceptible to Liver *yang* rising and Liver Fire ascending patterns.[22]

Similarly, Hu Suiyu and colleagues found that 5-HTTLPR polymorphism had significant differences in the frequency of distribution in the patients with Liver Fire ascending pattern when compared with the control group. 5-HTTLPR polymorphic SS genotype was higher in the Liver Fire ascending pattern group than the healthy control group. They also concluded that 5-HTTLPR polymorphic SS type individuals may be susceptible to Liver Fire rising pattern, but also stated this conclusion needs a further expanded sample size for study.[23]

Li Xing and others found that in those with Liver Fire ascending pattern, they had mutually coinciding characteristics, including: endogenous nerve-body fluid metabolism dysfunction, excessive sympathetic nerve function, and an inflammatory response. The study showed elevation in plasma norepinephrine (NE), epinephrine (E), cortisol (F), and aldosterone (Ald). They believe that when the body is in a state of stress, it can manifest in sympathetic–adrenal medulla and adrenal cortex hyperfunctioning.[24]

When conducting research on essential hypertension (EH) CM differential diagnosis patterns and plasma endogenous peptide content, Zheng Guanyi and others found that in the three pattern types of Liver Fire blazing, Phlegm-Damp abundance, and *yin* deficiency *yang* rising, the neuropeptide Y (NPY) and NE content was higher than in *yin yang* dual deficiency pattern type; while beta-endorphin (beta-EP) was by contrast lower.[25] In addition, there are also relevant research reports showing Liver stagnation Fire flaring pattern is closely related to serum rheology,[26] microcirculation,[27] and hemodynamics.[28]

Regarding the pathogenesis of hypertension with accompanying mental-emotional factors, from the point of view of condition-based medicine (state medicine), Zhou Lihua's[29] research demonstrates that hypertension is a pathological state secondary to other pathological states and the factors that lead to them. Under normal circumstances, blood vessels maintain a certain degree of tension to ensure the normal flow of blood circulation.

He posits that if there is long-term anxiety or depression, the organism can exhibit a high-tension state such as sympathetic nervous system hyper-functioning, which then elevates blood vessel tension. This in turn increases the shearing force of blood against the vessel walls, which results in blood pressure elevation and eventually contributes to the development of cardiovascular disease.

"Chinese herbs can reduce blood pressure moderately and concurrently act on multiple pathological segments such as patients' physiological as well as psychological pathomechanisms."

4. Discussion and Implications for Future Research

Hypertension is a disease caused by the interaction of both genetic and environmental factors. With the accelerated pace and increasing pressure of modern life, mental anxiety and depression are more prevalent and their impact on blood pressure is closely related. The existence of anxiety and/or depression along with hypertension makes for more complex disease and forms a vicious cycle, mutually interacting as both cause and effect by aggravating each other and thereby worsening disease.

Liver *qi,* as one of Chinese medicine's internal organs *qi,* is the material basis and motivation for the physiological function of Liver. Therefore, its disharmony can lead to the onset of many diseases, including hypertension. CM theory states that Liver's main function is that of dredging, with the role of maintaining the whole body's *qi* mechanism, thus promoting the movement of blood and body fluids as an integral component of homeostasis and normotension. Negative emotions cause Liver to lose its function of dredging and leads to stagnation of the *qi* mechanism. This then becomes a Liver *qi* knotted pattern, which belongs to the category of stagnation.

Although the effect is obvious, in the clinical use of antihypertensive medications along with anxiolytics and anti-depressants, the resulting side effects of drugs cannot be avoided. Chinese medicine plays an irreplaceable role in the treatment of patients with hypertension accompanied by psychological factors.

The CM pattern-differentiation type of diagnosis emphasizes individualized treatment such that in conjunction with pharmaceutical drugs to reduce blood pressure, more attention can

be given to patients' different personality characteristics and psychological factors. Furthermore, Chinese herbs can reduce blood pressure moderately and concurrently act on multiple pathological segments such as patients' physiological as well as psychological pathomechanisms. Multiple symptoms are therefore addressed, which can lead to an improvement of patients' quality of life.

CM recognizes that different mental states are correlated with different patterns of illnesses and, generally speaking, an excited mental state is correlated with illnesses of Excess, whereas a depressed mental state is correlated with illnesses of Deficiency.[1] Current CM research regarding hypertension with Liver stagnation has not differentiated CM patterns correlated with anxiety and depression.

Additional basic science research would benefit from exploration of the following hypothesis: Liver *qi* knotted pattern is static and can be seen as correlating with a depressed state; Liver stagnation Fire flaring pattern is dynamic and can be seen as having a correlation with an anxious state.

By utilizing CM's "course Liver and rectify *qi*" method to treat hypertension with Liver stagnation, patients' mental as well as physical symptoms can be simultaneously addressed. Studies have shown that not only is the antihypertensive effect of CM obvious, but also, in the absence of formal psychological therapy, the treatment can change the psychological factors of patients and thus achieve the effect of doing more with less.[19,30] Further clinical research using CM's differential diagnosis and emphasizing individualized treatment should also be explored, which in turn can enhance biomedicine's primary goal of simply lowering blood pressure.

To summarize, CM research regarding hypertension with Liver stagnation (section 3.3) shows that when Liver stagnation causes Fire, several things occur: the body's endogenous nerve-body fluid metabolism becomes imbalanced; sympathetic nerve function tends to elevate; and the hypothalamus-pituitary-target gland axis hormones have different degrees of secretion disorder. Catecholamines (norepinephrine, epinephrine) are especially more significantly increased. The incidence of Liver *qi*, Liver *yang* and Liver Fire all stem from Liver stagnation; therefore, Liver stagnation state is one of the important etiological pathogeneses in the theory of emotionally caused diseases, one of which is hypertension.

Other causes of disease, including emotional discontentment and overthinking or worry, will affect Liver's dredging and venting function. This in turn causes Liver *qi* to knot, which results in prolonged stagnation that then causes Fire. Subsequent *yang* rising injures *yin* and finally becomes Liver stagnation Fire flaring pattern, but this cannot be separated from Liver *qi* knotted.

"...if there is long-term anxiety or depression, the organism can exhibit a high-tension state such as sympathetic nervous system hyperfunctioning, which then elevates blood vessel tension. This in turn increases the shearing force of blood against the vessel walls, which results in blood pressure elevation and eventually contributes to the development of cardiovascular disease."

5. Conclusion

This review discusses hypertension as a disease that has both physical and mental (psychosomatic) factors. In addition, the authors put forth the hypothesis that both hypertension with Liver stagnation and hypertension with anxiety-depression are closely related: hypertension with Liver stagnation, including Liver *qi* knotted pattern and Liver stagnation Fire flaring pattern.

New ideas and methods for treatment stemming from the correlated mechanisms between hypertension concerning the Liver stagnation state and the anxiety-depression state should be pursued. This has the potential to influence modern medicine's strictly biologic model such that it can become a more holistic bio-psycho-social model.

Limitations to this critical review include non-comprehensive database search as well as potential bias in article selection due to limited personnel vetting articles for inclusion.

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(2) Chinese Medicine Administration – Evaluation of the efficacy of Chinese herbal medicine combined with psychological intervention in treating hypertension with Liver stagnation Fire blazing pattern (project number: 2015ZY02053).

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Electroacupuncture May Support Orthobiologic Therapeutic Outcomes for Knee Osteoarthritis: A Systematic Review

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Abstract

Objective

Osteoarthritis is a degenerative joint disease that affects nearly 27 million people in the United States, with the most common joints reported being hips, knees, and hands. A clinical diagnosis for osteoarthritis is pain, stiffness, and loss of function upon physical examination. Nearly nineteen percent of the American population over the age of forty-five have knee osteoarthritis, and this figure is expected to increase amid an aging population. The field of Cell Therapy emphasizes the physiological process of stimulating the repair of living tissue that was once believed to be irreparable by the body. Conventional therapies that treat osteoarthritis focus on reducing pain and improving function. Electroacupuncture has demonstrated immune modulation. This paper evaluates current literature to determine whether the immune response to electroacupuncture is complementary to cell therapy in the treatment of knee osteoarthritis, thereby creating a sub-discipline of Traditional Chinese Medicine within the field of Cell Therapy using Orthobiologics.

Methods

Search methods utilized PubMed, Google Scholar, and EBSCO host databases. Articles searched included years 2000 through 2018.

Results

Biochemical precursors to dopamine and acetylcholine, and cell signaling pathways within the extracellular environment, inhibit pro-inflammatory cytokine production. Standardization of protocols concerning the harvesting and processing of cell-based, orthobiologic products is strongly recommended by researchers to provide consistency among therapeutic outcomes.

Discussion

This systematic review represents a translational study of the immune modulatory effects of electroacupuncture as related to the use of cell therapy.

Conclusion

Evidence-based practices utilizing electroacupuncture to stimulate the vagus nerve demonstrates immune modulation. More research is needed to investigate the complementary effect of electroacupuncture to strengthen the clinical outcomes in the process of cell therapy using orthobiologics for the treatment of knee osteoarthritis.

Key Words: Regenerative medicine, electroacupuncture, knee osteoarthritis, platelet-rich plasma (PRP), inflammatory cytokines, and immunomodulation.

Introduction

Osteoarthritis (OA) is a degenerative joint disease[1] that affects nearly 27 million people in the United States, with the most common joints reported being hips, knees, and hands.[2] Nearly nineteen percent of the American population over the age of forty-five have been diagnosed with knee osteoarthritis, and this figure is expected to increase amid an aging population.[3]

Clinically, OA is evaluated by the presentation of pain, stiffness, and loss of function upon physical examination. This paper evaluates current literature to determine whether the immune response to electroacupuncture is complementary to cell therapy using orthobiologics in the treatment of knee osteoarthritis.

The Knee and Hip OsteoArthritis Screening Questionnaire (KHOA-SQ) offers high sensitivity and moderate specificity in the evaluation for osteoarthritis of the knees and hips.[4] The Western Ontario & McMaster Universities (WOMAC) Index is another commonly used survey to objectively evaluate the symptoms of patients with osteoarthritis.[5] A high score on either of these questionnaires is indicative of clinically progressive conditions of OA relating to increased pain and decreased function.

Radiographically, diagnostic markers for OA are based on the Kellgren/ Lawrence scale evaluating the severity of knee OA.[2] An accurate diagnosis shows both clinical and radiographic findings.

Traditional Chinese medicine (TCM) evaluates degenerative joint disease as a pattern involving bi Syndrome, including Wind *bi*, Damp *bi,* Cold *bi*, and Heat *bi*, or any combination of these patterns (i.e., Wind-Damp-Cold *bi* Syndrome).[6]

The National Institute of Biomedical Imaging and Bioengineering at the National Institutes of Health (NIH) describe the field of Regenerative Medicine as a broad field that includes tissue engineering to "recreate cells or rebuild organs."[7] Conventional therapies that treat osteoarthritis focus on reducing pain and improving function. As an extension of Regenerative Medicine, cell therapy proposes to reverse degenerative joint diseases with the use of orthobiologics,[7] whereas conventional therapies palliate symptoms.

"The objective of this paper considers the variability of outcomes in the application of orthobiologic products and offers a solution to scale back these inconsistencies. Many therapies in the treatment of knee OA focus on pain management and controlling inflammation because the most common symptoms are pain and loss of range of motion due to edema.[11]"

Electroacupuncture is a modality of TCM that applies a therapeutic electric current to sterile, single-use, solid filiform needles systematically inserted through viable human tissue in order to elicit a physiological response. The risk of infection, adverse side effects, bruising, and organ damage is possible, although very rare when performed by a licensed and trained practitioner. Electroacupuncture has demonstrated immunomodulation[8] (eliciting an immune response) and may be complementary to the outcomes of cell therapy using orthobiologics.

Cell therapies such as platelet-rich plasma (PRP) injections are increasingly being used to treat knee osteoarthritis.[9] The advantages of cell therapy using orthobiologics provide an alternative to surgical intervention and pharmacotherapy. Despite these advantages, the quality of orthobiologic products (i.e. PRP, bone marrow aspirate, etc.) is difficult to assess. Furthermore, various biomarkers and growth factors are used to characterize the therapeutic outcomes from orthobiologic products and this variety causes more difficulty to evaluate outcomes, objectively.[10]

The evaluation of current literature seeks evidence of physiological responses related to the immune modulation of electroacupuncture and whether the use of electroacupuncture can mitigate the deficits of cell therapy using orthobiologics in the treatment of degenerative joint disease. The objective of this paper considers the variability of outcomes in the application of orthobiologic products and offers a solution to scale back these inconsistencies. Many therapies in the treatment of knee OA focus on pain management and controlling inflammation because the most common symptoms are pain and loss of range of motion due to edema.[11]

This literature review is concerned with the immune modulation of electroacupuncture as complementary to cell therapy using orthobiologics in the treatment of knee osteoarthritis to repair soft tissue cartilage. Given prevalent turnover with the use of products in compliance with FDA regulation in the application of cell therapy using orthobiologics, the significance of this writing

focuses on the underlying mechanism of immunomodulation to control inflammation and support the extracellular environment to promote healing, irrespective of the use of specific products.

It is understood by the author that the immune response remains the same due to biochemistry and cell signaling mechanisms within the extracellular environment in response to various triggers, whether by physical trauma or endotoxin. Universal concepts of medical physiology and cell signaling are relevant to the mechanisms of immune function.

> "The outcome of the [cell signaling] is a physiologic response, such as secretion, movement, growth, division, or death. It is important to remember these physiologic responses are the collective result of a multitude of signaling messengers that transmit signals to the cells in various tissue."[12]

Moreover, much of the literature reviewed with respect to immune modulatory effects of electroacupuncture concerns endotoxins upregulating the immune response rather than chronic inflammatory conditions. Likewise, it is understood by the author that the immune response remains quite similar in the presence of inflammatory cytokines and tissue repair, regardless of endotoxin invasion or autologous cell infiltration based on physiologic responses to cell signaling pathways.[12]

According to the author, three influential processes that determine the success of regenerative therapies concern the role of neurotransmitters on limiting the inflammatory cascade, the cellular environment by which orthobiologic products are implanted, and the manufacturing process by which orthobiologic products are isolated from human tissue.[10, 18-22, 28-30] The following literature review investigates the immune response in the body related to these phenomena and will acknowledge a mechanism that electroacupuncture may provide to complement cell therapy using orthobiologics.[11, 25-27, 29]

Definition of Terms

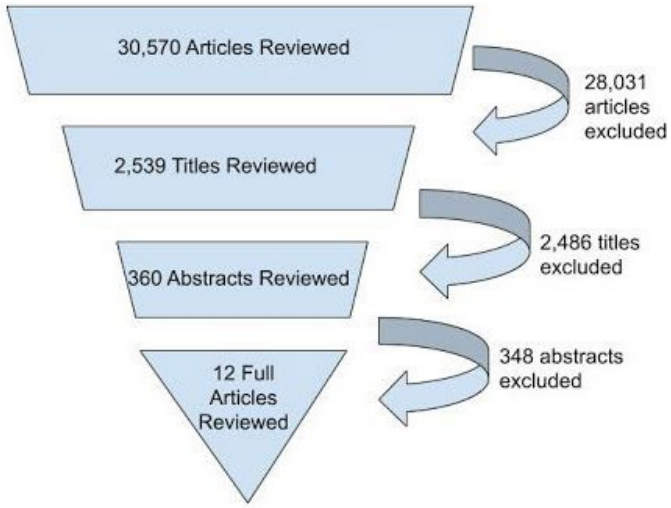
- "**Electroacupuncture**" is a combination of acupuncture and electrotherapy.[13] An electrode is clipped to the handle of a sterile, single-use, solid, filiform needle while inserted transdermally into the body at specific points and an electric current is transmitted through the needle.[14] Although electroacupuncture may be used to measure bioelectrical impedance,[15] this paper evaluated current literature on the use of electroacupuncture in relation to electrotherapy.
- "**Orthobiologic products**" refer to the manufacturing of Human Cells, Tissues, and Cellular and Tissue-based Products (HCT/Ps) defined in Title 21 of the Code of Federal Regulations Part 1271 (21 CFR 1271) as "*articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient.*" Orthobiologic products are intended for minimal manipulation and homologous use in treating conditions relating to bones, joints, and connective tissue.[16]
- "**Mesenchymal stem cells**" (MSCs) represent a classification of cells from human and mammalian bone marrow and periosteum that have the capacity, *in vitro,* to differentiate into a variety of mesodermal phenotypes and tissues.[17]
- "**Platelet-rich plasma**" refers to the processing of blood plasma to yield platelet concentrations significantly higher than that which is found in a normal sample of human blood.[10]

Methods

Search methods utilized PubMed, Google Scholar, and EBSCO host databases. The years of publication for the articles searched included the years 2000 through 2018. The total number of articles retrieved was 30,570 publications. The titles of 2,539 were reviewed with respect to inclusion/ exclusion criteria. Three hundred sixty abstracts were reviewed.

Twelve full articles were reviewed and comprise the literature review as presented in this writing (see **Figure 1**); however, an additional 12 full articles were reviewed for content presented as background information as provided in the introduction and were not included in the literature review.

Figure 1. Literature Review Inclusion Exclusion Flowchart



Overall, clinical trials in progress were study types excluded from the review as well as editorial commentary and study designs without a control group. Search terms used included acupuncture, electroacupuncture, dry needling, knee osteoarthritis, platelet-rich plasma (PRP), tissue growth, inflammatory cytokines, immune function, and immunomodulation.

Position articles and regulatory considerations published by special interest organizations and federal agencies, such as The Orthobiologic Institute (TOBI), the Center for Biologics Evaluation and Research, and the Food and Drug Administration pertaining to the classification, manipulation, and regulation of human cells, tissues, and cellular and tissue-based products (HCT/Ps) were reviewed for technical relevance but not included in the literature review.

As of July 2018, approximately 28,431 articles were retrieved in PubMed by searching the key term "acupuncture" (see **Table 1**). The inclusion criteria for this specific search result included publications with the keywords: knee osteoarthritis, laser therapy, electroacupuncture, immune modulation, warm acupuncture technique, knee pain, degenerative joint disease, ultrasound-guided acupuncture, auricular acupuncture, ST-36 zusanli, anti-inflammatory effects of acupuncture, and collagenous fibers (see **Table 4** on the following page).

Exclusion criteria for this key term search included other pathophysiological conditions unrelated to knee osteoarthritis (i.e., tendonitis, migraine, postmenopausal low bone mass density), cancer, autoimmune conditions unrelated to knee osteoarthritis (i.e., rheumatoid arthritis, Crohn's disease), meditation, and movement therapies (i.e., *tai chi* and *qi gong*).

Three hundred eighty-seven publications were retrieved in PubMed by searching the key term "dry needling." Research topics pertaining to musculoskeletal conditions (i.e., rotator cuff tendinopathy, migraine headaches, myofascial trigger points), anatomical structures, and pathogenicity unrelated to the knee (i.e., hip, shoulder, neck) were excluded from the review. Two hundred fifty-six publications were retrieved in PubMed by searching for key phrase "knee osteoarthritis + platelet rich plasma."

Publications excluded from the review consist of early-stage knee osteoarthritis and research topics published on neurodegenerative diseases and conditions, neural stem cell research including nerve growth outcomes, ischemic stroke and ischemic injury to neural tissue, traumatic brain injury, oncology research, umbilical cord blood-derived stem cells, ischemic injury to cardiac tissue, migraines, and diabetes. In addition, publication topics on gene expression associated with cholesterol-lowering effects of electroacupuncture, polycystic ovary syndrome, and lipid metabolism were excluded from the review (see **Table 1**).

Table 1. PubMed Search Criteria

Publication Years 2000 - 2018			
DATABASE	**ARTICLES**	**SEARCH TERMS**	**INCLUSION CRITERIA**
PubMed	28,431	Acupuncture	Knee Osteoarthritis, Laser Therapy, Electroacupuncture, Immune Modulation, Warm Needle Technique, Knee Pain, Degenerative Joint Disease, Ultrasound Guided Acupuncture, ST-36 zusanli, Anti-Inflammatory Effects of Acupuncture, Collagenous Fibers
	433	Acupuncture + Knee Osteoarthritis	
	387	Dry Needling	
	256	Knee Osteoarthritis + PRP	
	149	[Stem Cells Acupuncture]	
	25	Immune Modulation + Acupuncture	

Table 2. Google Scholar Search Criteria

Publication Years 2008 - 2018			
DATABASE	**ARTICLES**	**SEARCH TERMS**	**EXCLUSION CRITERIA**
Google Scholar	337	Electroacupuncture + [Inflammatory Cytokines] + [Knee Osteoarthritis] + [Immune Modulation] + [platelet rich plasma]	Early Knee Osteoarthritis, Musculoskeletal Injuries unrelated to knee osteoarthritis, Neurodegenerative conditions, Drug Therapy, Drug Interactions, Nutraceuticals, Herbal Remedies, Pain Management as a Singular Topic, Electromagnetic Fields, Ozone Therapy, *Tai Chi, Qi Gong*
	508	[Stem Cell Injection] + Knee + Tissue Growth	Early Knee Osteoarthritis, Musculoskeletal Injuries unrelated to knee osteoarthritis, Neurodegenerative conditions, Drug Therapy, Drug Interactions, Nutraceuticals, Herbal Remedies, Pain Management as a Singular Topic

Four hundred thirty-three publications were retrieved in PubMed by searching for key phrase "acupuncture knee osteoarthritis." One hundred forty-nine publications were retrieved in PubMed using key phrase "[stem cells] acupuncture." Twenty-five publications were retrieved in PubMed by the search of key phrase "immune modulation and acupuncture."

The years of publication for literature reviewed using Google Scholar were 2008-2018. As of July 2018, 337 publications were retrieved by Google Scholar search of key phrase "electroacupuncture + [inflammatory cytokines] + [knee osteoarthritis] + [immune modulation] + [platelet rich plasma]." Publication topics on early knee osteoarthritis, musculoskeletal injuries unrelated to knee osteoarthritis, neurodegenerative conditions, drug therapy and drug interactions, nutraceuticals and herbal remedies, pain management as a singular topic, electromagnetic fields, ozone therapy, *tai chi* and *qi gong* were excluded from review (see **Table 2** on the previous page).

Books and most annual meeting reports were excluded from review, with the exception of one article from the Mayo Clinic Proceedings authored by Evans, *Advances of Regenerative Orthopedics*. Five hundred and eight articles published in 2018 were retrieved by Google Scholar search with key phrase "[stem cell injections] knee + tissue growth." Publication topics relating to early knee osteoarthritis, musculoskeletal injuries unrelated to knee osteoarthritis, neurodegenerative conditions, drug therapy, nutraceuticals and herbal remedies, homeopathic remedies, and pain management as a singular topic were excluded from review.

The years 2010-2018 were used to search publication for literature reviewed using EBSCO host databases. Zero results were retrieved by searching for key phrase "platelet rich plasma and knee osteoarthritis and electroacupuncture." Forty-four publications were retrieved using key phrase "electroacupuncture and knee osteoarthritis" (see **Table 3**).

Inclusion criteria set for the methodology for this literature review was limited to therapies involving acupuncture, including electroacupuncture, warm-needling with moxibustion, ultrasound-guided acupuncture, laser acupuncture, and associations with Regenerative Medicine, including tissue engineering, platelet rich plasma injections, mesenchymal stem cells, adipose-derived stem cells, and bone marrow aspirate concentrate (see **Table 4**).

Inclusion criteria for study types included randomized-controlled trials, meta-analyses, systematic reviews, pilot studies, case reports, and animal studies. Inclusion criteria for study design included controls, standard of care models, and sham acupuncture. Publication topics relating to pain management as a single interest, early stage pathogenesis, behavior psychology, and postoperative care were excluded from review.

Table 3. EBSCO Host Search Criteria

Publication Years 2010 - 2018			
DATABASE	**ARTICLES**	**SEARCH TERMS**	**EXCLUSION CRITERIA**
EBSCO Host	0	Platelet Rich Plasma + Electroacupuncture + Knee Osteoarthritis	
	44	Electroacupuncture + Knee Osteoarthritis	Pain management as a singular topic Early knee osteoarthritis, Behavior Psychology, Post-Operative Care

Table 4. Review of Literature Inclusion Criteria across Databases

DATABASE	**INCLUSION CRITERIA**	
	Methodology	**Study Design**
PubMed	Electroacupuncture, Warm-needling with moxibustion, Ultrasound-guided acupuncture, Laser acupuncture, Regenerative Medicine, Tissue Engineering, Platelet-Rich Plasma, Mesenchymal Stem Cells Injection, Adipose-Derived stem cell injections, bone marrow aspirate concentrate injections	Randomized-controlled trials, Meta-analysis, Systematic reviews, Pilot studies, Case reports, Animal studies, Controls, Standard of Care Models, Sham Acupuncture
Google Scholar		
EBSCO Host		

Results

NEUROTRANSMITTER-RECEPTOR BINDING

Torres-Rosas et al. evaluates the immune modulatory effects of ST-36 zusanli in the incidence of sepsis.[18] This article is concerned with the control of systemic inflammation with the use of electroacupuncture to stimulate the sciatic nerve which demonstrates vagal activation. This thereby elicits an immune response of DOPA decarboxylase, a precursor to dopamine, a neurotransmitter, which inhibits cytokine production via dopaminergic type-1 receptors.[18]

In this study, cytokine production was measured by serum levels of pro-inflammatory cytokines such as tumor necrosis factor (TNF), Interleukin-6 (IL-6), monocyte chemotactic protein-1 (MCP-1), and interferon-γ (INF-γ). Clinically, common implications of vagal nerve stimulation are limited by anesthesia, and surgery required for the direct nerve stimulation. This animal study fixed mice by excising their adrenal glands to demonstrate increased susceptibility to pro-inflammatory cytokines in the presence of bacterial endotoxins.

Control models used electroacupuncture with a wooden toothpick or applied voltage-dependent stimulation at a non-acupoint 3cm distal to ST-36 zusanli and opposite the knee joint over the semitendinosus muscle. The needle used was 28 gauge x 12 mm length and insertion depth was 3 mm. The experiment group received electroacupuncture at ST-36 zusanli, with bilateral continuous stimulation for 15 minutes at 40 mA and 10 Hz.

Researchers observed a reduction in serum levels of all cytokines in the experiment group. Cytokine production was completely inhibited in the experiment group, yet control models did not inhibit cytokine production. Capsaicin was used to analyze local sensory signals by way of interfering with nociceptive and voltage-dependent neuronal pathways (similar to gait theory of mitigating pain perception). Painful irritation and surgical sectioning of the sciatic nerve completely interfered with the anti-inflammatory potential of electroacupuncture.

Additionally, Torres-Rosas et al. evaluated stress hormone production in the adrenal gland.[18] The experiment model demonstrated, in the presence of adrenal insufficiency, agonists to dopamine receptors suppress systemic inflammation and reduce the incidence of sepsis. Results support an anti-inflammatory mechanism mediated by both the sciatic and vagus nerves that downregulate the production of catecholamine when the adrenal gland is dysfunctional.

Oke et al. described an inherent anti-inflammatory reflex promoted by the use of electroacupuncture to release acetylcholine (ACh) upon vagal nerve stimulation as measured by heart rate variability.[19, 20, 21] In the author's manuscript, needling acupoint BL-15 xinshu, electroacupuncture was demonstrated to normalize high-frequency levels and low-frequency components of heart rate variability. Normalized high-frequency power of heart rate variability is widely recognized as the index of vagal stimulation.[20, 21] Cholinergic neurons inhibit inflammation just as the nervous system also controls heart rate.[22] Ascending fibers of the vagus nerve synapse with the upper medulla and activate nerve signals to inhibit pro-inflammatory cytokine release[23] by the sensory (afferent) arm of the inflammatory reflex.

The motor (efferent) arm of this inflammatory reflex involves the cholinergic anti-inflammatory pathway mediated by vagal stimulation and the release of ACh by the organs of the reticulo-endothelial system including the spleen, liver, and gastrointestinal tract.[23] ACh binds to receptors on the membranes of pro-inflammatory cytokine-producing cells, activated macrophages, within the extracellular environment, thereby promoting a cell signaling sequence to inhibit the release of TNF by macrophages.[24]

Song et al. evaluated a mechanism by which electroacupuncture at ST-36 zusanli attenuates pro-inflammatory cytokine release and organ dysfunction by activating a cholinergic pathway in rats with endotoxin challenge.[25] Electroacupuncture at ST-36 zusanli reduced levels of plasma Tumor Necrosis Factor-γ (TNF-γ) that were elevated in the presence of endotoxins. However, this animal study demonstrated that immune sufficiency is contingent upon adequate vagal stimulation. Bilateral cervical vagotomy in experimental animal subjects was performed and the effects of electroacupuncture in reducing pro-inflammatory cytokines were negated.

THE EXTRACELLULAR ENVIRONMENT

Chen, L et al., evaluated serum levels of anti-inflammatory cytokines attributed to electroacupuncture treatments at acupoint ST-36 zusanli.[26] This animal study demonstrated how electroacupuncture can enhance immune function by increasing serum levels of anti-inflammatory cytokines through ion channels located on the cell membrane of T-cells in the spleen. Sprague-Dawley rats were divided into three groups, including one control, one sham acupuncture group, and one acupuncture group. A 40 gauge (0.16 mm) acupuncture needle was inserted at ST-36 zusanli and electroacupuncture with mixed frequencies at 2 Hz and 15 Hz and 1 mA intensity was administered for 30 minutes (See **Figure 2** on following page).

Electroacupuncture was given daily for 1, 3, 7, or 14 days between the hours of 8 am and 12 pm to adjust for confounding variables due to circadian rhythms. Tissue extracts were analyzed around acupoint ST-36 zusanli, as well as blood serum levels, via ELISA assay for cytokine markers. Immunohistochemical analysis of spleen tissue extracts were processed. Results showed that three days of consecutive treatments at ST-36 zusanli significantly

increased serum levels of pro-inflammatory cytokine interferon-γ (IFN-γ), and extracts from spleen cells in rats contained higher levels of interleukin (IL)-2 and IL-17. Therefore, electroacupuncture at ST-36 zusanli demonstrated a mechanism for modulating immune function attributed to enhanced production of cytokines and T cells.

Da Silva et al. evaluated the release of IL-10 (anti-inflammatory) cytokines from M2 macrophages as a crucial component for the analgesic and anti-inflammatory effects of acupuncture to treat muscle pain.[27] This animal study used 112 mice of various genetic make-up (wildtype v. C57BL/6 v. IL-10-/-) to investigate the effects of manual acupuncture (MA) on regulating the anti-inflammatory immune response in mice with muscle inflammation. C57BL/6 mice and IL-10-/- mice are congenic. IL-10-/- mice have a targeted mutation deficient in IL-10.

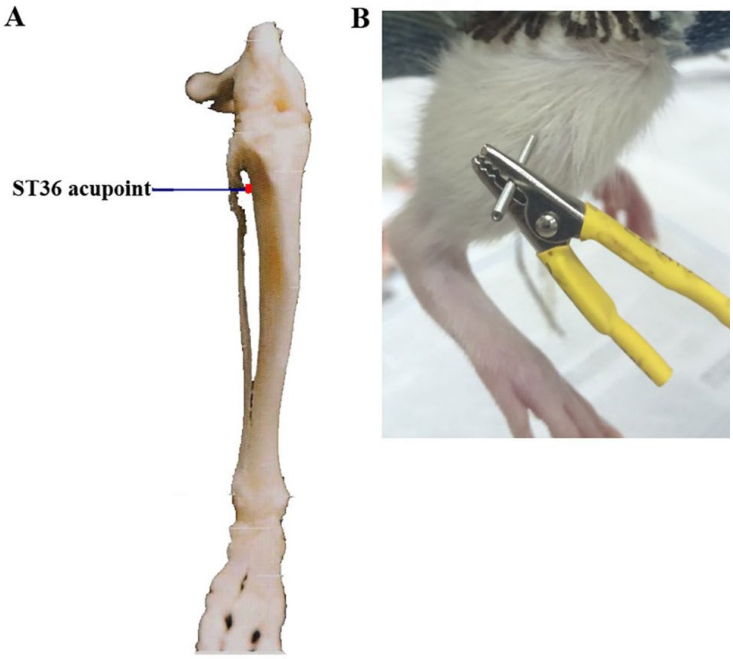
An injection of 3% carrageenan dissolved into sterile isotonic saline was used to elicit an inflammatory response. M1 macrophages demonstrated activation under the effects of acupuncture. M1 switched gene expression to M2 macrophages and secreted IL-10 cytokines within the experimental model. MA was applied at SP-6 sanyinjiao with oblique insertion of a stainless steel needle (0.17 x 7 mm) to a depth of 2-3 mm and the needle was retained for 10 minutes. MA was given once a day for 1, 5, or 13 days.

Inflammatory muscle pain exhibited neutrophil-dominant, primarily at the onset, and then converted to macrophage-dominant inflammation after 48 hours in the experiment model. Researchers concluded that manual acupuncture produced a phenotypic switch in macrophages and increased IL-10 levels to reduce pain and inflammation in muscle tissue. MA at SP-6 sanyinjiao increased or re-established IL-10 levels in inflamed control models after a single treatment, but MA at SP-6 sanyinjiao was ineffective in reducing pain behaviors and edema in IL-10-deficient mice.[27]

Chen, H et al. examined the anti-inflammatory effects attributed to blood serum after electroacupuncture treatments and the underlying mechanisms modulating chondrocyte inflammation.[28] The Ras-Raf-mitogen-activated protein kinase (MEK)1/2-extracellular signal-regulated kinase (ERK)1/2 (Ras-Raf-MEK1/2-ERK1/2) signaling pathway promotes the degradation of articular cartilage by enzymatic activity.[28] This animal study evaluated the anti-inflammatory effects of blood serum, after electroacupuncture treatments, on tumor necrosis factor (TNF)-α-mediated chondrocytes.

Chondrocytes were isolated from the knee cartilage of Sprague Dawley (SD) rats, cultured, and identified as type II collagen cells. Thirty Sprague Dawley (SD) rats were randomly divided into three even groups: one control and two electroacupuncture (EA) groups. The control (blank) group did not receive intervention. EA group I received fifteen minutes of electroacupuncture (2Hz and 2mA intensity) at acupoints EX-LE-4 neiguan and ST-35 waixiyan. EA group II received thirty minutes of treatment consistent with group I. A treatment cycle consisted of daily acupuncture for three days. Arterial blood samples were collected from the abdominal aorta of each group to process a serum fraction. Electroacupuncture serum group I and group II (EAS I and EAS II) were compared to the model group of TNF-α-treated chondrocytes. A total of four groups were evaluated. The control group received 10% serum from the blank group; the model group received 10 mcg/L of TNF-α and 10% serum from the blank group; the EAS I group received both 10 mcg/L of TNF-α and 10% serum from EA group 1; the EAS II group received both 10 mcg/L of TNF-α and 10% serum from EA group II.[28]

Figure 2. Chen, L et al. (2017) Experiment Model Point location of ST-36 zusanli in SD rats with electroacupuncture



Researchers observed the response of TNF-α-treated chondrocytes and Interleukin-1β (IL-1β) concentration levels in blood serum after 15 or 30 minutes of electroacupuncture.[28] There were no significant differences observed between EAS I and EAS II groups. Both EAS groups showed evidence of cell viability of TNF-α-treated chondrocytes. Both EAS groups also demonstrated a significant reduction in IL-1β concentrations. Furthermore, the protein expression levels of Ras, Raf, and MEK1/2 were reduced and activation of ERK1/2 kinase was inhibited by both EA groups but more significantly inhibited by the EAS II group, and thereby impeded the activation of pro-inflammatory regulators downstream. Therefore, electroacupuncture acts upon the extracellular environment conducive to anti-inflammatory mechanisms.[28]

A review article published by Fu et al. summarized a mechanism of tissue regeneration influenced by bioactive trophic effects of mesenchymal stem cells (MSCs) and emphasized the role of the extracellular environment and its structure.[29] Fu et al. suggested that the mechanism to promote inflammation, inhibit cell death, and stimulate endogenous repair is related to the secretion of cytokines and growth factors. There is strong evidence showing that MSCs elicit trophic factors mediated by growth factors delivered by extracellular vesicles and membrane nanotubes that increase bio-physio-communication with neighboring cells to enhance tissue repair.[29]

CH Evans contributed a review of various publications on "Advances in Regenerative Orthopedics" to the Mayo Clinic Proceedings.[30] This review highlighted MSCs as being among the most frequented types of cells used in regenerative therapies and they can be retrieved from many different types of tissue. However, Evans acknowledged a popular consensus that not all sources of MSCs are equal and that therapeutic outcomes are likely to be successful when recovered from the same tissue to be regenerated.[30]

Furthermore, Evans delineated four key components that contribute to the success of regenerative orthopedics: cell type, extracellular signaling, scaffolds, and mechanical stimulation.[30] Common practices in tissue engineering use strategies that combine these four components, but they present challenges with regard to feasibility and accessibility to patient populations.[30] Therefore, novel approaches in cell therapy using orthobiologics make full use of intrinsic biological processes *in vivo* to avoid the need for *ex vivo* expansion of autologous cells and multiple procedures.[30]

PRODUCT MANUFACTURING

From 2,138 initial articles, Raeissadat et al. conducted a review of 133 published studies by Iranian researchers in Iran that met criteria according to inclusion and exclusion of eligible articles.[10] Bone disorders were most prevalent among the published studies, and those on osteoarthritis accounted for eleven percent of all the studies reviewed, such that knee osteoarthritis comprised the most prevalent type of incidence.

This review of published studies outlined the variability in the manufacturing process of biologic products. Five main categories of platelet products were designated throughout the review, including pure platelet rich plasma (P-PRP), leukocyte platelet-rich plasma (L-PRP), pure platelet rich fibrin (P-PRF), leukocyte platelet-rich fibrin (L-PRF) and platelet rich growth factors (PRGF).

Inconsistencies prevail with regard to the venesection, centrifugation, aspiration of concentrate, and the use of activation methods. Researchers support protocol standardization for the preparation of platelet products such that the precise composition of platelets and growth factors are defined.[10] Researchers concluded by encouraging long-term follow-up studies on treatment efficacy of study subjects.[10]

Discussion

Conventional therapies use antibiotics to control infection but do not control inflammation. For example, a high level of infection indicates a high concentration of viral or bacterial proteins, whereas a high level of inflammation indicates pro-inflammatory cytokines due to vasodilation. In response to the upregulation of immune function, inhibiting a single cytokine along the cascade of pro-inflammatory cytokines has failed in clinical trials because multiple cytokines need to be inhibited to effectively control for sepsis.[18]

Researchers Torres-Rosas et al. observed the immune modulatory effects of electroacupuncture at acupoint ST-36 zusanli and analyzed neuronal networks supplied by the vagus and sciatic nerves. Evidence supports an anti-inflammatory mechanism by which DOPA decarboxylase, a pathway precursor of dopamine, activates an immune response to inhibit inflammatory cytokine production.[18]

Electroacupuncture near the sciatic nerve stimulates secretion of dopamine precursors in the adrenal medulla by subsequent vagal nerve activation. Evidence supports a mechanism by which D1-receptor agonists inhibit cytokine production in a negative feedback loop by which more dopamine secretion further inhibits systemic inflammation in response to the immune modulation effects of electroacupuncture at ST-36 zusanli.[18]

An anti-inflammatory mechanism occurs between the brain and peripheral nerves resulting from a negative feedback loop. Researchers Oke et al. described two phases of the inflammatory reflex mechanism, consisting of a sensory phase and a motor phase.[19] They cited various articles supporting the anti-inflammatory mechanisms attributed to peripheral nerve stimulation affecting the central nervous system to modulate inflammatory cytokine production by cholinergic receptors. Receptors on afferent vagal synapse terminals bind acetylcholine (ACh) and activate nerve signals in the brain to inhibit inflammatory cytokine production, namely TNF and IL-1β.[19]

Oke and Tracey evaluated the use of electroacupuncture to promote an inherent anti-inflammatory reflex facilitated by the release of ACh caused by stimulation of the vagus nerve.[19, 22] ACh inhibits the release of pro-inflammatory cytokines, thereby decreasing inflammation by downregulating the production of cytokines. Tumor necrosis factor (TNF) and other cytokines are synthesized by macrophages in response to bacterial endotoxins. Oke and Tracey observed a cholinergic anti-inflammatory

pathway, whereas Torres-Rosas attributed the anti-inflammatory pathway to dopamine receptors. Moreover, Song et al. evaluated a mechanism by which electroacupuncture at ST-36 zusanli attenuates pro-inflammatory cytokine release and organ dysfunction by also activating a cholinergic pathway.[25]

Torres-Rosas et al. characterize severe sepsis as an overwhelming inflammatory response leading to multiple organ failure. Researchers observed the effects of stimulating the vagus nerve with the use of electroacupuncture. Evidence supports immune modulation by neurotransmitters in the presence of endotoxins.[18] Although cell therapy using orthobiologics elicit the inflammatory process by mechanically increasing local concentration of cytokine proteins, the immune response is consistent with other inflammatory conditions, including endotoxemia and sepsis, due to the overproduction of inflammatory cytokines.[18]

Research suggests that pathogenesis depends on a cell communication as much as recovery depends on the signaling sequence mechanism of healing.[29] Much of the success of cell-based therapies is contingent upon the extracellular environment wherein orthobiologics are transplanted.[29]

Chen, L et al. evaluated serum levels of cytokines following electroacupuncture treatment at ST-36 zusanli acupoint.[27] Da Silva et al. evaluated the release of IL-10 cytokines from M2 macrophages as a crucial component for the analgesic and anti-inflammatory effects of acupuncture to treat inflammatory muscle pain.[28] Although musculoskeletal injuries unrelated to knee osteoarthritis were identified as exclusion criteria in the methodology of this literature review, this article[27] was included with exception to the exclusion criteria based on the context by which the immune modulation related to acupuncture was evaluated in the literature.[27]

Manual acupuncture (MA) at SP-6 sanyinjiao increased existing IL-10 levels and was effective in reducing pain and inflammation in mice with inflammation induced by a 3% carrageenan injection, thereby demonstrating pain control and anti-inflammatory effects in acute injury to muscle tissue after a single acupuncture treatment. Researchers observed a phenotypic change in macrophage expression of anti-inflammatory cytokine release under the influence of MA, thereby emphasizing protein expression as subsequent to a change in the extracellular environment.[27]

Chen, H et al. examined the anti-inflammatory effects attributed to blood serum after electroacupuncture treatments and the underlying mechanisms modulating chondrocyte inflammation.[28] Researchers concluded that electroacupuncture contributes biochemical properties to blood serum to inhibit TNF-α-treated chondrocyte inflammation and provide therapeutic outcomes in the treatment of osteoarthritis. Therefore, scientific evidence emphasizes the components of the extracellular environment as significant to the therapeutic outcome.[28]

A review article published by Fu et al. summarized a mechanism of tissue regeneration influenced by bioactive trophic effects of MSCs and emphasized the significance of the role and structure of the extracellular environment.[29] Bioactive trophic factors secreted cytokines, and growth factors stimulated resident cells to promote endogenous tissue repair. However, researchers offer explanations of two additional mechanisms that serve as important forms of intercellular communication to influence the behavior of recipient cells throughout the regenerative process.[29] Extracellular vesicles and membrane nanotubes promote angiogenesis by releasing growth factors directly into the medium, and reinforce the cell matrix to connect distant cells and proliferate MSCs.[29]

CH Evans summarized his review of various publications on the "Advances in Regenerative Orthopedics" in the Mayo Clinic Proceedings and classified MSCs as the most frequented types of cells used in regenerative therapies.[30] In agreement with Fu et al., Evans outlined four components significant to the success of regenerative orthopedics: cell type, extracellular signaling, scaffolds, and mechanical stimulation.[30]

Moreover, there is much to be said about the lack of standardized production protocol for the manufacturing of cell-based therapies. Raeissadat et al. criticized the inconsistencies that prevail with regard to the venesection, centrifugation, aspiration of concentrate, and the use of activation methods.[10] Research identifies a need for systematic protocol in the processing of orthobiologics and their concentrations of active ingredients.[10] Furthermore, research recommends a standardization of manufacturing process coupled with longitudinal studies on treatment applications.[10]

Conclusion

Evidence supports that cell therapy using orthobiologics to repair knee cartilage can slow the degenerative changes of knee osteoarthritis.[31] Throughout this systematic review, research has been evaluated and consolidated into three main categories that influence therapeutic outcomes of cell therapy using orthobiologics: Neurotransmitter Receptor Binding, the Extracellular Environment, and Product Manufacturing.

Electroacupuncture is effective in treating the symptoms of knee osteoarthritis to reduce pain and improve function.[11] Electroacupuncture also provides a mechanism of immune modulation by regulating the immune response in the presence of increased pro-inflammatory cytokines and attenuating cytokine production through an anti-inflammatory reflex elicited by vagal nerve stimulation.[19, 20, 21, 22] Moreover, the effects of electroacupuncture serve to support the extracellular environment conducive to tissue healing through the promotion of cell signaling and intercellular communication.[28, 29, 30]

The role of bioactive trophic proteins in the extracellular environment is supported by scientific evidence in contributing to the overall success of cell therapy using orthobiologics in tissue repair.[29] Furthermore, researchers conclude that a lack of standardization in the manufacturing process of orthobiologics contribute to inconsistencies in treatment outcomes in cell therapy.[29] Therefore, the immune modulatory effects of electroacupuncture may reinforce the overall success of cell therapy by promoting neurotransmitter receptor binding to modulate the immune system response to degeneration, assist hormone secretion in the extracellular environment to promote healing, and support standardization of product manufacturing in orthobiologics. More research is needed to investigate the complementary effect of electroacupuncture to strengthen the clinical outcomes in the process of repair of articular cartilage in the treatment of knee osteoarthritis.

This systematic review represents a translational study of the immune modulatory effects of electroacupuncture as they relate to the application of cell therapy using orthobiologics in the treatment of knee osteoarthritis. At present, scientific evidence directly evaluating the immune response to electroacupuncture as applied to the clinical outcomes of cell therapy is lacking.

Design of a pilot study is recommended to evaluate the immune modulatory effects of electroacupuncture at ST-36 zusanli with orthobiologic injections of mesenchymal stem cells into the knee joint to treat knee osteoarthritis. An obstacle to implementation of such a pilot study pertains to compliance with the Federal Drug Administration (FDA) and acquiring a Biologic License Application to use orthobiologic products as a drug treatment in a way that exceeds the definition of minimal manipulation under FDA regulation.[32]

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Case Report

Treating Cellulitis with Acupuncture and Chinese Herbs

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Abstract

As diabetes and obesity increase in prevalence, lower extremity infections such as cellulitis are increasingly common. Widespread repeated use of antibiotics has contributed to antibiotic resistant bacterial strains, which often exacerbates cellulitis infection. A 63-year-old male presented in June 2012 with cellulitis on his right big toe. Since 1994, he had suffered 14 recurrences of cellulitis and was treated solely with antibiotics each time. Recovery from episodes included pain and varying degrees of debilitation during the extended recovery time. This case of cellulitis included acupuncture treatment and internal and external herbs in addition to the antibiotic Keflex. The patient was not willing to forego antibiotics altogether, but the inclusion of herbs and acupuncture proved successful such that a second course of antibiotics was unnecessary. Recovery was also less painful. Adjunct treatment of acupuncture and herbs for cellulitis has the potential to assist medical practitioners whose patients seek faster recovery as well as relief from recurrence of cellulitis. This approach should be tried and evaluated further.

Key Words: Cellulitis, infection, suppuration, skin diseases, inflammation, skin and connective tissue diseases, acupuncture

Biomedical Perspective

Cellulitis is an acute infection of the skin and subcutaneous connective tissue including lymph. Diagnosis usually is made by visual examination.[1] Cardinal characteristics of cellulitis are the signs of calor, tumor, rubor and dolor. Cellulitis may involve a small area or spread vastly and quickly via lymph.[1] The most common site of infection is the lower extremities, with the trunk and upper extremities leading over the head and neck.[2]

The most common causative microorganisms are group A β-hemolytic streptococci and *Staphylococcus aureus*. Streptococci generally coincide with diffuse infections and staphylococci with localized infection including purulent and/or open lesions[1] or there may be

no site for infection to enter the skin.[1] Cellulitis is often comorbid with purulent skin infections such as abscesses and ulcers.[2,3]

Risks for abscesses and ulcers include spider bites, close physical contact with an infected person, recent use of antibiotics, and previous infection with methicillin-resistant *Staphylococcus aureus* (MRSA).[3] Comorbidity with diabetes further includes gangrene and osteomyletis.[4] Cellulitis often leaves the person with lymphedema. Lower-limb lymphedema and/or fungus creates an environment that may promote recurrent cellulitis.[5]

Treatment of cellulitis is most often handled on an outpatient basis with short-term oral antibiotics (Table 1)[1,3] and possible incision and drainage.[4,3] When there is no response to one antibiotic, the physician will usually try another, but in many cases, the infecting organism may not be responsive to this type of medication.[4,3]

Table 1. Commonly Used Antibiotics for Cellulitis

Intensity of Cellulitis	Antibiotic	Dosage	Frequency of dosage
Mild	Dicloxacillin	250 mg	Four times per day
Mild	Cephalexin	500 mg	Four times per day
Mild	Levofloxacin	250 mg	Daily
Severe	Oxacillin	1g IV	Every 6 hours
Severe?	Nafcillin	1g IV	Every 6 hours
MRSA or person is penicillin-allergic	Vancomycin	1g IV	Every 12 hours

Source: *The Merck Manual*[1]

Risks of antibiotic treatment involves gastrointestinal discomfort, pseudomembranous colitis (*Clostridium difficile*), or hypersensitivity, including anaphylaxis. Seizures are a risk with several of the antibiotics.[6] MRSA is a non-immediate risk.[3] In terms of differential diagnosis, deep vein thrombosis is also a condition that involves leg pain. Unlike cellulitis, deep vein thrombosis does not exhibit inflammation signs on the body surface such as hot skin with a red color.[1]

Public health issues commonly comorbid with cellulitis include obesity,[2] diabetes,[4] and administration of antibiotics.[2,3] A 2010 literature review and retrospective cohort study found obesity and skin abscesses to be the most common risk factors for community-associated methicillin-resistant *Staphylococcus aureus* cellulitis (CA-MRSA cellulitis).[2] In the cohort study on treatment of CA-MRSA cellulitis, the infection was overwhelmingly resistant to antibiotics.[2] Similarly, in a prospective prevalence study published in 2006, doctors in emergency rooms across the United States frequently gave patients with purulent abscesses and MRSA an antibiotic that also did not affect the organism.[3]

AOM Perspective

In traditional Chinese medicine (TCM), skin diseases are often classified as "external diseases." Literature in English on TCM dermatology shows no specific pattern differentiation for cellulitis. Signs and symptoms regarding skin disease lesions such as color and moisture aid in differentiation into eight pathogenic categories: Wind, Cold, Summer Heat, Dampness, Dryness, Fire, insects, Blood Stasis.[7] The diagnoses here follow from these signs and symptoms. Since cellulitis spreads quickly, we may consider pathogens of Fire-Toxin and Wind.

In a biomedical context, risk for cellulitis can result from an insect bite. Studies show co-occurrence between MRSA and insect bites.[2,3] Insect bites, a Chinese medicine disease called *chong shi yao shang*, may present with varied signs that include necrosis, pus and itching. Systemic reactions to insect bites may involve nausea, vomiting, fatigue and swelling that includes lymph nodes.[8]

The insect bite is most related to Toxin and Heat pathogens.[7,8] The treatment of Heat-Toxin from insect bite is Wu Wei Xiao Du Yin (Five-Ingredient Decoction to Eliminate Toxin) containing *jin yin hua* (Flos Lonicerae), *pu gong ying* (Herba Taraxaci), *zi hua di ding* (Herba Violae), *ye ju hua* (Flos Chrysanthemi Indici), *xi bei tian kui* (Herba Begoniae Fimbristipulatae).[8]

Case Description

First visit

In early summer 2012, a hypertensive patient presented requesting herbal medicine and acupuncture for treatment for right foot pain, redness, and swelling, primarily at his big toe. The onset of the current infection occurred when he returned by airplane from a brief, stressful family visit.

His infection cycle of cellulitis had been recurring since 1994. During the worst episodes, the entire right leg swelled and he experienced vomiting and nausea. With each episode, minimum recovery time was several weeks. He routinely took an antibiotic during each episode.

When he returned from his trip and experienced symptoms, he immediately contacted his MD and began a course of the antibiotic Keflex (cephalexin). The patient also sought immediate TCM treatment because he had found that acupuncture and herbs shortened the recovery time of his previous cellulitis recurrences. He was unable to receive his customized internal herbal medicine prescription from his usual acupuncturist on such short notice so he came to our nearby clinic. (This acupuncturist did not share chart notes.)

Since it was early summer, an insect bite was possibly the precipitating factor. He was absent other common contributing factors such as obesity and diabetes.

Patient body type was thin and lean. Tongue was peeled coat in front, greasy in back. Tongue body was red with many central cracks. Pulse was wiry and slippery.

This patient had been following an anti-inflammatory diet for two years. He ate no sugar or animal products except for yogurt and salmon. While on this diet he reported that he lost weight and generally experienced improved health. See Table 2 for full list of medications and supplements taken by the patient on an ongoing basis, including during treatment of the current complaint.

"In traditional Chinese medicine (TCM), skin diseases are often classified as 'external diseases.' Literature in English on TCM dermatology shows no specific pattern differentiation for cellulitis. Signs and symptoms regarding skin disease lesions such as color and moisture aid in differentiation into eight pathogenic categories: Wind, Cold, Summer Heat, Dampness, Dryness, Fire, insects, Blood Stasis.[7] "

Table 2. Medications and Supplements Taken by Patient

Long Term (before, during & after current treatment for cellulitis)		
Medication/Supplement	**Dose and Frequency**	**Drug Class**
Lisinopril	20 mg daily	ACE inhibitor, antihypertensive[3]
Hydrochlorothiazide(HCTZ)	25 mg daily	Thiazide diuretic, diuretic and antihypertensive[6]
Amlodipine besylate	10 mg daily	Dihydropyridine calcium channel blocker, antihypertensive[6]
Aspirin	Unknown dose daily	Salicylate[6]
Vitimin B12 (cyanocobalamin)	1000 mg every other day	Water–soluble vitamin
Zinc	15 mg daily	Trace element
DHA-EHA	Unknown dose daily	
Kelp liquid drops	Unknown dose daily	
Short Term (only during current treatment for cellulitis)		
Medication/Supplement	**Dose and Frequency**	**Drug Class**
Keflex (cephalexin)	500 mg four times a day	First-generation cephalosporin, antibiotic[6]
Ibuprofen	200 mg three times a day	NSAID, nonopioid analgesic, anti-inflammatory[6]

A longtime avid bicyclist, the patient reported now having low energy and he was unable to ride his bike a short distance to the clinic. He also reported chronic depression and expressed a feeling of catastrophe because he had looked forward to a year free of infection.

Diagnosis: Heat-Toxin. The supporting signs were recent sudden and rapid onset of a hot, swollen, red and painful big toe, red tongue, wiry and slippery pulse. Treatment methods were to, first, clear Heat-Toxin and, second, to calm the *shen*-spirit. See Table 3 for summary of points used.

Table 3. Acupuncture Points Needled During First Visit

Points	Rationale
Auricle *Shenmen*, Sympathetic, Kidney, Liver, Heart	Calm *shen*-spirit
LI-11 quchi, LI-4 hegu	Clear Heat and treat skin diseases[10]
LV-3 taichong	Relieve excess in the Liver channel, anchors floating Liver *yang*, create stability of emotions by using *yuan*-source point[10]
LV-1 dadun	Remove excess Heat from Liver by bleeding the *jing*-well point[10]
ST-36 zusanli	Create stability of emotions. Used in combination with LI-4 hegu to relieve hypertension.[10]

Herbal treatment included a custom-formulated powder of herbs to take internally as well as a custom-formulated external herbal soak for the foot that was dispensed in bulk herbs. The patient decocted these at home and soaked his foot at regular intervals (see Table 4). As far as this author knows, this was the first time the patient used external herbal soaking.

Table 4. Herb Formula Summaries

Internal Herbs	External Soaking Herbs
Powder, mostly 5:1 concentrate	Bulk raw herbs
Put prescribed amount of herbs into hot water, stir and drink. 5 grams, 3 times per day.	Soak herbs, bring to boil and simmer for 35 minutes. Strain decoction and when it cools down, soak the affected area for 30 minutes 2-3 times per day.
huang lian (Rhizoma Coptidis) 4 g, *huang qin* (Radix Scutellariae) 3 g, *huang bai* (Cortex Phellodendri) 3 g, *zhi zi* (Fructus Gardeniae) 4 g, *da huang* (Radix et Rhizoma Rhei) 1 g, *bai shao* (Radix Paeoniae Alba) 4 g, *pu gong ying* (Herba Taraxaci) 3 g, *zi hua di ding* (Herba Violae) 3 g. Take 5 g, three times a day.	*huang lian* (Rhizoma Coptidis) 10 g, *huang qin* (Radix Scutellariae) 15 g, *huang bai* (Cortex Phellodendri) 15 g, *zhi zi* (Fructus Gardeniae) 15 g, *yin chen hao* (Herba Artemisiae Scopariae) 60 g, *pu going ying* (Herba Taraxaci) 20 g, *zi hua di ding* (Herba Violae) 20 g, *jin yin hua* (Flos Lonicerae) 15 g

The formulas used were based on *Huang Lian Jie Du Tang* (Coptis Decoction to Relieve Toxicity) and *Wu Wei Xiao Du Yin* (Five-Ingredient Decoction to Relive Toxin). *Huang Lian Jie Du Tang* has the action to clear Heat and eliminate Toxin.

In their book, *Chinese Herbal Formulas and Applications: Pharmacological Effects & Clinical Research*, Chen and Chen indicate that *Wu Wei Xiao Du Yin* clears Heat-Toxin and is especially indicated for treating external sores such as furuncles and carbuncles, including cellulitis.[10] Chen and Chen also reported on a Chinese-language study in which the formula *Wu Wei Xiao Du Yin* specifically treated cellulitis.[10]

The patient refilled the external herbs the next day and continued the foot soaks. He finished the Keflex eleven days after his initial visit for acupuncture and herbal treatment.

Second visit

Two weeks later, the patient presented a slightly red but less swollen toe. The tongue was pink with central cracks, the center had a greasy coat, and the pulse was wiry. Although he reported improved appetite and increased exercise, he complained of continued fatigue after finishing the course of treatment with antibiotics. He said this contrasted with his usually high energy level.

Due to his continually feeling fatigued, the primary diagnosis was *qi* deficiency and the secondary diagnosis was Heat-Toxin from the remainder of the infection. Herbs and acupuncture, as noted in Table 5, each addressed Heat-Toxin, *qi* deficiency and *qi* stagnation. The base of the internal formula used at this visit was *Si Jun Zi Tang* (Four-Gentlemen Decoction) that tonifies *qi*. Several herbs were also retained from the previous formula to treat the Heat-Toxin. External herbs were discontinued.

Table 5. Second Visit Treatment Summary

Acupuncture		Internal Herbs, powder form, 4 g, 3 times per day	
CV-6 qihai	Remove *qi* stagnation along with LI-10 shousanli[10]	*he huan pi* (Cortex Albiziae) 16 g, *pu gong ying* (Herba Taraxaci) 16 g, *zi hua di ding* (Herba Violae) 9 g	Herbs used in previous formula to clear Heat-Toxin
CV-12 zhongwan	Tonify and regulate *qi*[10]	*ren shen* (Radix Ginseng) 6 g	*Si Jun Zi Tang* (Four-Gentlemen Decoction)
LI-4 hegu	See Table 3	*bai zhu* (Rhizoma Atractylodis Macrocephalae) 12 g	
LI-10 shousanli	Remove *qi* stagnation along with CV-12 zhongwan[10]	*fu ling* (Poria) 9 g	
ST-36 zusanli	See Table 3		
LV-3 taichong	See Table 3	*ye jiao teng* (Caulis Polygoni Multiflori) 9 g	Calm *shen*-spirit, nourish Blood
5-Needle Protocol	See Table 3	*shen qu* (Massa Fermentata) 9 g	Warm herb to harmonize the Stomach and relieve diarrhea

Third visit

Three weeks after the first visit, the patient reported that the foot pain was receding and he was able to ride his bicycle for 37-73 km (23-45 miles). He felt slight toe soreness after riding. Upon examination, the toe was slightly red, neutral temperature, slightly throbbing.

Though he reported "an increase in vitality," he also complained of fatigue in the morning that coincided with feelings of depression. His overall body temperature was warm. He sweat easily when he exercised and he experienced back pain when he sat too long.

Tongue was red with cracks. Tongue coat was wet, slightly white in the cracks only. The pulse was wiry on the left. The right pulse was tense in the *cun* with a weak and thin *guan* and *chi*. Diagnosis continued to be *qi* deficiency. Additional diagnosis was Kidney and Liver *yin* deficiency due to being warm and having back pain, hypertension, and long-term depressed feelings.

Treatment (Table 6) was thus shifted to support the Kidney and Liver in addition to tonification of *qi*. Acupuncture continued to release Heat from the body and support *qi*.

The patient's herbal treatment was revised. The new focus for the internal herbal formula was Spleen *qi* with continued use of *Si Jun Zi Tang* (Four-Gentlemen Decoction) and herbs for nourishing Kidney and Liver *yin*.

Table 6. Third Visit Treatment Summary

Acupuncture	Internal Herbs, powder form, 4 g, 3 times per day
LI-4 hegu, LI-10 shousanli, LI-11 quchi, ST-36 zusanli, LV-3 taichong, Rt side KI-7 fuliu, CV-3 zhongji, CV-6 qihai	*ren shen* (Radix Ginseng) 3 g, *bai zhu* (Radix Atractylodis Macrocephalae) 6 g, *fu ling* (Poria) 5 g, *zhi gan cao* (Radix Glycyrrhizae Preparata) 3 g, *he huan pi* (Cortex Albiziae) 6 g, *ye jiao teng Ye Jiao Teng* 6 g, *sheng di huang* (Radix Rhemanniae) 9 g, *gou qi zi* (Fructus Lycii) 6 g, *nu zhen zi* (Fructus Ligustri Lucidi) 6 g, *ye ju hua* (Flos Chrysanthemi Indici) 6 g, *ze xie* (Rhizoma Alismatis) 5 g, *du zhong* (Cortex Ecuommiae) 5 g, *he shou wu* (Radix Polygoni Multiflori) 5 g

"Long-term, this patient might better prevent infection by taking a TCM formula to nourish Kidney, Liver, and Spleen, following a Kidney and Spleen nourishing diet, and making lifestyle modifications that include more gentle physical exercise."

Fourth and Fifth Visits One Month After Onset of Symptoms

The toe remained tender but cool to touch. His tongue was pink rather than red. Acupuncture treatment continued to address *qi* deficiency and Kidney *yin*. The nourishing herbal formula was continued (Table 6). At the final visit, the patient showed ongoing visible improvement after a month during which he used the combined treatment of antibiotic, acupuncture, and external and internal herbal treatments.

Discussion

This case reports on a patient who had a long history of repeated bouts of cellulitis of the lower extremity. He eventually sought adjunct TCM in addition to antibiotics because he felt that recovery was quicker and he had less pain during each bout. While the patient was taking a course of antibiotics for this specific occurrence, he requested Chinese herbal medicine and acupuncture by this clinic. He recovered over a four-week period with no complications.

During the infection phase, the diagnosis was Heat-Toxin. During treatment, the background diagnoses of Spleen *qi* deficiency and Liver and Kidney *yin* deficiency quickly emerged. Prognosis was moderate due to many years of recurrent infection—this was evidenced by the patient's inability to fight infections effectively.

In TCM, antibiotics injure Spleen *qi,* often evidenced by short-term in fatigue and diarrhea. In the long term, successive courses of antibiotics reduce the Spleen's ability to make blood and promote healthy immunity. Spleen *qi* deficiency becomes further entrenched when Kidney and Liver are concurrently deficient, a trio involving both TCM controlling and generating cycle dysfunction.

Long-term, this patient might better prevent infection by taking a TCM formula to nourish Kidney, Liver, and Spleen, following a Kidney and Spleen nourishing diet, and making lifestyle modifications that include more gentle physical exercise.

Cellulitis is generally a self-limiting, non-recurring infection in primarily healthy people who do not have contributing factors such as obesity and diabetes. In a prospective cohort study of adult patients who had skin and soft tissue infections for not more than seven days, and presented at 11 emergency rooms in the United States, 96% of those contacted at 15–21 days after their visit to the emergency room (59% percent of the sample size) reported resolution or improvement whether or not the antibiotic fit the infection. Patients were included in the emergency room study based solely on their acute illness.[3] When a patient suffers from chronic illness, repeated emergency room visits are common.

Diabetic foot sores may linger for a long time and often present with cellulitis along with gangrene, osteomyletis and ulcers.[4]

Western research into new antibiotic agents seeks to find single substances or create combinations of two or three pharmaceuticals.[3] The Chinese herbs used in this case study contain a variety of molecules within each herb.[11] According to Chen and Chen, when used one at a time, herbs do not sustain antibiotic resistance, but when used in combination with several herbs in a formula, bacteria do not become resistant to the formula.[11]

Chen and Chen predominantly cite Chinese and Japanese research literature. In ratings of randomized controlled trials of acupuncture using the Oregon CONSORT STRICTA Instrument (OCSI), Chinese research was most represented and most consistently received the lowest scores, indicating lower quality in many areas of study design.[12] Though it is unknown how acupuncture RCTs compare to Chinese pharmacology studies, it points to the need to the need for standards in reporting research.

Conclusion

Because antibiotic resistance is a current-day problem, and conditions for cellulitis such as diabetes are prevalent, this case study points to an important area of care in which TCM may have a positive impact when integrated with western standards of care. In order to build on the success of cellulitis treatment, more investigation is needed into the combined use of TCM and antibiotics to achieve best results for this condition.

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Do You Have an Opinion About Any Important Issues Concerning Our Profession?

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The topic selected for this issue is:

How Do You Treat Leaky Gut in Your Clinic?

By Jenn Gibbons, MSTOM, LAc

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The digestive tract functions as an intermediary between the body and the external environment, taking in what it needs and expelling what it does not. To begin with, chewing food in the mouth cues the stomach to increase its production of stomach acid, which not only kills potential pathogens but also prompts the cascade of events that properly assimilates the incoming macronutrients. The pancreas then secretes enzymes and the gall bladder secretes bile such that the food is broken down into an absorbable form.

Absorption takes place through the single layer wall of the small intestine, which becomes permeable and allows these nutrients to pass into our bloodstream. The unabsorbed matter continues to move further into the large intestine as either food for the microbiome or waste product to be removed. If this intestinal layer is compromised, it will become hyper-permeable and allow contents to leak into the blood.

So what causes this layer to leak?

Anything that goes wrong above or below this absorption site can contribute to hyper-permeability. When nutrient-poor food is ingested, the body expends a lot of energy with little gain. Over time, this can lead to nutrient deficiencies and the overfeeding of the gut bacteria. When the bacteria in the upper gut are overfed, a reduction in the stomach acid can occur, thus impairing the release of enzymes and bile necessary to properly assimilate nutrients for absorption.

When the food then arrives at the absorption site and is not broken down sufficiently, it will not be absorbed. Rather, it will move into the large intestine and become food for the microbiome, thus leading to further bacterial overgrowth.

Bacterial overgrowth in the small intestine (SIBO) is often the cause of upper abdominal gas that can cause bloating, belching, reflux, pain and impaired nutrient absorption. This distention often interferes with normal peristalsis and impairs the function of the migrating-motor-complex, which handles the clearing of food fragments that remain in the upper gut.

If these fragments do remain, they are fermented by local bacteria, thereby creating more gas. This can interfere with normal bowel movements and lead to constipation or diarrhea. Bacterial overgrowth in the large intestine, or dysbiosis, is often the cause of lower abdominal gas that can also lead to bloating, pain, flatulence, and bowel irregularities.

The pressure along the digestive tract is enough to increase the permeability of the absorption site but this barrier also does have a regulator. The protein zonulin modulates the opening and closing of the tight junctions at the absorption site, controlling how permeable it is. Based on research by Dr. Alessio Fasano, SIBO and dysbiosis stimulate the production of zonulin, which increases intestinal permeability.[1]

Gluten, one of the most commonly consumed nutrient-poor food additives also stimulates zonulin. Dr. Fasano reports that gluten causes intestinal permeability in all of us, since humans lack the enzymes necessary to fully assimilate it. He also explains that these undigested gluten fragments are perceived as an enemy by the immune system and that if a person has a certain genetic predisposition, they may develop celiac disease as a result of overconsumption.

Comprehensive stool analysis tests such as the GI Map from Diagnostic Solutions can determine zonulin status. Food sensitivity labs such as KBMO and Cyrex Labs can also test for a patient's sensitivity to gluten. In addition, human leukocyte allele testing for celiac disease (HLA-DQ) can be performed to assess genetic risk.

Regardless of the result, a functional medicine practitioner is likely to advise their patient to optimize repair by adhering to the following points:

- prioritize eight hours of quality sleep
- avoid unnecessary stress
- improve your mood
- avoid an excess of either sedentary activities or strenuous overtraining
- and eat a nutrient-dense, anti-inflammatory diet that excludes acellular carbohydrates, added sugar, gluten, and any known food sensitivities.

They would also likely order both a SIBO breath test to determine whether or not there is bacterial overgrowth in the upper gut and a comprehensive stool analysis to see if there is a gut infection. This also can determine the state of the patient's microbiome and indicate how well they absorb their nutrients. Also, a thorough diet history and nutritional lab testing are useful to determine potential nutrient deficiencies.

In addition to treatment based on the lab tests, they will often recommend that the patient optimize their stomach's acidity by completing what is known as the "hydrochloric acid challenge" using betaine HCl with digestive enzymes. This not only protects the patient from potential pathogens but also helps to improve digestive function and thereby absorption.

In addition to advising on sleep, stress, movement and diet, Chinese medicine practitioners may also differentiate the patient's pattern of disharmony, which allows them to further personalize their patient's treatment plan. Reflecting on the different presentations above, a patient might present with Excess in the Stomach, Small Intestine, or Large Intestine. This Excess may impede the descending function of Stomach-*qi,* causing Counterflow. It may also back up the Liver and Gall Bladder, creating Stagnation of *qi* and Blood.

Patients often turn to antacids or proton-pump inhibitors to reduce their Stomach-Counterflow symptoms. This anchors the ascension, but it also reduces digestive strength and invites Cold. When dysbiosis is present, the Liver may be burdened with increased toxicity causing *qi* Stagnation and Heat. The increase in pressure and Heat throughout the digestive tract can burn off fluids reducing precious *yin*. The reduction in digestive function and nutrients can lead to deficiency patterns of the Spleen manifesting as Damp-Accumulation. Over time, the overworked Spleen can lose support from the Kidneys, which can lead to weakness along the entire digestive tract wall. This can present as a leaky esophagus or a leaky blood-brain barrier.

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JASA: *The Journal of the American Society of Acupuncturists* is seeking submissions for its summer 2020 Clinical Pearl topic:

"How Do You Treat Chronic (Primary) Low Back Pain in Your Clinic?"

Clinical Pearl submissions may be sent to Clinical Pearls Editor Tracy Soltesz at kesrya@gmail.com by June 1, 2020.

Please refer to our website for Author Guidelines and submission information: http://www.meridiansjaom.com/author-guidelines.html

How Do You Treat Leaky Gut in Your Clinic?

by Atara Noiade, DAOM, LAc

Atara Noiade holds an MBioSci from John Hopkins University and in 2016 she received her DAOM from Emperor's College in Santa Monica, CA. Dr. Noiade is also an NCCAOM Diplomate in Herbal Medicine. Active in promoting and protecting access to Chinese medicine since 2001, she served on the Executive Board of the Washington State Association where she helped assure Washington State's passage of the law permitting East Asian medicine practitioners to recommend and treat with Chinese herbs. Dr. Noiade currently practices in Alexandria, Virginia. Email: dranoiade@gmail.com

Increased intestinal permeability is considered by many medical periodicals as mainly a theoretical digestive condition by which bacteria is able to permeate the intestinal wall. The common term often used is "leaky gut syndrome."

While many articles claim there is no evidence of this syndrome, Chinese medicine does not attempt to decipher whether there is a specific correlation between symptoms to a specific conventional diagnosis. Rather, the focus is placed on the presentation of symptoms and the constitution of the patient when determining a Chinese medicine diagnosis.

"Naturally, depending upon the particular needs of the patient, the treatment protocol may vary substantially."

Often, what is described by the patient as "leaky gut syndrome" is a Deficiency pattern. This most typically presents as Spleen *qi-xu*, Stomach *qi-xu*, or Stomach *yin-xu*.

Naturally, depending upon the particular needs of the patient, the treatment protocol may vary substantially. Based on these above three diagnoses, the following treatment options may be utilized.

(Herbal formulas used for these diagnoses presume there is no additional complicating diagnosis, so the practitioner should examine the ingredients closely to be sure the match is appropriate. These treatments also presume that the patient is not pregnant.)

Spleen *qi-xu*

Acupuncture: 4 Gates: LI-4 and LR-3, SP-3, SP-1, KI-3, ST-36, LU-9

Herbal formula: *Xiang She Liu Jun Wan or Bu Zhong Yi Qi Wan*

Stomach *qi-xu*

Acupuncture: 4 Gates: LI-4 and LR-3, ST-36, UB-18, UB-20, UB-21, ST-42, SP-3

Herbal formula: *Shu Gan Wan or Shuang Bao Su Kou Fu Ye*

Stomach *yin-xu*

This typically occurs secondary to another diagnosis, so look carefully at the symptoms to determine the primary cause.

Acupuncture: 4 Gates: LI-4 and LR-3, ST-36, UB-15, UB-16, UB-18, UB-20, UB-21, SP-6, KI-6, KI-1

Herbal formula: Will vary based upon deficient Kidney, deficient Liver-*xue*, Empty Heart-fire, generalized *qi-xu*. The Practitioner will need to closely examine the symptoms to determine the best formula and will likely need to use a combination of formulas.

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How Do You Treat Leaky Gut in Your Clinic?

By Greg Lee, LAc

Greg Lee received his Master's of Acupuncture from the Traditional Acupuncture Institute, now Maryland University of Integrative Health (MUIH). He is the founder and director of the Lyme Research & Healing Center in Frederick, Maryland. www.GoodbyeLyme.com/heal-leaky-gut

He can be reached at: 301.228.3764, greg@GoodbyeLyme.com

At the Lyme Research & Healing Center, approximately 70% of our patients have symptoms of or have been diagnosed with "leaky gut." A combination of eleven different treatments and remedies is used to target the underlying pathogens, reduce the toxins and inflammation, and heal the leaks in the gut. A multipronged targeted treatment and remedy approach may help the patient to heal leaky gut symptoms more quickly and effectively.

"A multipronged targeted treatment and remedy approach may help the patient to heal leaky gut symptoms more quickly and effectively."

Treatment 1: Diet modification

Modify the diet to lower consumption of inflammatory foods, increase healthy organic foods rich in minerals and vitamins, and remove foods known to contain glyphosate, xenoestrogens and toxins.

Treatment 2: Custom programmed Frequency Specific Micro-Current (FSM)

Using electro-dermal scan data, the location of specific pathogens and inflammatory compounds is identified and targeted with anti-microbial, anti-toxin, anti-biofilm, anti-inflammatory and tissue healing micro-current frequencies. The most common areas treated for infections and leaky gut symptoms are the sinuses, digestion tract, liver, gall bladder, blood, brain and joints.

Treatment 3: Essential oils

Over 40 different organic and wild-crafted essential oils, including oregano, thyme, cinnamon, peppermint, ginger, turmeric, fennel and eucalyptus, are used in combinations to target specific infections, reduce inflammation, and heal leaks in the gut. These oils are synergistic with acupuncture and moxibustion and are delivered to the gut using methods such as suppositories, enemas and micro-particle delivery.

Treatment 4: Supplements

For leaky gut repair, patients are provided a range of supplements, including arabinogalactan, de-glycerized licorice, glutamine, white fish protein, bitters, HCL, digestive enzymes, aloe vera, probiotics or prebiotics, quercetin, methylsulfonylmethane (MSM), glucosamine, zinc, glutathione and melatonin.

Treatment 5: Homeopathic remedies

Gut infections like Lyme disease, Candida, Clostridia, E. coli, Bartonella, viruses and parasites are targeted with homeopathic remedies. Detoxifying homeopathic remedies are also given to lower gut discomfort, systemic inflammation, neurological symptoms, biotoxins and heavy metals, painful emotions and joint pains.

Treatment 6: Herbs

Similar to essential oils and homeopathics, herbs are also used to target specific infections, inflammatory compounds like tumor necrosis factor-alpha (TNF-a), and endotoxins that can aggravate leaky gut. *Ren Dong Teng* (Honeysuckle vine), *Lian Qiao* (forsythia), *Ku Shen* (sophora), *Huang Lian* (coptis), *Jiang Huang* (turmeric), *Qing Hao* (artemisia) and *Dan Shen*

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How Do You Treat Leaky Gut in Your Clinic?

Becky Thoroughgood, LOM, Dipl Ac (NCCAOM)

Becky Thoroughgood, LOM, DiplAc (NCCAOM) is a 2003 graduate of the Traditional Acupuncture Institute, now the Maryland University of Integrative Health (MUIH), and has been in practice in Harrisburg, PA, since 2004. She completed her Chinese Medicine Herbology certificate at MUIH in 2013. In addition to her clinic, she devotes much study time to the microbiome and digestive health. Becky is currently writing a book about how traditional Asian medicine and those she has been privileged to serve have transformed her life. Email: becky@well-pointacupuncture.com

When working with a patient diagnosed or suspected to have "leaky gut," clinical observations from the 12th century's Earth School Master Li Dong Yuan prove relevant today. Master Yuan observed that dietary intemperance, poor quality foods, emotional strain and overwork damage the Stomach and Spleen and give rise to a myriad of illnesses. Modern day insults such as repeated courses of antibiotics, pain relievers, acid-reducing drugs and chemotherapy add to the mix.

> "Leaky gut presents as a complex pattern of Excess and Deficiency, so our patients are encouraged to receive treatment for a minimum of three months."

Leaky gut presents as a complex pattern of Excess and Deficiency, so our patients are encouraged to receive treatment for a minimum of three months. The treatment plan follows a "4Rs" gut healing strategy: Remove, Restore, Re-inoculate and Repair. Pulses and patient progress determine how long each phase lasts.

Remove *qi*-stagnation, Food-Stagnation, Damp and Heat

Points such as LI-4, LI-11, LV-3, GB-34, SP-9, SP-6, SP-4, PC-6, SP-2, ST-44, SI-3, auricular *shen men*, and *yin tang* are used to move the *qi,* calm the mind and reduce accumulations. Chong Mai, Hua Tuo and Back Shu points are palpated for tight painful areas and then treated. Although the priority is to reduce Excesses, tonifying points such as ST-36, ST-37, KI-3, KI-6, KI-7, HT-7 and LV-8 can be incorporated. Kiiko Matsumoto's treatment strategies and abdominal palpation is applied to identify and release reflexes for the adrenals, immune system, and digestive organs.[1]

Assuming the patient can tolerate herbal formulas, Liver *qi*-regulating formulas are prescribed. These include *Shu Gan Wan, Chai Hu Shu Gan Wan* or *Yue Ju Wan*. Heat and Damp clearing formulas such as B*an Xia Xie Xin Tang* can also be used. Harmonizing formulas such as *Jia Wei Xiao Yao* and *Xiao Chai Hu Tang* are another possibility.[2] If Food-Stagnation is present, formulas such as *Bao He Wan* or aromatic herbs such as *cang zhu, hou po, huo xiang, pei lan,* or *sha ren* might be needed.

Patients are encouraged to abstain from alcohol, sugar, dairy, soy and gluten for at least 14-30 days. A whole foods diet, such as Whole30,®[3] with emphasis on warm soups, stews, and porridges rather than cold and raw meals, is also encouraged.

When bloating is present, a low FODMAP diet can help control symptoms. Monash University is an excellent resource.[4] For histamine responses such as itching, hives and rhinorrhea, following a low histamine diet for several weeks is also suggested.

Restore proper function

In this phase, continue to monitor and treat Excess patterns as well as the state of Kidney *yin* and *yang*. Consider switching to previously mentioned harmonizing or multipurpose formulas, such as *Xiang Sha Liu Jun Zi Tang, Bu Zhong Yi Qi Tang,* or *Sheng Yang Yi Wei Tang*.

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Exceptional Results in Traditional Chinese Medicine and Oncology: A Focus Dryness and Heat Part Two, Hormonal Treatments: Internal Dryness

By Yair Maimon, OMD, PhD, Ac

Dr. Maimon heads the Tal Integrative Cancer Research Center, Institute of Oncology-Sheba Academic Hospital, Tel Hashomer, Israel. He serves as the president of the International Congress of Chinese Medicine in Israel (ICCM) and the head of the Refuot Integrative Medicine Center. With over 30 years of clinical, academic, and research experience in the field of integrative and Chinese medicine, Dr. Maimon combines scientific research with the inspiration from a deep understanding of Chinese medicine. He has been a keynote speaker for numerous congresses and TCM postgraduate courses. Dr. Maimon is the founder and director of a new innovative eLearning academy, the TCM Academy of Integrative Medicine, www.tcm.ac.

The treatment of cancer patients using traditional Chinese medicine (TCM) presents both new challenges and great opportunities for acupuncturist to understand and develop their skills in the emerging field of oncology acupuncture (OA). A growing body of research concerning this topic has been done over the past several years.

It also should be remembered that long established Chinese medical knowledge as it concerns oncology can also be applied to the treatment of immune system and prevention of disease in general. Getting acquainted with the research results and protocols can enable TCM practitioners to communicate better with the western medical community and the oncologist in particular by helping to bridge East and West.

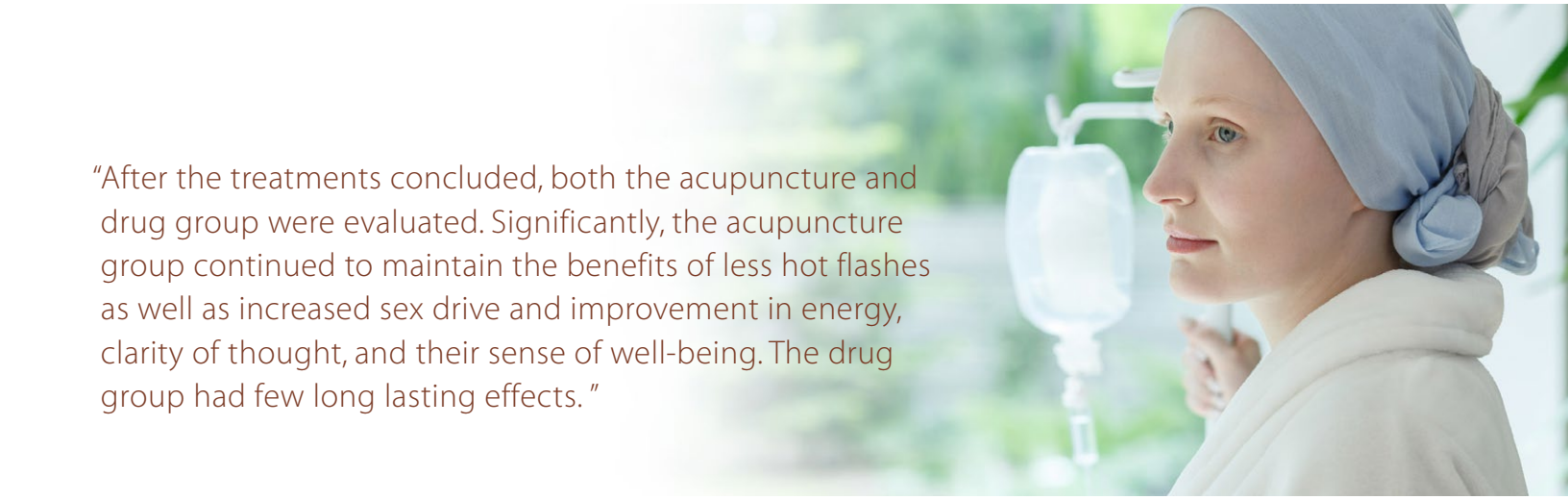
Part one of this article focused on the treatment of external symptoms, one of which is the result of exposure to radiation, one of the common types of western medicine treatments in cancer. Part two focuses on internal symptoms that arise during cancer treatments.

Dryness - *external and internal*

There are two types of unusual dryness that occur during the treatment of cancer. One is from external causes, often due to exposure to radiation treatments, while the other is from internal causes, mainly the treatment using anti-hormonal (especially anti-estrogen) medicine. Because cancer cells are sensitive to estrogen, this type of treatment is often given to women diagnosed with breast cancer over long periods, often up to 5-7 years.

The use of anti-estrogen hormone treatment (such as Tamoxifen) causes hot flashes and is actually drying the *chong mai*. One interesting study was carried out on breast cancer patients who received this anti-estrogen drug and suffered from hot flashes.[1]

The study compared two groups: one received an antidepressant drug (venlafaxine)—a common treatment for hot flashes—and the other received acupuncture treatments. The results showed improved reduction in hot flashes in both groups as well as significant improvements in mental health.



"After the treatments concluded, both the acupuncture and drug group were evaluated. Significantly, the acupuncture group continued to maintain the benefits of less hot flashes as well as increased sex drive and improvement in energy, clarity of thought, and their sense of well-being. The drug group had few long lasting effects."

After the treatments concluded, both the acupuncture and drug group were evaluated. Significantly, the acupuncture group continued to maintain the benefits of less hot flashes as well as increased sex drive and improvement in energy, clarity of thought, and their sense of well-being. The drug group had few long lasting effects.[1]

The treatment duration of the study was 12 weeks. All patients were treated using primary acupuncture points: Bladder-23, Kidney-3, and Spleen-6 for general menopausal symptoms. Secondary points were used as needed. According to the TCM diagnosis they included: Du-14, Gb-20, Lu-9, Liv-3, Du-20, St-36, Ren-6, Pc-7, and Ht-7.[1]

Two additional studies by Bokmand (2013)[2] and Liljegren (2012)[3] on the treatment of anti-hormonal treatment causing hot flashes used points from the Heart and Kidney channels Ht-6 and Kid-3 (Bokman) versus Ht -6 and KId-7(Liljegren). Both studies used Liv-3 and Sp-6; Li-4, Liv-3, and St-36 were added in the Liljegren study.

Personal comment: I find that the selection of the points in these studies does not accurately reflect the TCM diagnosis of dryness which from my point of view needs to address the extramerians Ren Mai and Chong Mai. Nevertheless, even the above point selection showed good results.

Protection - from side effects and more

In the last decade a study on one specific formula that was designed to address internal dryness was conducted by a hospital department of oncology as well as four cancer research centers and cancer laboratories world-wide. Results of this human study showed that the Chinese herbal formula LCS101 (Protectival), which was administered to breast cancer patients during chemotherapy, had significant clinical benefits in preventing chemotherapy side effects that included: anemia, leucopenia, fatigue and vomiting[4] and overall quality of life of cancer patients.[5] It also showed reduction of chemotherapy's side effects of more than 50% on both white and red blood cell counts.[5]

Additional studies on LCS101 (Protectival) demonstrate its multifaceted effects on the immune system. This protects against the side effects of chemotherapy and at the same time provides an anti-cancer effect. The multi-compound herbal formula LGS101 (Protectival), with its wide effect, is a prime example of the essence of Chinese medicine and its holistic approach.[6]

Final note

Combining different strategies in TCM, in both acupuncture and herbal medicine, has had a vast contribution by allowing faster and better healing with fewer side effects for cancer patients. By fusing oncology and biological science with TCM traditions, the significance of the TCM paradigm can be validated and provides an important step towards the integration of such healing options in cancer care.

To learn more about LCS101 research in cancer care, TCM Academy https://www.tcm.ac/course/treatment-of-radiation-side-effects/

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January 22, 2020

Dear Colleagues, Patients, and Supporters of Acupuncture:

On Tuesday, January 21st the Centers for Medicare and Medicaid Services (CMS) announced the historic decision to not only cover acupuncture for low back pain, but also to go out of their way to include Licensed Acupuncturists as the key group of providers for acupuncture services, along with physicians. This unprecedented support of a licensure group who is not currently a part of Medicare, as well as the endorsement of our academic system, speaks to the care and trust they put in us, and the desire for Medicare beneficiaries to receive the best care possible. **Please, recognize how phenomenal these actions are, and, if you choose to contact CMS, *thank them.***

Many providers are unclear as to why supervision is indicated and why the term "auxiliary personnel" is used. The answers to these questions are simple: CMS is only empowered to approve independent care for provider groups who are already within Medicare via the Social Security Act. Their options are to exclude the group, or find a way to include practitioners such as Licensed Acupuncturists with supervision by a provider within the structure of CMS. This is neither a slight to the profession, nor an error in any way. Provider types outside of Medicare are by CMS definition "auxiliary personnel". Auxiliary personnel must be supervised by Medicare providers. This is the maximal freedom that can be granted until the Social Security Act is amended to include LAcs, by an act of Congress. **The power to do that does not lie with CMS, but with our profession.**

Many questions naturally arise from this transformation in non-pharmacologic care for chronic low back pain for Medicare beneficiaries. How will the care be billed? How will payment be arranged? What type of supervision is required? How many units can be billed in a single session? Can we use electrical stimulation? The answers to these questions must remain forthcoming at present, as many of the procedural components of this have not yet been developed by CMS itself, and many clarifications are needed.

What we do know about this new expansion of care is the following:

1. Up to 20 visits will be allowed per year, with 12 visits in the first 90 days with demonstration of improvement. This is both a generous allotment, and truly allows a fair trial of acupuncture.
2. Only a physician as defined by Medicare in 1861(r)(1) (i.e. an MD or DO), and those with "a masters or doctoral level degree in acupuncture or Oriental Medicine from a school accredited by the Accreditation Commission on Acupuncture and Oriental Medicine (ACAOM)" may furnish acupuncture. This clearly prevents those with substandard training from providing services, protecting the quality of care for beneficiaries.
3. The type of supervision required was changed at the request of the LAc profession from "direct" to "the appropriate level". This accommodation adds tremendous latitude for collaborative agreements between LAcs and MD/DO providers, nurse practitioners, clinical nurse specialists,

and physician assistants, allowing the maximum freedom within CMS' power. While nurse practitioners, clinical nurse specialists, and physician assistants may not practice acupuncture, their supervisory availability also vastly expands the potential for collaborative agreements. It is implicit in this that these providers are not specifically directing the nature of the acupuncture treatment, but rather are collaboratively assuring patient diagnoses, safety, follow-up, and connection to the established care system.

4. Dry Needling is clearly defined as a "type of acupuncture" within the determination.

For a full read of the CMS decision, please see the CMS Decision Memo.

The American Society of Acupuncturists and the NCCAOM are proud to stand among those many groups lending support and high-level information to CMS towards their determination.

We recognize especially ASA member organizations:

- ASDC - Acupuncture Society of Washington, DC
- ASNY - Acupuncture Society of New York
- CalATMA - California Acupuncture and Traditional Medicine Association
- CTSA - Connecticut Society of Acupuncturists
- MAA - Minnesota Acupuncture Association

And our allied acupuncture groups:

- AAOA - American Alliance of Acupuncture
- AAQ - Association of Acupuncturists Quebec
- ANF - Acupuncture Now Foundation
- CAOMA - Council of Acupuncture and Oriental Medicine Associations
- IHPC – Integrative Health Policy Consortium
- NCASI - National Center for Acupuncture Safety and Integrity
- SAR - Society for Acupuncture Research

This is a monumental step towards improving access to acupuncture and licensed acupuncturists for all Americans, and we should take a moment to enjoy this evolution, which was many years in the making.

The next steps towards the inclusion of licensed acupuncturists in American healthcare are up to us as a unified group. **The single best way to get involved with this process is to join us at the second annual American Society of Acupuncturist national meeting, May 2-4, 2020 in Washington, D.C. where we will discuss this and much more!**

We will also be updating you regularly as we learn more.

Sincerely,

The Board of the American Society of Acupuncturists

The National Certification Commission for Acupuncture and Oriental Medicine

CLINICAL PEARLS - GREG LEE CONTINUED FROM PAGE 38

(salvia root) are some of the top herbs given for detoxing and healing leaky gut. These herbs are usually delivered in a micro-particle or suppository to target specific tissues or digestion organs.

Treatment 7: Liver-Gall Bladder flushes

To prevent reinfection of the gut from the liver and gall bladder, patients perform a one-day liver and gall bladder flush at home. The patient takes a combination of magnesium and amino acids which enlarges the ducts in the liver and gall bladder. A few hours later, he will take a combination of citrus juice and oil which squeezes the ducts closed and pushes out pathogens, parasites, stones, fat deposits and biofilms.

Treatment 8: Binders and movers

Patients with diarrhea are provided supplements and herbs that bind to and eliminate toxins as well as inflammatory compounds such as zeolite, bamboo charcoal, clays, pectin and *Wu Bei Zi* (galla chinensis). In the case of slow moving bowels or constipation, supplements and herbs which move the bowels are included, such as *Da Huang* (rhubarb), cascara sagrada, magnesium, vitamin C and glycerin.

Treatment 9: Visceral manipulation

Leaky gut symptoms of bloating, swelling, and pain have been quickly relieved with hands-on manipulation of the inflamed tissues and organs using visceral manipulation therapy.

Treatment 10: Hot needle acupuncture and moxibustion

Patients have reported rapid relief of deep tissue chronic gut pain and inflammation soon after burning moxa on the handles of 1" needles inserted into ST-25, LR-14 and SP-15. Burning moxa may be repeated on a single needle as many as eight times, as long as the patient continues to report improvement.

Treatment 11: Peptides

Peptides are a relatively new remedy in the prescription and supplement market. They are smaller versions of proteins. Research shows great potential for accelerated healing of tissues, reducing inflammation, and targeting pathogens. BPC-157 and Thymosin Beta 4 peptides are effective for rapid gut tissue repair, lowering inflammation, and protecting organs.

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CLINICAL PEARLS - BECKY THOROUGHGOOD CONTINUED FROM PAGE 39

Patients with slow motility and weak or rebellious Stomach *qi* are encouraged to use prokinetics such as digestive bitters, bitter greens or ginger before meals. Some may benefit from digestive enzymes or *Jian Pi Wan*.

Chewing thoroughly is integral to proper digestion. Since the sweeping movement of undigested material through the gastrointestinal tract requires periods of fasting, patients should not snack. Space meals every 3-4 hours.

Re-inoculate and Repair—Let food be your medicine

Throughout treatment, patients are urged to include bone broth for its gelatin rich, gut healing properties and demulcent herbs, including slippery elm, licorice and aloe. Supplements and foods containing quercetin, such as onions, apples, grapes, berries, broccoli, citrus fruits, cherries, tea and capers have been found to help seal the tight junctions in the intestines.[5]

While certain probiotic strains and fermented foods can help balance dysbiosis, prebiotic foods and plant fiber diversity are paramount to re-establishing healthy gut ecology, which is responsible for nutrient absorption and healing leaky gut. Once the digestion is more robust, patients should include prebiotic foods such as green tea, asparagus, garlic, onions, dandelion greens, slightly underripe bananas, chicory root, Jerusalem artichokes, leeks, apples with the skins, carrots and cocoa.[6] The diet should include 30-40 different plant-based foods during each week.

In addition to a varied diet, patients must attend to their emotional stressors through relaxation or meditation practices or therapy. They must also prioritize regular exercise and sleep.

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St – 45 厲兌
Li Dui, Severe Mouth

By Yair Maimon, DOM, PhD, Ac and Bartosz Chmielnicki, MD

Please see bios at end of the article.

The pictures are part of a project called the "Gates of Life" portraying the nature, action, and *qi* transformation of acupuncture channels and points made by the CAM team © (Chmielnick, Ayal, Maimon). Illustration by painter Mrs. Martyna "Matti" Janik.

Explanation of the picture:

St-45 is a Metal point on the Stomach channel, which is symbolized in the picture by the pile of metal coins. It is also a *jing-well* point; therefore, a well is also depicted next to the coins. These images serve as metaphors to remind us about the nature of the point.

There is Shennong (also called LiShi) sitting in front of a cave at Mount Li. He holds a frying pan in his hand, which he is using to extinguish a fire. This is a symbol of the Metal quality giving borders to Fire energy.

The trigram "*Dui*" painted on the wall reminds us of the joy and open mouth of the Stomach.

Characters of the Name:

厲 – Li – This character is a pictogram of a scorpion hiding under a rock. It means severe and stern, also like a whetstone sharpening the Metal.

Mount Li is the birthplace of **神農**, Shennong. He was an early agriculture hero who taught the Chinese people how to cultivate the soil, use the plow, and dig wells. He also instructed on the medical values of all herbs. When connected with the character of Wind, **厲風**, LiFeng, it means evil and pathologic wind.

兌 – Dui – This character shows breath coming out of mouth. It means to speak, to gratify, to exchange, but it also signifies mouth and, by extension, hole.

Meaning of the Name:

Severe Mouth

This translation is relevant on many levels. St-45 as a Metal point on the Stomach channel treats many diseases of the mouth, gums, teeth and throat, especially when related with inflammatory processes. On the other hand, "open mouth" is the symbol of hunger and needs that are never satisfied.

Main Actions and Indications:

Li Dui gathers the nourishment—the effect of digestion—and passes it to the Spleen so it can be distributed with Blood to all the organs of the body.

As the Metal point it has strong concentrating movement, gathering the Essences, and is also used to treat all Heat/Fire pathologies of *YangMing* division.

1. St-45 is a *jing-well* point and the last point of the channel.

1.1 Influences the other side of the channel – face, eyes, nose, mouth, throat

As a *jing-well* point, St-45 strongly influences the other end of the channel—the area of face, head and orifices, and especially the eyes. *YangMing* is associated with Autumn, Metal and general movement of energy downwards and inwards, which enables the function of digestion. As St-45 is the Metal point, these associations makes St-45 one of the strongest point for treating Fire/Heat disorders, especially when expressed in the head or face in various forms of infectious diseases, often accompanied by pus and inflammation.

1.2 TMM (Tendo Muscular Meridian)

St-45 is the starting point of the Sinew channel passing through the knee, hip joint, groin above the genitals, abdomen, breast, and neck. It terminates below the eyelids and in front of the ear. All physical manifestations of the Sinew channel, such as pains, swellings, stiffness along its pathway (including facial paralysis, abscesses of breasts and so on), can be successfully treated with St-45.

2. St-45 is the Metal point

Metal gives borders to Fire. The main function is to help bring energy down from Heaven to Earth, from Fire to Water; therefore, Metal points naturally help in regulating the Fire and preventing its over activity. Therefore St-45 is effective in reducing Fire/Heat pathologies of *YangMing* division.

Metal's energy works to condense, moving downwards, while the Fire energy goes upward and outward. The Metal quality can control the Fire and bring it to its limits, thereby reducing Fire.

On the physical level, Heat in *YangMing* causes fever, inflammation and swelling on the face—in the sinuses, nose, teeth, mouth—and in the throat, breasts, digestive tract, or knees.

On the emotional level, *YangMing* Heat results in insomnia, irritability, uncontrolled desires, hunger, or even manic behavior.

3. *Shen* transformations

The Stomach provides the nourishment on different levels. It enables pleasure and satisfaction in life. When there is excessive Heat/Fire in the Stomach, people crave for pleasure but are never satisfied; they never having enough. They continuously hunger for more food, more drink, more sexual pleasure, and so on. On the other hand, they are also not satisfied with themselves.

Metal phase is the manifestation of refinement and clarity. St-45 as the Metal point on the Stomach channel gives boundaries to the Heat/Fire, helping to control the cravings. This function results in the ability to digest (absorb) reality and feel satisfied.

Metal gives to Earth its solidity and fertility like the precious metals in the Earth do. This makes it abundant and gives its borders a sense of solidarity.

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What's the Difference Between a Systematic Review and a Literature Review?

By Jennifer Stone, MSOM, LAc

For the science research community, it's a question that deserves discussion. As an editor, I see confusion and misunderstanding by both authors and peer reviewers across many different types of scholarly reviews.

Here are the definitions of each of them:

A **literature review** is a critical analysis of a segment of a published body of knowledge about a specific topic. This is done through: 1. Summary/overview of the topic; 2. Classification of the topic; and 3. Comparisons of prior research studies, reviews of literature, and theoretical articles.

A **systematic review** answers a defined research question by collecting and summarizing all empirical evidence that fits pre-specified eligibility criteria. Note: A **meta-analysis** is the use of statistical methods to summarize the results of these studies that are included in a systematic review.

A systematic review is not just a research paper. It's a full-blown non-biased research study of the existing literature on a topic. The systematic review is used to inform clinical decision-making or the creation of clinical practice guidelines. It can also be used as evidence to inform policy change (such as whether Medicare should cover acupuncture). A systematic review is a long-term project that involves multiple researchers working together following structured guidelines.

Most of the reviews submitted to JASA are literature reviews. Many DAOM candidates prepare a literature review as a part of their capstone project and they submit the literature review to a peer reviewed journal for publication.

In this issue, we include both a literature review and a systematic review. Please read both to understand the differences between them.

This chart from the Mayo Clinic library resource page nicely summarizes their differences:

	Systematic Review	Literature Review
Definition	High-level overview of primary research on a focused question that identifies, selects, synthesizes, and appraises all high quality research evidence relevant to that question	Qualitatively summarizes evidence on a topic using informal or subjective methods to collect and interpret studies.
Goals	"Answer a clinical question Eliminate bias"	Provide summary or overview of topic
Question	Clearly defined and answerable clinical question Recommend using PICO as a guide	Can be a general topic or a specific question
Components	Pre-specified eligibility criteria Systematic search strategy Assessment of the validity of findings Interpretation and presentation of results Reference list	Introduction Methods Discussion Conclusion Reference list
Number of Authors	Three or more	One or more
Timeline	Months to years Average eighteen months	Weeks to months
Requirements	Thorough knowledge of topic Perform searches of all relevant databases Statistical analysis resources (for meta-analyses)	Understanding of topic Perform searches of one or more databases
Value	Connects practicing clinicians to high quality evidence Supports evidence-based practice	Provides summary of literature on a topic

https://libraryguides.mayo.edu/systematic-reviews

For ambitious authors who wish to undergo a systematic review with or without a meta-analyses, I recommend the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) website. www.prisma-statement.org

into the correlation between IMI, male health, and fetal development requires further research.

Acupuncture can offer a safe, minimally-invasive approach to addressing suboptimal sperm numbers with no noted side effects. The results of the studies described above show that acupuncture may have a role in the treatment of IMI by having a positive effect on sperm parameters. More research and follow up is needed to test the long term effects on male health following acupuncture treatment for IMI in addition to higher quality studies with larger samples sizes.

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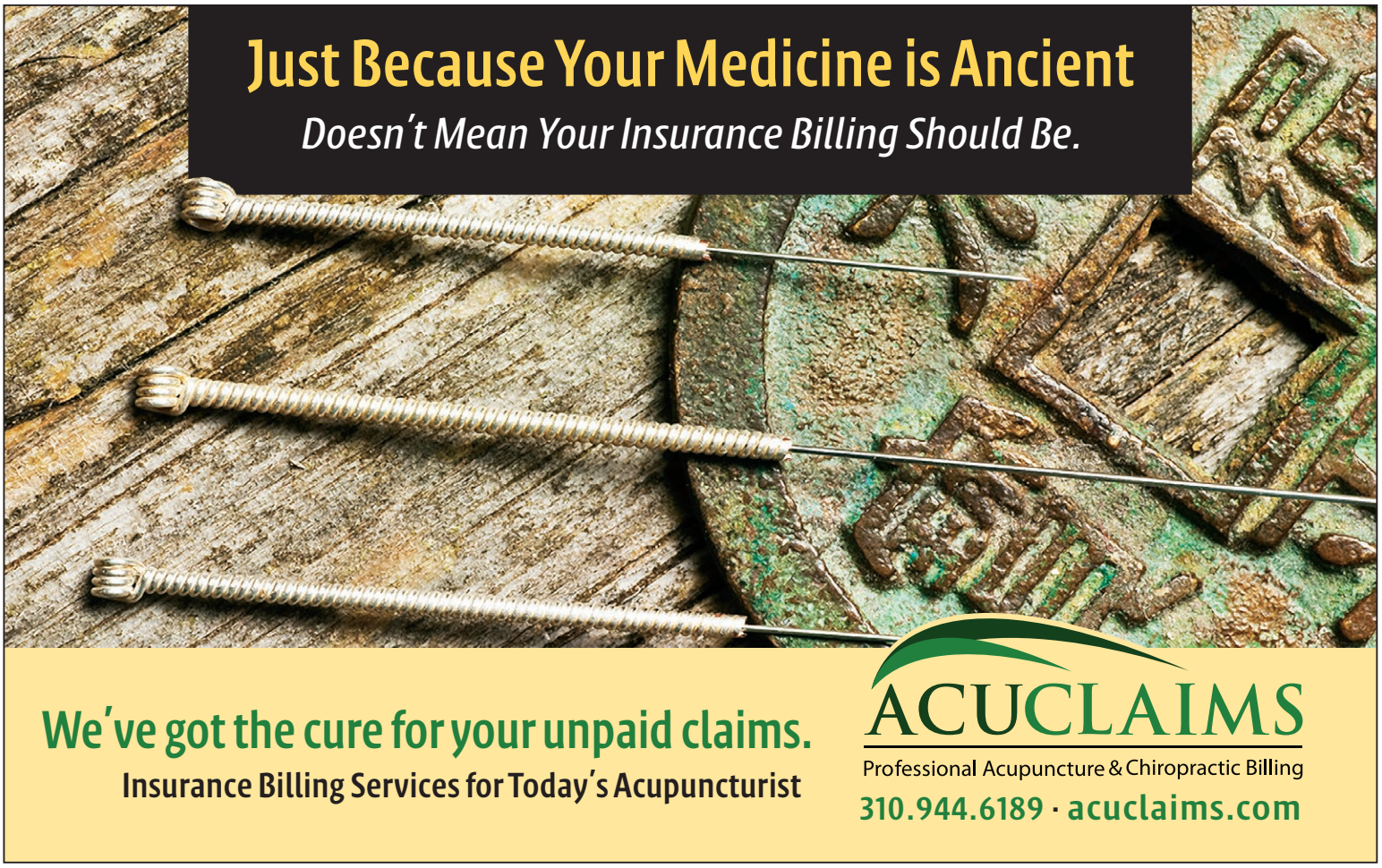
Footnotes

i. a sensation of warmth, numbness, tingling, soreness, and/or tension resulting from stimulation affecting muscle nerve afferents[3]

ii. total number (or concentration, depending on outcome reported) of spermatozoa, and percentages of progressively motile (pr) spermatozoa, below the lower reference limits



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