

Clinical Practice Guideline: **Acupuncture for the Treatment of Rheumatoid Arthritis**

Date of Implementation: **March 18, 2010**

Product: **Specialty**

POLICY

American Specialty Health – Specialty (ASH) clinical committees have determined that acupuncture for the treatment of pain and dysfunction associated with rheumatoid arthritis (RA) is professionally recognized and may have a favorable benefit:risk profile. A trial period of acupuncture for the treatment of pain and dysfunction associated with RA to assess effectiveness for individual patients is supported by the available evidence. However, the clinical effectiveness of acupuncture for treatment of the underlying inflammatory process related to RA is inconclusive and requires further study to determine its efficacy as compared with the currently accepted professional standard means of treatment.

PROCESS AND DEFINITIONS

When developing, reviewing, and approving clinical policy, ASH peer-review committees consider whether the technique/procedure:

- Is established as clinically effective by:
 - Scientific information published in an acceptable peer-reviewed clinical science resource, and
 - The consensus opinion of the Evidence Evaluation Committee (EEC) when available;
- Is professionally recognized by:
 - Inclusion in the educational standards accepted by the majority of the professions' educational institutions,
 - Wide acceptance and use of the practice, and
 - Recommendations for use made by healthcare practitioners practicing in the relevant clinical area;
- Poses a health and safety risk; and
- Is plausible or implausible
 - A belief, theory, or mechanism of health and disease that can be explained within the existing framework of scientific methods, reasoning, and available knowledge is considered plausible.
 - A treatment intervention or diagnostic procedure that requires the existence of forces, mechanisms, or biological processes that are not known to exist within the current framework of scientific methods, reasoning, and available knowledge is considered implausible.

Substitution harm (indirect harm): Compromised clinical outcomes caused by:

- Utilizing a specific diagnostic or therapeutic procedure when the safety, clinical effectiveness, or diagnostic utility is either unknown or is known to be unsafe, ineffective, or of no diagnostic utility, *instead of* a diagnostic or therapeutic procedure known to be safe, be clinically effective, or to have diagnostic utility; or
- The utilization of a diagnostic or therapeutic procedure that is substantially less effective or safe than another procedure with established safety, and clinical effectiveness or utility.

Labeling effects (non-specific harm): The harm that results from identifying in a patient a condition or a finding that is not clinically valid.

Safe: The terms “safe” and “safety,” are used only with specific reference to the absence of direct harm. Direct harm would include any injury to a patient caused by the mechanical, thermal, biological, chemical, pharmacological, electrical, electromagnetic, or psycho-dynamic properties of a diagnostic or therapeutic procedure, and as such, the procedure would be considered unsafe.

Direct harm: Any injury to a patient caused by the mechanical, thermal, biological, chemical, pharmacological, electrical, electromagnetic, or psycho-dynamic properties of a diagnostic or therapeutic procedure.

Benefit versus risk profile: The relative effectiveness or utility of a therapeutic intervention or diagnostic procedure versus its potential for direct harm.

- Positive (benefits outweigh risks),
- Negative (risks outweigh benefits), or
- Equivocal (available information is inconclusive).

Acupuncture Safety

- Major adverse events associated with acupuncture are exceedingly rare.
- Minor adverse events (e.g., bruising, soreness at needle insertion point) associated with acupuncture were found to be common and transient.
- The incidence of adverse events of acupuncture is substantially lower than that of many drugs or other accepted invasive procedures.
- Proper patient selection and acupuncture technique are very important for acupuncture safety.

Description/Background

Rheumatoid arthritis (RA) is an autoimmune disorder causing persistent, destructive, symmetrical polyarthritis often associated with the hands and feet, although it may involve any synovial joint. The diagnosis is based on clinical exam and systematized

1 diagnostic criteria: number of swollen and tender joints, erythrocyte sedimentation rate
 2 (ESR), C-reactive protein (CRP), levels of rheumatoid factor (RF), and anti-cyclic
 3 citrullinated peptide (anti-CCP) (Combe et al., 2007).

4
 5 RA is the most common inflammatory disease of the joints and affects approximately
 6 0.6% of the total US population, with estimates of prevalence ranging from 1-6 per 1,000
 7 for men and 3-12 per 1,000 for women (Helmick et al., 2008; Lawrence et al., 2008;
 8 Combe et al., 2007). RA typically presents between 35 and 45 years of age, yet occurs
 9 with increased frequency as persons age. Although specific genes have yet to be
 10 identified a genetic link is suggested. The only identified modifiable risk factor is
 11 smoking cessation (Woolf & Akesson, 2007). Treatment strategies should focus on
 12 reductions in pain, inflammation, disability, radiological damage, and the development of
 13 co-morbidities (Combe et al., 2007).

14 15 **Evidence and Research**

16 The review by Wang et al. highlights key methodological flaws that limit the ability to
 17 appropriately perform meta-analyses of acupuncture trials (Wang et al., 2008).
 18 Heterogeneity of trials is endemic in the field of acupuncture research, and includes
 19 issues related to participants, outcomes, and treatments (acupuncture dose/intensity,
 20 control type, and duration variations). The authors highlight the differing styles of
 21 acupuncture of the included trials, e.g., wide variation in the number of acupuncture
 22 points (acupoints) (1-24) and treatments (1,180). Astute observation of these issues led to
 23 recommendations for future studies to focus on the optimum dose (effective evidence-
 24 based dose/intensity including number of acupuncture points, frequency of acupuncture
 25 sessions, and intervention duration) of acupuncture treatments for RA.

26
 27 The review by Lee et al. chose to interpret the data comparing acupuncture to
 28 pharmaceutical interventions in a negative light, despite the equivalence of findings (Lee
 29 et al., 2008b). It has been suggested that acupuncture should be held to the same level of
 30 effectiveness as currently accepted therapies, i.e., acupuncture is at least as good as the
 31 current usual care, yet with less adverse effects (Hammerschlag, 1998). Lee et al.
 32 comment that 75% (6/8) of randomized controlled trials (RCTs) reported mild overall
 33 adverse effects of acupuncture treatment. They go further to report, “In comparison to
 34 those of standard drug treatments such as NSAIDs, these were mild, infrequent, and
 35 perhaps even negligible.” The review also addressed the methodological limitations of
 36 the included trials and specifically highlighted the small sample size of the two (2) most
 37 recent placebo controlled trials (Tam et al., 2007; Zanette et al., 2007). The authors go so
 38 far as to warn against drawing firm conclusions from the literature resultant to these
 39 limitations.

40
 41 A few additional trials are worth mentioning as they highlight potential mechanisms,
 42 treatment optimization, and synergistic effects of acupuncture and related modalities for

the treatment of RA. The most recent is a brief report of an outcomes trial investigating the hypothesis, “Acupuncture modulates oxidative stress by enhancing the activity of antioxidants in RA patients” (Kim et al., 2009). This report is an addendum to a pilot project investigating the feasibility of acupuncture in the symptom management of RA (Lee et al., 2008a). Participants (n=25) received fourteen (14) individualized acupuncture treatments over six (6) weeks to observe the standardized criteria of the American College of Rheumatology (ACR) as well as antioxidant status (e.g., Superoxide dismutase[SOD]) and total antioxidant status (TAS). As part of the exploratory analysis, participants were divided into two groups, responders (>50% reduction in swollen joint counts) or non-responders (<50% reduction in swollen joint counts) (Kim et al., 2009). The findings suggest the reduction in the number of swollen joints (Lee et al., 2008a) was significantly related to the up-regulation of SOD activity as acupuncture induced increased activities of SOD as compared to non-responders (Kim et al., 2009).

A recent exploratory outcomes trial on acupuncture in RA patients (n=6) reports on the potential use of positron-emission tomography (PET) as a relevant biomarker (Sato et al., 2009). Participants received ten (10) standardized sessions over eight (8) weeks and outcome assessments included: PET imaging to ascertain potential regional inflammatory findings, systemic inflammatory markers (ESR), and subjective (visual analog scale [VAS]) and objective (range of motion [ROM]) assessment. The results indicate that acupuncture relieved pain, enhanced physical function, and improved quality of life, yet no statistically significant change was shown either in systemic inflammatory markers (ESR) or in regional inflammatory findings (PET). Contrary to the previously stated findings reported by Kim et al. and Lee et al., the authors suggest that the regional effects of acupuncture are unlikely to be induced through reduction of regional inflammation.

As highlighted in the review by Wang et al., numerous RCTs are subject to methodological flaws in treatment adequacy (Wang et al., 2008). An outcomes trial from China followed participants (n=47) treated with a total of six (6) courses of acupuncture (one [1] course equal to ten [10] treatments) and assessed inflammatory markers (e.g., ESR) and objective measures (e.g., swelling and pain of joints) at the end of three (3) and six (6) courses of treatment (Wang et al., 2007). As compared to results at the end of three (3) courses of treatment, six (6) courses offered significant improvements in all outcomes, highlighting the call for investigations into “an evidence-based assessment on frequency and intervention duration of acupuncture session” (Wang et al., 2008). In line with the need for mirroring treatment plans that appropriately reflect clinical practice, assessment of potential additive (or synergistic) effects of co-interventions of acupuncture are needed.

As noted, no large scale RCTs have been conducted on the benefits of acupuncture for the treatment of rheumatoid arthritis. The five (5) systematic reviews are a result of

several small scale pilot RCTs. The lack of large scale, well-designed RCTs precludes firm conclusions from being drawn.

Conclusions

The evidence is insufficient to support or refute the use of acupuncture for the treatment of rheumatoid arthritis.

References

- Acupuncture. (1997). *NIH Consensus Statement*, 15(5), 1-34. Retrieved January 4, 2010, from <http://consensus.nih.gov/1997/1997Acupuncture107PDF.pdf>
- Bernateck M, Becker M, Schwake C, Hoy L, Passie T, Parlesak A, Fischer MJ, Fink M, Karst M. Adjuvant auricular electroacupuncture and autogenic training in rheumatoid arthritis: a randomized controlled trial. Auricular acupuncture and autogenic training in rheumatoid arthritis. *Forsch Komplementmed*. 2008 Aug;15(4):187-93. Epub 2008 Jul 29.
- Bhatt-Sanders D. Acupuncture for rheumatoid arthritis: an analysis of the literature. *Semin Arthritis Rheum*. 1985 May;14(4):225-31. Review.
- Casimiro L, Barnsley L, Brosseau L, Milne S, Robinson VA, Tugwell P, Wells G. Acupuncture and electroacupuncture for the treatment of rheumatoid arthritis. *Cochrane Database Syst Rev*. 2005 Oct 19;(4):CD003788. Review.
- Combe B, Landewe R, Lukas C, Bolosiu HD, Breedveld F, Dougados M, Emery P, Ferraccioli G, Hazes JM, Klareskog L, Machold K, Martin-Mola E, Nielsen H, Silman A, Smolen J, Yazici H. EULAR recommendations for the management of early arthritis: report of a task force of the European Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). *Ann Rheum Dis*. 2007 Jan;66(1):34-45. Epub 2006 Jan 5.
- Dixon WG, Symmons DP. Does early rheumatoid arthritis exist? *Best Pract Res Clin Rheumatol*. 2005 Feb;19(1):37-53. Review.
- Eisenberg DM, Davis RB, Ettner SL, Appel S, Wilkey S, Van Rompay M, Kessler RC. Trends in alternative medicine use in the United States, 1990-1997: results of a follow-up national survey. *JAMA*. 1998 Nov 11;280(18):1569-75.
- Freedman J. An audit of 500 acupuncture patients in general practice. *Acupunct Med*. 2002 Mar;20(1):30-4.

- 1 Grigor C, Capell H, Stirling A, McMahon AD, Lock P, Vallance R, Kincaid W, Porter D.
2 Effect of a treatment strategy of tight control for rheumatoid arthritis (the TICORA
3 study): a single-blind randomised controlled trial. *Lancet*. 2004 Jul 17-
4 23;364(9430):263-9.
- 5
- 6 Hammerschlag R. Methodological and ethical issues in clinical trials of acupuncture. *J*
7 *Altern Complement Med*. 1998 Summer;4(2):159-71. Review.
- 8
- 9 Han, JS. Acupuncture: neuropeptide release produced by electrical stimulation of
10 different frequencies. *Trends Neurosci*. 2003 Jan;26(1):17-22. Review.
- 11
- 12 Han, JS. Acupuncture and endorphins. *Neurosci Lett*. 2004 May 6;361(1-3):258-61.
13 Review.
- 14
- 15 Helmick CG, Felson DT, Lawrence RC, Gabriel S, Hirsch R, Kwoh CK, Liang MH,
16 Kremers HM, Mayes MD, Merkel PA, Pillemer SR, Reveille JD, Stone JH; National
17 Arthritis Data Workgroup. Estimates of the prevalence of arthritis and other
18 rheumatic conditions in the United States. Part I. *Arthritis Rheum*. 2008 Jan;58(1):15-
19 25.
- 20
- 21 Jäntti J, Aho K, Kaarela K, Kautiainen H. Work disability in an inception cohort of
22 patients with seropositive rheumatoid arthritis: a 20 year study. *Rheumatology*
23 (Oxford). 1999 Nov;38(11):1138-41.
- 24
- 25 Kim ST, Kim YJ, Lee JY, Lee H, Yin CS, Choi SM, Chae Y, Lee H, Park HJ.
26 Acupuncture enhances superoxide dismutase (SOD) activity in the serum of
27 rheumatoid arthritis patients. *Clin Exp Rheumatol*. 2009 Mar-Apr;27(2):384.
- 28
- 29 Langevin HM, Bouffard NA, Badger GJ, Churchill DL, Howe AK. Subcutaneous tissue
30 fibroblast cytoskeletal remodeling induced by acupuncture: Evidence for a
31 mechanotransduction-based mechanism. *J Cell Physiol*. 2006A Jun;207(3):767-74.
- 32
- 33 Langevin HM, Bouffard NA, Churchill DL, Badger GJ. Connective tissue fibroblast
34 response to acupuncture: dose-dependent effect of bidirectional needle rotation. *J*
35 *Altern Complement Med*. 2007 Apr;13(3):355-60.
- 36
- 37 Langevin HM, Churchill DL, Wu J, Badger GJ, Yandow JA, Fox JR, Krag MH.
38 Evidence of connective tissue involvement in acupuncture. *FASEB J*. 2002
39 Jun;16(8):872-4. Epub 2002 Apr 10.

- 1 Langevin HM, Konofagou EE, Badger GJ, Churchill DL, Fox JR, Ophir J, Garra BS.
2 Tissue displacements during acupuncture using ultrasound elastography techniques.
3 *Ultrasound Med Biol*. 2004 Sep;30(9):1173-83.
4
- 5 Langevin HM, Storch KN, Cipolla MJ, White SL, Buttolph TR, Taatjes DJ. Fibroblast
6 spreading induced by connective tissue stretch involves intracellular redistribution of
7 alpha- and beta-actin. *Histochem Cell Biol*. 2006B May;125(5):487-95. Epub 2006
8 Jan 14.
9
- 10 Langevin HM, Yandow JA. Relationship of acupuncture points and meridians to
11 connective tissue planes. *Anat Rec*. 2002 Dec 15;269(6):257-65.
12
- 13 Lawrence RC, Felson DT, Helmick CG, Arnold LM, Choi H, Deyo RA, Gabriel S,
14 Hirsch R, Hochberg MC, Hunder GG, Jordan JM, Katz JN, Kremers HM, Wolfe F;
15 National Arthritis Data Workgroup. Estimates of the prevalence of arthritis and other
16 rheumatic conditions in the United States. Part II. *Arthritis Rheum*. 2008
17 Jan;58(1):26-35.
18
- 19 Lee H, Lee JY, Kim YJ, Kim S, Yin C, Khil JH, Kwon K, Choi SM, Lee H, Park HJ.
20 Acupuncture for symptom management of rheumatoid arthritis: a pilot study. *Clin*
21 *Rheumatol*. 2008A May;27(5):641-5. Epub 2008 Jan 10.
22
- 23 Lee MS, Shin BC, Ernst E. Acupuncture for rheumatoid arthritis: a systematic review.
24 *Rheumatology* (Oxford). 2008B Dec;47(12):1747-53. Epub 2008 Aug 18. Review.
25
- 26 Li A, Lao L, Wang Y, Xin J, Ren K, Berman BM, Tan M, Zhang R. Electroacupuncture
27 activates corticotrophin-releasing hormone-containing neurons in the paraventricular
28 nucleus of the hypothalamus to alleviate edema in a rat model of inflammation.
29 *BMC Complement Altern Med*. 2008 May 12;8:20.
30
- 31 Li P, Ayannusi O, Reid C, Longhurst JC. Inhibitory effect of electroacupuncture (EA) on
32 the pressor response induced by exercise stress. *Clin Auton Res*. 2004 Jun;14(3):182-
33 8.
34
- 35 Linde K, Vickers A, Hondras M, ter Riet G, Thormählen J, Berman B, Melchart D.
36 Systematic reviews of complementary therapies - an annotated bibliography. Part 1:
37 Acupuncture. *BMC Complement Altern Med*. 2001;1:3. Epub 2001 Jul 16. Review.
38
- 39 Nahin RL, Barnes PM, Stussman BJ, Bloom B. Costs of complementary and alternative
40 medicine (CAM) and frequency of visits to CAM practitioners: United States, 2007.
41 *Natl Health Stat Report*. 2009 Jul 30;(18):1-14.

- 1 Napadow V, Ahn A, Longhurst J, Lao L, Stener-Victorin E, Harris R, Langevin HM. The
2 status and future of acupuncture research. *J Altern Complement Med.* 2008
3 Sep;14(7):861-9.
- 4
- 5 Napadow V, Kettner N, Liu J, Li M, Kwong KK, Vangel M, Makris N, Audette J, Hui
6 KK. Hypothalamus and amygdala response to acupuncture stimuli in carpal tunnel
7 syndrome. *Pain.* 2007 Aug;130(3):254-66. Epub 2007 Jan 19.
- 8
- 9 Sato M, Inubushi M, Shiga T, Hirata K, Okamoto S, Kamibayashi T, Tanimura K,
10 Tamaki N. Therapeutic effects of acupuncture in patients with rheumatoid arthritis: a
11 prospective study using (18)F-FDG-PET. *Ann Nucl Med.* 2009 May;23(3):311-6.
12 Epub 2009 Apr 1.
- 13
- 14 Smith LA, Oldman AD, McQuay HJ, Moore RA. Teasing apart quality and validity in
15 systematic reviews: an example from acupuncture trials in chronic neck and back
16 pain. *Pain.* 2000 May;86(1-2):119-32.
- 17
- 18 Tam LS, Leung PC, Li TK, Zhang L, Li EK. Acupuncture in the treatment of rheumatoid
19 arthritis: a double-blind controlled pilot study. *BMC Complement Altern Med.* 2007
20 Nov 3;7:35.
- 21
- 22 Ulett GA, Han S, Han JS. Electroacupuncture: mechanisms and clinical application. *Biol*
23 *Psychiatry.* 1998 Jul 15;44(2):129-38. Review.
- 24
- 25 Wang C, de Pablo P, Chen X, Schmid C, McAlindon T. Acupuncture for pain relief in
26 patients with rheumatoid arthritis: A systematic review. *Arthritis Rheum.* 2008 Sep
27 15;59(9):1249-56. Review.
- 28
- 29 Wang R, Jiang C, Lei Z, Yin K. The role of different therapeutic courses in treating 47
30 cases of rheumatoid arthritis with acupuncture. *J Tradit Chin Med.* 2007
31 Jun;27(2):103-5.
- 32
- 33 White P, Lewith G, Berman B, Birch S. Reviews of acupuncture for chronic neck pain:
34 pitfalls in conducting systematic reviews. *Rheumatology (Oxford).* 2002
35 Nov;41(11):1224-31. Review.
- 36
- 37 Woolf AD, Akesson K. Can we reduce the burden of musculoskeletal conditions? The
38 European action towards better musculoskeletal health. *Best Pract Res Clin*
39 *Rheumatol.* 2007 Feb;21(1):1-3.

- 1 Yang X, Li JS, Yang SQ, Zhang XX, Zhang TS, Zhou HY, Liu XG. [Influence of
2 moxibustion on JAK-STAT signal transduction pathways of synovial cells in
3 rheumatoid arthritis rabbits]. *Zhen Ci Yan Jiu*. 2007 Apr;32(2):75-82. Chinese.
4
- 5 Zanette Sde A, Born IG, Brenol JC, Xavier RM. A pilot study of acupuncture as
6 adjunctive treatment of rheumatoid arthritis. *Clin Rheumatol*. 2008 May;27(5):627-
7 35. Epub 2007 Nov 8.
8
- 9 Zhang RX, Lao L, Wang X, Fan A, Wang L, Ren K, Berman BM. Electroacupuncture
10 attenuates inflammation in a rat model. *J Altern Complement Med*. 2005
11 Feb;11(1):135-42.