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ACUPUNCTURE TREATMENT OF VASOMOTOR SYMPTOMS IN MEN WITH PROSTATIC CARCINOMA: A PILOT STUDY

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ABSTRACT

Purpose: Most men who undergo castration therapy for prostatic carcinoma will have vasomotor symptoms that usually persist for years. Vasomotor symptoms are elicited from the thermoregulatory center, possibly due to a decrease in hypothalamic opioid activity induced by low sex steroid concentrations. Acupuncture treatment in women, which stimulates hypothalamic opioid activity, alleviates vasomotor symptoms. We report on men treated with acupuncture for relief of vasomotor symptoms after castration therapy.

Materials and Methods: We asked 7 men with vasomotor symptoms due to castration therapy to receive acupuncture treatment 30 minutes twice weekly for 2 weeks and once a week for 10 weeks. Effects on flushes were recorded in logbooks.

Results: Of the 7 men 6 completed at least 10 weeks of acupuncture therapy and all had a substantial decrease in the number of hot flushes (average 70% after 10 weeks). At 3 months after the last treatment the number of flushes was 50% lower than before therapy. Therapy was discontinued after 10 weeks because of a femoral neck fracture in 1 man and after 3 weeks due to severe back pain in 1.

Conclusions: Acupuncture may be a therapeutic alternative in men with hot flushes after castration therapy and merits further evaluation.

KEY WORDS: vasomotor system, men, prostatic neoplasms, castration, acupuncture

Vasomotor symptoms, including hot flushes and sweating, occur in about 3 of 4 women at menopause as a consequence of decreasing sex hormone levels.[1–5] These symptoms may also be induced in men by current therapies for advanced carcinoma of the prostate, such as bilateral orchiectomy or medical castration with gonadotropin-releasing hormone (Gn-RH) analogues. This condition has received little attention in the urological literature, possibly because hot flushes are thought to be self-limiting.

In 1896 Cabot studied the effect of castration for treatment of prostate enlargement and reported "uncomfortable flushes of heat, similar to those experienced by women at the time of the menopause."[6] In the 1930s McCullagh and Renshaw reported that after castration 7 of 12 men complained of sudden flushes and sensations of hot or cold. "The hot flushes occurred as many as four or five times daily for a period of several years and tended gradually to decrease in number and severity."[7] Huggins et al reported that 9 of 21 patients had episodic hot flushes and perspiration beginning 2 to 6 weeks after orchiectomy.[8] Ginsburg and O'Reilly reported hand blood flow during a hot flush,[9] and changes in skin blood flow and water evaporation during flushes in 13 patients after orchiectomy.[10] Reports emphasized that hot flushes were sometimes the most distressing symptom after orchiectomy[10,11] and after Gn-RH analogue treatment.[12,13] Frequent flushes affect the quality of life profoundly and are experienced by up to 85% of women.[1,2,14,15] The symptoms, which often cause sleep disturbances, fatigue and irritability, may disappear after 2 to 5 years but can persist for more than 15.[1–3,15] Vasomotor symptoms in men usually persist for more than 5 years.[16]

A sudden downward shift of the set point of the hypothalamic thermoregulatory center is believed to induce flushes.[1,4,17–19] This theory is supported by observations during flushes of increases in peripheral blood flow, pulse rate, skin conductance and skin temperature with a concomitant decrease in body core temperature.[1,2,14,18–21] These phenomena lead to or are signs of heat loss. The flushes are sometimes followed by chills or shivering if significant heat loss has occurred.[2,18] The cause of alterations in the thermoregulatory center remains unknown. Altered autonomic activity probably causes increased blood flow.[20] Increased circulating epinephrine during a flush correlates with the increased heart rate, and a lower concentration of norepinephrine correlates with increased blood flow since circulation through the skin of the hands is under α-adrenergic vasoconstrictor control.[18,20] Increased blood flow may also be induced by the potent vasodilatory neuropeptide, calcitonin gene-related peptide (CGRP).[22,23]

The role of estrogen in the etiology of hot flushes in women is not clear. Some studies have reported decreased circulating levels of estrogen,[24,25] whereas others have found no such correlation.[21,26] Possibly hypothalamic factors associated with the release of Gn-RH are involved in vasomotor symptom genesis.[14,19,27,28] The flushes characteristically coincide with peaks in luteinizing hormone and Gn-RH secretion.[14,18,21,27–29] A hypothetical model of the genesis of hot flushes presented by Lomax and Schönbaum is based on the fact that noradrenergic and pacemaker neurons stimulate hypothalamic Gn-RH release.[14] The negative feedback of estradiol might be mediated by β-endorphin induced inhibition of the noradrenergic pathways. Ovarian failure leads to a decrease in hypothalamic β-endorphin activity and disinhibition of the noradrenergic drive, and increased Gn-RH release. The Gn-RH neurons are close to the thermoregulatory center and enhanced activity in the hypothalamus could lead to a transient reduction in the thermoregulatory set point, thus triggering the hot flush.[14] Also, opioids have direct

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effects on thermoregulation, and a decrease in hypothalamic β-endorphin activity may make thermoregulation less stable.[30]

Therapy that affects hypothalamic β-endorphin activity in women, such as estrogen, physical exercise or acupuncture, is associated with a lower prevalence of vasomotor symptoms.[14,23,31,32] Menopausal women with hot flushes may be successfully treated with hormone replacement therapy. There are few nonpharmacological alternatives to hormone replacement therapy but behavioral therapy and acupuncture have been suggested.[23,33,34] Acupuncture therapy increases hypothalamic β-endorphin activity and decreases the frequency of hot flushes in postmenopausal women.[23] Treatment with diethylstilbestrol or megestrol acetate in men reduces flushes more effectively than nonhormonal therapies.[35,36] To our knowledge no studies of alternative therapies have been reported in men with vasomotor symptoms. We established whether acupuncture therapy could be used to treat vasomotor symptoms in men who underwent castration therapy for prostatic carcinoma.

MATERIALS AND METHODS

We asked 7 men with vasomotor symptoms after castration therapy to participate in the pilot study (see table). All men attended the outpatient clinic at the department of surgery at the County Hospital of Ludvika, Sweden, and had vasomotor symptoms during continuous treatment with Gn-RH analogue. After the men received verbal and written information they consented to take part in the study. Acupuncture therapy was given for 30 minutes twice a week for 2 weeks and thereafter once a week for 10 weeks. Acupuncture therapy for women and men with vasomotor symptoms was approved by the Ethical Committee at the Faculty of Health Sciences, University of Linköping. The mode of acupuncture therapy was the same as that used in our current study on women with vasomotor symptoms and breast cancer with a slight modification.

The acupuncture points used are shown in the Appendix. A bilateral 2 Hz. current was used at BL 23 and BL 32. Acupuncture was administered by a physiotherapist (M. H.). Effects on flushes were recorded in logbooks, which the men were asked to complete daily for 1 week before therapy, every day for 1 week after 2, 6 and 10 weeks of therapy, and 3 months after the end of therapy (week 24). They were asked to record daily the total number of flushes during the previous day and night. The number of flushes per week was calculated for each man and analyzed with computer software. Nonparametric methods were used for descriptive and comparative purposes.

RESULTS

Of the 7 men 6 completed at least 10 weeks of acupuncture therapy and all had a substantial decrease in hot flushes (see table). Data on these 6 men were used for statistical analysis. Two men stopped therapy for medical reasons. Patient 6 had a femoral neck fracture after 10 weeks of therapy and patient 7 had such severe back pain at 3 weeks that he could not lie down during therapy. Patient 5 had a long distance to travel for therapy and was so satisfied with the effects after 10 weeks that he decided to forego the last 2 treatments. In this patient the daily number of flushes had decreased from 5 to 7 before to 1 to 2 at week 10. Pairwise comparison of the number of flushes per week before and during therapy demonstrated a statistically significant decrease after 6, 10 and 24 weeks ($p < 0.05$). One factor analysis of variance repeated measures revealed a statistically significant decrease with time and treatments ($p = 0.0037$), which was confirmed with the nonparametric Friedman test ($p = 0.0065$).

DISCUSSION

Vasomotor symptoms with hot flushes and sweating are common in men with prostatic carcinoma who have undergone castration therapy.[9,10] Some endocrine therapies are available but there are few alternatives.[35,36] In this small nonrandomized pilot study we demonstrated that electrostimulated acupuncture may be an alternative for men with hot flushes after castration therapy and should be further evaluated in larger randomized studies using controls and a placebo. The more than 50% reduction in number of flushes during therapy in our study has not been previously reported to our knowledge in placebo studies of hot flushes in women or men.[34,35] Freedman and Woodward reported almost no placebo effect in women with hot flushes treated with behavioral therapy.[34] In a double-blind study of men with vasomotor symptoms after orchiectomy the number of flushes decreased less than 20% with placebo and more than 95% with diethylstilbestrol.[35] In our men who received 10 to 12 weeks of electrostimulated acupuncture once or twice a week for 30 minutes each the number of vasomotor attacks decreased and remained at 50% for at least 3 months after completion of therapy. Such a treatment effect is greater than that reported by Freedman and Woodward after behavioral therapy for hot flushes in women with paced respiration[34] and similar to that reported by us after electrostimulated acupuncture in women with hot flushes.[23]

Today hormone replacement therapy is the treatment of choice for climacteric women with vasomotor symptoms. Changes in hypothalamic neurotransmitter activity, such as β-endorphin, noradrenalin or catechol estrogens, have been suggested as the reason for these symptoms.[2,14,17,18,21] Regular physical activity and acupuncture affect hypothalamic β-endorphin activity and may be beneficial for vasomotor symptoms. Postmenopausal women who regularly exercise had fewer vasomotor symptoms than controls,[31] and electrostimulated acupuncture for 8 weeks significantly reduced hot flushes.[23]

The use of logbooks for daily recordings of the number and intensity of hot flushes and sweating appears to be a good way to monitor vasomotor symptoms. According to a previous study, the most valid method of monitoring such symptoms is to measure the total number of flushes during the day and

Data on 7 men treated with acupuncture due to vasomotor symptoms after castration therapy with Gn-RH analogue

Pt. No. — Age	Mos. Since Start of Therapy	Av. No. Flushes/Day				
		1 Wk. Before Therapy	2 Wks.	6 Wks.	10 Wks.	24 Wks.
1 — 67	18	6.9	4.9	2.4	1.7	6.0
2 — 65	8	5.1	2.9	1.3	1.4	3.3
3 — 74	5	4.3	1.6	1.0	1.1	1.9
4 — 76	3	12.3	15.6	12.0	8.4	6.7
5* — 70	12	5.9	2.4	2.9	1.6	3.3
6* — 79	Greater than 12	12.7	4.7	4.1	1.0	0.6
7† — 80	3	11.9	17.4			
Average in pts. 1–6		7.9	5.3	4.0	2.5	3.6

* Stopped therapy after 10 weeks.
† Stopped therapy after 3 weeks (5 treatments).

night.[23] No further information was obtained when flushes were counted separately day and night or when flushes were weighted according to severity day, night or for 24 hours. Therefore, in our study men were asked only to count the total number of flushes per 24 hours and to record it daily in the logbook.

Scientific evaluation of acupuncture has primarily concerned treatment of pain and to our knowledge there have been no previously reported scientific studies on acupuncture for vasomotor symptoms in men. There are certain problems with evaluating acupuncture and most trials have been considered poor.[37,38] Some studies have been difficult to evaluate due to a variable number of treatment sessions for different patients,[39] which we avoided through a project plan that included a fixed number of treatments, although that plan could not be followed by all men. Studies have usually been uncontrolled and as such provide little or no information concerning specific versus nonspecific factors responsible for the effectiveness of treatment.[39] Generally acupuncture might well be expected to have a powerful nonspecific placebo effect considering that it is a form of therapy with an aura of mysticism[39] and, therefore, it may be difficult to justify the need for a control study. Although placebo controlled trials have been performed on correct versus incorrect points of acupuncture (sham acupuncture), few have revealed significant differences between classical and sham acupuncture, whereas most have included too few patients for statistical comparisons.[39] In our study the choice of points was based on previous experience with acupuncture for primary dysmenorrhea[40] and in women with hot flushes.[23] In both studies stimulation of the same acupuncture points was effective, probably at least partially through general effects on β-endorphin production. However, lack of previous scientific reports on acupuncture treatment of hot flushes in men made it impossible to consider certain points as correct and others as control.

Electrostimulated acupuncture and transcutaneous electrical stimulation have been compared to manual stimulation.[41–44] Classical acupuncture and high frequency (80 Hz.) electrostimulated acupuncture for chronic pain had more marked and sustained effects than superficial needle insertion and low frequency (2 Hz.) electrostimulated acupuncture. Electrostimulated acupuncture appeared to have more long lasting effects than superficial needle insertion in menopausal women treated for hot flushes.[23] Although we did not compare superficial needle insertion with electrostimulated acupuncture in this study, our promising results merit a randomized, controlled trial on, for example, superficial needle insertion versus low frequency (2 Hz.) electrostimulated acupuncture to distinguish the specific effects of acupuncture from the nonspecific placebo effects. Placebo treatment has been suggested to induce β-endorphin release based on the fact that placebo-induced pain relief could be blocked by naloxone.[45] If endorphins are involved in vasomotor symptoms, this may explain why symptoms decrease during placebo or superficial needle insertion acupuncture treatment.[23] However, the long lasting effects for at least 3 months in our patients suggest something more than placebo. In a study in which controls received muscle relaxation or α-wave feedback the number of flushes per day did not decrease.[36] Compared to those results the more than 50% decrease in the number of flushes induced by acupuncture in our study does not seem to be a placebo effect. Although a crossover design may be ideal, the persistent acupuncture effects in our studies[23] require a washout period of more than 3 months, which probably would be difficult to prescribe.

Acupuncture and transcutaneous electrical stimulation increase the threshold for pain and affect central neuronal activity.[43,46] The acupuncture points used in our study are thought to have general effects on patients with pain.[40] However, other points, and different treatment duration and intervals could be more effective in treating postmenopausal women with vasomotor symptoms. We do not yet know with certainty that acupuncture induced anything but a placebo effect. In the etiology of climacteric vasomotor symptoms disturbances of the regulatory role of opioids have been suggested. It is possible that changed hormonal levels result in sensitization of peripheral and central neurons making them more susceptible to neural input.

In a previous study of women CGRP-like immunoactivity levels were increased in urine 24 hours before compared to after successful acupuncture therapy.[23] CGRP produces vasodilatation and hot flushes when administered intravenously in healthy young men.[47] The significant decrease in CGRP after acupuncture[23] could explain the reduction of symptoms, and may be related to the fact that β-endorphins seem to inhibit the release of CGRP.[48] In conclusion, 6 men with vasomotor symptoms after castration therapy had decreasing frequency of hot flushes after 10 to 12 weeks of acupuncture treatment. Acupuncture appears to be an appropriate subject for further studies aimed at increasing the armamentarium for treatment of men with vasomotor symptoms.

APPENDIX: ACUPUNCTURE POINTS AND ANATOMICAL POSITIONS FOR NEEDLE INSERTION

Acupuncture Point	Anatomical Localization
Bilaterally at:	
UB/BL 15 Bladder	Thoracic part of back
UB/BL 23 Bladder (stimulated with 2 Hz.)	Lumbar part of back
UB/BL 32 Bladder (stimulated with 2 Hz.)	Lumbar part of back
Unilaterally at:	
GV 20 Governor vessel	Top of head
H/HT 7 Heart	Ulnar side of wrist
P/PC 6 Pericardium	Volar side of distal forearm
Liv/LR3 Liver	Dorsum pedis
SP 6 Spleen	Lower leg, medial side
SP 9 Spleen	Lower leg, medial side just below knee

REFERENCES

1. Rebar, R. W. and Spitzer, I. B.: The physiology and measurement of hot flushes. Amer. J. Obst. Gynec., **156:** 1284, 1987.
2. Kronenberg, F.: Hot flushes: epidemology and physiology. Ann. N. Y. Acad. Sci., **592:** 52, 1990.
3. Berg, G., Gottvall, T., Hammar, M. and Lindgren, R.: Climacteric symptoms among women aged 60–62 in Linköping, Sweden, in 1986. Maturitas., **10:** 193, 1988.
4. Hammar, M., Berg, G., Fåhraeus, L. and Larsson-Cohn, U.: Climacteric symptoms in an unselected sample of Swedish women. Maturitas., **6:** 345, 1984.
5. Jaszmann, L. J. B.: Epidemiology of the climacteric syndrome. In: The Management of the Menopause and Postmenopausal Years. Edited by S. Campbell. Lancaster: MTP Press, pp. 11–23, 1976.
6. Cabot, A. T.: The question of castration for enlarged prostate. Amer. Surg., **24:** 265, 1896.
7. McCullagh, E. P. and Renshaw, J. F.: The effects of castration in the adult male. J.A.M.A., **103:** 1140, 1934.
8. Huggins, C., Stevens, R. E. and Hodges, C. V.: Studies on prostatic cancer: II. The effects of castration on advanced carcinoma of the prostate gland. Arch. Surg., **43:** 209, 1941.
9. Ginsburg, J. and O'Reilly, B.: Short reports: climacteric flushing in man. Brit. Med. J., **287:** 262, 1983.
10. Frödin, T., Ålund, G. and Varenhorst, E.: Measurement of skin blood-flow and water evaporation as a means of objectively assessing hot flushes after orchidectomy in patients with prostatic cancer. Prostate, **7:** 203, 1985.
11. Charig, C. R. and Rundle, J. S.: Flushing. Long-term side effect of orchiectomy in treatment of prostatic carcinoma. Urology, **33:** 175, 1989.

12. Parmar, H., Edwards, L., Phillips, R. H., Allen, L. and Lightman, S. L.: Orchiectomy versus long acting D-trp-6-LHRH in advanced prostatic cancer. Brit. J. Urol., **59:** 248, 1987.
13. Smith, J. A.: Androgen suppression by a gonadotropin releasing hormone analogue in patients with metastatic carcinoma of the prostate. J. Urol., **131:** 1110, 1984.
14. Lomax, P. and Schönbaum, E.: Postmenopausal hot flushes and their management. Pharmacol. Ther., **57:** 347, 1993.
15. Oldenhave, A., Jaszmann, L. J. B., Haspels, A. A. and Everaerd, W. T. A. M.: Impact of climacteric on well-being. A survey based on 5213 women 39 to 60 years old. Amer. J. Obst. Gynec., **168:** 772, 1993.
16. Karling, P., Hammar, M. and Varenhorst, E.: Prevalence and duration of vasomotor symptoms after surgical or medical castration in men with prostatic carcinoma. J. Urol., **152:** 1170, 1994.
17. Tataryn, I. V., Lomax, P., Bajorek, J. G., Chesarek, W., Meldrum, D. R. and Judd, H. L.: Postmenopausal hot flushes: a disorder of thermoregulation. Maturitas., **2:** 101, 1980.
18. Kronenberg, F., Cote, L. J., Linkie, D. M., Dyrenfurth, I. and Downey, J. A.: Menopausal hot flashes: thermoregulatory, cardiovascular, and circulating cathecholamine and LH changes. Maturitas., **6:** 31, 1984.
19. Tataryn, I. V., Lomax, P., Meldrum, D. R., Bajorek, J. G., Chesarek, W. and Judd, H. L.: Objective techniques for the assessment of postmenopausal hot flashes. Obst. Gynec., **57:** 340, 1981.
20. Ginsburg, J., Swinhoe, J. and O'Reilly, B.: Cardiovascular responses during the menopausal hot flush. Brit. J. Obst. Gynaec., **88:** 925, 1981.
21. Meldrum, D. R., Tataryn, I. V., Frumar, A. M., Erlik, Y., Lu, K. H. and Judd, H. L.: Gonadotropins, estrogens, and adrenal steroids during the menopausal hot flash. J. Clin. Endocr. Metab., **50:** 685, 1980.
22. Chen, J.-T., Hirai, Y., Seimiya, Y., Hasumi, K. and Shiraki, M.: Menopausal flushes and calcitonin-gene-related peptide. Lancet, **342:** 49, 1993.
23. Wyon, Y., Lindgren, R., Lundeberg, T. and Hammar, M.: Effects of acupuncture on climacteric vasomotor symptoms, quality of life, and urinary excretion of neuropeptides among postmenopausal women. Menopause, **2:** 3, 1995.
24. Erlik, Y., Meldrum, D. R. and Judd, H. L.: Estrogen levels in postmenopausal women with hot flashes. Obst. Gynec., **59:** 403, 1982.
25. Hagen, C., Christiansen, C., Christensen, M. S. and Transboel, I.: Climacteric symptoms, fat mass, and plasma concentrations of LH, FSH, Prl, oestradiol-17 and androstenedione in the early post-menopausal period. Acta Endocr., **101:** 87, 1982.
26. Hutton, J. D., Jacobs, H. S., Murray, M. A. F. and James, V. H. T.: Relation between plasma oestrone and oestradiol and climacteric symptoms. Lancet, **1:** 678, 1978.
27. Tataryn, I. V., Meldrum, D. R., Lu, K. H., Frumar, A. M. and Judd, H. L.: LH, FSH and skin temperature during the menopausal hot flash. J. Clin. Endocr. Metab., **49:** 152, 1979.
28. Casper, R. F., Yen, S. S. C. and Wilkes, M. M.: Menopausal flushes: a neuroendocrine link with pulsatile luteinizing hormone secretion. Science, **205:** 823, 1979.
29. Meldrum, D. R., Defazio, J. D., Erlik, Y., Lu, J. K. H., Wolfsen, A. F., Carlson, H. E., Hershman, J. M. and Judd, H. L.: Pituitary hormones during the menopausal hot flash. Obst. Gynec., **64:** 752, 1984.
30. Cagnacci, A., Melis, G. B., Soldani, R., Paoletti, A. M. and Fioretti, P.: Effect of sex steroids on body temperature in postmenopausal women. Role of endogenous opioids. Life Sci., **50:** 515, 1992.
31. Hammar, M., Berg, G. and Lindgren, R.: Does physical exercise influence the frequency of postmenopausal hot flushes? Acta Obst. Gynec. Scand., **69:** 409, 1990.
32. Wardlaw, S. L., Wehrenberg, W. B., Ferin, M., Antunes, J. L. and Frantz, A. G.: Effect of sex steroids on -endorphin in hypophyseal portal blood. J. Clin. Endocr. Metab., **55:** 877, 1982.
33. Wijma, K., Melin, A., Nedstrand, E. and Hammar, M.: Treatment of menopausal symptoms with applied relaxation: a pilot study. J. Behav. Ther. Exp. Psychiat., **28:** 251, 1997.
34. Freedman, R. R. and Woodward, S.: Behavioral treatment of menopausal hot flushes: evaluation by ambulatory monitoring. Amer. J. Obst. Gynec., **167:** 436, 1992.
35. Atala, A., Amin, M. and Harty, J. I.: Diethylstilbestrol in treatment of postorchiectomy vasomotor symptoms and its relationship with serum follicle-stimulating hormone, luteinizing hormone, and testosterone. Urology, **39:** 108, 1992.
36. Smith, A.: A prospective comparison of treatments for symptomatic hot flushes following endocrine therapy for carcinoma of the prostate. J. Urol., **152:** 132, 1994.
37. Levith, G. T.: Can we assess the effects of acupuncture? Brit. Med. J., **288:** 1475, 1984.
38. Ter Reit, G., Kleijnen, J. and Knipschild, P.: Acupuncture and chronic pain: a criteria-based meta-analysis. J. Clin. Epidemiol., **43:** 1191, 1990.
39. Baldry, P. E.: Scientific evaluation of acupuncture. In: Acupuncture, Trigger Points and Musculoskeletal Pain. New York: Churchill Livingstone, pp. 125–138, 1993.
40. Thomas, M., Lundeberg, T., Björk, G. and Lundström-Lindstedt, V.: Pain and discomfort in primary dysmenorrhea is reduced by preemptive acupuncture or low frequency TENS. Eur. J. Rehab., in press, 1999.
41. Richardson, P. H. and Vincent, C. A.: Acupuncture for the treatment of pain: a review of evaluative research. Pain, **24:** 15, 1986.
42. Fox, E. J. and Melzack, R.: Transcutaneous electrical stimulation and acupuncture: comparison of treatment for low-back pain. Pain, **2:** 141, 1976.
43. Haker, E. and Lundeberg, T.: Acupuncture treatment in epicondylalgia: a comparative study of two acupuncture techniques. Clin. J. Pain, **6:** 221, 1990.
44. Thomas, M. and Lundeberg, T.: Importance of modes of acupuncture in the treatment of chronic nociceptive low back pain. Acta Anesthesiol. Scand., **38:** 63, 1994.
45. Levine, J. D., Gordon, N. C. and Fields, H. L.: The mechanism of placebo analgesia. Lancet, **2:** 654, 1978.
46. Chapman, R. C. and Benedetti, C.: Analgesia following transcutaneous electrical stimulation and its partial reversal by a narcotic antagonist. Life Sci., **21:** 1645, 1977.
47. Jernbeck, J., Edner, M., Dalsgaard, C.-J. and Pernow, B.: The effect of calcitonin gene-related peptide (CGRP) on human forearm blood flow. Clin. Physiol., **10:** 335, 1990.
48. Collin, E., Frechilla, D., Pohl, M., Bourgoin, S., Le Bars, D., Hamon, M. and Cesselin, F.: Opioid control of the release of calcitonin gene-related peptide-like material from the rat spinal cord in vivo. Brain Res., **609:** 211, 1993.