



# Menopause

The Journal of The North American Menopause Society

VOLUME 17, ISSUE 2, 2010

## CONTENTS

---

### Editorials

---

223

**Hot flashes and hormone use: harbingers of heart disease?**

Eliot A. Brinton, MD, FAHA, FNLA

226

**Long-term outcomes of vasomotor symptom treatments: what happens after we pull the plug—or the needles**

Claudio N. Soares, MD, PhD, FRCPC

228

**The role of acupuncture in treating menopausal hot flashes**

Nancy E. Avis, PhD and Remy R. Coeytaux, MD, PhD

231

**Selective estrogen receptor modulator: the saga continues**

Steven R. Goldstein, MD

233

**Beyond identifying women at risk for coronary heart disease and osteoporosis**

Jill Attaman, MD

235

**The Women's Health Initiative tells us more about what estrogen can and cannot do but does not give us the answer**

Marcie K. Richardson, MD

237

**Another multibotanical for vasomotor symptoms: some lessons learned**

Katherine M. Newton, PhD

239

**Cognitive performance test research and clinical perils**

Quentin R. Regestein, MD

*(continued)*

---

*Menopause: The Journal of The North American Menopause Society* (ISSN 1072-3714) is published bimonthly for The North American Menopause Society by Lippincott Williams & Wilkins, 16522 Hunters Green Parkway, Hagerstown, MD 21740-2116. Business and production offices are located at 530 Walnut Street, Philadelphia, PA 19107-3621. All rights reserved. Printed on acid-free paper. Periodical postage paid at Hagerstown, Maryland, and at additional mailing offices. Copyright © 2010 by The North American Menopause Society.

**POSTMASTER:** Send address changes to *Menopause: The Journal of The North American Menopause Society*, P.O. Box 1550, Hagerstown, MD 21740.

## Position Statement

---

242

### **Estrogen and progestogen use in postmenopausal women: 2010 position statement of The North American Menopause Society**

*The North American Menopause Society has made significant additions and modifications to its recommendations on this important topic. This update incorporates current evidence into practical clinical recommendations, with consideration for the therapeutic benefit-risk ratio at various times through menopause and beyond.*

## Articles

---

256

### **History of hot flashes and aortic calcification among postmenopausal women**

Rebecca C. Thurston, PhD, Lewis H. Kuller, MD, DrPH,  
Daniel Edmundowicz, MD, MS, and Karen A. Matthews, PhD

*Among postmenopausal women using hormone therapy, a longer prospectively measured history of reporting hot flashes was associated with increased aortic calcification, controlling for traditional cardiovascular risk factors.*

262

### **The Acupuncture on Hot Flashes Among Menopausal Women study: observational follow-up results at 6 and 12 months**

Einar Kristian Borud, MD, MPH, Terje Alraek, PhD, Adrian White, MD, PhD,  
and Sameline Grimsgaard, MD, MPH, PhD

*Acupuncture can contribute to a more rapid reduction in vasomotor symptoms and an increase in health-related quality of life in highly bothered postmenopausal women but probably has no long-term effects.*

269

### **Effects of acupuncture on hot flashes in perimenopausal and postmenopausal women—a multicenter randomized clinical trial**

Kun Hyung Kim, OMD, MS, Kyung Won Kang, MS, Dong Il Kim, OMD, PhD,  
Hyung Jun Kim, OMD, PhD, Hyun Min Yoon, OMD, PhD,  
Jin Moo Lee, OMD, PhD, Jae Cheol Jeong, OMD, MS, Myeong Soo Lee, PhD,  
Hee Jung Jung, MS, and Sun-Mi Choi, OMD, PhD

*In this multicenter, randomized, controlled trial, 12 sessions of acupuncture plus usual care conducted over 4 weeks showed significant reduction of hot flash activities and menopause-related symptoms compared to usual care alone group without serious adverse events, indicating the potential therapeutic role of acupuncture on menopausal hot flashes in day-to-day clinical practice.*

281

### **A randomized, placebo- and active-controlled trial of bazedoxifene/conjugated estrogens for treatment of moderate to severe vulvar/vaginal atrophy in postmenopausal women**

Risa Kagan, MD, FACOG, R. Stan Williams, MD, Kaijie Pan, MS,  
Sebastian Mirkin, MD, and James H. Pickar, MD

*Bazedoxifene/conjugated estrogens effectively treat moderate to severe vulvar/vaginal atrophy and its symptoms, supporting their use as a menopausal therapeutic option.*

290

**Prevention of coronary heart disease and osteoporosis in women aged 45 to 49 years: a challenging role for general practitioners**

Hedwig M.M. Vos, MD, Annemiek van Kuik, MD, Manon E.J. Janse, MD, Francois G. Schellevis, MD, PhD, and Toine L.M. Lagro-Janssen, MD, PhD

*Women aged 45 to 49 years with a low socioeconomic status have more risk factors for coronary heart disease and osteoporosis than do women with middle or the highest socioeconomic status. The general practitioner should therefore be a key player in the prevention of coronary heart disease and osteoporosis related to an unhealthy lifestyle in premenopausal women.*

295

**Hormone therapy and physical function change among older women in the Women's Health Initiative: a randomized controlled trial**

Yvonne L. Michael, ScD, Rachel Gold, PhD, MPH, JoAnn E. Manson, MD, DrPH, Erin M. Keast, MPH, Barbara B. Cochrane, RN, PhD, Nancy F. Woods, RN, PhD, Robert G. Brzyski, MD, PhD, S. Gene McNeeley, MD, and Robert B. Wallace, MD, MS

*Hormone therapy provided no overall protection against functional decline during 6 years of follow-up of nondisabled postmenopausal women aged 65 to 79 years at enrollment. However, this study did not address the influence of hormone therapy for women of younger ages.*

303

**Use of a multibotanical (Nutrafem) for the relief of menopausal vasomotor symptoms: a double-blind, placebo-controlled study**

Joan Tan Garcia, MD, Florante Gonzaga, MD, Delfin Tan, MD, Toon Yaa Ng, MSc, Pau Ling Oei, MRCOG, and Cathryn W.B. Chan, MRCOG

*The findings of this phase III, double-blind, randomized, placebo-controlled trial suggest that Nutrafem is an effective and safe botanical therapy for alleviating menopausal vasomotor symptoms.*

309

**Raloxifene improves verbal memory in late postmenopausal women: a randomized, double-blind, placebo-controlled trial**

Didy E. Jacobsen, MD, Monique M. Samson, PhD, Marielle H. Emmelot-Vonk, MD, and Harald J.J. Verhaar, PhD

*This randomized, double-blind, placebo-controlled trial found that raloxifene treatment for 1 year significantly improved verbal memory when compared with placebo in late postmenopausal women.*

315

**Association between vasomotor hot flashes and heart rate variability in recently postmenopausal women**

Hanna Hoikkala, MD, Petri Haapalahti, MD, PhD, Matti Viitasalo, MD, PhD, Heikki Väänänen, Lic Sc, Anssi R.A. Sovijärvi, MD, PhD, Olavi Ylikorkala, MD, PhD, and Tomi S. Mikkola, MD, PhD

*In recently postmenopausal women, overall heart rate variability failed to show an association with hot flashes; however, during a hot flash episode, heart rate variability indicated an increase in sympathetic activity and a decrease in parasympathetic activity.*

321

**Hyperinsulinemia in nonobese women reporting a moderate weight gain at the beginning of menopause: a useful early measure of susceptibility to insulin resistance**

André Lemay, MD, PhD, Lucile Turcot, MD, PhD, Francine Déchêne, DtP, MSc, Sylvie Dodin, MD, MSc, and Jean-Claude Forest, MD, PhD

*Almost one in five nonobese women reporting a moderate weight gain at the beginning of menopause and showing an enlarged waist circumference has increased fasting insulin levels with an early increase in TG level, a decrease in high-density lipoprotein cholesterol level, and an abnormal response to oral glucose test. Because those changes are characteristic of insulin resistance, the measurement of fasting insulin along with glucose, lipids, and waist circumference may help to identify menopausal women who are at higher risk of developing glucose intolerance, diabetes, and cardiovascular disease and to implement early preventive measures.*

326

**Effect of St John's wort on severity, frequency, and duration of hot flashes in premenopausal, perimenopausal and postmenopausal women: a randomized, double-blind, placebo-controlled study**

Khadijeh Abdali, MSC, Marjan Khajehei, MSC, and Hamid Reza Tabatabaee, MSC

*This study showed that St. John's wort can be an effective treatment for vasomotor symptoms affecting perimenopausal or postmenopausal women.*

332

**Urinary incontinence is associated with lower psychological general well-being in community-dwelling women**

Roslin Botlero, MD, Robin J. Bell, MD, PhD, Donna M. Urquhart, PhD, and Susan R. Davis, MD, PhD

*This study found that not only is urinary incontinence associated with a significant reduction in well-being in community-dwelling women, but also the relationship between different types of urinary incontinence and well-being appears to differ.*

338

**Paroxetine increases brain-derived neurotrophic factor in postmenopausal women**

Alessandra Cubeddu, MD, Andrea Giannini, MD, Fiorella Bucci, MD, Sara Merlini, MD, Elena Casarosa, PhD, Nicola Pluchino, MD, Stefano Luisi, MD, PhD, Michele Luisi, MD, PhD, and Andrea R. Genazzani, MD, PhD

*In this study, we observed that, in postmenopausal women, treatment with paroxetine 10 mg/day for 6 months is able to increase brain-derived neurotrophic factor plasma levels to plasma values similar to those obtained in women treated with estrogen and progestogen therapy, significantly improving climacteric symptoms.*

344

**Hormone therapy and the medical encounter: a qualitative analysis of women's experiences**

Abbey Hyde, PhD, Jean Nee, MA, Jonathan Drennan, PhD, Michelle Butler, PhD, and Etaoine Howlett, PhD

*This study explored women's experiences in biomedical consultations for menopause symptoms, with a particular focus on hormone therapy. Results show shifts in the prescribing practices of physicians and how women themselves influence hormone therapy prescribing. In addition, women using hormone therapy tended to use it for temporary relief of symptoms.*

351

**Prospective follow-up of changes in menopausal complaints and hormone status after surgical menopause in a Malaysian population**

Ron Collaris, MD, Kiren Sidhu, MD, MRCOG, and Joe M. Chan, MD

*Results from this small prospective pilot project among Malaysian women undergoing hysterectomy with and without ovarian preservation suggests that in most women, symptoms are relatively mild and develop only by the third week after the surgical procedure.*

359

**Clustering of cardiometabolic risk factors in Asian Indian women: Santiniketan women study**

Minakshi Bhagat, MSc, Sangita Mukherjee, MTech, Priyanka De, MTech, Riddhi Goswami, MSc, Susil Pal, PhD, Mithun Das, MSc, and Arnab Ghosh, PhD

*Asian Indian women are worse than men in many aspects of cardiometabolic risk factors. This article explains the clustering of cardiometabolic risk factors in Asian Indian women during natural menopause.*

365

**Dysregulation of subcutaneous adipose tissue blood flow in overweight postmenopausal women**

Jonas Andersson, MD, Lars-Göran Sjöström, MD, Marcus Karlsson, MSc, Urban Wiklund, PhD, Magnus Hultin, MD, PhD, Fredrik Karpe, MD, PhD, and Tommy Olsson, MD, PhD

*Adipose tissue blood flow decreases in overweight postmenopausal women. This may influence the development of metabolic dysfunction linked to cardiovascular disease.*

372

**Soy isoflavones, Mediterranean diet, and physical exercise in postmenopausal women with insulin resistance**

Placido Llaneza, MD, PhD, Celestino Gonzalez, PhD, Jose Fernandez-Iñarrea, MD, Ana Alonso, PhD, Maria J. Diaz-Fernandez, PhD, Ignacio Arnott, MD, and Javier Ferrer-Barriendos, MD, PhD

*Daily intake of 40 mg of soy isoflavones together with a Mediterranean diet and exercise reduced insulin resistance in postmenopausal women who had insulin resistance in the first place. The reduction was significantly better than those seen with lifestyle changes alone.*

379

**Red clover extract: a source for substances that activate peroxisome proliferator-activated receptor  $\alpha$  and ameliorate the cytokine secretion profile of lipopolysaccharide-stimulated macrophages**

Monika Mueller, MSc, PhD, Stefanie Hobiger, BSc, and Alois Jungbauer, MSc, PhD

*Red clover extracts and isoflavones currently used for amelioration of menopausal symptoms also show putative anti-inflammatory activity in in vitro assays and putative hypolipidemic activity through PPAR- $\alpha$  activation. Several metabolites also exert these activities.*

388

**Factors associated with metabolic syndrome in a sample of women in Puerto Rico**

Josefina Romaguera, MD, MPH, Ana P. Ortiz, PhD, Fernando J. Roca, MD, Giancarlo Colón, BA, and Erick Suárez, PhD

*The association between the metabolic syndrome and demographic, health, and lifestyle characteristics in a sample of women living in Puerto Rico was the focus of this study. Results confirmed that obesity is an important risk factor associated with metabolic syndrome in this study sample, whereas alcohol consumption and a higher education level appear to lower its prevalence.*

393

**Extract and fraction from *Ulmus wallichiana* Planchon promote peak bone achievement and have a nonestrogenic osteoprotective effect**

Kunal Sharan, MSc, Jawed A. Siddiqui, MSc, Gaurav Swarnkar, MSc, Abdul Malik Tyagi, MSc, Avinash Kumar, MSc, Preeti Rawat, MSc, Manmeet Kumar, MSc, Geet K. Nagar, BSc, Kamal R. Arya, PhD, Lakshmi Manickavasagam, MSc, Girish K. Jain, PhD, Rakesh Maurya, PhD, and Naibedya Chattopadhyay, PhD

*A standardized fraction from *Ulmus wallichiana*, containing several flavonoid-C-glucoside compounds, promotes peak bone mass achievement and prevents estrogen deficiency-induced bone loss. Given the identification and determination of bioactive markers and a favorable oral dose of 50 mg kg<sup>-1</sup> day<sup>-1</sup>, this standardized fraction has therapeutic potential in menopausal osteoporosis.*

403

**Cardiovascular hemodynamics during stress in premenopausal versus postmenopausal women**

Andrew Sherwood, PhD, Sat Byul Park, MD, Joel W. Hughes, PhD, James A. Blumenthal, PhD, Alan Hinderliter, MD, Ranak Trivedi, MS, and Judith McFetridge-Durdle, PhD, RN

*This study showed that postmenopausal women were characterized by increased sympathetic nervous system activity and increased systemic vascular resistance compared with premenopausal women. These postmenopausal alterations in autonomic and hemodynamic regulation may contribute to increased cardiovascular risk after menopause.*

410

**Self-reported anxiety, depressive, and vasomotor symptoms: a study of perimenopausal women presenting to a specialized midlife assessment center**

Andreea L. Seritan, MD, Ana-Maria Iosif, PhD, Ju Hui Park, PhD, Deborah DeatherageHand, RN, BSN, Richard L. Sweet, MD, and Ellen B. Gold, PhD

*Multiple logistic regression analyses showed an association of vasomotor symptoms bothersomeness with anxiety and/or depressive symptoms in perimenopausal and postmenopausal women. Perimenopausal women were also significantly more likely to report anxiety and/or depressive symptoms than were postmenopausal women.*

416

**Bone mineral density after concurrent chemoradiation in patients with uterine cervical cancer**

Jong Ha Hwang, MD, Seung Hun Song, MD, PhD, Jae Kwan Lee, MD, Nak Woo Lee, MD, and Kyu Wan Lee, MD

*Bone mineral density was significantly lower in patients with cervical cancer treated with concurrent chemoradiation. Therefore, postmenopausal women with uterine cervical cancer treated by concurrent chemoradiation should be considered to be at risk for osteoporosis.*

421

**Clinical characteristics of bladder urothelial tumors in female patients**

Nian-zhao Zhang, PhD, MD, Jun Chen, PhD, MD, Hong-qiang Wang, MM, and Zhi-shun Xu, PhD, MD

*Menopause may have an unfavorable influence on the clinical characteristics of bladder urothelial tumors in female patients.*

---

**Review Article**

426

**Black cohosh and suspected hepatotoxicity: inconsistencies, confounding variables, and prospective use of a diagnostic causality algorithm.**

**A critical review**

Rolf Teschke, MD

*The analysis of 69 cases with primarily suspected hepatotoxicity by black cohosh revealed major inconsistencies and confounding variables, not supporting the concept of hepatotoxicity in a causal relationship to the use of black cohosh.*

---

**Letters to the Editor**

441

---

Lippincott Williams & Wilkins and The North American Menopause Society cannot be held responsible for errors or for any consequences arising from the use of the information contained in this journal. All advertising material published in this journal is expected to conform to regulatory and medical standards. The appearance of advertising in this publication does not constitute a guarantee or endorsement by The North American Menopause Society or Lippincott Williams & Wilkins of the quality or value of such a product or service or any claims made by its marketer.

PERMISSION TO PHOTOCOPY ARTICLES: This publication is protected by copyright. Permission to reproduce copies of articles for noncommercial use may be obtained from the Copyright Clearance Center, 222 Rosewood Drive, Danvers, MA 01923, Tel: (978) 750-8400, FAX: (978) 750-4470, URL: <http://www.copyright.com>

*Menopause: The Journal of The North American Menopause Society* is a registered trademark of The North American Menopause Society.

**Menopause: The Journal of The North American Menopause Society** (ISSN 1072-3714) is published bimonthly by Lippincott Williams & Wilkins, 16522 Hunters Green Parkway, Hagerstown, MD 21740-2116. Business offices are located at 530 Walnut Street, Philadelphia, PA 19106-3621. Periodical postage paid at Hagerstown, MD, and at additional mailing offices. **Annual subscription rates:** *United States*—\$322 Individual, \$582 Institution. *Rest of World*—\$362 Individual, \$647 Institution. Single copy rate \$107. All prices include a handling charge. Subscriptions outside of North America must add \$11 for airfreight delivery. United States residents of AL, CO, DC, FL, GA, HI, IA, ID, IN, KS, KY, LA, MD, MO, ND, NM, NV, PR, RI, SC, SD, UT, VT, WA, WV add state sales tax. The GST tax of 7% must be added to all orders shipped to Canada (Lippincott Williams & Wilkins' GST Identification #895524239, Publications Mail Agreement #1119672). Subscription prices outside the United States must be prepaid. Prices subject to change without notice. Visit us online at [www.lww.com](http://www.lww.com). Individual subscription rates include print and access to the online version. Institutional rates are for print only; online subscriptions are available via Ovid. Institutions can choose to purchase a print and online subscription together for a discounted rate. Institutions that wish to purchase a print subscription, please contact Lippincott Williams & Wilkins, 16522 Hunters Green Parkway, Hagerstown, MD 21740-2116; phone 800-638-3030 (outside the United States 301-223-2300); fax 301-223-2400. Institutions that wish to purchase an online subscription or online with print, please contact the Ovid Regional Sales Office near you or visit [www.ovid.com/site/index.jsp](http://www.ovid.com/site/index.jsp) and select Contact and Locations. **Address for subscription information, orders, or change of address:** Lippincott Williams & Wilkins, P.O. Box 1580, Hagerstown, MD 21741-1580; phone 800-638-3030 (outside the United States 301-223-2300); fax 301-223-2400. In Japan, contact LWW Igaku-Shoin Ltd., 3-23-14 Hongo, Bunkyo-ku, Tokyo 113-0033; phone 81-3-5689-5400; fax 81-3-5689-5402. In Bangladesh, India, Nepal, Sri Lanka, and Pakistan, contact Globe Publications Pvt. B-13 3rd Floor, A Block, Shopping Complex, Naraina Vihar, Ring Road, New Delhi, 110028; phone 91-11-579-3211; fax 91-11-579-8876. Address advertising inquiries to Rene Artuso at Lippincott Williams & Wilkins, 530 Walnut Street, Philadelphia, PA 19106 USA

**Postmaster:** Send address changes to *Menopause: The Journal of The North American Menopause Society*, P.O. Box 1550, Hagerstown, MD 21740.

Copyright © 2010 by The North American Menopause Society. All rights reserved. Printed in the USA.