Randomized Controlled Trial Evidence That Estrogen Replacement Therapy Reduces the Progression of Subclinical Atherosclerosis in Healthy Postmenopausal Women Without Preexisting Cardiovascular Disease

To the Editor:

Two articles have appeared in Circulation1,2 that have cited the Estrogen in the Prevention of Atherosclerosis Trial (EPAT)3 as supportive evidence that hormone replacement therapy (HRT) has no benefit on atherosclerosis in women with established cardiovascular disease (CVD). Citation of EPAT as supportive evidence for such a statement is incorrect on 2 major grounds, as follows: (1) EPAT was a randomized, double-blind, placebo-controlled, 2-year, serial arterial imaging trial conducted in healthy postmenopausal women without preexisting CVD, and (2) the overall primary trial outcome of EPAT demonstrated a positive beneficial effect of unopposed estrogen replacement therapy (ERT) on the progression of subclinical atherosclerosis.

In the placebo-treated group, the average rate of progression of subclinical atherosclerosis measured by carotid artery intima-media thickness was +0.0036 mm/year, whereas in the unopposed ERT group, subclinical atherosclerosis regressed at a rate of −0.0017 mm/year (P=0.046 for difference between treatment groups). Among the women who did not use lipid-lowering medication, the placebo-unopposed ERT difference (benefit) in the average rates of atherosclerosis progression was even greater (P=0.002). EPAT supports the growing body of data that indicate that the preexisting state of health of the vasculature and the timing (relative to menopause) of initiation of ERT determine whether atherosclerosis will respond beneficially to hormone therapy.4 Many important and complex questions generated by the recent body of data remain to be addressed in the area of cardiovascular health and HRT.4 As pointed out by Mendelsohn and Karas,5 misinterpretation of data in the field of CVD and hormone replacement therapy? Curr Atheroscler Rep. 2003;5:1–11.


Response

We apologize for any confusion created by a regrettable editing error concerning the citation of the Estrogen in the Prevention of Atherosclerosis Trial (EPAT) study in the 2 aforementioned papers.1,2 The reference to the EPAT trial was mistakenly included in a list of other randomized trials of hormone replacement therapy (HRT), giving the impression that EPAT found no evidence of benefit of HRT on atherosclerosis in women with established cardiovascular disease. We have accurately cited the EPAT study in a recent review of HRT clinical trials.3 An erratum will be published in a future issue of Circulation.

David M. Herrington, MD, MHS
Timothy D. Howard, PhD
Bridget Brosnihan, PhD
Gregory A. Hawkins, PhD
David M. Rebouissin, PhD
Jianfeng Xu, PhD
Siqun L. Zheng, MD
Deborah A. Meyers, PhD
Eugene R. Bleeker, MD
Wake Forest University School of Medicine
Winston-Salem, NC
Donald P. McDonnell, MD
Xiaolin Li, PhD
Department of Pharmacology and Cancer Biology
Duke University Medical Center
Durham, NC
Randomized Controlled Trial Evidence That Estrogen Replacement Therapy Reduces the Progression of Subclinical Atherosclerosis in Healthy Postmenopausal Women Without Preexisting Cardiovascular Disease
Howard N. Hodis, Wendy J. Mack and Roger A. Lobo

_Circulation_. 2003;108:e5
doi: 10.1161/01.CIR.0000080080.76333.38
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2003 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/108/1/e5

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org/subscriptions/