


Vol 110, No 17, October 26, 2004  
ISSN 0009-7322  
<http://circ.ahajournals.org>

American Heart Association®   
*Learn and Live*™

SUPPLEMENT TO

RC681.A1 C8

# Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

Abstracts  
from

scientific  
sessions  
2004

Sessions: November 7–10  
Exhibits: November 7–9  
New Orleans, Louisiana  
[scientificsessions.org](http://scientificsessions.org)



basic science



clinical science



population science

## Named and Invited Lectures 2004

2004 Russell Ross Memorial Lectureship in Vascular Biology • 2004 George Lyman Duff Memorial Lecture • 2004 Sol Sherry Distinguished Lecture in Thrombosis • 2004 Thomas W. Smith Memorial Lecture • 2004 George E. Brown Memorial Lecture • 2004 Dickinson W. Richards Memorial Lecture • 2004 Katharine A. Lembricht Award • 2004 William W. L. Glenn Lecture • 2004 William J. Rashkind Memorial Lecture • 2004 T. Duckett Jones Memorial Lecture • 2004 Charles T. Dotter Memorial Lecture • 2004 Laennec Society Lecture • 2004 Ancel Keys Lecture • 2004 Lewis K. Dahl Memorial Lecture • 2004 Robert I. Levy Endowed Lecture in Lipid Metabolism

## New and Young Investigator Award/Prize Abstract Finalists

Lewis N. and Arnold M. Katz Basic Science Research Prize for Young Investigators • Melvin L. Marcus Young Investigator Awards in Cardiovascular Science • Cournand and Comroe Young Investigators Prizes in Cardiopulmonary and Critical Care • Outstanding Research Award in Pediatric Cardiology • Melvin Judkins Young Investigator Award in Cardiovascular Radiology • Vivian Thomas Young Investigator Award • Martha N. Hill New Investigator Awards • Elizabeth Barrett-Connor Research Award in Epidemiology and Prevention for Investigators in Training • Samuel A. Levine Young Clinical Investigator Awards • Laennec Society Young Clinician Award • NPAM New Investigator Award

## Abstracts From the Scientific Sessions 2004



# Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION

## Editorial Correspondence

 (Additional information available on the Internet at <http://www.circulationaha.org/misc/about.shtml>)

**EDITORIAL CORRESPONDENCE** should be sent to Joseph Loscalzo, MD, PhD, Editor, *Circulation*, 560 Harrison Ave, Suite 502, Boston, MA 02118. Phone 617-414-8780. Fax 617-414-8781. E-mail [circ@bu.edu](mailto:circ@bu.edu)

**INSTRUCTIONS TO AUTHORS** appear in the first issue of each month. Authors should consult these instructions before submitting manuscripts to *Circulation*.

**AUTHOR COSTS** include page charges, cost of color figures, and cost of reprints, if ordered.

Statements, opinions, and results of studies published in *Circulation* are those of the authors and do not reflect the policy or position of the American Heart Association, and the American Heart Association provides no warranty as to their accuracy or reliability.

## Business Correspondence

 (Additional information available on the Internet at <http://www.circulationaha.org/misc/about.shtml>)

**BUSINESS CORRESPONDENCE** should be sent to American Heart Association, Lippincott Williams & Wilkins Subscription Fulfillment Dept, 351 West Camden Street, Baltimore, MD 21201-2436. Telephone 800-787-8984. Fax 800-787-8985. E-mail: [custserv@lww.com](mailto:custserv@lww.com); outside the U.S.: Telephone 410-361-8080; Fax 410-361-8048.

**CHANGE OF ADDRESS:** Please supply old and new addresses. Allow 4 weeks for changes.

**ANNUAL SUBSCRIPTION RATES:** U.S.: Personal \$303.00; Institutional \$576.00; Single copy \$17.00. **Outside the U.S.:** Personal \$519.00; Institutional \$781.00; Single copy \$17.00.

Medical professionals and scientists in training may subscribe for \$162 in the United States and \$271 outside the United States if payment is accompanied by a letter from the department chair verifying post held and completion date.

Prepayment is required. Make check, draft, or money order payable to the American Heart Association in US dollars drawn on a US bank, with *Circulation* on the face of the check. To charge with a credit card, include account number, expiration date, and name as it appears on card.

**REPRINTS:** Authors may purchase reprints of their article by dialing Kathryn Welch, Author Reprint Department, Lippincott Williams & Wilkins at 1-800-341-2258; or, via E-mail at [ReprintsGroup@lww.com](mailto:ReprintsGroup@lww.com); an Author Reprint Order Form may be accessed through the Internet at <http://www.services.lww.com/periodicals/author-reprints>. Single copies of reprints are available from the corresponding authors. Reprints in large quantities, for commercial or academic use, may be purchased from the publisher. For information and prices: telephone 410-528-4121, E-mail [kgray@lww.com](mailto:kgray@lww.com)

## Advertising Correspondence

 (Additional information available on the Internet at <http://www.circulationaha.org/misc/about.shtml>)

**US ADVERTISING SALES:** The Jackson-Gaeta Group, Inc., 33 Smull Avenue, Caldwell, NJ 07006. Telephone 973-403-7677. Fax 973-403-7795. Contact Joe Jackson, Paul Nalbandian, or Charles Novak. For media kits, contact Tina Auletta.

**JAPAN ADVERTISING SALES:** Biomedis International LTD, ASK Ginza Bldg, 10-6, 7-Chome Ginza, Chuo-ku, Tokyo 104-0061, Japan. Telephone (03) 3575-1611. Fax (03) 3569-0155. Contact Hiromu Furukawa. E-mail [hiromu-f@biomedis.co.jp](mailto:hiromu-f@biomedis.co.jp)

**REST OF WORLD SALES:** Fran Grega, 3205 Douglas Point Court, Riva, MD 21140. Telephone 410-956-9861. Fax 410-956-9862. E-mail [fgrega@comcast.net](mailto:fgrega@comcast.net)

**ADVERTISING PRODUCTION:** Contact Randy Ezell, Lippincott Williams & Wilkins, 351 West Camden Street, Baltimore, MD 21201-2436, telephone 410-528-8533, E-mail [rezell@lww.com](mailto:rezell@lww.com)

**SPONSORED GIFT SUBSCRIPTIONS:** Contact Carol Bak, Lippincott Williams & Wilkins, 351 West Camden Street, Baltimore, MD 21201-2436, telephone 410-528-4163, fax 410-528-4305, E-mail [cbak@lww.com](mailto:cbak@lww.com)

**CLASSIFIED ADVERTISING:** Contact Jennifer Williams, Lippincott Williams & Wilkins, 351 West Camden Street, Baltimore, MD 21201-2436, telephone 1-800-528-1843, E-mail [jwilliam@lww.com](mailto:jwilliam@lww.com)

Advertisements in this issue have been reviewed to comply with the principles governing advertising in American Heart Association publications. A copy of these principles is available on request. *The appearance of an advertisement in an AHA publication is neither an AHA guarantee nor endorsement of the product or service or the claims for the product or service made by the advertiser.*

## Secondary Services

**INDEXED OR ABSTRACTED** in *Biological Abstracts*, *CABS*, *CINAHL*, *Chemical Abstracts*, *Current Contents*, *EMBASE/Excerpta Medica*, and *Index Medicus*.

**AVAILABLE ONLINE** from Ovid Online, 333 Seventh Avenue, 4th Floor, New York, NY 10001. Telephone 800-950-2035.

**MICROFORM EDITION** available from University Microfilms International, 300 North Zeeb Road, Ann Arbor, MI 48106-1346. Telephone 313-761-4700. Also available from Princeton Microfilm Corporation, Alexander Road, Box 2073, Princeton, NJ 08540. Telephone 609-452-2066.

**AUTHORIZATION TO PHOTOCOPY** items from this publication for personal and internal use, the personal or internal use of specific clients, or for educational use, is granted by the American Heart Association on the condition that the copier pay the appropriate fee to the Copyright Clearance Center, Inc. (CCC), 222 Rosewood Drive, Danvers, MA 01923. Telephone 978-750-8400. Fax 978-750-4744. This consent does not extend to copying for advertising or promotional purposes, for creating new collective works, or for resale. Individuals may make single photocopies for personal, noncommercial use without obtaining permission. For all other use, permission should be sought directly from the Rights & Permissions Desk, Lippincott Williams & Wilkins, 351 West Camden Street, Baltimore, MD 21201-2436; telephone 410-528-4016; fax 410-528-8550; E-mail [journalpermissions@lww.com](mailto:journalpermissions@lww.com)

*Circulation* (ISSN 0009-7322) is published weekly by Lippincott Williams & Wilkins, 351 West Camden Street, Baltimore, MD 21201-2436.

GST Registration Number 89552 4239 RT.

Printed in the USA. © 2004 American Heart Association, Inc.



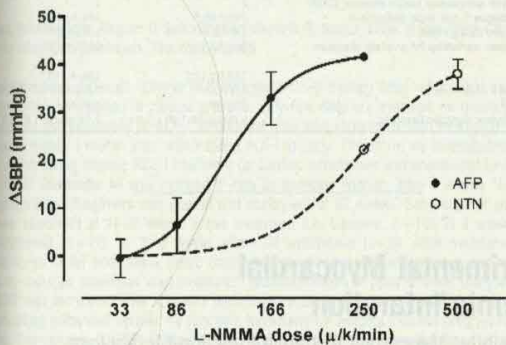
of membranous RhoA and phosphorylated ERM in brainstem were greater both in angiotensin II-treated rats and SHR than in WKY. Valsartan reduced the expression levels of membranous RhoA in angiotensin II-treated rats and SHR. In addition, Y-27632 or valsartan reduced the expression levels of phosphorylated ERM in both groups. Subcutaneous infusion of phenylephrine increased SBP to the same level of angiotensin II infusion in WKY. However, it did not alter the expression levels of membranous RhoA and phosphorylated ERM. Conclusions: These results suggest that 1) the pressor response induced by central infusion of angiotensin II is substantially mediated by activation of Rho/Rho-kinase pathway in brainstem via AT1 receptors, 2) this pathway may also be involved in hypertensive mechanism in SHR.

1412

**Endothelial Nitric Oxide and Hypertension in Autonomic Failure**

Alfredo Gamboa, Cyndya Shibus, Andre Diedrich, Bonnie K Black, Ginnie Farley, Satish R Raj, David Robertson, Italo Biagiogni; Vanderbilt Univ, Nashville, TN

More than half of patients with autonomic failure (AF) have severe supine hypertension despite low or unresponsive norepinephrine levels and often undetectable plasma renin activity. Supine hypertension is related to increased vascular resistance but the mechanism is not known. To test the hypothesis that nitric oxide deficiency contributes to supine hypertension we blocked endogenous nitric oxide synthase with L-NMMA in 5 AF patients and 7 normal controls (supine SBP 173±6 and 107±5 mmHg, respectively). Systolic blood pressure (SBP) was normalized to 110 mmHg in AF with graded head-up tilt, and baroreflexes were eliminated with trimethaphan in normal controls to mimic autonomic failure. The pressor response to graded doses of L-NMMA was shifted to the left in AF (Figure); The dose necessary to increase SBP by 30 mmHg was 3.4-fold lower in AF compared to controls (136±24 and 465±103 µg/k/min respectively, p<0.02). In conclusion, contrary to our original hypothesis, our results suggest an increased tonic release of nitric oxide in AF. Thus, NO deficiency does not contribute to supine hypertension in autonomic failure. On the contrary, this enhanced tonic NO may contribute to orthostatic hypotension in these patients.



1413

**Oral Administration of a Mineralocorticoid Receptor Antagonist Reduces Brain, Heart, and Blood-borne Proinflammatory Cytokines in Heart Failure**

Yu-Ming Kang, Carver College of Med, Univ of Iowa, Iowa City, IA; Ralph F Johnson, Univ of Iowa, Iowa City, IA; Zhi-Hua Zhang, Carver College of Med, Univ of Iowa, Iowa City, IA; Robert M Weiss, Carver College of Med, Univ of Iowa and VA Med Ctr, Iowa City, IA; Alan K Johnson, Univ of Iowa, Iowa City, IA; Robert B Felder; Carver College of Med, Univ of Iowa and VA Med Ctr, Iowa City, IA

**Introduction:** Brain and blood-borne cytokines may contribute to neurohumoral excitation in heart failure (HF). We previously reported that blockade of mineralocorticoid receptors (MR) in the central nervous system with spironolactone (SL) reduces circulating tumor necrosis factor (TNF)-α in HF rats. The effect of SL on proinflammatory cytokines (PIC) in the brain and on other important circulating PIC - interleukin (IL)-1β and IL-6 - was not determined. **Hypothesis:** Chronic treatment with oral SL will reduce brain and blood-borne PIC in rats with HF following MI. **Methods and Results:** Rats underwent coronary artery ligation to induce MI (48.2±2.0% of left ventricle, with ejection fraction of 35.5±4.1% by echocardiography), or sham surgery (SHAM). Six weeks later, immunohistochemistry of the paraventricular nucleus (PVN) of hypothalamus, a region critical to cardiovascular regulation, revealed more PVN neurons (MI vs SHAM, \*\*P<0.01) positive for TNF-α (59.5±3.3\*\* vs 10.8±0.9) and IL-1β (70.7±3.9\*\* vs 13.8±1.2) in MI (n=6) than in SHAM (n=6) rats. Double staining demonstrated that these neurons were distributed among PVN neurons expressing Fra-like immunoreactivity, indicating chronic neuronal activation. MI rats (n=6) treated with SL (1 mg/kg/day orally for 6 weeks) had fewer (MI+SL vs MI, #P<0.01) Fra-like positive PVN neurons (85.5±5.4# vs 183.8±5.0), and fewer PVN neurons positive for TNF-α (22.4±1.8# vs 32.4±1.7%) and IL-1β (19.1±1.3# vs 38.4±2.1%). Levels of TNF-α, IL-1β and IL-6 in brain and heart tissues and in plasma were also lower in MI rats treated with SL (see table). **Conclusion:** In rats with ischemia-induced heart failure, orally administered SL has a global inhibitory influence on the appearance of proinflammatory cytokines in brain, heart and plasma. The beneficial influence of MR antagonism in patients with HF may result at least in part from blocking aldosterone-induced

Group	plasma IL-1β (pg/ml)	plasma IL-6 (pg/ml)	heart IL-1β (pg/mg protein)	hypo-thalamus IL-1β (pg/mg protein)	hypo-thalamus TNF-α (pg/mg protein)	brain-stem TNF-α (pg/mg protein)	brain-stem IL-6 (pg/mg protein)	cortex IL-1β (pg/mg protein)	heart/BW Ratio (mg/g)	lung/BW Ratio (mg/g)
MI+VEH (n=7)	131.1±10.9	119.5±9.7	53.4±6.5	47.1±7.9	6.8±0.7	6.1±0.9	67.1±10.1	26.4±4.1	7.2±0.2	13.5±0.6
MI+SL (n=7)	57.5±3.1*	53.3±8.6*	32.6±5.9*	29.4±5.1*	3.9±0.6*	2.8±0.5*	39.4±5.5*	25.8±5.2	6.4±0.3*	12.1±0.6*
SHAM+SL (n=6)	48.2±3.6	33.7±2.8	23.7±6.5	17.4±4.8	2.8±0.7	2.1±0.6	25.3±4.8	24.3±4.9	3.3±0.1	5.2±0.3
SHAM+VEH (n=6)	53.9±2.4	36.1±2.6	27.6±5.4	18.8±4.0	3.2±0.9	2.4±0.8	28.0±8.7	23.6±6.5	3.4±0.1	5.1±0.3

**Pulmonary Arterial Hypertension: New Therapies**

Subspecialty: Integrative Biology

Wednesday

Ernest N Morial Convention Center, Hall 12

Abstracts 1414-1418

1414

**Inhaled Treprostinil Sodium (TRE) For the Treatment of Pulmonary Hypertension**

Robert Voswinckel, Beate Enke, Andre Kreckel, Frank Reichenberger, Stefanie Krick, Henning Gall, Tobias Gessler, Thomas Schmehl, Markus G Kohstall, Friedrich Grimminger, Hossein A Ghofrani, Werner Seeger, Horst Olschewski; Univ Hosp Giessen, Giessen, Germany

**Objective:** To evaluate the effects of inhaled TRE on pulmonary hemodynamics and gas exchange in severe pulmonary hypertension (PH) and to assess safety, tolerability and clinical efficacy in patients with severe PH. **Background:** TRE is a stable prostacyclin analogue that has been approved for treatment of pulmonary arterial hypertension as a continuous subcutaneous infusion. Iloprost, another prostacyclin analogue, has been shown to be efficacious in a randomised controlled study as repetitive inhalation. **Methods:** In an open-label study a preservative free solution of inhaled TRE was applied to 17 patients with severe pulmonary hypertension during Swan-Ganz catheter investigation. Patients received a TRE inhalation by use of the pulsed OptiNeb® ultrasound nebulizer (3 single breaths, TRE solution 600 µg/ml). Hemodynamics were observed for 2 hours. Two patients with idiopathic PAH received compassionate treatment with 4 inhalations of TRE per day after the acute test. **Results:** Patients (male/female = 4/13) suffered from iPAH (n=5), PAH other (n=8) and CTEPH (n=4); PVR 948 ± 112 dyn\*s\*cm<sup>-5</sup>, PAP 48.3 ± 2.7 mmHg, PAWP 8.9 ± 0.5 mmHg, CVP 10.8 ± 1.6 mmHg, CO 3.8 ± 0.3 l/min, SvO2 61.8 ± 1.8 %. TRE inhalation resulted in a sustained, highly pulmonary selective vasodilatation over 120 minutes. Maximum PVR decrease was -31.2 ± 4.5 % after 30 min. PVR and SVR at 120 minutes after inhalation were 89.2 ± 4.2 % and 101.0 ± 4.0 % of the baseline values, respectively. The AUC for the observation period (120min) was -22.9 ± 3.8 % for PVR and -4.9 ± 3.2% for SVR. The compassionate use patients had been treated for more than 3 months. In both patients NYHA class improved (from IV to III and from III to II), and six minute walk increased (from 0 m (bedridden) to 143 m, and from 310 m to 486 m, respectively). No side effects have been observed by the patients during long-term treatment. **Conclusion:** Inhaled TRE shows strong pulmonary selective vasodilatory efficacy with a long duration of effect following single acute dosing. Tolerability is excellent even at high drug concentrations and short inhalation times (3 breaths). Long-term treatment effects are very promising. The current results warrant controlled studies investigating this approach in a larger series of patients. Supported by Lung RX

1415

**Rho-kinase in Pulmonary Hypertension**

Ken Ishikura, Norikazu Yamada, Akihiro Tsujii, Satoshi Ota, Mashio Nakamura, Masaaki Ito, Naoki Isaka, Takeshi Nakano; Mie Univ Sch of Med, Tsu, Japan

**Objectives:** Pulmonary hypertension (PH) is a poor prognostic disease with limited treatment. Rho-kinase is involved in the pathophysiology of several diseases underlying smooth muscle hypercontraction. But the role of it is unknown. The purpose of this preliminary report was to indicate the efficacy of fasudil, a Rho-kinase inhibitor in patients with pulmonary hypertension using interventional hemodynamic assessment. **Methods:** Fasudil was intravenously injected in 10 patients (9 female, mean ± SD, 46 ± 15 years, NYHA II n=2, III n=7, IV n=1) with primary (n=5) and secondary (n=5) PH who were not received any vasodilator. Fasudil was administered 30mg with 1mg/min. Hemodynamic data were measured using Swan-Ganz catheter until 60 minutes after starting administration of fasudil. Hemodynamic and arterial blood gas data of baseline and the lowest total pulmonary resistance (TPR) time were compared. **Results:** The lowest TPR time was within 30 to 60 minutes after administration. Administration of fasudil significantly decreased TPR from 13.6 ± 6.8 U to 10.3 ± 4.9 U (-23.2 ± 9.2 %, p < 0.001) and mean pulmonary arterial pressure (mPAP) from 43.6 ± 14.5 mmHg to 38.8 ± 13.9 mmHg (-11.6 ± 10.4 %, p < 0.02). Cardiac index (CI) was significantly increased from 2.39 ± 0.66 L/min/m<sup>2</sup> to 2.74 ± 0.73 L/min/m<sup>2</sup> (+16.5 ± 15.1 %, p < 0.01). Although TPR was equally decreased in both primary and secondary PH, the changes in the parameters that prescribed TPR, namely CI and mPAP, were different between the two groups subjects. Increased CI was a major factor into reducing TPR in primary PH, while reduced mPAP