MESSAGE FROM THE CHAIR

The 63rd Annual Fall Conference of the Councils on High Blood Pressure Research and Kidney on Cardiovascular Disease has concluded and it was a great success. The conference was held at the InterContinental Chicago O’Hare Hotel, Sept. 23–26. Over 350 abstracts were presented at the meeting. Highlights included our conference awards and activities sponsored by the Trainee Advocacy Committee. As noted by those who attended, the conference continues to grow and evolve in a highly positive manner. The Program Committee, headed by Rhian Touyz, is to be congratulated. A complete report of the meeting will be presented in an upcoming edition of Hypertension.

Another highlight of the conference was AHA Immediate Past President Clyde Yancy’s participation. He had the opportunity to learn more about what’s important to the membership, and heard the concerns of our community. For example, one item of business that was brought up during our meeting in Chicago related to the AHA’s decision to put the Established Investigator Award (EIA) on hiatus for a year. We approached AHA Director of Research Administration, Ms. Patricia Hinton, for additional information. Because this may be of general interest, I’ll summarize her response here.

The EIA was not offered this past July in anticipation of a reduction in the AHA research budget. The National Center Research budget is based upon the prior year’s actual audited revenue. The National Research Program receives 52 percent of all National Center revenue, whether it is from affiliate fundraising efforts or income from investments, Scientific Sessions, scientific publications or other sources. As revenue increases or decreases from these sources, the national research budget is directly affected.

Early this year, AHA research volunteers realized that projections of AHA revenues for the 2008–09 fiscal year predicted a sharp decline in the funds available to the National Research Program for allocation in FY 2009–10. Last March, the projection of funds to be available to the National Research Program for 09–10 was $35–40 million, as opposed to the $51.5 million available for 08–09. The National Research Program Subcommittee had to determine the best course of action for the National Research Program offerings for programs to offer for the July 2009 application deadline. In 2008, the EIA, the Scientist Development Grant, the Innovative Research Grant and the Clinical Research Program had been available for the July deadline.

In March, the National Research Program Subcommittee considered a number of options and finally decided that putting the EIA on hiatus for a year would cover much of the projected budget reduction of $12–17 million. The Subcommittee also decided to delay offering the Innovative Research Program (IRG) until January 2010, at the earliest. A number of factors were considered, including the cost of the program and the alignment of each program with the Research Strategic Plan (key components: early career recruitment, innovation, collaborative approaches, increasing AHA funding of patient-oriented research, and international focus). This was a difficult decision for the subcommittee, and they fully anticipated revisiting the EIA for 2010. In fact, they noted that should the research budget outlook improve and the EIA be reinstated for the July 2010 deadline, they wanted to be sure to include anyone who had missed the opportunity to apply in 2009. They anticipated making an exception for those who would have been eligible for the EIA in 2009 but by 2010 would have exceeded the experience limit (6–9 years since first appointment as assistant professor or equivalent).

Now it is October, and we know that the national research awards budget will be about $39 million for 2009–10. The projections were pretty close, we will have a significantly reduced research budget, and so the decision to put the EIA on hiatus for a year seems to have been a good one. It will minimize the impact on the paylines of the other programs that the AHA is offering this year. The National Research Program Subcommittee will be meeting in early November to discuss the national research programs to offer for the July 2010 and January 2011 deadlines. The Subcommittee will be discussing the EIA at that time, and the input from the HBPR Leadership Committee meeting will be included in that discussion.

I would like to thank Ms. Hinton for her helpful background information. In future issues of Connections we will continue to keep you posted on changing aspects of the AHA Research Portfolio.

In addition to the fall conference, the plans for our next hypertension summer school continue to develop. The goal of this program is to attract and motivate postdoctoral fellows, students and clinical trainees into careers in hypertension and cardiovascular disease. The chair of the organizing committee for the school is Ray Townsend. Dates and location for the 2010 Hypertension Summer School as follows:

Portland State University, Portland, Ore. Saturday, July 31–Wednesday, Aug. 4

Remember that Scientific Sessions will be held in Orlando, Fla., at the Orange County Convention Center from Nov. 14–18, 2009.

Finally, I would like to say that this is an exciting time for the members of our Council. The next meeting of the Leadership Committee is March 2010 and we welcome suggestions for agenda items. We are here to serve you.
As Program Chair of the 63rd Annual Fall Conference of the Council on High Blood Pressure Research and Kidney on Cardiovascular Disease it is a pleasure to report back on the great success of this meeting, which was held at the InterContinental Chicago O’Hare Hotel from Sept. 23–26, 2009.

The American Heart Association's High Blood Pressure Research Conference is considered to be amongst the most important and prestigious medical meetings on hypertension in the world, designed as a scientific program that focuses on disseminating information about recent advances in hypertension research. This program provides an opportunity for learning, interacting and networking between scientists, basic and clinical. Over the past few years there has been significant growth in attendance at the meeting and in 2009, there was a record number of 749 registrants from over 20 countries. The conference was preceded by a one-day workshop, titled “Systems Medicine Strategies in Hypertension — From Molecules to Patients,” and focused on state-of-the-art technologies and approaches to better understand molecular and physiological mechanisms of hypertension in experimental and clinical settings. The workshop attracted over 250 registrants, with standing room only, and was the largest ever at a Council for High Blood Pressure meeting. The committee of the workshop program, Drs. E.L. Schiffrin (McGill Univ.), T. Coffman (Duke Univ.), and A. Dominiczak (Univ. Glasgow), designed a comprehensive program comprising four sections to study hypertension 1) at the gene level, 2) at the molecular level, 3) at the vascular level, and 4) at the clinical level. World-renowned investigators led the workshop with presentations and discussions. The workshop was closed and the official meeting opened by Dr. Daniel Levy, Framingham, Mass., who gave a wonderful talk on “genes, molecules, systems biology and epidemiology — bringing it together through Framingham.” The scientific program of the conference was abstract-based and included over 350 reviewed abstracts presented in oral and poster sessions. In addition, numerous named award lectures were given by the most outstanding investigators in the hypertension community. The objectives of the meeting were certainly met and by the end of the one-day workshop and 2.5-day conference attendees should have satisfactorily been able to:

- understand the genetic underpinnings involved in the pathogenesis of hypertension and the translation into clinical practice in terms of prevention, diagnosis and treatment.
- identify the mechanisms involved in cardiovascular and renal remodeling and available treatments that target these pathways.
- appreciate the role of the immune system and inflammation in the pathophysiology of hypertension and the effect of available treatments upon this system.
- understand the outcomes of recent major trials in hypertension and cardiovascular disease and incorporate new information into clinical practice.

Novartis Award for Excellence in Hypertension Research
Drs. Curtis Sigmund and Carlos Ferrario

Harriet Dunstan Award
Recipient Dr. Nancy Brown with Rhian Touyz and R. Clinton Webb
– identify the hormonal and metabolic mechanisms that link hypertension, obesity and diabetes
– describe the functioning of the RAAS and its role in hypertension, cardiovascular disease and kidney disease.
– understand the outcomes of recent major trials in hypertension and cardiovascular disease and incorporate new information from these trials into clinical practice.

The scientific program was enriched by the contributions of the many awardees of the council for High Blood Pressure Research. These included the Irvine Page-Alva Bradley Lifetime achievement award (Leopoldo Raij), the Donald Seldin lecture (Roger Wiggins), the Arthur C. Corcoran Memorial lecture (Toshiro Fujita), the Harry Goldblatt New Investigator awards (Christian Delles) and Goldblatt finalists (Eric Lazartigues and Weirong Zhang), the Lewis K. Dahl Memorial Lecture (Christian Deschepper) and the Harriet Dustan Award (Nancy J. Brown). In addition the two Novartis awardees, Drs. Curt Sigmund and Carlos Ferrario, shared their life’s work in hypertension research with the meeting participants.

Supporting the next generation of hypertension investigators is a priority of the CHBPR. As such it is with pride that the council actively supports many trainees to attend the annual CHBPR conference. In 2009, 12 new investigator awards were supported by the CHBPR, two new investigator awards were supported by the Council on Kidney in Cardiovascular Disease, five European new investigator awards were supported by Astra Zeneca and four new investigator travel awards were provided by the CHBPR trainee advocacy committee. The strengths and contributions of the members of the CHBPR were further recognized at the annual meeting when it was announced that two of our members were recipients of awards from the American Heart Association. Congratulations to Dr. Tadashi Inagami as the Distinguished Scientist awardee and to Dr. Ronald G. Victor on receiving the Louis B. Russell Jr. Memorial Award.

A new initiative of the 2009 program was to include a presentation from...
the top trainee of the High Blood Pressure Research Council of Australia, given by Mr. T. Michael De Silva. Over the next few years, the CHBPR will reciprocate this gesture and provide support for young awardees from our council to participate in the annual meeting of the High Blood Pressure Research Council of Australia. Such an initiative allows for excellent international opportunities for the next generation of hypertension scientists.

I have no doubt that everyone benefited from the 63rd meeting, whether through gaining new personal knowledge and insights in hypertension research, through changes in scientific approaches in the laboratory or through novel therapeutic strategies in the management of patients with hypertension and associated conditions.

The success of the meeting would not have been possible without the tremendous assistance from the AHA staff, particularly Susan Kunish, the guidance and support from Drs Clinton Webb (current chair) and Gabby Navar (past chair), the hard work by the Program Committee and the many hours spent reviewing abstracts by the reviewers. Thanks are expressed to all.

The 64th meeting will take place in Washington next year, Oct. 13–16. I look forward to welcoming you to another great meeting of the Councils on High Blood Pressure Research and Kidney in Cardiovascular Disease.

- Drs. Carlos Ferrario and Curtis Sigmund, Novartis Award for Hypertension Research
- Dr. Leopoldo Raij, Irvine Page-Alva Bradley Lifetime Achievement Award in Hypertension
- Dr. Nancy Brown, Harriet Dustan Award (Sponsored by Lippincott Williams and Wilkins)
- Dr. Toshiro Fujita, Arthur C. Corcoran Memorial Lecture
- Dr. Christian Deshepper, Lewis K. Dahl Lecture
- Dr. Roger Wiggins, Donald Seldin Lecture
- Dr. Christian Delles, Harry Goldblatt New Investigator Award; finalists for this award included Drs. Eric Lazartigue and Weirong Zhang

Harry Goldblatt New Investigator Award
Recipient Dr. Christian Delles with R. Clinton Webb and Rhian Touyz

Harry Goldblatt New Investigator Award
Finalist Dr. Eric Lazartigue with R. Clinton Webb and Rhian Touyz

Harry Goldblatt New Investigator Award
Finalist Dr. Weirong Zhang with R. Clinton Webb and Rhian Touyz

Kidney Council New Investigator Award
Jeff Sands, Kidney Council Chair, with recipients Xiao Li and Deyin Lu, and David Ellison, Kidney Council Vice Chair
• Drs. Tadashi Inagami and Ronald G. Victor, Distinguished Achievement Awards of the CHBPR and CKCD, respectively.

Twenty-four young investigators received travel awards sponsored by the Hypertension Council, the Kidney Council, Astra Zeneca (European Fellows) and the CHBPR Trainee Advocacy Committee. The awardees were:

**Annual High Blood Pressure Research Conference New Investigator Award**
Sponsored by the Council for High Blood Pressure Research
Hyehun Choi
Carmen De Miguel
Mohammed Haque
Shannon Harlan
Zhanjun Jia
Pimonrat Ketsawatsomkron
James Luther
Augusto Montezano
Meena Madhur
Guillermo Silva
Ana Silva
Frederique Yiannikouris

**Kidney Council New Investigator Award**
Sponsored by the Council on Kidney in Cardiovascular Disease
Xiao Li
Deyin Lu

**New Investigator Award for European Fellows**
Supported by a grant from Astra Zeneca
Matej Durik
Alexandra Hlavacova
Marlette Kappers
Agnes Machnik
Virginia Reverte

**High Blood Pressure Research Council of Australia New Investigator Award**
T. Michael De Silva

**New Investigator Travel Awards**
Sponsored by the Council for High Blood Pressure Research Trainee Advocacy Committee
Andreas Beyer
Marcela Herrera
Chiara Marchesi
Sydney Murphy

**Annual HBPR Conference New Investigator Award**

**New Investigator Award for European Fellows**
Alexandra Hlavacova, Matei Durik, Agnes Machnik, Marlette Kappers, Virginia Reverte

**High Blood Pressure Research Council of Australia New Investigator Award**
Recipient T. Michael De Silva with R. Clinton Webb, Kate M. Denton [Program Secretary for HBPRCA] and Rhian Touyz
I was born in Bahia Blanca, then a sleepy city on the Atlantic coast about 370 miles south of Buenos Aires, Argentina. My parents were immigrants from Russia and Austria that arrived in Argentina as teenagers and worked very hard to become middle class. I found high school boring but my education outside school was exciting thanks to close friends Beto, Mario and Jorge who exposed me to books, music and to humanistic and social issues. Movies were my connection with a confusing world that was necessary to know and certainly to understand: whereas European movies dealt with human imperfection and the misery of the war and postwar, American movies dealt with the conquest of the West, the victory in the 2nd world war and the American dream!

At age 16 I went to Buenos Aires and eventually to Rosario, the second largest city in Argentina. I attended Medical School in Rosario where I fell in love with the human and scientific components of medicine. Although access to science in Rosario was difficult and restricted to encyclopedic learning with no Internet access, I was surrounded by wonderful mentors and teachers who reminded me that Argentine investigators such as Bernardo Houssay (Nobel laureate, 1947), and Braun-Menendez made major scientific contributions to the world. Interestingly this Lifetime Achievement Award honors Irvine Page who, together with Braun-Menendez, discovered and named angiotensin, a substance that has occupied a great part of my own scientific career.

Given the social and economic situation in Argentina, North America was an easier place to find a good position than Buenos Aires. I was at the top of my class and, encouraged by my professors and my lack of fear, perhaps because of the example of my parents, I emigrated. After a short stop in Canada I went to Chicago for clinical training at the Michael Reese Hospital, a place well supported and full of outstanding basic scientists and clinical investigators. I did not have the opportunity to do research there but the exposure to outstanding scientists convinced me to stay in academic medicine.

My involvement with medical science developed at the University of Minnesota where I worked with Alfred Michael’s pediatric nephrology group, at that time one of the best in the world. The general atmosphere in the lab was one of fostering creativity. It was common to hear: “It is a great idea, you should explore it further” and with that encouragement … I did.

I initiated a series of studies to investigate the regulation of the flow of plasma and macromolecules through the mesangium...
by angiotensin II and by hemodynamic changes. Epidemiological studies drew attention to the role of hypertension in renal failure progression. Micropuncture studies reported that hypertensive Dahl but not SHR rats develop glomerular hypertension but good studies of the renal pathology and progression of glomerular injury in hypertension were lacking. I developed a semi-quantitative and reproducible method to evaluate histological changes in coronal sections of kidneys. This method permitted separate quantification of mesangial expansion and segmentally or globally sclerosis of the glomeruli. It also concomitantly determined whether the injury was more prominent in the juxtamedullary or in the cortical glomeruli. This technique with minor modifications continues to be used today by many investigators. With the aid of this technique, we established that during hypertension, glomerular injury occurs because there is defective preglomerular autoregulation and therefore the coexistence of systemic and glomerular hypertension (1984-85). ACE inhibitors came to the market and, based on our previous studies, we explored the renoprotective qualities of ACE inhibitors. By 1986, Bob Furchgott had discovered EDRF (nitric oxide) and Paul Vanhoutte headed a group of young scholars working on EDRF at the Mayo Clinic, 70 miles from Minneapolis. With Paul and Tom Luscher, then a postdoc, we demonstrated that in hypertension, EDRF was greatly impaired in hypertensive Dahl rats but not in SHR. Our studies predicted what was subsequently shown in hypertensive humans by J. Panza. With Hiroshi Hayakawa we further demonstrated that the differences in EDRF between Dahl and SHR rats were linked to quantitative differences in vascular and renal NO synthase in response to hypertension.

With great collaborators such as M. Zhou and E. Jaimes, I have continued to work on the biology of NO in the vessels and in the kidney in relation with hypertension, dyslipidemia, atherosclerosis and diabetes. It has been a great ride and I am confident that we made quite a few contributions that are endowed with clinical relevance; after all I am a clinical scientist. As a final note, this wonderful award made me think about what I would like to strive for in the years to come, provided my health and energy are maintained. My interest in science, clinical medicine and social issues will continue to be there. I must confess, however, that my grandchildren are becoming more and more of an attractant by the minute.

Thank you once more and I sincerely hope that I can continue to see my peers at the AHA CHBPR meetings and that we maintain the same enthusiasm for years to come.

Report From The Trainee Advocacy Committee

Erika Boesen, PhD
Trainee Advocacy Committee Representative

Once again there was great participation by students and postdocs at the annual Fall High Blood Pressure Research Conference, with 264 trainees and students attending the meeting. This year’s annual Trainee Workshop/Mixer, sponsored by the
Trainee Advocacy Committee, featured Dr. John Glick as our invited speaker. Dr. Glick, a collaborator of Dr. Patch Adams of the Gesundheit Institute, entertained and spoke with us about the healing power of humor and the importance of caring for one another. The hilarity of “getting in the underpants” was followed by a well-attended karaoke session, complete with prizes for the best two performances. Special thanks go to the following for their support of this event: the AHA, Drs. Joey Granger, Stephanie Watts and Greg Fink, Michigan State University’s Department of Pharmacology/Dr. J.R. Haywood, and the Medical College of Georgia’s Department of Physiology/Dr. Clinton Webb and Vascular Biology Center/Drs. David and Jennifer Pollock. Please pass on suggestions for speakers at next year’s Trainee Workshop to myself or the incoming Trainee Advocacy Committee Co-chair, Dr. Justin Grobe (justin-grobe@uiowa.edu).

Research Briefs

September 2009:

Hypertension. 2009;54:482-488. Effect of Modest Salt Reduction on Blood Pressure, Urinary Albumin, and Pulse Wave Velocity in White, Black, and Asian Mild Hypertensives. He FJ, Marciniak M, Visagie E, Markandu ND, Anand V, Dalton RN, MacGregor GA. This small study in 21 patients used implantable carotid sinus stimulators to determine the effect on autonomic activity in patients with drug-resistant hypertension. After 3 months of chronic baroreceptor stimulation, there was a significant fall in blood pressure of 30 mmHg with an accompanying fall in heart rate and a decrease in sympathetic activity as monitored by heart rate variability analysis. There was a significant correlation between the fall in blood pressure and the decrease in HR variability suggesting that in addition to the effects of baroreceptor stimulation to decrease blood pressure it also improves sympathetic overactivity in hypertension.

Hypertension. 2009;54(3):619-624. Endogenous Interleukin-10 Inhibits Angiotensin II-Induced Vascular Dysfunction. Didion SP, Kinzenbaw DA, Schrader LI, Chu Y, Faraci FM. This study used IL-10 knockout mice and found that this antiinflammatory cytokine protected mice from developing endothelial dysfunction after angiotensin II infusion. This was true in mice treated for ten days (1.4 mg/kg/day) and in arteries.

Announcements

The NHLBI recently published a RFA in the NIH Guide focusing on the relationship between large artery stiffening and the development of hypertension. If you would like information regarding this RFA, here is a link to the announcement:

If you need additional information, contact:
Terry N. Thrasher, Ph.D., Program Director Vascular Biology and Hypertension Branch Division of Cardiovascular Diseases, NIH 6701 Rockledge Drive, MSC 7940 Bethesda, MD 20892-7940 Tel. 301 435 0560 Fax 301 480 2858 E-mail: thrashertn@nhlbi.nih.gov

The 23rd Scientific Meeting of the International Society of Hypertension (ISH 2010), to be held Sept. 26–30, 2010, in beautiful Vancouver, Canada, is on! This important international meeting, focusing on global cardiovascular risk reduction, will be at the forefront of new concepts in basic, clinical and population science. Be sure to register by Jan. 15, 2010, to take advantage of the Super Early Bird rates.
incubated overnight with angiotensin II (1 nmol/L). Moreover, treating arteries (PEG-SOD) or mice (tempol) with antioxidants prevented the impaired dilator response caused by the angiotensin II treatments. This was in spite of similar levels of blood pressure in the IL-10 KO and wildtype mice. Thus IL-10 appears to vasoprotective independent of changes in blood pressure and activation of inflammatory pathways in response to angiotensin II may cause at least some of the vascular pathologies associated with high levels of the peptide.

**October 2009:**

**Hypertension.** 2009;54(4):744-750

Losartan metabolite EXP3179 blocks NADPH oxidase-mediated superoxide production by inhibiting protein kinase C.

Fortuno A, Bidegain J, Robador PA, Hermida J, López-Sagasta J, Beloqui O, Díez J, Zalba G.

Several studies suggest losartan’s cardiovascular protective effects are in part independent of AT1R blockade. This study investigated metabolic effects of two major metabolites of losartan, EXP3174 and EXP3179. The data suggest that EXP3174, the more long-lived and well-characterized metabolite, potently inhibits the AT1R. In contrast, the more short-lived EXP3179 inhibits NADPH oxidase in an AT1R independent manner. This inhibition by EXP3170 appears to be mediated by upstream inhibition of PKC. Thus at least a portion of the antioxidant effects of losartan may be due to EXP3179 inhibition of PKC, independent of AT1R effects.

**Hypertension.** 2009;54(4):751-755

Dieet-dependent net acid load and risk of incident hypertension in United States women.

Zhang L, Curhan GC, Forman JP.

This prospective study used subjects in the Nurses Health Study to test the hypothesis that a higher diet-dependent acid load is associated with an increased risk for developing hypertension. In women with a BMI <25 kg/m2, the correlation of increased acid load with increased hypertension incidence was highly significant but less so in women with a higher BMI. The results suggest that a diet high in fruits and vegetables and low in meat and cheese reduces the total acid load and decreases the risk of incident hypertension.

**Hypertension.** 2009;54(4):852-859

Role of sympathetic nervous system in Schlagener genetically hypertensive mice.

Davern PJ, Nguyen-Huu TP, La Greca L, Abdelkader A, Head GA.

A spontaneously hypertensive mouse strain was developed in the 1970s by Schlagener and Sides. Subsequent studies suggest the hypertension is caused by sympathetic overactivity but the mechanisms mediating hypertension in this strain, the Schlagner BPH/2J mice, have never been well-characterized. This study describes elevated central neurogenic activity in the medial amygdala and an exaggerated day/night difference in BP compared to the normotensive control strain, BPN/2J mice. In addition, locomotor activity was tightly correlated with circadian changes in blood pressure. Spectral analysis and ganglion blockade studies revealed an apparent increase in central sympathetic activity in the hypertensive strain. This model of genetic neurogenic hypertension suggests that the medial amygdala aong with the hypothalamus might regulate circadian rhythms of blood pressure and activity and might be an important site to look for changes leading to forms of hypertension with a strong circadian rhythm such as non-dippers.

**November 2009:**

**Hypertension.** 2009;54:1014-1020

Effect of Cardiorespiratory Fitness on Vascular Regulation and Oxidative Stress in Postmenopausal Women.


This cross-sectional study in white postmenopausal women examined the relationship between fitness and cardiovascular parameters. The findings demonstrate that fitness level and regular physical activity appear to be highly protective against oxidative stress by maintaining antioxidant enzyme efficiency. These results further suggest that oxidative stress and NO production modulate both blood pressure and cerebrovascular conductance and may be beneficial to maintaining cognitive performance during aging. Although this small study (42 subjects) needs to be replicated in a larger study, it does support a role for exercise in moderating oxidative stress to promote cardiovascular health in postmenopausal women.

**Hypertension.** 2009;54:1028-1034.

Pressure-Induced Vascular Oxidative Stress Is Mediated Through Activation of Integrin-Linked Kinase 1/βPix/Rac-1 Pathway.


It has long been appreciated that biomechanical forces elicit signaling in vascular wall cells. Indeed, myogenic tone and flow induced signaling are well established in almost all vascular beds. This study examines another signaling response to increased wall stress during elevated luminal pressure, activation of NADPH oxidase via integrin signaling. The results demonstrate that increasing pressure in isolated arteries from 100 to 180 mmHg increases activation of Rac-1 and integrin-linked kinase (ILK) upstream of NADPH oxidase activation. The resultant increase in oxidative stress was associated with diminished endothelium-dependent dilation. This novel observation clearly links mechanotransduction to oxidative stress in initiating endothelial dysfunction.

**Hypertension.** 2009;54:1077-1083

Intrarenal Dopamine Attenuates Deoxycorticosterone Acetate/High Salt–Induced Blood Pressure Elevation in Part Through Activation of a Medullary Cyclooxygenase 2 Pathway.

Yao B, Harris RC, Zhang.

The authors used catechol-o-methyl-transferase knockout mice to elevate renal dopamine content and investigate the role of intrarenal dopamine on the development of DOCA-salt hypertension. They found that the increase in blood pressure and in renal oxidative stress was significantly attenuated in the COMT (-/-) mice. The (-/-) mice also had greater urinary sodium excretion and elevated renal medullary COX-2 expression. COX-2 inhibition eliminated the renoprotective effect of COMT (-/-) without elevating blood pressure. Thus it appears that intrarenal dopamine may protect renal function and ameliorate the development of hypertension by elevating medullary COX-2 dependent prostaglandin production.